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著者(和文)	呉侖澤
Author(English)	OH Yun-Taek
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Iron-catalyzed Selective Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Sulfones, Phosphine Oxides, and Phosphonates and Its Synthetic Application

09D52065 Yun Taek Oh

September, 2013

Urabe-Hata Laboratory
Department of Biomolecular Engineering
Graduate School of Bioscience and Biotechnology
Tokyo Institute of Technology

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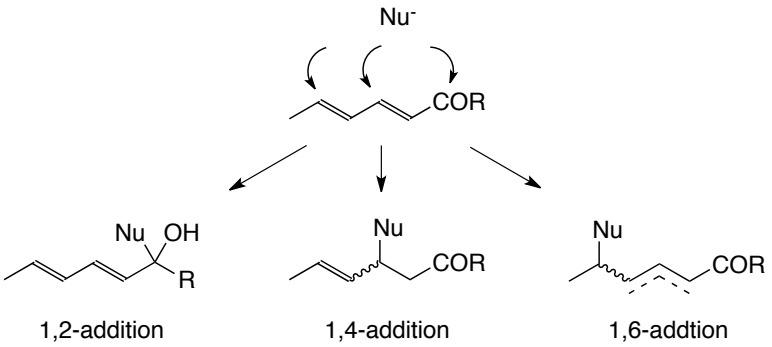
Chapter 1. Introduction

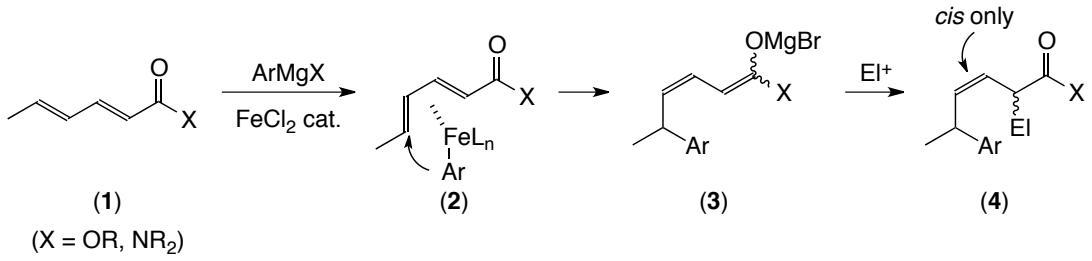
The transition metal-catalyzed conjugate addition of organometallic reagents to electron-deficient olefins is one of the most versatile methods for the selective carbon-carbon bond formation. Actually, there are numerous reports on the nucleophilic addition to electron-deficient mono-olefins. However, similar reactions to the corresponding dienes have been rarely reported. For example, the selective addition to α,β,γ,δ-unsaturated carbonyl compounds has not been amply solved, because they have multiple reaction sites (e.g., 1,2-, 1,4-, and 1,6-addition) and there are additional issues on the regioselection (β- and δ-addition) and the stereoselection (*E* or *Z*) of the remaining olefinic bond as illustrated in Scheme 1.[1]

Scheme 1. Conjugate Addition to α,β,γ,δ-Unsaturated Carbonyl Compounds.



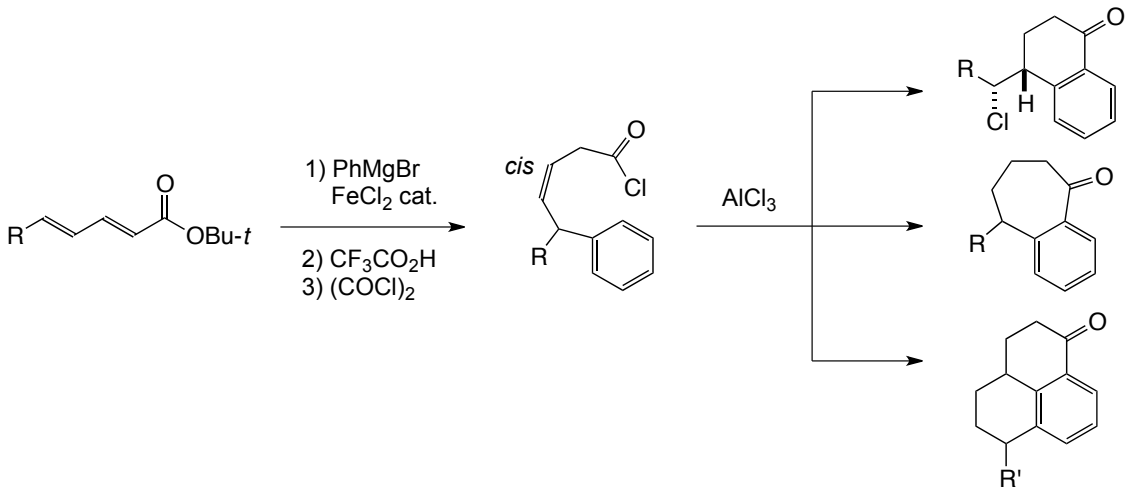
Although copper salts have been mainly used as the catalysts in these reactions,[2,3] our laboratory reported a notable role of an iron catalyst[4] in the 1,6-selective addition of aryl Grignard reagents to dienoates or dienamides **1**, giving stereo-defined *cis*-4-aryl-2-alkenoates or -amides **4** (Scheme 2).[5a,b,6] This reaction may involve the intermediary formation of the *s-cis*-diene-iron complex **2**, which effects the aryl transfer from iron to the terminal position of the dienoate to give the observed *cis*-product after hydrolysis ($El^+ = H^+$). The magnesium dienolate **3**, most likely generated *in situ*, could be also used for the reactions with other electrophiles (for example El^+ = alkyl halides),[5] giving again exclusively the desired products with a *cis*-olefinic bond.

Scheme 2. Iron-catalyzed 1,6-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Dienoate or Dienamide.



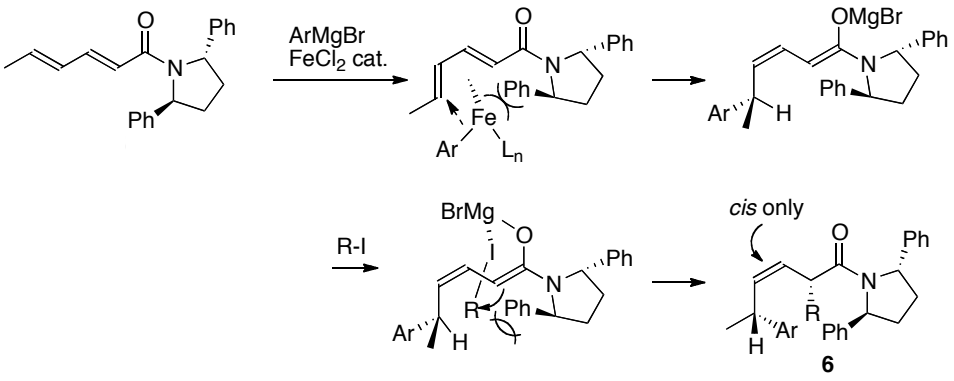
The above *cis*-alignment of the incoming aryl group and the carbonyl group on the other side of the allylic system was readily applied to the preparation of cyclic products of various ring systems via the Fridel-Crafts reaction as shown in Scheme 3.[7]

Scheme 3. Application to the Preparation of Bicyclic Products.



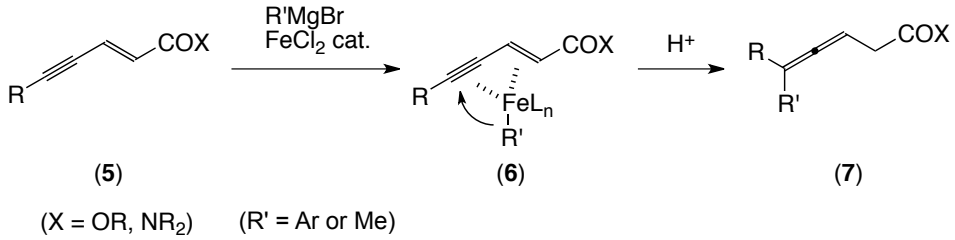
Another application is a highly efficient asymmetric δ-addition as shown in Scheme 4, where the *s-cis*-diene-iron intermediate appears to play an important role to control the stereochemistry of the first aryl addition at the remote position from the chiral auxiliary (Scheme 4).[5b]

Scheme 4. Application to the Asymmetric Multi-Component Coupling.

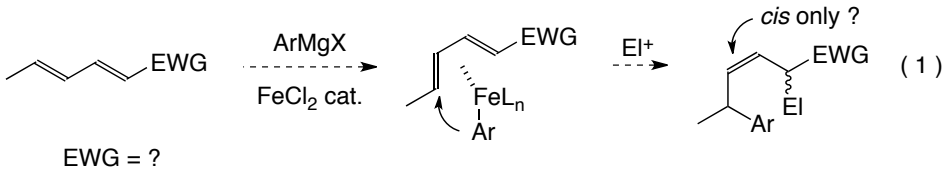


The nature of iron effecting the selective 1,6-addition was also found in the conjugate addition to enynoates or –amides **5**, giving exclusively 3,4-alkadienoates or -amides **6** (Scheme 5).[5c]

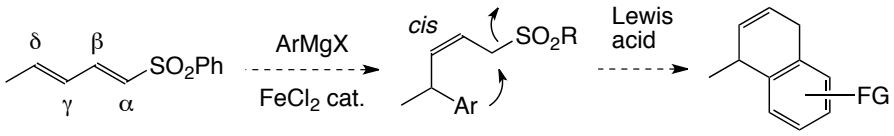
Scheme 5. Iron-catalyzed 1,6-Addition of Aryl or Methyl Grignard Reagents to Enynoates and -amides.



Seeing this successful iron-catalyzed 1,6-addition to α,β,γ,δ-unsaturated esters and amides, we began to turn our attention to other electron-deficient dienes as illustrated in eq 1 (EWG = electron-withdrawing group), hoping to develop different valuable reactions. The following chapters will show our study along this line.



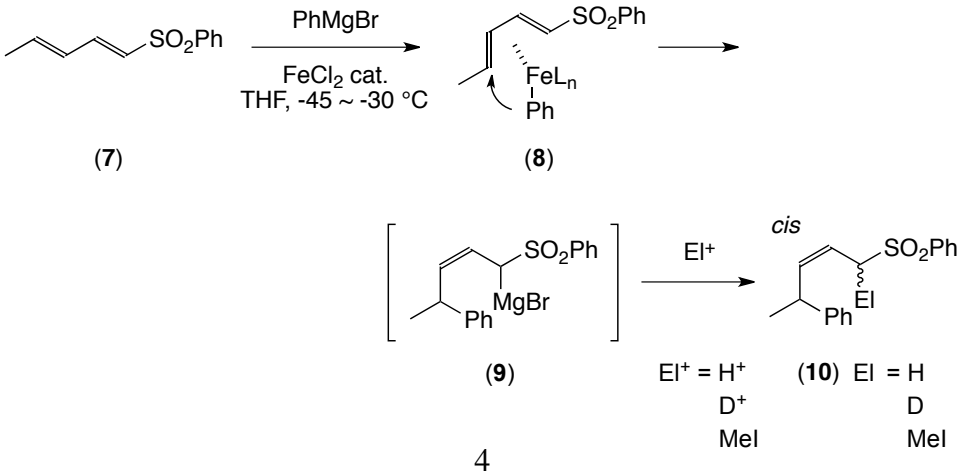
Chapter 2 of this Thesis describes the successful iron-catalyzed conjugate addition of aryl Grignard reagents to α,β,γ,δ-unsaturated sulfones. As already shown in Scheme 2, the iron-catalyzed selective conjugate addition of aryl Grignard reagents to α,β,γ,δ-unsaturated carbonyl compounds has been reported from our laboratory. The *cis*-alignment of the incoming aryl group and the carbonyl group on the other side of the allylic system was readily applied to the preparation of cycloheptanones and other ring systems via the Fridel-Crafts reaction as shown in Scheme 3. In order to expand the applicability of this series of transformations, the author planned to use a new functional group, sulfonyl, in the electron-deficient dienes.[8] The electron-withdrawing ability of sulfonyl group, comparable to the previous carbonyl groups, may effect the addition of aryl Grignard reagent to the δ position of the diene[9] and the Fridel-Crafts type cyclization of the resultant product,[10] which are illustrated in eq 2.



(2)

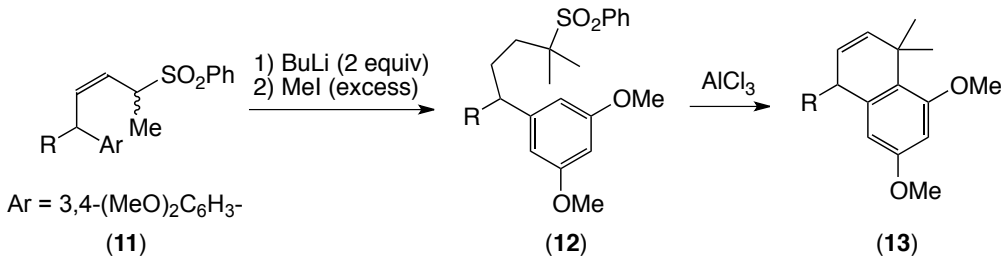
Our expection was found actually true. When sulfonyldiene **7** was treated with PhMgBr in the presence of a catalytic amount of $FeCl_2$, allyl sulfone **10** having a *cis*-olefin geometry was obtained in a highly regio- and steroselective manner (Scheme 6). Deuteriolysis and methylation also afforded the corresponding products **10** (El = D or Me), showing the presence of the intermediate magnesiated sulfone **9** and also its synthetic versatility.

Scheme 6. Iron-catalyzed Selective δ-Addition of Phenyl Grignard Reagent to (1*E*,3*E*)-1,3-Pentadienyl Phenyl Sulfone.

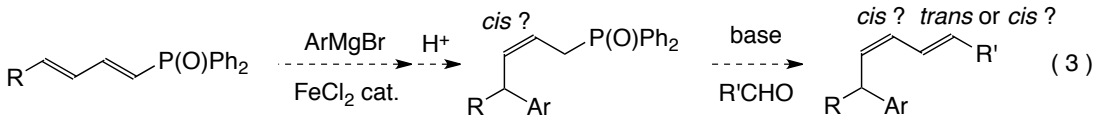


After the conversion of the produced allyl sulfone **11** to α,α-dimethylallyl sulfone **12** by *n*-BuLi and MeI, its intramolecular Friedel-Crafts reaction with $AlCl_3$ was executed to give 1,4-dihydronaphthalenes **13** in good yield (Scheme 7). Thus, the transformation initially planned in eq 2 has been achieved.

Scheme 7. Application to Fridel-Crafts Cyclization.



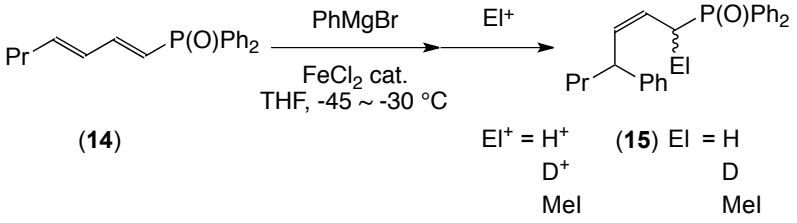
Chapter 3 describes iron-catalyzed selective conjugate addition of aryl Grignard reagents to α,β,γ,δ-unsaturated phosphine oxides and its synthetic application. As we had succeeded in the new iron-catalyzed selective addition to α,β,γ,δ-unsaturated sulfones, we were then interested in other electron-deficient dienes having a different heteroatom group. It is known that vinyl phosphorus compounds are good Michael-type acceptors.[11] However, its extension to dienyl phosphorus compounds is quite rare and has not been investigated, presumably for the same reason shown in Scheme 1. Thus we began to investigate the reaction shown in eq 3. It should be noted that the product this time is the stereo-defined precursor of Wittig reagents. Thus the synthetic utility of the products could be readily attested in the possible synthesis of stereo-defined 1-aryl-2,4-dienes as illustrated in eq 3.



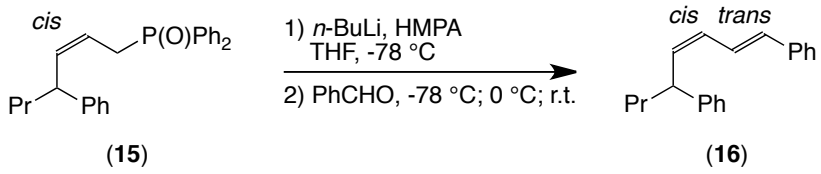
When [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**14**) was treated with PhMgBr in the presence of $FeCl_2$, the addition reaction nicely proceeded to give [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide (**13**) in good yield after hydrolysis (Scheme 8). The deuteration

and methylation could be preformed to give **15** (El = D or Me) in good yield, which is also shown in Scheme 8.

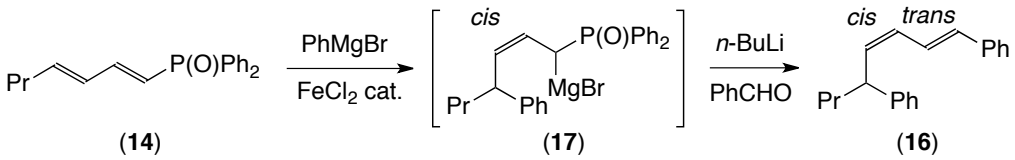
Scheme 8. Iron-catalyzed Selective δ-Addition of Phenyl Grignard Reagent to [(1*E*,3*E*)-1,3-Heptadienyl]diphenylphosphine Oxide.



Our next interest was the utility of the above product in the stereoselective preparation of dienes via the Wittig reaction.[12] After considerable optimization of the reaction conditions, when [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide (**13**) was treated with BuLi and benzaldehyde (eq 4), (1*E*,3*Z*)-1,5-diphenyl-1,3-octadiene (**14**) was obtained with high stereoselectivities. An attempt towards the one-pot δ-addition of Grignard reagent and Wittig reaction as shown in eq 5 will be also mentioned.



(4)

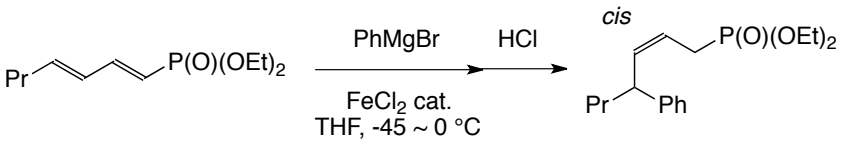


(5)

Chapter 4, the iron-catalyzed δ-addition of aryl Grignard reagents to α,β,γ,δ-unsaturated phosphonates is described. There are two major types of stable phosphorus functional groups useful for the conjugate nucleophilic addition to their substituted olefins. One is phosphine oxide, whose utility has been described in the preceding chapter, and the other is phosphonate.[11] We were interested in this alternative phosphorus group for the same propose as that described in Chapter 3. One concern is that a phosphonate group is of less electron-withdrawing character than the corresponding phosphine oxide so that the nucleophilic addition to a diene having the former

functional group appears less feasible.[13] When [(1*E*,3*E*)-1,3-heptadienyl]phosphonate **18** was treated with PhMgBr and a catalytic amount of $FeCl_2$, the reaction took place without any difficulty to give virtually single [(*Z*)- 4-phenyl-2-heptenyl]phosphonate **19** after hydrolysis (Scheme 9).

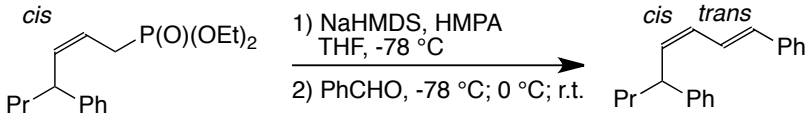
Scheme 9. Iron-catalyzed Selective δ-Addition of Phenyl Grignard Reagent to [(1*E*,3*E*)-1,3-Heptadienyl]phosphonate.



(**18**) (**19**)

Our next interest was the utility of the above product in the stereoselective preparation of dienes via the Wittig reaction.[11,14] After considerable optimization of the reaction conditions, when [(*Z*)-4-phenyl-2-heptenyl]phosphonate **19** was treated with NaHMDS (HMDS= hexamethyldisilazide) and benzaldehyde (Scheme 10), (1*E*,3*Z*)-1,5-diphenyl-1,3-octadiene (**16**) was produced with high stereoselectivity.

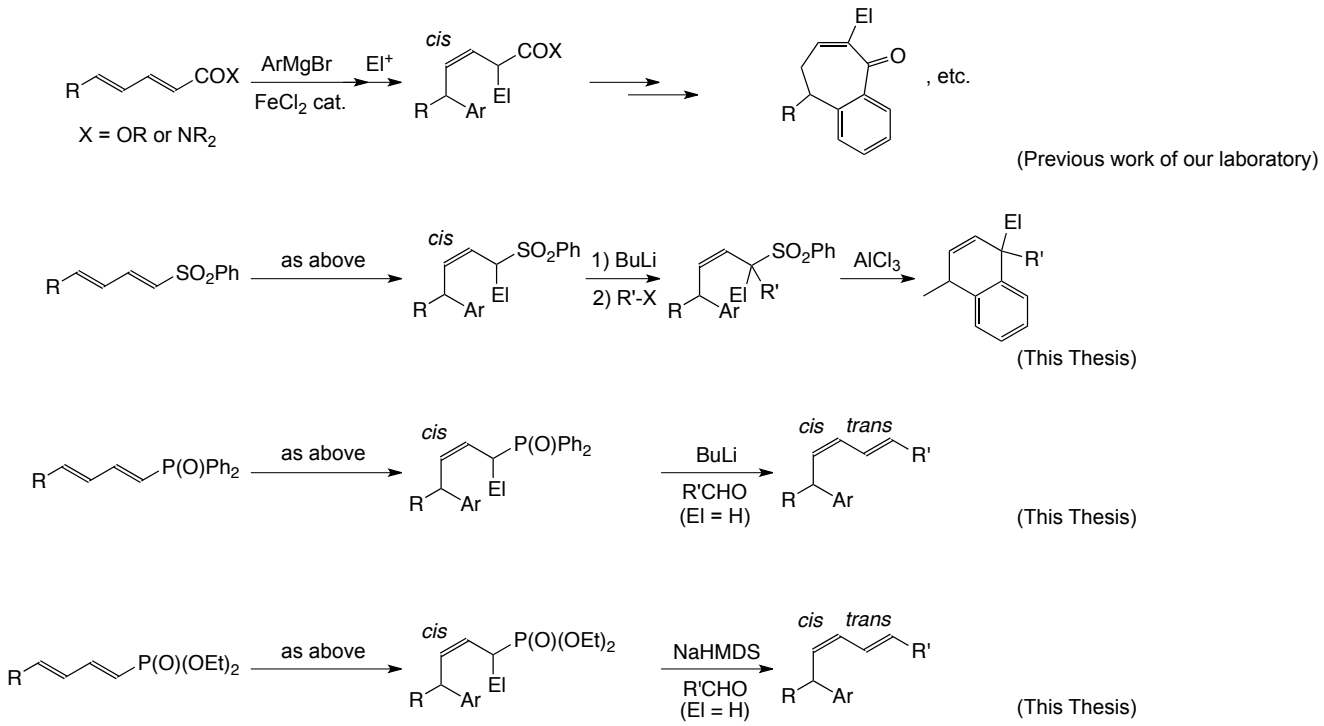
Scheme 10. Wittig Reaction from [(*Z*)- 4-Phenyl-2-heptenyl]phosphonate.



(**19**) (**16**)

Chapter 5 describes the summary of this thesis, which is shown in Scheme 11.

Scheme 11. Summary of this Thesis.



Some outlook for the contents of this thesis is also described.

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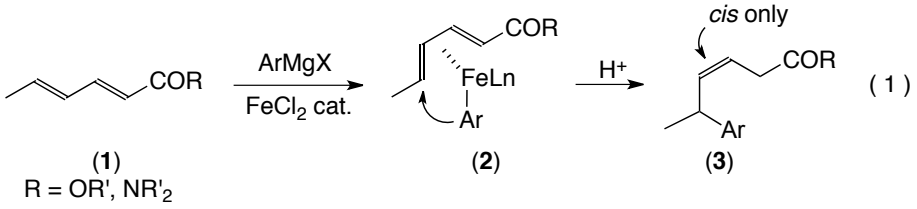
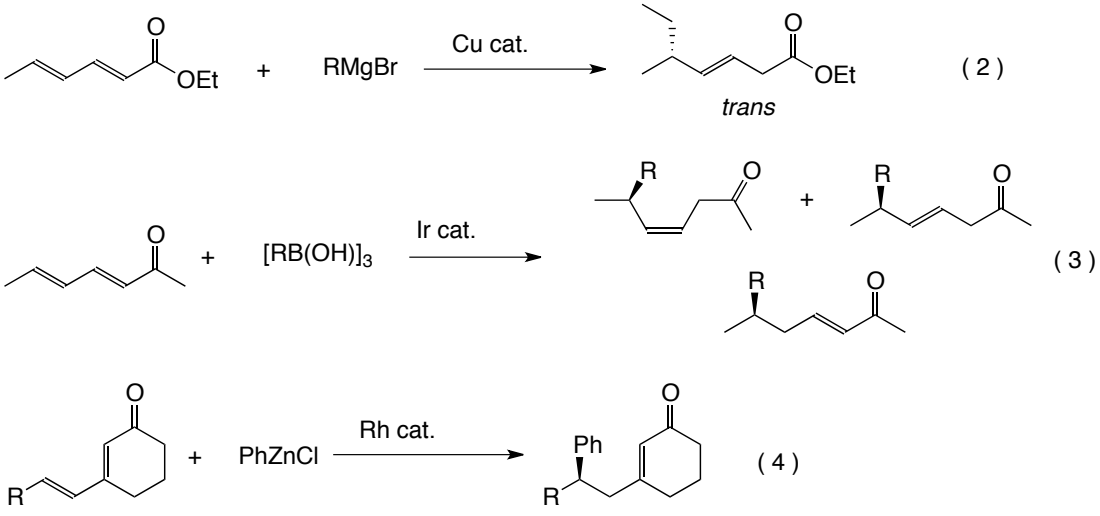
Chapter 2. Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Sulfones and Its Synthetic Application

Introduction

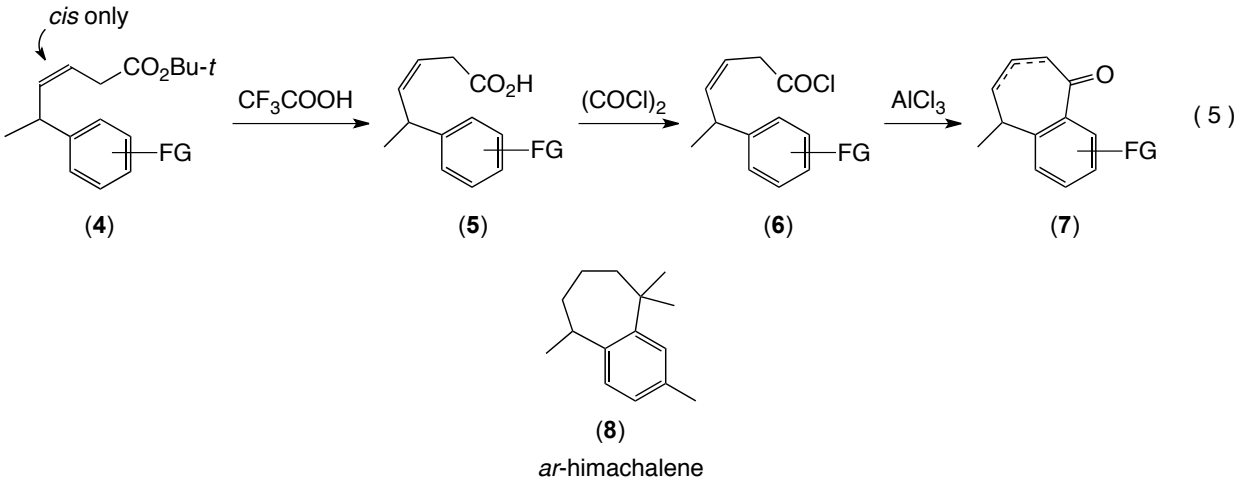
1,6-Addition to α,β,γ,δ-unsaturated carbonyl compounds **1** is a useful method to prepare bifunctional synthons, provided that a single product is obtained with high regio- and stereoselectivities. Recently our laboratory reported a solution to this issue by using an iron catalyst and aryl Grignard reagent as shown in eq 1, where the 1,6-addition product **3** with a *cis*-olefinic bond was exclusively formed, presumably via *s-cis*-diene-iron complex **2**.[1-4]



The above feature of *cis*-olefin formation can be well contrasted with other recently reported selective 1,6-additions of organometallic reagents to α,β,γ,δ-unsaturated carbonyl compounds shown in eq 2-4.[5] In eq 2, the *trans*-olefin was selectively formed under copper catalysis, which may be complementary with the result of our laboratory (eq 1). Ir-catalyzed reaction of eq 3 showed a moderate selectivity regarding both regio- and stereochemistries of the olefinic bond. The Rh-catalyzed reaction of eq 4 afforded the product having a conjugated double bond, which is again in stark contrast to the outcome of eq 1.

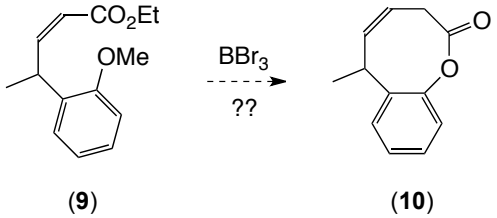


The *cis*-alignment of the incoming aryl group and the functional group on the other side of the allylic system highlighted in eq 1 prompted our laboratory to investigate the cyclization between these two groups. There might be a few variations possible to realize this idea. Equation 5 shows one possible strategy involving the Friedel-Crafts reaction, and this has been realized by Yokomizo and Goto of our group.[6,7] The product of eq 1, *t*-butyl *cis*-5-aryl-3-alkenoate **4**, was first converted to the corresponding carboxylic acid **5** with CF_3CO_2H. The carboxylic acid **5** was then led to the corresponding acid chloride **6** with a standard reagent, $(COCl)_2$, with the fragile *cis*-olefinic portion remained intact. Although the formation of a seven-membered ring is generally challenging, the cyclization of **6** under the Fridel-Crafts conditions with $AlCl_3$ nicely took place, perhaps with the assistance of *cis*-olefinic bond, to give the benzocycloheptenone **7** (eq 5). This method has been applied to the total synthesis of *ar*-himachalene (**8**).[7]



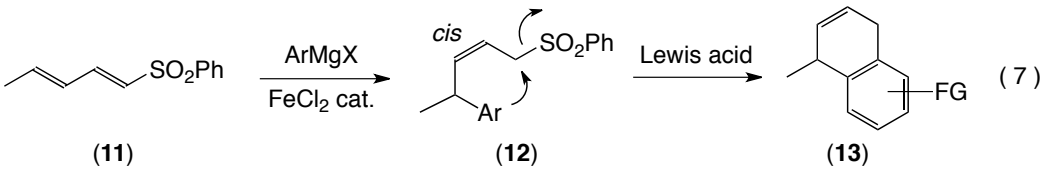
(5)

Another way to take advantage of this *cis*-olefinic bond may be based on an aromatic functional group, an example of which is illustrated in eq 6. Thus, demethylation of the anisole residue of **8** followed by the cyclization may give an 8-membered lactone **10**, but this transformation has not been examined yet.



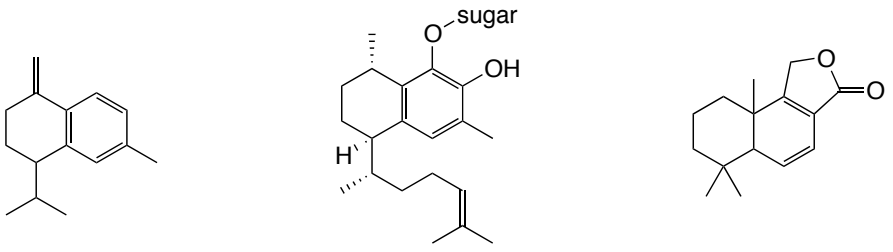
(6)

As shown above, our group has successfully utilized the products resulting from α,β,γ,δ-unsaturated esters and Grignard reagents. We then turned our attention to develop a different substrate having a new functional group that would effect the 1,6-addition as well as the cyclization to the aromatic ring. After survey of the literature,[8] we were glad to reach a plan, in which we use sulfonyl group as the above candidate according to the formulation of eq 7. It is well known that a sulfonyl group is a potent electron-withdrawing group so that α,β-unsaturated sulfones are good Michael acceptors comparable to α,β-unsaturated carbonyl compounds.[9] Thus, we were interested in the iron-catalysis to effect the transformation from α,β,γ,δ-unsaturated sulfone **11** to **12**. On the other hand, allylic sulfones are known as useful synthetic intermediates.[8] For example, they serve as a reactive allylation reagent to aromatic rings under Friedel-Crafts (Lewis acid) conditions.[10] Applying these reactions to **12** will result in the formation of **13**, which is a useful intermediate for the synthesis of terpenoids such as those shown in Chart 1.



(7)

Chart 1. Cyclic Naturally Occurring Terpenes.

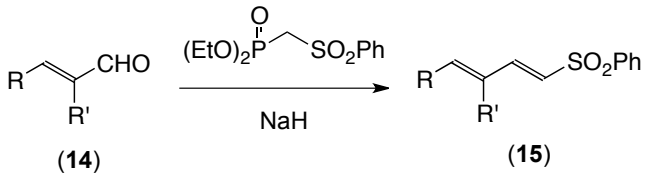


calacorene *seco*-pseudopterosin A bemadienolide

Results and Discussions

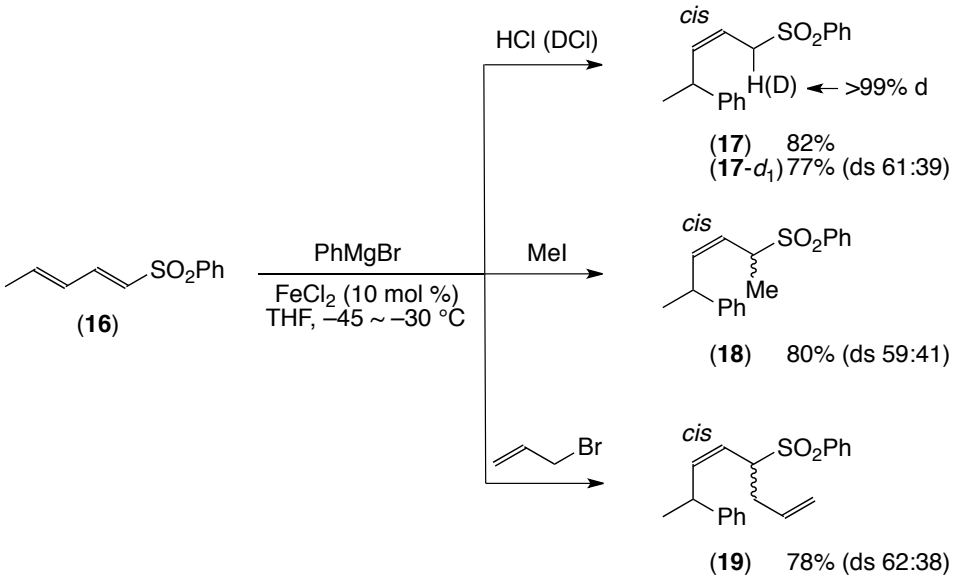
The required starting sulfonydienes **15** were readily prepared by the reaction of α,β-unsaturated aldehydes **14** with the Horner-Emmons reagent[11] in good yield and as a single olefinic isomer as shown in Scheme 1.

Scheme 1. Preparation of the Starting Sulfonyldienes.



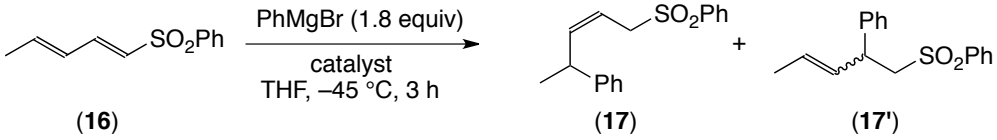
We then examined the feasibility of the iron-catalyzed conjugate addition of aryl Grignard reagents to α,β,γ,δ-unsaturated sulfones. Thus, sulfonyldiene **16** was treated with PhMgBr in the presence of 10 mol% $FeCl_2$ to afford virtually single allyl sulfone **17** after hydrolysis. Instead of hydrolysis, deuteriolysis or the treatment with alkyl halides gave **17**-d_1 with high deuterium incorporation or the alkylated products **18** and **19** in good yields (Scheme 2).

Scheme 2. Iron-catalyzed Selective Conjugate Addition of PhMgBr to Sulfonyldiene **16**.



Quite recently, impurities contained in iron reagents, particularly Cu, have been reported to be an actual promoter for many iron-catalyzed reactions.[12] As conjugate addition of Grignard reagents to α,β,γ,δ-unsaturated carbonyl compounds is well catalyzed by a copper salt, we decided to negate the possibility that a copper impurity effected the above reaction. Thus, $FeCl_2$ of the purity of 99.998% (Aldrich) achieved the similar yield and selectivity as the routine $FeCl_2$ (99.9%, in Scheme 1) as shown in Scheme 3. On the contrary, the conjugate addition was attempted by using a catalytic amount of $CuBr•SMe_2$, and it, in fact, afforded an intractable mixture of β-adduct (**17**) and δ-adduct (**20**), confirming that this reaction truly requires the iron catalyst.

Scheme 3. The Outcome of the Reaction Dependent on the Purity of $FeCl_2$.



(**16**) (**17**) (**17'**)

		yield (%)	
catalyst	Make	1,6-addition (**17**)	1,4-addition (**17'**)
$FeCl_2$ (99.9%) routinely used	Soekawa	82[c]	0[a,c]
$FeCl_2$ (99.998%)	Aldrich	82[c]	0[a,c]
$CuBr•SMe_2$	Aldrich	39[a]	15[a,b]

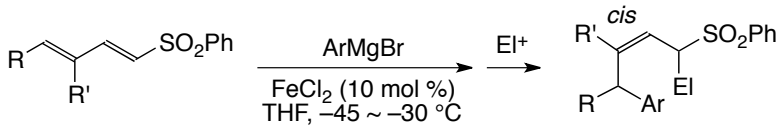
[a]NMR yield. [b]The olefinic stereochemistry was not determined. [c]Isolated yield

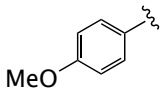
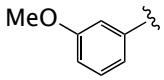
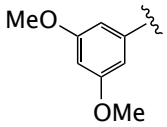
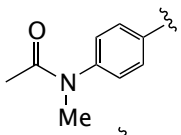
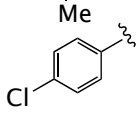
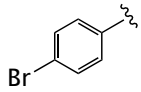
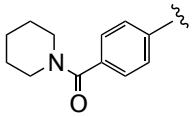
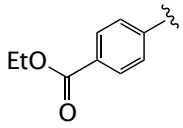
Other products prepared from various sulfonyldienes, Grignard reagents, and electrophiles are summarized in Table 1. Besides methyl derivative of sulfonylbutadiene **16**, propyl and cyclohexyl substituted ones **21** and **22** participated in the addition as well, to give allyl sulfones **25** and **26** as single isomers (entries 5 and 6). Even γ-substituted and γ,δ-disubstituted sulfonyldienes **23** and **24** reacted smoothly with a Grignard reagent to produce the corresponding allyl sulfones **27** and **28** in high yields (entries 7 and 8).

As far as the Grignard reagents are concerned, in addition to phenylmagnesium bromide, 3-methoxyphenyl-, 4-methoxyphenyl-, and 3,5-dimethoxyphenylmagnesium bromide afforded single allyl sulfones and their alkylated homologues with *cis*-olefin in good yields (entries 9-16). (Acetylamino)phenyl Grignard reagent (prepared from the corresponding iodide and

isopropylmagnesium bromide *in situ*[13]) afforded the desired product **37** as well (entry 17). Even halogenated Grignard reagents took part in the addition to give **38** and **39**, with their halogen moieties remaining unattacked (entries 18 and 19). In addition, aryl Grignard reagents having an electron-withdrawing group such as 4-(piperidinocarbony)- or 4-(ethoxycarbonyl)phenylmagnesium halides underwent the addition to dienyl sulfone **16** to give the desired products **40** and **41** (entries 20 and 21), showing the good compatibility of functional groups in this transformation.

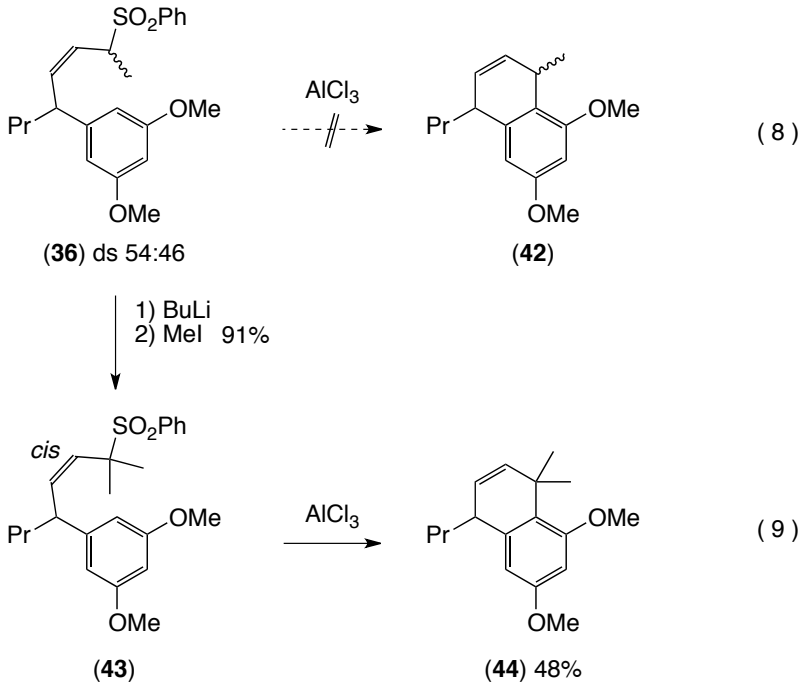
Table 1. Preparation of Various Allyl Sulfones.



	Sulfonyldiene		ArMgBr			Product		
entry	R	R'	Ar	(equiv)	El+	El	isolated yield (%)	ds
1	Me	H (**16**)		(1.8)	HCl	H	82 (**17**)	–
2	Me	H (**16**)		(1.8)	DCl	D	77 (**17**-d_1) (>99% d)	61:39
3	Me	H (**16**)		(2.5)	MeI	Me	80 (**18**)	59:41
4	Me	H (**16**)		(2.5)	CH_2=$CHCH_2Br$	CH_2=$CHCH_2$-	78 (**19**)	62:38
5	Pr	H (**21**)		(1.8)	HCl	H	76 (**25**)	–
6	*c*-C_6H_{11}	H (**22**)		(1.8)	HCl	H	76 (**26**)	–
7	H	Me (**23**)		(1.8)	HCl	H	73 (**27**)[a]	–
8	Pr	Et (**24**)		(1.8)	HCl	H	75 (**28**)[a]	–
9	Me	H (**16**)		(1.8)	HCl	H	82 (**29**)	–
10	Me	H (**16**)		(1.8)	HCl	H	90 (**30**)	–
11	Me	H (**16**)		(1.8)	HCl	H	84 (**31**)	–
12	Me	H (**16**)		(2.5)	MeI	Me	87 (**32**)	53:47
13	Me	H (**16**)		(2.5)	BuI	Bu	73 (**33**)	61:39
14	Me	H (**16**)		(2.5)	$MeOCH_2Cl$	$MeOCH_2$-	92 (**34**)	61:39
15	Pr	H (**21**)		(2.5)	HCl	H	70 (**35**)	–
16	Pr	H (**21**)		(2.5)	MeI	Me	74 (**36**)	59:41
17	Me	H (**16**)		(2.5)	HCl	H	58 (**37**)	–
18	Me	H (**16**)		(2.5)	HCl	H	62 (**38**)	–
19	Me	H (**16**)		(2.5)	HCl	H	55 (**39**)	–
20	Me	H (**16**)		(2.5)	HCl	H	63 (**40**)	–
21	Me	H (**16**)		(3.0)	HCl	H	48 (**41**)	–

[a] The stereochemistry of the olefin was confirmed by ^{1}H NMR NOESY experiments.

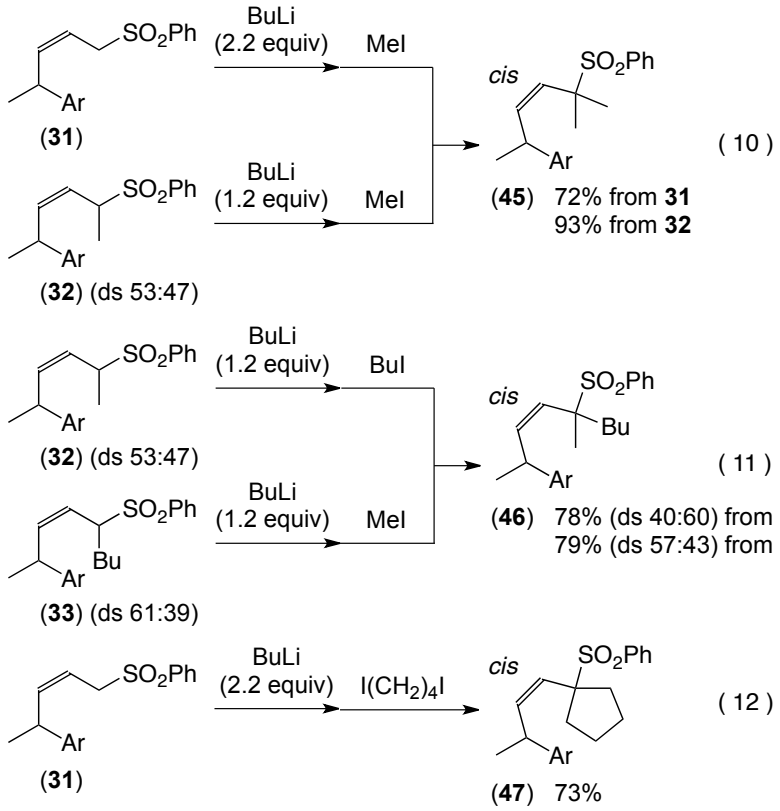
Having established the iron-catalyzed preparation of *cis*-4-aryl-2-alkenyl sulfones, we focused our attention on the allyl transfer ability of these allylic sulfones under the Fridel-Crafts conditions, where the *cis* olefinic structure should have an important role for the smooth ring closure between the aryl group and the allylic sulfone. To attest the whole sequence that we planned in eq 7, we executed a couple of preliminary reactions on the cyclization of allyl sulfones. The cyclization of **36**, the product of entry 16 in Table 1, in the presence of $AlCl_3$ even under forcing conditions did not afford the desired product **42**, due perhaps to the insufficient stabilization of the secondary-allylic cation for the Friedel-Crafts reaction. Accordingly, we next examined metallation and alkylation of allyl sulfones[14] to obtain its α,α-dialkylallyl derivatives to facilitate the formation of the intermediate cation, despite the concern on the preservation of the *cis*-stereochemical integrity during the deprotonation and alkylation steps. Nonetheless, lithiation and methylation of allyl sulfone **36** with butyllithium and MeI did not accompany isomerization of the *cis*-olefin to give the desired sulfone **43.** Its intramolecular Friedel-Crafts reaction as before gratifyingly afforded 1,4-dihydronaphthalene **44** albeit in a moderated yield (eq 9), achieving the transformation of eq 7.



In addition to products **31** and **32** directly obtained from the conjugate addition (entries 12 and 13 in Table 1), more substituted allylic sulfones are readily prepared by the deprotonation and alkylation of these products as shown in Scheme 4. For example, treatment of **31** and **32** with 2.2 or 1.2 equiv of BuLi generated the corresponding di- or mono-anion, which upon reaction with methyl

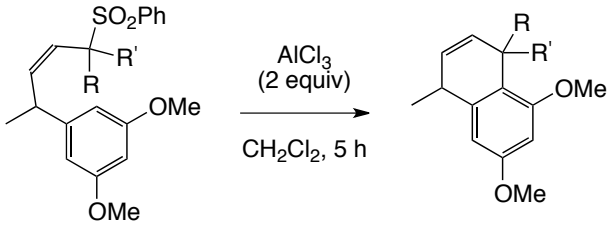
iodide gave product **45** having a fully substituted carbon α to sulfone in good yields (eq 10). Other products **46** and **47** were prepared in the same way (eqs 11 and 12). In any case in Scheme 4, it should be emphasized that the olefin isomerization from *cis* to *trans* was not observed.

Scheme 4. Alkylation of Allyl Sulfones (Ar = 3,5-$(MeO)_2C_6H_3$-).



With these substrates in hand, we further optimized reaction conditions for the cyclization. The attempted cyclization of **30** or **31** with $AlCl_3$ did not afford the desired products even under forcing condition (entries 1 and 2, Table 2), as mentioned in eq 8. However, gratifyingly, α,α-dialkylated allylic sulfones **45**-**47** afforded 1,4-dihydronaphthalenes **48**-**50** in good yields (entries 3-5).[10,15] These byciclic skeletons having a quaternary carbon adjacent to the ring junction are often found in naturally occurring products (see Chart 1).

Table 2. Cyclization of Allyl Sulfones with $AlCl_3$.



entry	R	R'			temp. (°C)	product yield (%)		
1	H	H	(**31**)		r.t.		0	
2	Me	H	(**32**)	(ds 53:47)	r.t.		0	
3	Me	Me	(**45**)		0	(**48**)	55	
4	Me	Bu	(**46**)	(ds 57:43)	0	(**49**)	61	(ds 77:23)
5	-$(CH_2)_4$-		(**47**)		0	(**50**)	74	

Summary

In conclusion, we reported the iron-catalyzed selective δ-addition of aryl Grignard reagents to sulfonyldienes and its synthetic utility. It is worthy to note that the sulfonyl group plays a triple role: (i) to effect the selective δ-conjugate addition, (ii) to enable alkylation at allylic terminus, and (iii) to work as a leaving group in the Friedel-Crafts reaction. Further investigation on the utility of these reactions is now in progress.

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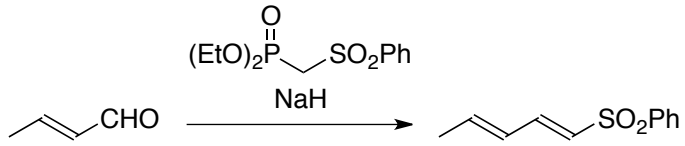
15. The yields of **48** remained lower with other Lewis acids (BF_3•OEt_2 : 0%, $FeCl_3$: trace, $TiCl_4$: 34%, and Et_2AlCl : 40%)

Experimental section (Chapter 2)

General. ^{1}H and ^{13}C NMR spectra were taken on a Varian Gemini-300 spectrometer at 300 and 75 MHz or an Agilent 400-MR spectrometer at 400 and 100 MHz, respectively. Unless otherwise specified in spectral data, the former was always used. $CDCl_3$ was used as the solvent. Chemical shifts are reported in parts per million shift (δ value) from Me_4Si (δ 0 ppm for ^{1}H) or based on the middle peak of the solvent ($CDCl_3$) (δ 77.00 ppm for ^{13}C NMR) as an internal standard. Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in Hertz. Infrared (IR) spectra were recorded on a JASCO A-100 spectrometer and are reported in wave numbers (cm^{-1}). High resolution mass spectra (HRMS) were obtained on a Bruker micrOTOF II by the positive electrospray ionization (ESI) method calibrated with sodium formate at the Suzukake-dai Material Analysis Center, Technical Department, Tokyo Institute of Technology. All reactions were carried out under argon. $FeCl_2$ (99.9%) used routinely was purchased from Soekawa Chemicals Co. (Japan). $FeCl_2$ (99.998%) for control experiments was purchased from Sigma-Aldrich Co. (USA). Dry solvents (THF, diethyl ether, and CH_2Cl_2) were purchased from Kanto Chemicals Co. (Japan). Chemicals were purified or dried in a standard manner, if necessary.

(1*E*,3*E*)-1,3-Pentadienyl phenyl sulfone (16).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a solution of methyl phenyl sulfone (3.12 g, 20.0 mmol) in THF (20 mL) was added *n*-BuLi (28.0 mL, 1.57 M solution in hexane, 44.0 mmol) at 0 °C. After the mixture was stirred at 0 °C for 30 min, diethyl chlorophosphate (3.45 mL, 24.0 mmol) was added dropwise at 0 °C. After the reaction mixture was warmed up to room temperature, it was stirred for 1 h. The reaction was quenched with aqueous saturated NH_4Cl solution. After the mixture was evaporated to remove bulk of the THF, water and CH_2Cl_2 were added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford diethyl [(benzenesulfonyl)methyl]phosphonate (5.46 g, 93%) as a white solid.

^{1}H NMR δ 1.30 (t, *J* = 7.2 Hz, 6H, -P(O)($OCH_2C\underline{H}_3$)$_2$), 3.77 (d, *J* = 16.8 Hz (P-C-H), 2H, -$C\underline{H}_2SO_2Ph$), 4.16 (dq, *J* = 8.4 (P-O-C-H), 7.2 Hz, 2H, -P(O)($OC\underline{H}_2CH_3$)$_2$), 7.58 (t, *J* = 7.5 Hz, 2H, -$SO_2\underline{Ph}$), 7.68 (t, *J* = 7.5 Hz, 1H, -$SO_2\underline{Ph}$), 8.00 (d, *J* = 7.5 Hz, 2H, -$SO_2\underline{Ph}$).

^{13}C NMR δ 16.15 (d, *J* = 6.2 Hz ($\underline{C}$-C-O-P)), 53.72 (d, *J* = 137.0 Hz (P-C)), 63.31 (d, *J* = 6.3 Hz (C-O-P)), 128.27 (2 carbons), 129.06 (2 carbons), 134.04, 139.91.

IR (KBr) 3066 (Ar), 2982, 2903, 1585, 1482, 1448, 1398, 1370, 1320, 1255, 1154 cm^{-1}.

These spectral properties were in good agreement with those reported in the above literature. However, the reported ^1H NMR δ value for -C<u>H</u>$_2$SO$_2$Ph in this literature, δ 4.11 ppm (d, *J* = 16.8 Hz, 2H), should be wrong, because an alternative literature (Enders, D.; von Berg, S.; Jandeleit, B. *Org. Synth*. **2002**, *78*, 169-176) showed the peak position to be δ 3.77 ppm (d, *J* = 16.8 Hz, 2H), which is consistent with our record.

To a suspension of sodium hydride (260 mg of a 60% suspension in mineral oil, 6.50 mmol) in THF (15 mL) was added diethyl [(benzenesulfonyl)methyl]phosphonate (1.75 g, 6.00 mmol) in THF (10 mL) at 0 °C under argon. After the mixture was stirred at room temperature for 10 min, it was again cooled to 0 °C. After (*E*)-2-butenal (0.410 mL, 5.00 mmol) was added, the mixture was warmed to room temperature and stirred for 1 h. The reaction was terminated by the slow addition of water. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, ^1H NMR analysis of which did not show the presence of olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (930 mg, 89%) exclusively with an *E*,*E*-olefinic bond and as a white solid.

^1H NMR δ 1.87 (d, *J* = 6.9 Hz, 3H, <u>Me</u>CH=CH-), 6.12 (dd, *J* = 10.8, 15.1 Hz, 1H, MeCH=C<u>H</u>CH=CHSO$_2$Ph), 6.24 (d, *J* = 14.8 Hz, 1H, MeCH=CHCH=C<u>H</u>SO$_2$Ph), 6.27 (dq, *J* = 15.1, 6.9 Hz, 1H, MeC<u>H</u>=CHCH=CHSO$_2$Ph), 7.25 (dd, *J* = 10.8, 14.8 Hz, 1H, MeCH=CHC<u>H</u>=CHSO$_2$Ph), 7.49-7.64 (m, 3H, -SO$_2$<u>Ph</u>), 7.88 (d, *J* = 8.1 Hz, 2H, -SO$_2$<u>Ph</u>).

^{13}C NMR δ 18.74, 127.34, 127.41 (2 carbons), 127.45, 129.18 (2 carbons), 133.10, 141.05, 142.46, 142.72.

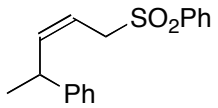
IR (KBr) 3052 (Ar and C=CH), 3014 (Ar), 2962, 2906, 1644 (C=C), 1595, 1446, 1306 (SO_2), 1149 (SO_2), 1082, 992, 832, 752, 716 cm^{-1}.

Anal. Calcd for $C_{11}H_{12}O_2S$: C, 63.43; H, 5.81. Found: C, 63.78; H, 5.97.

M.p. 51-53 °C.

The *E*,*E*-diene stereochemistry was confirmed by ^1H NMR coupling constants.

(*Z*)-4-Phenyl-2-pentenyl phenyl sulfone (17).



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 2 mL of THF was added phenylmagnesium bromide (0.330 mL, 1.09 M solution in THF, 0.360 mmol) at –45 °C under argon. After the mixture was stirred at –45 ~ –30 °C for 3 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in*

vacuo to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (46.9 mg, 82%) as a white solid.

^{1}H NMR δ 1.11 (d, *J* = 6.9 Hz, 3H, MeCHPh), 3.43 (dq, *J* = 9.9, 6.9 Hz, 1H, MeCHPh), 3.86 (dd, *J* = 7.5, 14.2 Hz, 1H, -CH=CHCH$_2$SO$_2$Ph), 3.99 (dd, *J* = 8.4, 14.2 Hz, 1H, -CH=CHCH$_2$SO$_2$Ph), 5.43 (ddd, *J* = 7.5, 8.4, 9.9 Hz, 1H, -CH=CHCH$_2$SO$_2$Ph), 5.85 (t, *J* = 9.9 Hz, 1H, -CH=CHCH$_2$SO$_2$Ph), 7.01 (d, *J* = 6.9 Hz, 2H, Ph-H), 7.13-7.27 (m, 3H, Ph-H), 7.52 (t, *J* = 7.3 Hz, 2H, -SO$_2$Ph), 7.63 (t, *J* = 7.3 Hz, 1H, -SO$_2$Ph), 7.89 (d, *J* = 7.3 Hz, 2H, -SO$_2$Ph).

NOESY experiments showed the correlation between the peaks at δ 3.43 ppm (MeCHPh) and at δ 3.86 ppm (-CH=CHCH$_2$SO$_2$Ph), and at δ 5.43 ppm (-CH=CHCH$_2$SO$_2$Ph) and at δ 5.85 ppm (-CH=CHCH$_2$SO$_2$Ph). Thus, the stereochemistry of the olefin was assigned to *Z*.

^{13}C NMR δ 21.52, 37.42, 55.25, 114.18 (C=C), 126.31, 126.63 (2 carbons), 128.44 (2 carbons), 128.53 (2 carbons), 129.07 (2 carbons), 133.71, 138.56, 143.53, 144.41 (C=C).

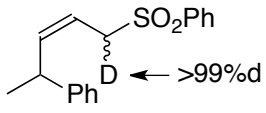
IR (KBr) 3060 (Ar), 3033 (Ar and C=CH), 2966, 2933, 2888, 1653 (C=C), 1600, 1580, 1446, 1306 (SO$_2$), 1138 (SO$_2$), 1082, 1022, 733, 686, 566 cm^{-1}.

Anal. Calcd for $C_{17}H_{18}O_2S$: C, 71.30; H, 6.34. Found: C, 71.37; H, 6.33.

M.p. 71-72 °C.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants as well as ^{1}H NMR NOESY experiments.

A 61:39 diastereomeric mixture of (*Z*)-1-deuterio-4-phenyl-2-pentenyl phenyl sulfone (17-d_1).



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.459 mL, 1.09 M solution in THF, 0.500 mmol) at –45 °C under argon. After the mixture was stirred at –45 ~ –30 °C for 3 h, the reaction was terminated by the addition of 1 N DCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the diastereoselectivity of the product was 61:39. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (44.1 mg, 77%) as an oil and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^{1}H NMR δ 1.11 (d, *J* = 6.9 Hz, 3H, MeCHPh), 3.43 (dq, *J* = 10.8, 6.9 Hz, 1H, MeCHPh), 3.84 (d, *J* = 7.2 Hz, 1H, -CH=CHCHDSO$_2$Ph), 5.42 (dd, *J* = 7.2, 10.8 Hz, 1H, -CH=CHCHDSO$_2$Ph), 5.86 (t, *J* = 10.8 Hz, 1H, -CH=CHCHDSO$_2$Ph), 7.01 (d, *J* = 7.8 Hz, 2H, Ph-H), 7.13-7.25 (m, 3H, Ph-H), 7.52 (t, *J* = 7.5 Hz, 2H, -SO$_2$Ph), 7.63 (t, *J* = 7.5 Hz, 1H, -SO$_2$Ph), 7.89 (d, *J* = 7.5 Hz, 2H, -SO$_2$Ph).

Minor isomer: ^{1}H NMR (characteristic peaks are shown) δ 1.12 (d, *J* = 6.9 Hz, 3H, MeCHPh), 3.96 (d, *J* = 8.1 Hz, 1H, -CH=CHCHDSO$_2$Ph).
The integration of peak areas at δ 3.84 ppm (-C=CHCHDSO$_2$Ph) and δ 3.96 ppm (-C=CHCHDSO$_2$Ph) decreased its original value (2 H) to total 1.0 H to show >99% deuterium incorporation at these positions.
The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

Control experiment: Addition of phenylmagnesium bromide to (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (16) using a catalytic amount of FeCl$_2$ (99.998% purity).

To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (20.8 mg, 0.100 mmol) and FeCl$_2$ (1.3 mg, 0.010 mmol, purity: 99.998% purchased from Sigma-Aldrich Co., USA) in 1 mL of THF was added phenylmagnesium bromide (0.183 mL, 0.985 M solution in THF, 0.180 mmol) at –45 °C under argon. After the mixture was stirred at –45 ~ –30 °C for 3 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated NaHCO$_3$ solution and brine, dried over Na$_2$SO$_4$, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford (*Z*)-4-phenyl-2-pentenyl phenyl sulfone (23.6 mg, 82%) as a white solid.

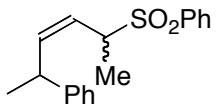
For spectral data, see: (*Z*)-4-phenyl-2-pentenyl phenyl sulfone (**5**) shown above.

Control experiment: Addition of phenylmagnesium bromide to (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (16) using a catalytic amount of CuBr·SMe$_2$.

To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (20.8 mg, 0.100 mmol) and CuBr·SMe$_2$ (2.1 mg, 0.010 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.183 mL, 0.985 M solution in THF, 0.180 mmol) at –45 °C under argon. After the mixture was stirred at –45 ~ –30 °C for 3 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated NH$_4$Cl solution, aqueous saturated NaHCO$_3$ solution, and brine, dried over Na$_2$SO$_4$, and concentrated *in vacuo* to give a crude oil, which contained (*Z*)-4-phenyl-2-pentenyl phenyl sulfone (**17**) in 39% yield, 2-phenyl-3-pentenyl phenyl sulfone in 15% yield, and (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone in 36% by ^{1}H NMR analysis with an internal standard. Isolation of a pure sample was not undertaken.

2-Phenyl-3-pentenyl phenyl sulfone.
^{1}H NMR (characteristic peaks are shown) δ 1.87 (d, *J* = 6.9 Hz, 3H, MeCH=CH-), 3.25 (m, 1H, PhCH-), 3.52 (dd, *J* = 3.0, 7.5 Hz 1H, -CH$_2$SO$_2$Ph), 5.30-5.56 (m, 2H, -CH=CH-).
The olefinic stereochemistry of 2-phenyl-3-pentenyl phenyl sulfone could not be determined.

A 59:41 diastereomeric mixture of (*Z*)-5-phenyl-3-hexen-2-yl phenyl sulfone (18) prepared by phenyl Grignard addition to sulfonyldiene 4, followed by *in situ* methylation.



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.459 mL, 1.09 M solution in THF, 0.500 mmol) at –45 °C under argon. After the mixture was warmed up to 0 ºC over 3 h, iodomethane (0.062 mL, 1.00 mmol) was added and the reaction mixture was heated in an oil bath maintained at 50 °C for 12 h. The reaction was terminated at room temperature by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was 59:41. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (47.8 mg, 80%) as a white solid and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^{1}H NMR δ 1.24 (d, *J* = 6.9 Hz, 3H, MeCHPh), 1.52 (d, *J* = 6.9 Hz, 3H, -CH(Me)SO_2Ph), 3.45 (dq, *J* = 10.0, 6.9 Hz, 1H, MeCHPh), 4.04-4.17 (m, 1H, -CH=CHCH(Me)SO_2Ph), 5.32 (t, *J* = 10.0 Hz, 1H, -CH=CHCH(Me)SO_2Ph), 5.71 (t, *J* = 10.0 Hz, 1H, -CH=CHCH(Me)SO_2Ph), 6.78-6.85 (m, 2H, Ph-H), 7.06-7.31 (m, 3H, Ph-H), 7.40 (t, *J* = 8.1 Hz, 2H, -SO_2Ph), 7.57 (t, *J* = 8.1 Hz, 1H, -SO_2Ph), 7.78 (d, *J* = 8.1 Hz, 2H, -SO_2Ph).

^{13}C NMR δ 14.23, 21.81, 37.41, 58.81, 121.68, 126.08, 126.59 (2 carbons), 128.30 (2 carbons), 128.77 (2 carbons), 128.88 (2 carbons), 133.46, 137.45, 141.05, 144.04.

Minor isomer: ^{1}H NMR (characteristic peaks are shown) δ 0.95 (d, *J* = 6.9 Hz, 3H, MeCHPh), 1.38 (d, *J* = 6.9 Hz, 3H, -CH(Me)SO_2Ph), 3.37 (dq, *J* = 10.0, 6.9 Hz, 1H, MeCHPh), 4.04-4.17 (m, 1H, -CH=CHCH(Me)SO_2Ph), 5.26 (t, *J* = 10.0 Hz, 1H, -CH=CHCH(Me)SO_2Ph), 5.72 (t, *J* = 10.0 Hz, 1H, -CH=CHCH(Me)SO_2Ph), 6.78-6.85 (m, 2H, Ph-H), 7.06-7.31 (m, 3H, Ph-H), 7.52 (t, *J* = 7.2 Hz, 2H, -SO_2Ph), 7.66 (t, *J* = 7.2 Hz, 1H, -SO_2Ph), 7.91 (d, *J* = 7.2 Hz, 2H, -SO_2Ph).

^{13}C NMR (characteristic peaks are shown) δ 13.84, 21.24, 37.72, 59.10, 121.79, 126.31, 126.53 (2 carbons), 128.58 (2 carbons), 129.20 (2 carbons), 133.62, 137.50, 141.52, 144.84.

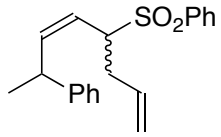
IR (KBr) 3060 (Ar), 3023 (Ar and C=CH), 2969, 2924, 1654 (C=C), 1600, 1583, 1493, 1445, 1305 (SO_2), 1147 (SO_2), 1086, 762, 529 cm^{-1} for a 59:41 mixture of diastereoisomers.

Anal. Calcd for $C_{18}H_{20}O_2S$: C, 71.96; H, 6.71. Found: C, 72.27; H, 6.58 for a 59:41 mixture of diastereoisomers.

(M.p. 93-94 °C.)

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

A 62:38 diastereomeric mixture of (5*Z*)-7-phenyl-1,5-octadien-4-yl phenyl sulfone (19) prepared by phenyl Grignard addition to sulfonyldiene 4, followed by *in situ* allylation.



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (62.5 mg, 0.300 mmol) and $FeCl_2$ (3.8 mg, 0.030 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.688 mL, 1.09 M solution in THF, 0.750 mmol) at –45 °C under argon. After the mixture was warmed up to 0 ºC over 3 h, allyl bromide (0.130 mL, 1.50 mmol) was added and the reaction mixture was heated in an oil bath maintained at 60 °C for 12 h. The reaction was terminated at room temperature by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was 62:38. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (76.5 mg, 78%) as an oil and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^{1}H NMR δ 1.20 (d, *J* = 6.9 Hz, 3H, MeCHPh), 2.46 (m, 1H, -CH(CH_2CH=CH_2)SO_2Ph), 3.02 (m, 1H, -CH(CH_2CH=CH_2)SO_2Ph), 3.32 (dq, *J* = 9.9, 6.9 Hz, 1H, MeC*H*Ph), 3.98 (dt, *J* = 9.6, 9.9 Hz, 1H, -C*H*(CH_2CH=CH_2)SO_2Ph), 5.14 (md, *J* = 9.9 Hz, 1H, -CH(CH_2CH=CH_2)SO_2Ph), 5.19 (md, *J* = 17.1 Hz, 1H, -CH(CH_2CH=CH_2)SO_2Ph), 5.26 (t, *J* = 9.9 Hz, 1H, -CH=C*H*CHSO_2Ph), 5.72 (ddt, *J* = 9.9, 17.1, 7.2 Hz, 1H, -CH(CH_2C*H*=CH_2)SO_2Ph), 5.79 (t, *J* = 9.9 Hz, 1H, -C*H*=CHCHSO_2Ph), 6.71-6.78 (m, 1H, Ph-H), 7.04-7.28 (m, 4H, Ph-H), 7.37 (t, *J* = 7.5 Hz, 2H, -SO_2*Ph*), 7.57 (t, *J* = 7.5 Hz, 1H, -SO_2*Ph*), 7.77 (d, *J* = 7.5 Hz, 2H, -SO_2*Ph*).

^{13}C NMR δ 21.72, 32.17, 37.45, 63.62, 118.73, 119.77, 126.03, 126.54, 128.28 (2 carbons), 128.79 (2 carbons), 128.88 (2 carbons), 133.05, 133.52, 137.56, 142.54, (2 carbons), 143.97.

Minor isomer: ^{1}H NMR (characteristic peaks are shown) δ 0.86 (d, *J* = 6.9 Hz, 3H, MeCHPh), 2.31-2.39 (m, 1H, -CH(CH_2CH=CH_2)SO_2Ph), 2.83-2.92 (m, 1H, -CH(CH_2CH=CH_2)SO_2Ph), 3.25 (dq, *J* = 9.9, 6.9 Hz, 1H, MeC*H*Ph), 4.02 (dt, *J* = 9.6, 9.9 Hz, 1H, -C*H*(CH_2CH=CH_2)SO_2Ph), 4.91 (md, *J* = 9.9 Hz, 1H, -CH(CH_2CH=CH_2)SO_2Ph), 5.01 (qd, *J* = 1.5, 17.1 Hz, 1H, -CH(CH_2CH=CH_2)SO_2Ph), 5.21 (t, *J* = 9.9 Hz, 1H, -CH=C*H*CHSO_2Ph), 5.40 (ddt, *J* = 9.9, 17.1, 7.2 Hz, 1H, -CH(CH_2C*H*=CH_2)SO_2Ph), 5.79 (t, *J* = 9.9 Hz, 1H, -C*H*=CHCHSO_2Ph), 7.50 (t, *J* = 7.5 Hz, 2H, -SO_2*Ph*), 7.67 (t, *J* = 7.5 Hz, 1H, -SO_2*Ph*), 7.92 (d, *J* = 7.5 Hz, 2H, -SO_2*Ph*).

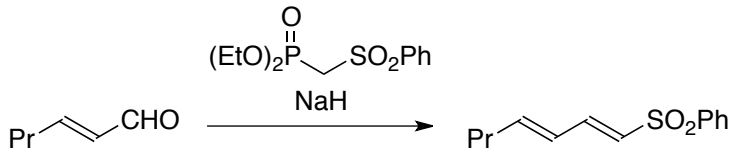
^{13}C NMR (characteristic peaks are shown) δ 21.11, 32.28, 37.74, 118.30, 120.24, 126.28, 126.76, 128.44 (2 carbons), 129.25 (2 carbons), 132.77, 133.71, 137.73, 143.20 (2 carbons), 144.65.

IR (neat) 3062 (Ar and C=CH_2), 3027 (Ar and C=CH), 2967, 1654 (C=C), 1601, 1548, 1480, 1446, 1306 (SO_2), 1147 (SO_2), 733, 699 cm^{-1} for a 62:38 mixture of diastereoisomers.

Anal. Calcd for $C_{20}H_{22}O_2S$: C, 73.58; H, 6.79. Found: C, 73.82; H, 6.86 for a 62:38 mixture of

diastereoisomers.
The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

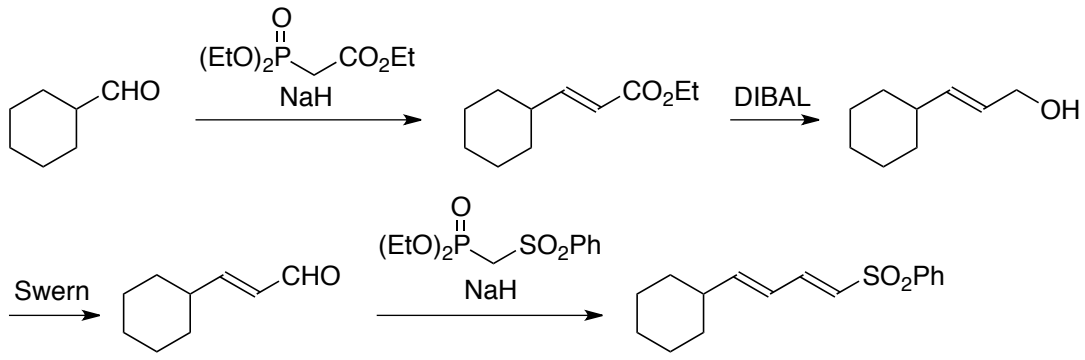
(1*E*,3*E*)-1,3-Heptadienyl phenyl sulfone (21).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a suspension of sodium hydride (52.0 mg of a 60% suspension in mineral oil, 1.30 mmol) in THF (5 mL) was added diethyl [(benzenesulfonyl)methyl]phosphonate (350 mg, 1.20 mmol) in THF (2 mL) at 0 °C under argon. After the mixture was stirred for 10 min at room temperature, it was again cooled to 0 °C. Then, (*E*)-2-hexenal (0.115 mL, 1.00 mmol) was added and the mixture was warmed up to room temperature and was stirred overnight. The reaction was terminated by the slow addition of water. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, ^{1}H NMR analysis of which did not show the presence of olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (190 mg, 79%) exclusively with an *E*,*E*-olefinic bond and as a white solid.
^{1}H NMR δ 0.91 (t, *J* = 7.2 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$-), 1.45 (sextet, *J* = 7.2 Hz, 2H, CH$_3$C$\underline{H}_2$CH$_2$-), 2.15 (q, *J* = 7.2 Hz, 2H, allyl-H), 6.10 (dd, *J* = 10.6, 14.7 Hz, 1H, PrCH=C$\underline{H}$CH=CHSO$_2$Ph), 6.25 (d, *J* = 14.7 Hz, 1H, PrCH=CHCH=C$\underline{H}$SO$_2$Ph), 6.26 (dt, *J* = 14.7, 7.2 Hz, 1H, PrC$\underline{H}$=CHCH=CHSO$_2$Ph), 7.25 (dd, *J* = 10.6, 14.7 Hz, 1H, PrCH=CHC$\underline{H}$=CHSO$_2$Ph), 7.49-7.63 (m, 3H, -SO$_2\underline{Ph}$), 7.89 (d, *J* = 6.9 Hz, 2H, -SO$_2\underline{Ph}$).
^{13}C NMR δ 13.51, 21.57, 34.90, 126.07, 127.31 (2 carbons), 127.42, 129.11 (2 carbons), 133.03, 140.98, 142.78, 147.49.
IR (KBr) 3051 (Ar and C=CH), 2957, 2923, 2871, 1639 (C=C), 1591, 1446, 1306 (SO$_2$), 1142 (SO$_2$), 1083, 998, 823, 754 cm^{-1}.
Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82. Found: C, 65.73; H, 6.79.
M.p. 40-41 °C.
The *E*,*E*-diene stereochemistry was confirmed by ^{1}H NMR coupling constants.

(1*E*,3*E*)-4-Cyclohexyl-1,3-butadienyl phenyl sulfone (22).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a suspension of NaH (780 mg of a 60% suspension in mineral oil, 19.5 mmol) in THF (50 mL) was added triethyl phosphonoacetate (3.60 mL, 18.0 mmol) at 0 °C under argon. After the reaction mixture was stirred at room temperature for 10 min, it was cooled to 0 °C and cyclohexanecarbaldehyde (1.68 g, 15.0 mmol) in THF (10 mL) was added dropwise. The reaction mixture was allowed to warm up to room temperature over 1 h and quenched with water (50 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford ethyl (*E*)-3-cyclohexylpropenoate (3.12 g, 100%) as an oil.

To a solution of ethyl (*E*)-3-cyclohexylpropenoate (2.73 g, 15.0 mL) in CH_2Cl_2 (50 mL) was added DIBAL (43.7 mL, 1.03 M solution in hexane, 45.0 mmol) at –78 °C under argan. The reaction mixture was allowed to warm up to 0 °C over 5 h and quenched with 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with saturated aqueous $NaHCO_3$ solution, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford (*E*)-3-cyclohexyl-2-propenol (1.88 g, 89%) as an oil.

To a solution of oxalyl chloride (0.515 mL, 6.00 mmol) in CH_2Cl_2 (20.0 mL) was added DMSO (630 mg, 8.10 mmol) in CH_2Cl_2 (2 mL) dropwise at –78 °C. After the solution was stirred at room temperature for 20 min, (*E*)-3-cyclohexyl-2-propenol (420 mg, 3.00 mmol) in CH_2Cl_2 (2 mL) was added dropwise and the reaction mixture was stirred at –78 ºC for 1 h. Then, Et_3N (3.04 mL, 22.0 mmol) was added and the reaction mixture was allowed to warm up to 0 °C. After the reaction mixture was stirred at 0 ºC for 20 min, aqueous saturated NH_4Cl solution was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give (*E*)-3-cyclohexyl-2-propenal (551 mg, 100%) as a yellow oil, which was essentially pure by ^1H NMR analysis and was used in the next step without purification.

To a suspension of sodium hydride (156 mg of a 60% suspension in mineral oil, 3.90 mmol) in THF (15 mL) was added diethyl [(benzenesulfonyl)methyl]phosphonate (1.05 g, 3.60 mmol) in THF (5 mL)

at 0 °C under argon. After the reaction mixture was stirred at room temperature for 10 min, it was again cooled to 0 °C. Then, (*E*)-3-cyclohexyl-2-propenal (415 mg, *ca*. 3.00 mmol) in THF (5 mL) was added. After the reaction mixture was warmed to room temperature, it was stirred for 1 h. The reaction was terminated by the slow addition of water. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, ^{1}H NMR analysis of which did not show the presence of olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (774 mg, 93%) exclusively with an *E*,*E*-olefinic bond and as a white solid.

^{1}H NMR δ 1.04-1.35 (m, 5H, alkyl-H), 1.60-1.80 (m, 5H, alkyl-H), 2.10 (m, 1H, allyl-H), 6.05 (dd, *J* = 10.6, 15.6 Hz, 1H, -CH=C<u>H</u>CH=CHSO$_2$Ph), 6.20 (dd, *J* = 6.6, 15.6 Hz, 1H, -C<u>H</u>=CHCH=CHSO$_2$Ph), 6.26 (d, *J* = 14.8 Hz, 1H, -CH=CHCH=C<u>H</u>SO$_2$Ph), 7.24 (dd, *J* = 10.6, 14.8 Hz, 1H, -CH=CHC<u>H</u>=CHSO$_2$Ph), 7.49-7.63 (m, 3H, -SO$_2$<u>Ph</u>), 7.89 (d, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>).

^{13}C NMR δ 25.66 (2 carbons), 25.86, 31.98 (2 carbons), 41.12, 123.56, 127.43 (2 carbons), 127.53, 129.18 (2 carbons), 133.07, 141.12, 143.29, 153.02.

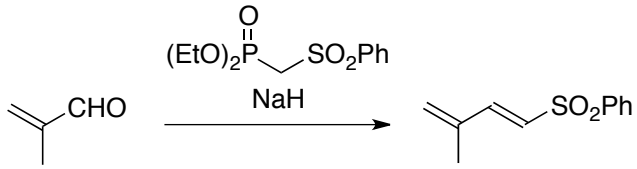
IR (KBr) 3051 (Ar and C=CH), 3014 (Ar), 2922, 2849, 1636 (C=C), 1585, 1447, 1308 (SO$_2$), 1145 (SO$_2$), 997, 832, 754, 685 cm^{-1}.

Anal. Calcd for $C_{16}H_{20}O_2S$: C, 69.53; H, 7.29. Found: C, 69.49; H, 7.25.

M.p. 63-64 °C.

The *E*,*E*-diene stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*E*)-3-Methyl-1,3-butadienyl phenyl sulfone (23).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a suspension of sodium hydride (52.0 mg of a 60% suspension in mineral oil, 1.30 mmol) in THF (5 mL) was added diethyl [(benzenesulfonyl)methyl]phosphonate (350 mg, 1.20 mmol) in THF (2 mL) at 0 °C under argon. After the mixture was stirred for 10 min at room temperature, it was again cooled to 0 °C. After 2-methyl-2-propenal (0.082 mL, 1.00 mmol) was added, the mixture was warmed up to room temperature and was stirred for 1 h. The reaction was terminated by the slow addition of water. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, ^{1}H NMR analysis of which did not show the presence of olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (207 mg, 82%) exclusively with an *E*-olefinic bond and as a white solid.

^{1}H NMR δ 1.84 (s, 3H, <u>Me</u>), 5.45 (s, 1H, <u>H$_2$</u>C=C(Me)CH=CHSO$_2$Ph), 5.48 (s, 1H,

$\underline{H_2}$C=C(Me)CH=CHSO$_2$Ph), 6.32 (d, *J* = 15.2 Hz, 1H, H$_2$C=C(Me)C$\underline{H}$=CHSO$_2$Ph), 7.35 (d, *J* = 15.2 Hz, 1H, H$_2$C=C(Me)CH=C$\underline{H}$SO$_2$Ph), 7.51-7.66 (m, 3H, -SO$_2\underline{Ph}$), 7.91 (d, *J* = 7.5 Hz, 2H, -SO$_2\underline{Ph}$).

^{13}C NMR δ 18.03, 126.88, 127.58 (2 carbons), 127.79, 129.27 (2 carbons), 133.30, 138.75, 140.71, 144.79.

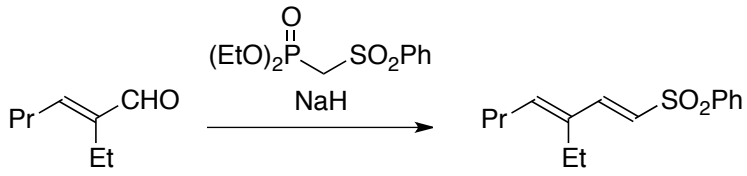
IR (KBr) 3047 (Ar and C=CH), 2980, 2950, 2906, 1623 (C=C), 1589, 1447, 1306 (SO$_2$), 1142 (SO$_2$), 1085, 918, 852, 720 cm^{-1}.

Anal. Calcd for $C_{11}H_{12}O_2S$: C, 63.43; H, 5.81. Found: C, 63.66; H, 5.83.

M.p. 63-64 °C.

The *E*-olefin stereochemistry was confirmed by ^{1}H NMR coupling constants.

(1*E*,3*E*)-3-Ethyl-1,3-heptadienyl phenyl sulfone (24).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a suspension of sodium hydride (52.0 mg of a 60% suspension in mineral oil, 1.30 mmol) in THF (5 mL) was added diethyl [(benzenesulfonyl)methyl]phosphonate (350 mg, 1.20 mmol) in THF (2 mL) at 0 °C under argon. After the reaction mixture was stirred for 10 min at room temperature, it was again cooled to 0 °C. After (*E*)-2-ethyl-2-hexenal (0.148 mL, 1.00 mmol) was added, the reaction mixture was warmed up to room temperature and stirred overnight. The reaction was terminated by the slow addition of water. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, ^{1}H NMR analysis of which did not show the presence of olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (250 mg, 94%) exclusively with an *E*,*E*-olefinic bond as an oil.

^{1}H NMR δ 0.94 (t, *J* = 7.5 Hz, 3H, $\underline{Me}$), 0.95, (t, *J* = 7.5 Hz, 3H, $\underline{Me}$), 1.46 (sextet, *J* = 7.5 Hz, 2H, CH$_3$C$\underline{H_2}$CH$_2$-), 2.12-2.23 (m, 4H, allyl-H), 5.96 (t, *J* = 7.5 Hz, 1H, PrC$\underline{H}$=C(Et)-), 6.24 (d, *J* = 15.1 Hz, 1H, -CH=C$\underline{H}$SO$_2$Ph), 7.22 (d, *J* = 15.1 Hz, 1H, -C$\underline{H}$=CHSO$_2$Ph), 7.50-7.63 (m, 3H, -SO$_2\underline{Ph}$), 7.89 (d, *J* = 6.9 Hz, 2H, -SO$_2\underline{Ph}$).

NOESY experiments showed the correlation between the peaks at δ 5.96 ppm (PrC$\underline{H}$=C(Et)-) and at δ 7.22 ppm (-C$\underline{H}$=CHSO$_2$Ph).

^{13}C NMR δ 13.04, 13.83, 19.86, 22.21, 30.65, 123.81, 127.32 (2 carbons), 129.15 (2 carbons), 132.98, 137.39, 141.38, 144.72, 146.44.

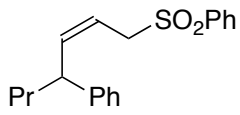
IR (neat) 3058 (Ar and C=CH), 2964, 2934, 2873, 1623 (C=C), 1591, 1446, 1306 (SO$_2$), 1146 (SO$_2$), 1086, 848, 753 cm^{-1}.

Anal. Calcd for $C_{15}H_{20}O_2S$: C, 68.14; H, 7.62. Found: C, 68.11 ; H, 7.55.

The *E*,*E*-diene stereochemistry was confirmed by ^{1}H NMR NOESY experiments and ^{1}H NMR coupling

constants.

(*Z*)-4-Phenyl-2-heptenyl phenyl sulfone (25).



To a solution of (1*E*,3*E*)-1,3-heptadienyl phenyl sulfone (**21**) (47.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.330 mL, 1.09 M solution in THF, 0.360 mmol) at –45 °C under argon. After the mixture was stirred at –45 ~ –30 ºC for 3 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (47.8 mg, 76%) as an oil.

^{1}H NMR δ 0.78 (t, *J* = 7.2 Hz, 3H, $\underline{CH_3}CH_2CH_2$-), 0.93-1.10 (m, 2H, alkyl-H), 1.30 (m, 1H, alkyl-H), 1.53 (m, 1H, alkyl-H), 3.18 (td, *J* = 7.5, 10.9 Hz, 1H, PrC$\underline{H}$Ph), 3.84 (dd, *J* = 7.5, 14.5 Hz, 1H, -CH=CHC$\underline{H_2}SO_2$Ph), 3.96 (dd, *J* = 8.1, 14.5 Hz, 1H, -CH=CHC$\underline{H_2}SO_2$Ph), 5.46 (ddd, *J* = 7.5, 8.1, 10.9 Hz, 1H, -CH=C$\underline{H}CH_2SO_2$Ph), 5.86 (t, *J* = 10.9 Hz, 1H, -C$\underline{H}$=CHCH$_2$SO$_2$Ph), 6.95 (d, *J* = 6.9 Hz, 2H, Ph-H), 7.10-7.27 (m, 3H, Ph-H), 7.50 (t, *J* = 7.8 Hz, 2H, -SO$_2\underline{Ph}$), 7.61 (t, *J* = 7.8 Hz, 1H, -SO$_2\underline{Ph}$), 7.86 (d, *J* = 7.8 Hz, 2H, -SO$_2\underline{Ph}$).

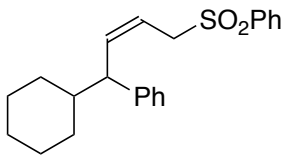
^{13}C NMR δ 13.89, 20.29, 38.63, 43.54, 55.43, 115.03 (C=C), 126.25, 127.08 (2 carbons), 128.41 (2 carbons), 128.52 (2 carbons), 129.02 (2 carbons), 133.65, 138.50, 142.46, 143.58 (C=C).

IR (neat) 3059 (Ar), 3026 (Ar and C=CH), 2957, 2923, 2870, 1654 (C=C), 1601, 1585, 1447, 1307 (SO_2), 1141 (SO_2), 1086, 728, 688 cm^{-1}.

Anal. Calcd for $C_{19}H_{22}O_2S$: C, 72.57; H, 7.05. Found: C, 72.63; H, 7.02.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-4-Cyclohexyl-4-phenyl-2-butenyl phenyl sulfone (26).



To a solution of (1*E*,3*E*)-4-cyclohexyl-1,3-butadienyl phenyl sulfone (**22**) (111 mg, 0.400 mmol) and $FeCl_2$ (5.1 mg, 0.040 mmol) in 2 mL of THF was added phenylmagnesium bromide (0.661 mL, 1.09 M solution in THF, 0.720 mmol) at –45 °C under argon. After the reaction mixture was gradually warmed up to room temperature over 5 h, the reaction was terminated by the addition of 1 N HCl solution (2 mL).

The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (108 mg, 76%) as an oil.

^{1}H NMR δ 0.48-0.75 (m, 2H, alkyl-H), 0.97-1.62 (m, 9H, alkyl-H), 2.89 (t, *J* = 10.1 Hz, 1H, (cyclohexyl)C<u>H</u>Ph), 3.81 (dd, *J* = 7.2, 14.4 Hz, 1H, -CH=CHC<u>H</u>$_2$SO$_2$Ph), 3.93 (dd, *J* = 8.1, 14.4 Hz, 1H, -CH=CHC<u>H</u>$_2$SO$_2$Ph), 5.49 (ddd, *J* = 7.2, 8.1, 10.1 Hz, 1H, -CH=C<u>H</u>CH$_2$SO$_2$Ph), 5.94 (t, *J* = 10.1 Hz, 1H, -C<u>H</u>=CHCH$_2$SO$_2$Ph), 6.92 (d, *J* = 6.6 Hz, 2H, Ph-H), 7.10-7.24 (m, 3H, Ph-H), 7.46 (t, *J* = 7.2 Hz, 2H, -SO$_2$<u>Ph</u>), 7.57 (t, *J* = 7.2 Hz, 1H, -SO$_2$<u>Ph</u>), 7.83 (d, *J* = 7.2 Hz, 2H, -SO$_2$<u>Ph</u>).

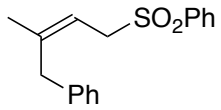
^{13}C NMR δ 26.19, 26.27 (2 peaks), 30.74, 30.92, 42.93, 50.43, 55.51, 115.84 (C=C), 126.14, 127.72 (2 carbons), 128.38 (2 carbons), 128.41 (2 carbons), 128.99 (2 carbons), 133.60, 138.61, 141.16, 142.66 (C=C).

IR (neat) 3068 (Ar), 3026 (Ar and C=CH), 2925, 2851, 1654 (C=C), 1600, 1585, 1447, 1308 (SO_2), 1142 (SO_2), 832, 729 cm^{-1}.

Anal. Calcd for $C_{22}H_{26}O_2S$: C, 74.54; H, 7.39. Found: C, 74.27; H, 7.55.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-3-Methyl-4-phenyl-2-butenyl phenyl sulfone (27).



To a solution of (*E*)-3-methyl-1,3-butadienyl phenyl sulfone (**23**) (83.3 mg, 0.400 mmol) and $FeCl_2$ (5.1 mg, 0.040 mmol) in 2 mL of THF was added phenylmagnesium bromide (0.667 mL, 1.08 M solution in THF, 0.720 mmol) at –45 °C under argon. After the reaction mixture was gradually warmed up to room temperature over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (84.0 mg, 73%) as an oil.

^{1}H NMR δ 1.64 (s, 3H, <u>Me</u>), 3.10 (s, 2H, PhC<u>H</u>$_2$-), 3.93 (d, *J* = 7.8 Hz, 2H, -C=CHC<u>H</u>$_2$SO$_2$Ph), 5.40 (t, *J* = 7.8 Hz, 1H, -C=C<u>H</u>CH$_2$SO$_2$Ph), 6.92 (d, *J* = 7.8 Hz, 2H, Ph-H), 7.12-7.24 (m, 3H, Ph-H), 7.57 (t, *J* = 7.2 Hz, 2H, -SO$_2$<u>Ph</u>), 7.68 (t, *J* = 7.2 Hz, 1H, -SO$_2$<u>Ph</u>), 7.91 (d, *J* = 7.2 Hz, 2H, -SO$_2$<u>Ph</u>).

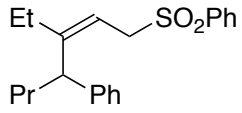
NOESY experiments showed the correlation between the peaks at δ 3.10 ppm (PhC<u>H</u>$_2$-) and at δ 3.93 ppm (-C=CHC<u>H</u>$_2$SO$_2$Ph). Thus, the stereochemistry of the olefin was assigned to *Z*.

^{13}C NMR δ 23.55, 37.60, 56.05, 112.02, 126.28, 128.37 (2 carbons), 128.43 (2 peaks of 2 carbons), 129.12 (2 carbons), 133.64, 138.09, 138.81, 144.59.

IR (neat) 3060 (Ar), 3027 (Ar and C=CH), 2973, 2916, 1663 (C=C), 1601, 1584, 1495, 1446, 1307 (SO_2),

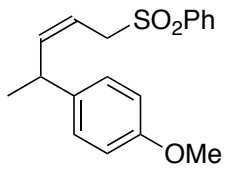
1148 (SO_2), 1082, 734 cm^{-1}.
Anal. Calcd for $C_{17}H_{18}O_2S$: C, 71.30; H, 6.34. Found: C, 71.57; H, 6.44.
The *Z*-stereochemistry was confirmed by ^1H NMR NOESY experiments.

(*Z*)-3-Ethyl-4-phenyl-2-heptenyl phenyl sulfone (28).



To a solution of (1*E*,3*E*)-3-ethyl-1,3-heptadienyl phenyl sulfone (**24**) (52.9 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 2 mL of THF was added phenylmagnesium bromide (0.330 mL, 1.09 M solution in THF, 0.360 mmol) at –45 °C under argon. After the reaction mixture was gradually warmed up to room temperature over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (51.6 mg, 75%) as an oil.
^1H NMR δ 0.83 (t, *J* = 7.5 Hz, 3H, Me), 0.84 (t, *J* = 7.5 Hz, 3H, Me), 1.08-1.13 (m, 2H, alkyl-H), 1.40 (m, 1H, alkyl-H), 1.56-1.81 (m, 2H, alkyl-H), 1.89 (m, 1H, alkyl-H), 3.61 (t, *J* = 7.5 Hz, 1H, PrCHPh), 4.03 (dd, *J* = 8.0, 11.2 Hz, 1H, -C=CHC$H_2$$SO_2$Ph), 4.08 (dd, *J* = 8.0, 11.2 Hz, 1H, -C=CHC$H_2$$SO_2$Ph), 5.29 (t, *J* = 8.0 Hz, 1H, -C=CHC$H_2$$SO_2$Ph), 6.92 (d, *J* = 7.5 Hz, 2H, Ph-H), 7.10-7.22 (m, 3H, Ph-H), 7.56 (t, *J* = 7.5 Hz, 2H, -SO_2Ph), 7.68 (t, *J* = 7.5 Hz, 1H, -SO_2Ph), 7.92 (d, *J* = 7.5 Hz, 2H, -SO_2Ph).
NOESY experiments showed the correlation between the peaks at δ 3.61 ppm (PrCHPh) and at δ 4.03 ppm (-C=CHC$H_2$$SO_2$Ph). Thus, the stereochemistry of the olefin was assigned to *Z*.
^{13}C NMR δ 12.44, 14.16, 20.73, 24.12, 33.39, 45.59, 56.05, 109.79 (C=C), 126.16, 127.66 (2 carbons), 128.17 (2 carbons), 128.57 (2 carbons), 129.11 (2 carbons), 133.62, 138.87, 141.95, 152.76 (C=C).
IR (neat) 3060 (Ar), 3026 (Ar and C=CH), 2959, 2932, 2871, 1654 (C=C), 1600, 1585, 1447, 1307 (SO_2), 1150 (SO_2), 1085, 745, 700, 688 cm^{-1}.
Anal. Calcd for $C_{21}H_{26}O_2S$: C, 73.64; H, 7.65. Found: C, 73.93; H, 7.62.
The *Z*-stereochemistry was confirmed by ^1H NMR NOESY experiments.

(*Z*)-4-(4-Methoxyphenyl)-2-pentenyl phenyl sulfone (29).



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5

mg, 0.020 mmol) in 2 mL of THF was added (4-methoxyphenyl)magnesium bromide (0.310 mL, 1.17 M solution in THF, 0.360 mmol) at –45 °C under argon. After the mixture was stirred at –45 ~ –30 °C for 3 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (52.2 mg, 82%) as a white solid.

^{1}H NMR δ 1.08 (d, *J* = 6.9 Hz, 3H, MeCHAr), 3.39 (dq, *J* = 9.9, 6.9 Hz, 1H, MeCHAr), 3.77 (s, 3H, Ar-OMe), 3.85 (dd, *J* = 7.5, 14.6 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 3.98 (dd, *J* = 8.4, 14.6 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 5.40 (ddd, *J* = 7.5, 8.4, 9.9 Hz, 1H -CH=CHC$H_2$$SO_2$Ph), 5.82 (t, *J* = 9.9 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 6.76 (d, *J* = 8.7 Hz, 2H, -C_6H_4-OMe), 6.93 (d, *J* = 8.7 Hz, 2H, -C_6H_4-OMe), 7.53 (t, *J* = 7.5 Hz, 2H, -SO_2Ph), 7.64 (t, *J* = 7.5 Hz, 1H, -SO_2Ph), 7.88 (d, *J* = 7.5 Hz, 2H, -SO_2Ph).

^{13}C NMR δ 21.55, 36.56, 55.22, 55.24, 113.81 (C=C), 113.90 (2 carbons), 127.56 (2 carbons), 128.45 (2 carbons), 129.06 (2 carbons), 133.68, 136.51, 138.61, 143.89, 158.00 (C=C).

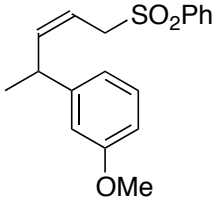
IR (KBr) 3065 (Ar), 3021 (Ar and C=CH), 2969, 2840, 1654 (C=C), 1610, 1581, 1511, 1445, 1314 (SO_2), 1142 (SO_2), 1071, 1027, 832, 688 cm^{-1}.

Anal. Calcd for $C_{18}H_{20}O_3S$: C, 68.33; H, 6.37. Found: C, 68.43; H, 6.31.

M.p. 50-51 °C.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-4-(3-Methoxyphenyl)-2-pentenyl phenyl sulfone (30).



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added (3-methoxyphenyl)magnesium bromide (0.320 mL, 1.11 M solution in THF, 0.360 mmol) at –45 °C under argon. After the mixture was stirred at –45 ~ –30 °C for 3 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (56.8 mg, 90%) as an oil.

^{1}H NMR δ 1.10 (d, *J* = 6.9 Hz, 3H, MeCHAr), 3.41 (dq, *J* = 9.9, 6.9 Hz, 1H, MeCHAr), 3.77 (s, 3H, Ar-OMe), 3.86 (dd, *J* = 7.5, 14.3 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 3.98 (dd, *J* = 8.4, 14.3 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 5.42 (br td, *J* = 8.4, 9.9 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 5.85 (t, *J* = 9.9 Hz, 1H, -

C<u>H</u>=CHCH$_2$SO$_2$Ph), 6.60 (br s, 2H, C$_6$<u>H</u>$_4$-OMe), 6.70 (d, *J* = 8.1 Hz, 1H, -C$_6$<u>H</u>$_4$-OMe), 7.15 (t, *J* = 8.1 Hz, 1H, -C$_6$<u>H</u>$_4$-OMe), 7.52 (t, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>), 7.62 (t, *J* = 7.5 Hz, 1H, -SO$_2$<u>Ph</u>), 7.89 (d, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>).

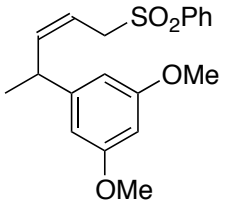
^{13}C NMR δ 21.58, 37.53, 55.15, 55.34, 111.42, 112.92, 114.41, 119.07 (C=C), 128.42 (2 carbons), 129.05 (2 carbons), 129.51, 133.64, 138.88, 143.37, 146.22, 159.84 (C=C).

IR (neat) 3061 (Ar), 3026 (Ar and C=CH), 2973, 2917, 1648 (C=C), 1600, 1447, 1585, 1307 (SO$_2$), 1149 (SO$_2$), 1082, 739 cm^{-1}.

Anal. Calcd for C$_{18}$H$_{20}$O$_3$S: C, 68.33; H, 6.37. Found: C, 68.25; H, 6.59.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-4-(3,5-Dimethoxyphenyl)-2-pentenyl phenyl sulfone (31).



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (1.04 g, 5.00 mmol) and FeCl$_2$ (63.4 mg, 0.500 mmol) in 10 mL of THF was added (3,5-dimethoxyphenyl)magnesium bromide (9.78 mL, 0.920 M solution in THF, 9.00 mmol) at –45 °C under argon. After the mixture was stirred at –45 ~ –30 °C for 3 h, the reaction was terminated by the addition of 1 N HCl solution (15 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated NaHCO$_3$ solution and brine, dried over Na$_2$SO$_4$, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (1.47 g, 84%) as an oil.

^{1}H NMR δ 1.09 (d, *J* = 6.9 Hz, 3H, <u>Me</u>CHAr), 3.38 (dq, *J* = 9.7, 6.9 Hz, 1H, MeC<u>H</u>Ar), 3.76 (s, 6H, Ar-(O<u>Me</u>)$_2$), 3.85 (dd, *J* = 7.2, 13.8 Hz, 1H, -CH=CHC<u>H$_2$</u>SO$_2$Ph), 3.97 (dd, *J* = 8.4, 13.8 Hz, 1H, -CH=CHC<u>H$_2$</u>SO$_2$Ph), 5.41 (ddd, *J* = 7.2, 8.4, 9.7 Hz, 1H, -CH=C<u>H</u>CH$_2$SO$_2$Ph), 5.84 (t, *J* = 9.7 Hz, 1H, -C<u>H</u>=CHCH$_2$SO$_2$Ph), 6.23 (d, *J* = 2.4 Hz, 2H, -C$_6$<u>H</u>$_3$-(OMe)$_2$), 6.28 (t, *J* = 2.4 Hz, 1H, -C$_6$<u>H</u>$_3$-(OMe)$_2$), 7.52 (t, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>), 7.62 (t, *J* = 7.5 Hz, 1H, -SO$_2$<u>Ph</u>), 7.88 (d, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>).

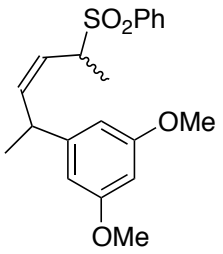
^{13}C NMR δ 21.46, 37.58, 55.16 (2 peaks consisting of 1 carbon and 2 carbons), 97.83 (MeO-C-<u>C</u>-C-MeO), 104.90 (2 carbons, MeO-C-<u>C</u>-C-<u>C</u>-C-MeO), 114.26, 128.29 (2 carbons), 128.97 (2 carbons), 133.65, 138.50, 143.19, 146.93, 160.77 (2 carbons).

IR (neat) 3064 (Ar), 3020 (Ar and C=CH), 2996, 2965, 2924, 1654 (C=C), 1596, 1447, 1318 (SO$_2$), 1151 (SO$_2$), 1033, 934, 740 cm^{-1}.

Anal. Calcd for C$_{19}$H$_{22}$O$_4$S: C, 65.87; H, 6.40. Found: C, 65.84; H, 6.35.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

A 53:47 diastereomeric mixture of (*Z*)-5-(3,5-dimethoxyphenyl)-3-hexen-2-yl phenyl sulfone (32) prepared by aryl Grignard addition to sulfonyldiene 16, followed by *in situ* methylation.



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (312 mg, 1.50 mmol) and $FeCl_2$ (19.0 mg, 0.150 mmol) in 5 mL of THF was added (3,5-dimethoxyphenyl)magnesium bromide (4.52 mL, 0.830 M solution in THF, 3.75 mmol) at –45 °C under argon. After the mixture was warmed up to 0 ºC over 3 h, iodomethane (0.470 mL, 7.50 mmol) was added. After the reaction mixture was heated in an oil bath maintained at 50 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (5 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was 53:47. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (473 mg, 87%) as an oil and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^{1}H NMR δ 1.22 (d, *J* = 6.9 Hz, 3H, MeCHAr), 1.48 (d, *J* = 6.9 Hz, 3H, -CH(Me)SO_2Ph), 3.44 (dq, *J* = 10.4, 6.9 Hz, 1H, MeCHAr), 3.76 (s, 6H, Ar-(OMe)$_2$), 4.09 (m, 1H, -CH=CHCH(Me)SO_2Ph), 5.27 (t, *J* = 10.4 Hz, 1H, -CH=CHCHSO_2Ph), 5.73 (t, *J* = 10.4 Hz, 1H, -CH=CHCHSO_2Ph), 6.16 (d, *J* = 2.4 Hz, 2H, -C_6H_3-(OMe)$_2$), 6.27 (t, *J* = 2.4 Hz, 1H, -C_6H_3-(OMe)$_2$), 7.39 (t, *J* = 7.2 Hz, 2H, -SO_2Ph), 7.57 (t, *J* = 7.2 Hz, 1H, -SO_2Ph), 7.76 (d, *J* = 7.2 Hz, 2H, -SO_2Ph).

NOESY experiments showed the correlation between the peaks at δ 3.44 ppm (MeCHAr) and at δ 4.09 ppm (-CH=CHCH(Me)SO_2Ph), and at δ 5.27 ppm (-CH=CHCHSO_2Ph) and at δ 5.73 ppm (-CH=CHCHSO_2Ph). Thus, the stereochemistry of the olefin was assigned to *Z*.

^{13}C NMR δ 14.50, 21.92, 37.72, 55.20 (2 carbons), 58.82, 97.92, 104.95 (2 carbons), 121.69, 128.83 (2 carbons), 128.86 (2 carbons), 133.48, 137.20, 140.87, 146.74, 160.64 (2 carbons).

Minor isomer: ^{1}H NMR (characteristic peaks are shown) δ 0.93 (d, *J* = 6.9 Hz, 3H, MeCHAr), 1.39 (d, *J* = 6.9 Hz, 3H, -CH(Me)SO_2Ph), 3.29 (dq, *J* = 10.4, 6.9 Hz, 1H, MeCHAr), 3.75 (s, 6H, Ar-(OMe)$_2$), 5.26 (t, *J* = 10.4 Hz, 1H, -CH=CHCHSO_2Ph), 5.70 (t, *J* = 10.4 Hz, 1H, -CH=CHCHSO_2Ph), 6.24 (d, *J* = 2.4 Hz, 2H, -C_6H_3-(OMe)$_2$), 6.28 (t, *J* = 2.4 Hz, 1H, -C_6H_3-(OMe)$_2$), 7.50 (t, *J* = 7.2 Hz, 2H, -SO_2Ph), 7.66 (t, *J* = 7.2 Hz, 1H, -SO_2Ph), 7.90 (d, *J* = 7.2 Hz, 2H, -SO_2Ph).

^{13}C NMR δ 13.96, 21.19, 37.91, 55.19 (2 carbons), 59.07, 97.70, 104.87 (2 carbons), 122.01, 128.66 (2 carbons), 129.20 (2 carbons), 133.62, 137.52, 141.17, 147.33, 160.86 (2 carbons).

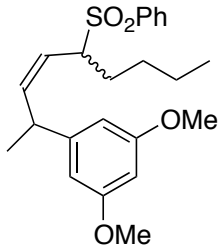
For full ^{1}H NMR data, see: the major isomer of (*Z*)-5-(3,5-dimethoxyphenyl)-3-hexen-2-yl phenyl sulfone.

IR (neat) 3064 (Ar and C=CH), 2964, 2933, 1610, 1460, 1306 (SO_2), 1150 (SO_2), 1086, 834, 689 cm^{-1} for a 53:47 mixture of diastereoisomers.

Anal. Calcd for $C_{20}H_{24}O_4S$: C, 66.64; H, 6.71. Found: C, 66.59; H, 6.75 for a 53:47 mixture of diastereoisomers.

The *Z*-stereochemistry was confirmed by ^{1}H NMR NOESY experiments as well as ^{1}H NMR coupling constants.

A 61:39 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-3-nonen-5-yl phenyl sulfone (33) prepared by aryl Grignard addition to sulfonyldiene 16, followed by *in situ* butylation.



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added (3,5-dimethoxyphenyl)magnesium bromide (0.602 mL, 0.830 M solution in THF, 0.500 mmol) at –45 °C under argon. After the mixture was warmed up to 0 ºC over 3 h, iodobutane (0.110 mL, 1.00 mmol) was added. After the reaction mixture was heated in an oil bath maintained at 60 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was 61:39. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (58.6 mg, 73%) as an oil and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^{1}H NMR δ 0.91 (t, *J* = 7.2 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$-), 1.21 (d, *J* = 6.9 Hz, 3H, $\underline{Me}$CHAr), 1.15-1.66 (m, 5H, alkyl-H), 2.16 (m, 1H, alkyl-H), 3.40 (dq, *J* = 10.5, 6.9 Hz, 1H, MeC$\underline{H}$Ar), 3.77 (s, 6H, Ar-(O$\underline{Me}$)$_2$), 3.96 (dt, *J* = 3.0, 10.5 Hz, 1H, -CH=CHC$\underline{H}$(Bu)SO$_2$Ph), 5.15 (t, *J* = 10.5 Hz, 1H, -CH=C$\underline{H}$CH(Bu)SO$_2$Ph), 5.83 (t, *J* = 10.5 Hz, 1H, -C$\underline{H}$=CHCH(Bu)SO$_2$Ph), 6.16 (d, *J* = 2.1 Hz, 2H, -C$_6\underline{H}_3$-(OMe)$_2$), 6.26 (t, *J* = 2.1 Hz, 1H, -C$_6\underline{H}_3$-(OMe)$_2$), 7.35 (t, *J* = 7.2 Hz, 2H, -SO$_2\underline{Ph}$), 7.57 (t, *J* = 7.2 Hz, 1H, -SO$_2\underline{Ph}$), 7.74 (d, *J* = 7.2 Hz, 2H, -SO$_2\underline{Ph}$).

^{13}C NMR δ 13.79, 21.92, 22.37, 27.49, 28.80, 37.82, 55.23 (2 carbons), 63.95, 97.91, 104.96 (2 carbons), 120.52, 128.58 (2 carbons), 128.83 (2 carbons), 133.40, 137.43, 142.31, 146.70, 160.62 (2 carbons).

Minor isomer: ^{1}H NMR (characteristic peaks are shown) δ 0.75 (t, *J* = 6.9 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$-), 0.86 (d, *J* = 6.9 Hz, 3H, $\underline{Me}$CHAr), 3.19 (dq, *J* = 10.4, 6.9 Hz, 1H, MeC$\underline{H}$Ar), 3.75 (s, 6H, Ar-(O$\underline{Me}$)$_2$), 3.90 (dt, *J* = 3.0, 10.4 Hz, 1H, -CH=CHC$\underline{H}$(Bu)SO$_2$Ph), 5.17 (t, *J* = 10.4 Hz, 1H, -CH=C$\underline{H}$CH(Bu)SO$_2$Ph), 5.79 (t, *J* = 10.4 Hz, 1H, -C$\underline{H}$=CHCH(Bu)SO$_2$Ph), 6.23 (d, *J* = 2.1 Hz, 2H, -C$_6\underline{H}_3$-(OMe)$_2$), 6.27 (t, *J* =

2.1 Hz, 1H, -$C_6\underline{H}_3$-$(OMe)_2$), 7.45 (t, *J* = 7.2 Hz, 2H, -$SO_2\underline{Ph}$), 7.66 (t, *J* = 7.2 Hz, 1H, -$SO_2\underline{Ph}$), 7.90 (d, *J* = 7.2 Hz, 2H, -$SO_2\underline{Ph}$).

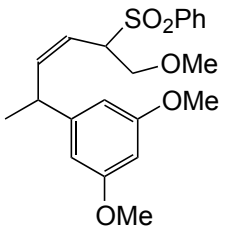
^{13}C NMR (characteristic peaks are shown) δ 13.66, 21.40, 22.29, 27.35, 28.75, 38.08, 55.17 (2 carbons), 64.05, 97.86, 121.33, 129.25 (2 carbons), 133.57, 137.93, 142.84, 147.52, 160.82 (2 carbons).

IR (neat) 3060 (Ar and C=CH), 2996, 2958, 2871, 1610, 1596, 1459, 1305 (SO_2), 1149 (SO_2), 1085, 746, 689 cm^{-1} for a 61:39 mixture of diastereoisomers.

Anal. Calcd for $C_{23}H_{30}O_4S$: C, 68.62; H, 7.51. Found: C, 68.95; H, 7.59 for a 61:39 mixture of diastereoisomers.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

A 61:39 diastereomeric mixture of (*Z*)-5-(3,5-dimethoxyphenyl)-1-methoxy-3-hexen-2-yl phenyl sulfone (34) prepared by aryl Grignard addition to sulfonyldiene 16, followed by *in situ* methoxymethylation.



To a solution of (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added (3,5-dimethoxyphenyl)magnesium bromide (0.540 mL, 0.920 M solution in THF, 0.500 mmol) at –45 °C under argon. After the mixture was warmed up to 0 ºC over 4 h, chloromethyl methyl ether (0.075 mL, 1.00 mmol) and HMPA (0.350 mL, 2.00 mmol) were added in this order. After the reaction mixture was heated in an oil bath maintained at 50 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was *cis* and the diastereoselectivity of the product was 61:39. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (71.5 mg, 92%) as an oil, and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^{1}H NMR (400 MHz) δ 1.26 (d, *J* = 6.8 Hz, 3H, $\underline{Me}$CHAr), 3.34 (s, 3H, -$CH_2O\underline{Me}$), 3.50 (dq, *J* = 10.0, 6.8 Hz, 1H, MeC$\underline{H}$Ar), 3.72 (dd, *J* = 7.2, 10.0 Hz, 1H, -C$\underline{H}_2$OMe), 3.78 (s, 6H, -$C_6H_3(O\underline{Me})_2$), 3.98 (dd, *J* = 4.4, 10.0 Hz, 1H, -C$\underline{H}_2$OMe), 4.30 (m, 1H, -CH=CHC$\underline{H}$$SO_2$Ph), 5.36 (dd, *J* = 6.8, 10.0 Hz, 1H, -CH=C$\underline{H}$CHSO_2Ph), 5.87 (t, *J* = 10.0 Hz, 1H, -C$\underline{H}$=CHCHSO_2Ph), 6.21 (d, *J* = 2.0 Hz, 2H, -$C_6\underline{H}_3(OMe)_2$), 6.28 (t, *J* = 2.0 Hz, 1H, -$C_6\underline{H}_3(OMe)_2$), 7.40 (t, *J* = 7.6 Hz, 2H, -$SO_2\underline{Ph}$), 7.57 (t, *J* = 7.6 Hz, 1H, -$SO_2\underline{Ph}$), 7.76 (d, *J* = 7.6 Hz, 2H, -$SO_2\underline{Ph}$).

^{13}C NMR (100 MHz) δ 21.75, 37.87, 55.27 (2 carbons), 59.14, 63.75, 70.16, 98.01, 105.06 (2 carbons), 118.23, 128.76 (2 carbons), 129.15 (2 carbons), 133.60, 138.12, 143.10, 146.77, 160.70 (2 carbons).

Minor isomer: ^{1}H NMR (400 MHz, characteristic peaks are shown) δ 0.97 (d, *J* = 6.8 Hz, 3H,

MeCHAr), 3.23 (s, 3H, -CH_2OMe), 3.39 (dq, *J* = 10.0, 6.8 Hz, 1H, MeCHAr), 3.70 (dd, *J* = 6.8, 10.0 Hz, 1H, -CH_2OMe), 3.75 (s, 6H, -C_6H_3(OMe)$_2$), 3.88 (dd, *J* = 4.4, 10.0 Hz, 1H, -CH_2OMe), 5.33 (dd, *J* = 6.8, 10.0 Hz, 1H, -CH=CHCHSO_2Ph), 5.80 (t, *J* = 10.0 Hz, 1H, -CH=CHCHSO_2Ph), 6.31 (d, *J* = 2.0 Hz, 2H, -C_6H_3(OMe)$_2$), 7.52 (t, *J* = 7.6 Hz, 2H, -SO_2Ph), 7.67 (t, *J* = 7.6 Hz, 1H, -SO_2Ph), 7.91 (d, *J* = 7.6 Hz, 2H, -SO_2Ph).

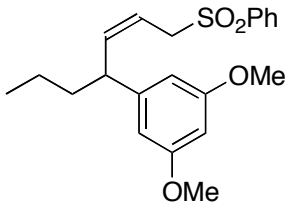
^{13}C NMR (100 MHz, characteristic peaks are shown) δ 20.53, 37.82, 55.23 (2 carbons), 58.95, 63.90, 69.95, 105.19 (2 carbons), 118.40, 128.85 (2 carbons), 133.73, 138.44, 143.34, 146.95, 160.84 (2 carbons).

IR (neat) 3064 (Ar), 3029 (Ar and C=CH), 2961, 2928, 2838, 1605 (C=C), 1596, 1461, 1448, 1307 (SO_2), 1204, 1149 (SO_2), 1084, 935, 835, 745, 607, 540 cm^{-1} for a 61:39 mixture of diastereoisomers.

HRMS (ESI) Calcd for $C_{21}H_{26}O_5SNa$ $[M+Na]^+$: 413.1393. Found: 413.1390 for a 61:39 mixture of diastereoisomers.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-4-(3,5-Dimethoxyphenyl)-2-heptenyl phenyl sulfone (35).



To a solution of (1*E*,3*E*)-1,3-heptadienyl phenyl sulfone (**21**) (47.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added (3,5-dimethoxyphenyl)magnesium bromide (0.490 mL, 1.02 M, solution in THF, 0.500 mmol) at –45 °C under argon. After the mixture was warmed up to room temperature over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (50.5 mg, 70%) as an oil.

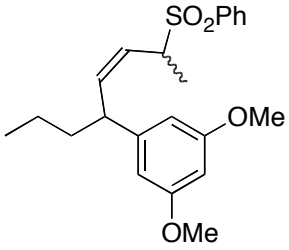
^{1}H NMR (400 MHz) δ 0.78 (t, *J* = 7.2 Hz, 3H, $CH_3CH_2CH_2$-), 0.95-1.12 (m, 2H, alkyl-H), 1.29 (m, 1H, alkyl-H), 1.51 (m, 1H, alkyl-H), 3.13 (td, *J* = 7.2, 10.0 Hz, 1H, PrCHAr), 3.76 (s, 6H, Ar-(OMe)$_2$), 3.84 (dd, *J* = 7.6, 14.4 Hz, 1H, -CH=CHCH_2SO_2Ph), 3.94 (dd, *J* = 8.4, 14.4 Hz, 1H, -CH=CHCH_2SO_2Ph), 5.44 (ddd, *J* = 7.6, 8.4, 10.0 Hz, 1H, -CH=CHCH_2SO_2Ph), 5.85 (t, *J* = 10.0 Hz, 1H, -CH=CHCH_2SO_2Ph), 6.18 (d, *J* = 2.4 Hz, 2H, -C_6H_3(OMe)$_2$), 6.27 (t, *J* = 2.4 Hz, 1H, -C_6H_3(OMe)$_2$), 7.50 (t, *J* = 7.2 Hz, 2H, -SO_2Ph), 7.60 (t, *J* = 7.2 Hz, 1H, -SO_2Ph), 7.85 (d, *J* = 7.2 Hz, 2H, -SO_2Ph).

^{13}C NMR (100 MHz) δ 13.90, 20.31, 38.62, 43.79, 55.23 (2 carbons), 55.45, 97.85 (C_4 of 3,5-(MeO)$_2C_6H_3$-), 105.43 (2 carbons, C_2 of 3,5-(MeO)$_2C_6H_3$-), 115.22, 128.38 (2 carbons), 129.00 (2 carbons), 133.64, 138.54, 142.21, 146.11, 160.81 (2 carbons).

IR (neat) 3020 (Ar and C=CH), 2954, 2925, 1655 (C=C), 1589, 1460, 1302 (SO_2), 1159 (SO_2), 1140,

1065, 820 cm^{-1}.
HRMS (ESI) Calcd for $C_{21}H_{26}O_4SNa$ $[M+Na]^+$: 397.1449. Found: 397.1448.
The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.

A 59:41 diastereomeric mixture of (*Z*)-5-(3,5-dimethoxyphenyl)-3-octen-2-yl phenyl sulfone (36) prepared by aryl Grignard addition to sulfonyldiene 21, followed by *in situ* methylation.



To a solution of (1*E*,3*E*)-1,3-heptadienyl phenyl sulfone (**21**) (47.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 2 mL of THF was added (3,5-dimethoxyphenyl)magnesium bromide (0.490 mL, 1.02 M solution in THF, 0.500 mmol) at –45 °C under argon. After the mixture was warmed up to 0 ºC over 3 h, iodomethane (0.063 mL, 1.00 mmol) was added. After the reaction mixture was heated in an oil bath maintained at 50 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (2 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was 59:41. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (57.4 mg, 74%) as an oil and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^1H NMR (400 MHz) δ 0.72 (t, *J* = 7.2 Hz, 3H, $\underline{CH_3}CH_2CH_2$-), 0.80-1.24 (m, 2H, alkyl-H), 1.26 (m, 1H, alkyl-H), 1.33 (d, *J* = 7.2 Hz, 3H, $\underline{Me}CHSO_2Ph$), 1.41 (m, 1H, alkyl-H), 3.02 (td, *J* = 7.6, 10.4 Hz, 1H, PrC$\underline{H}$Ar), 3.75 (s, 6H, Ar-(O$\underline{Me}$)$_2$), 4.04 (m, 1H, -CH=CHC$\underline{H}$(Me)SO_2Ph), 5.30 (t, *J* = 10.4 Hz, 1H, -CH=C$\underline{H}$CHSO_2Ph), 5.73 (t, *J* = 10.4 Hz, 1H, -C$\underline{H}$=CHCHSO_2Ph), 6.21 (d, *J* = 2.4 Hz, 2H, -$C_6\underline{H}_3$(OMe)$_2$), 6.27 (t, *J* = 2.4 Hz, 1H, -$C_6\underline{H}_3$(OMe)$_2$), 7.32 (t, *J* = 7.6 Hz, 2H, -$SO_2\underline{Ph}$), 7.57 (t, *J* = 7.6 Hz, 1H, -$SO_2\underline{Ph}$), 7.90 (d, *J* = 7.6 Hz, 2H, -$SO_2\underline{Ph}$).
^{13}C NMR (100 MHz) δ 13.75, 13.92, 20.18, 38.49, 44.09, 55.22 (2 carbons), 59.29, 97.68, 105.39 (2 carbons), 122.82, 128.89 (2 carbons), 129.20 (2 carbons), 133.56, 137.77, 140.28, 146.57, 160.88 (2 carbons).

Minor isomer: ^1H NMR (400 MHz, characteristic peaks are shown) δ 0.86 (t, *J* = 7.6 Hz, 3H, $\underline{CH_3}CH_2CH_2$-), 1.49 (d, *J* = 6.8 Hz, 3H, $\underline{Me}CHSO_2Ph$), 3.19 (td, *J* = 7.2, 10.0 Hz, 1H, PrC$\underline{H}$Ar), 5.31 (t, *J* = 10.0 Hz, 1H, -CH=C$\underline{H}$CHSO_2Ph), 5.69 (t, *J* = 10.0 Hz, 1H, -C$\underline{H}$=CHCHSO_2Ph), 6.10 (d, *J* = 2.0 Hz, 2H, -$C_6\underline{H}_3$(OMe)$_2$), 6.25 (t, *J* = 2.0 Hz, 1H, -$C_6\underline{H}_3$(OMe)$_2$), 7.43 (t, *J* = 7.6 Hz, 2H, -$SO_2\underline{Ph}$), 7.66 (t, *J* = 7.6 Hz, 1H, -$SO_2\underline{Ph}$), 7.71 (d, *J* = 7.6 Hz, 2H, -$SO_2\underline{Ph}$).
^{13}C NMR (100 MHz) δ 13.92, 14.34, 20.58, 38.87, 43.84, 55.22 (2 carbons), 59.11, 97.89, 105.33 (2 carbons), 122.73, 128.55 (2 carbons), 128.80 (2 carbons), 133.39, 137.13, 139.61, 145.94, 160.59 (2

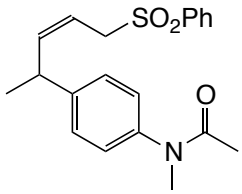
carbons).

IR (neat) 3066 (Ar and C=CH), 2956, 2931, 2871, 2840, 1655 (C=C), 1597, 1462, 1306 (SO_2), 1147 (SO_2), 1086, 690 cm^{-1} for a 59:41 mixture of diastereoisomers.

HRMS (ESI) Calcd for $C_{22}H_{28}O_4SNa$ $[M+Na]^+$: 411.1606. Found: 411.1607 for a 59:41 mixture of diastereoisomers.

The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.

(*Z*)-4-[4-[Acetyl(methyl)amino]phenyl]-2-pentenyl phenyl sulfone (37).



The arylmagnesium reagent was generated according to the following literature [Boudier, A.; Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 4414-4435].

To a solution of *N*-(4-iodophenyl)-*N*-methylacetamide (138 mg, 0.500 mmol) in THF (1 mL) was added *i*-PrMgBr (0.900 mL, 0.560 M solution in THF, 0.504 mmol) dropwise at 0 °C under argon. After the resulting solution was stirred at 0 °C for 1 h and cooled again to –45 °C, (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF were added. The reaction mixture was allowed to warm up to room temperature over 7 h. The reaction was terminated by the addition of 1 N HCl solution (2 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (41.3 mg, 58%) as an oil.

^1H NMR (400 MHz) δ 1.15 (d, *J* = 6.8 Hz, 3H, MeCHAr), 1.85 (s, 3H, -COMe), 3.23 (s, 3H, -NMe), 3.54 (dq, *J* = 10.0, 6.8 Hz, 1H, MeCHAr), 3.89 (dd, *J* = 8.0, 14.0 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 3.97 (dd, *J* = 8.0, 14.0 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 5.47 (dt, *J* = 10.0, 8.0 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 5.85 (t, *J* = 10.0 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 7.06 (d, *J* = 8.4 Hz, 2H, -$C_6H_4$$NR_2$), 7.10 (d, *J* = 8.4 Hz, 2H, -$C_6H_4$$NR_2$), 7.56 (t, *J* = 7.6 Hz, 2H, -SO_2Ph), 7.66 (t, *J* = 7.6 Hz, 1H, -SO_2Ph), 7.91 (d, *J* = 7.6 Hz, 2H, -SO_2Ph).

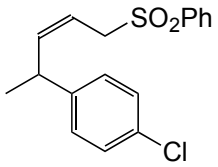
^{13}C NMR (100 MHz) δ 21.34, 22.40, 37.02, 37.13, 55.23, 114.50, 127.13, 128.00 (2 carbons), 128.48 (2 carbons), 129.16 (2 carbons), 133.78 (2 carbons), 138.82, 142.86, 143.10, 143.96, 170.54 (C=O).

IR (neat) 3091 (Ar), 3054 (Ar), 3027 (Ar), 2971, 2931, 1660 (C=O), 1606 (C=C), 1509, 1309 (SO_2), 1140 (SO_2), 1086. 737, 688, 573, 533 cm^{-1}.

HRMS (ESI) Calcd for $C_{20}H_{23}NO_3SNa$ $[M+Na]^+$: 380.1291. Found: 380.1287.

The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.

(*Z*)-4-(4-Chlorophenyl)-2-pentenyl phenyl sulfone (38).



The arylmagnesium reagent was generated according to the following literature [Boudier, A.; Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 4414-4435].

To a solution of 1-chloro-4-iodobenzene (119 mg, 0.500 mmol) in THF (1 mL) was added *i*-PrMgCl (0.580 mL, 0.865 M solution in THF, 0.502 mmol) dropwise at 0 °C under argon. After the resulting solution was stirred at 0 °C for 1 h and cooled again to –45 °C, (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF were added. The reaction mixture was allowed to warm up to room temperature over 7 h. The reaction was terminated by the addition of 1 N HCl solution (2 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (39.6 mg, 62%) as a white solid.

^{1}H NMR (400 MHz) δ 1.12 (d, *J* = 6.8 Hz, 3H, MeCHAr), 3.45 (dq, *J* = 10.0, 6.8 Hz, 1H, MeCHAr), 3.87 (dd, *J* = 8.0, 14.4 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 3.94 (dd, *J* = 8.0, 14.4 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 5.44 (dt, *J* = 10.0, 8.0 Hz, 1H, -CH=CHCH$_2$$SO_2$Ph), 5.82 (t, *J* = 10.0 Hz, 1H, -CH=CHCH$_2$$SO_2$Ph), 6.94 (d, *J* = 8.4 Hz, 2H, -C_6H_4Cl), 7.19 (d, *J* = 8.4 Hz, 2H, -C_6H_4Cl), 7.52 (t, *J* = 8.0 Hz, 2H, -SO_2Ph), 7.64 (t, *J* = 7.2 Hz, 1H, -SO_2Ph), 7.88 (d, *J* = 8.0 Hz, 2H, -SO_2Ph).

^{13}C NMR (100 MHz) δ 21.56, 36.89, 55.27, 114.73, 128.04 (2 carbons), 128.42 (2 carbons), 128.64 (2 carbons), 129.10 (2 carbons), 132.05, 133.72, 138.68, 142.94 (2 peaks).

IR (KBr) 3065 (Ar), 3029 (Ar), 2977, 2899, 1969, 1903, 1664 (C=C), 1683, 1491, 1313 (SO_2), 1141 (SO_2), 1085, 901, 742, 686, 574, 520 cm^{-1}.

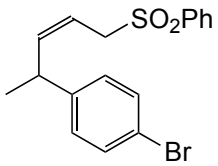
M.p. 73-74 °C.

HRMS (ESI) Calcd for $C_{17}H_{17}Cl^{35}O_2SNa$ $[M+Na]^+$: 343.0530. Found: 343.0530.

HRMS (ESI) Calcd for $C_{17}H_{17}Cl^{37}O_2SNa$ $[M+Na]^+$: 345.0501. Found: 345.0508.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-4-(4-Bromophenyl)-2-pentenyl phenyl sulfone (39).



The arylmagnesium reagent was generated according to the following literature [Boudier, A.;

Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 4414-4435].

To a solution of 1,4-dibromobenzene (118 mg, 0.500 mmol) in THF (1 mL) was added *i*-PrMgCl (0.580 mL, 0.865 M solution in THF, 0.502 mmol) dropwise at 0 °C under argon. After the resulting solution was stirred at 0 °C for 1 h and cooled again to –45 °C, (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF were added. The reaction mixture was allowed to warm up to room temperature over 7 h. The reaction was terminated by the addition of 1 N HCl solution (2 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (40.5 mg, 55%) as a white solid.

^{1}H NMR (400 MHz) δ 1.11 (d, *J* = 6.8 Hz, 3H, MeCHAr), 3.45 (dq, *J* = 10.0, 6.8 Hz, 1H, MeCHAr), 3.90 (dd, *J* = 8.0, 14.4 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 3.91 (dd, *J* = 8.0, 14.4 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 5.46 (dt, *J* = 10.0, 8.0 Hz, 1H, -CH=CHCH$_2$$SO_2$Ph), 5.81 (t, *J* = 10.0 Hz, 1H, -CH=CHCH$_2$$SO_2$Ph), 6.88 (d, *J* = 8.0 Hz, 2H, -C_6H_4Br), 7.34 (d, *J* = 8.0 Hz, 2H, -C_6H_4Br), 7.52 (t, *J* = 8.0 Hz, 2H, -SO_2Ph), 7.64 (t, *J* = 8.0 Hz, 1H, -SO_2Ph), 7.87 (d, *J* = 8.4 Hz, 2H, -SO_2Ph).

^{13}C NMR (100 MHz) δ 21.52, 36.94, 55.24, 114.76, 120.07, 128.41 (2 carbons), 128.42 (2 carbons), 129.10 (2 carbons), 131.59 (2 carbons), 133.74, 138.58, 142.84, 143.46.

IR (KBr) 3054 (Ar), 3027 (Ar), 2952, 2922, 1584 (C=C), 1487, 1445, 1394, 1302 (SO_2), 1133 (SO_2), 901, 826, 649, 568, 529 cm^{-1}.

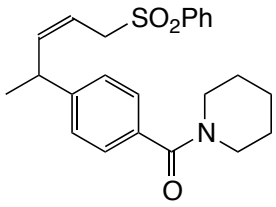
M.p. 62-63 °C.

HRMS (ESI) Calcd for $C_{17}H_{17}Br^{79}O_2SNa$ [M+Na]$^+$: 387.0025. Found: 387.0015.

HRMS (ESI) Calcd for $C_{17}H_{17}Br^{81}O_2SNa$ [M+Na]$^+$: 389.0005. Found: 388.9995.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-4-[4-[(1,5-Pentylidene)carbamoyl]phenyl]-2-pentenyl phenyl sulfone (40).



The arylmagnesium reagent was prepared by a literature method [Dohle, W.; Lindsay, D. M.; Knochel, P. *Org. Lett.* **2001**, *3*, 2871-2873].

To a solution of *N*,*N*-(1,5-pentylidene)-4-iodobenzamide (168 mg, 0.500 mmol) in THF (1 mL) was added *i*-PrMgBr (0.900 mL, 0.560 M solution in THF, 0.504 mmol) dropwise at 0 °C under argon. After the resulting solution was stirred at 0 °C for 1 h and cooled again to –45 °C, (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (41.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF were added. The reaction mixture was allowed to warm up to room temperature over 7 h. The

reaction was terminated by the addition of 1 N HCl solution (2 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (50.3 mg, 63%) as an oil.

^{1}H NMR (400 MHz) δ 1.13 (d, J = 7.2 Hz, 3H, MeCHAr), 1.40-1.78 (br m, 6H, alkyl-H), 3.34 (br m, 2H, -NCH_2-), 3.51 (dq, J = 10.0, 7.2 Hz, 1H, MeCHAr), 3.70 (br m, 2H, -NCH_2-), 3.87 (dd, J = 14.4, 7.6 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 3.96 (dd, J = 14.4, 8.4 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 5.45 (ddd, J = 7.6, 8.4, 10.0 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 5.85 (t, J = 10.0 Hz, 1H, -CH=CHC$H_2$$SO_2$Ph), 7.04 (d, J = 8.0 Hz, 2H, -$C_6H_4$$NR_2$), 7.26 (d, J = 8.0 Hz, 2H, -$C_6H_4$$NR_2$), 7.54 (t, J = 7.6 Hz, 2H, -SO_2Ph), 7.64 (d, J = 7.6 Hz, 1H, -SO_2Ph), 7.89 (d, J = 7.6 Hz, 2H, -SO_2Ph).

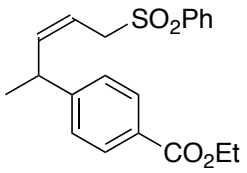
^{13}C NMR (100 MHz) δ 21.46, 24.59, 25.62 (br), 26.53 (br), 37.32, 43.15 (br), 48.77 (br), 55.26, 114.59, 126.71 (2 carbons), 127.16 (2 carbons), 128.42 (2 carbons), 129.14 (2 carbons), 133.80, 134.56, 138.60, 143.05, 145.80, 170.10 (C=O).

IR (neat) 3061 (Ar), 3021 (Ar), 2934, 2856, 1622 (C=O), 1608 (C=C), 1446, 1308 (SO_2), 1278, 1143 (SO_2), 1086, 1002, 845, 758, 532 cm^{-1}.

HRMS (ESI) Calcd for $C_{23}H_{27}NO_3SNa$ [M+Na]$^+$: 420.1604. Found: 420.1607.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-4-[4-(Ethoxycarbonyl)phenyl]-2-pentenyl phenyl sulfone (41).



The arylmagnesium reagent was prepared by a literature method [Delacroix, T.; Bérillon, L.; Cahiez, G.; Knochel, P. *J. Org. Chem.* **2000**, *65*, 8108-8110].

To a solution of ethyl 4-iodobenzoate (0.150 mL, 0.900 mmol) in THF (1 mL) was added *i*-PrMgBr (1.22 mL, 0.740 M solution in THF, 0.900 mmol) dropwise at –10 °C under argon. After the resulting solution was stirred at –10 °C for 1.5 h and cooled again to –45 °C, (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone (**16**) (62.5 mg, 0.300 mmol) and $FeCl_2$ (3.8 mg, 0.030 mmol) in 1 mL of THF were added. The reaction mixture was allowed to warm up to room temperature over 7 h. The reaction was terminated by the addition of 1 N HCl solution (2 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (51.5 mg, 48%) as an oil.

^{1}H NMR δ 1.15 (d, J = 6.9 Hz, 3H, MeCHAr), 1.38 (t, J = 7.2 Hz, 3H, -$CO_2CH_2CH_3$), 3.51 (dq, J = 10.2,

6.9 Hz, 1H, MeC<u>H</u>Ar), 3.87 (dd, *J* = 7.8, 14.3 Hz, 1H, -CH=CHC<u>H</u>$_2$SO$_2$Ph), 3.96 (dd, *J* = 8.1, 14.3 Hz, 1H, -CH=CHC<u>H</u>$_2$SO$_2$Ph), 4.36 (q, *J* = 7.2 Hz, 2H, -CO$_2$C<u>H</u>$_2$CH$_3$), 5.47 (ddd, *J* = 7.8, 8.1, 10.2 Hz, 1H, -CH=C<u>H</u>CH$_2$SO$_2$Ph), 5.85 (t, *J* = 10.2 Hz, 1H, -C<u>H</u>=CHCH$_2$SO$_2$Ph), 7.07 (d, *J* = 8.2 Hz, 2H, -C$_6$<u>H</u>$_4$-CO$_2$Et), 7.51 (t, *J* = 7.2 Hz, 2H, -SO$_2$<u>Ph</u>), 7.63 (t, *J* = 7.2 Hz, 1H, -SO$_2$<u>Ph</u>), 7.87 (d, *J* = 7.2 Hz, 2H, -SO$_2$<u>Ph</u>), 7.90 (d, *J* = 8.2 Hz, 2H, -C$_6$<u>H</u>$_4$-CO$_2$Et).

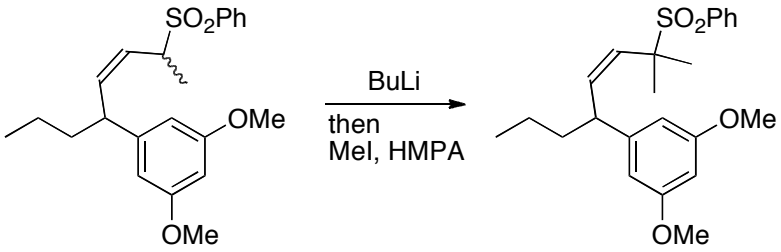
^{13}C NMR δ 14.29, 21.46, 37.49, 55.20, 60.82, 114.96, 126.63 (2 carbons), 128.38 (2 carbons), 128.58, 129.08 (2 carbons), 129.82 (2 carbons), 133.76, 138.47, 142.56, 149.59, 166.35 (C=O).

IR (neat) 3064 (Ar), 3025 (Ar and C=CH), 2978, 2930, 1716 (C=O), 1653 (C=C), 1609, 1559, 1447, 1308 (SO$_2$), 1143 (SO$_2$), 1018, 732, 688 cm^{-1}.

Anal. Calcd for C$_{20}$H$_{22}$O$_4$S: C, 67.01; H, 6.19. Found: C, 66.92; H, 6.13.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-5-(3,5-Dimethoxyphenyl)-2-methyl-3-octen-2-yl phenyl sulfone (43) prepared by lithiation and methylation of a 54:46 diastereomeric mixture of (*Z*)-5-(3,5-dimethoxyphenyl)-3-octen-2-yl phenyl sulfones (36).



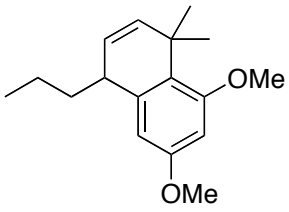
To a solution of a 54:46 diastereomeric mixture of (*Z*)-5-(3,5-dimethoxyphenyl)-3-hexen-2-yl phenyl sulfone (**36**) (21.9 mg, 0.056 mmol, prepared by aryl Grignard addition to sulfonyldiene **21**, followed by *in situ* methylation) in THF (1 mL) was added BuLi (0.060 mL, 1.67 M solution in hexane, 0.101 mmol) at 0 °C under argon. After the mixture was stirred at 0 °C for 30 min, iodomethane (0.026 mL, 0.420 mmol) and HMPA (0.146 mL, 0.240 mmol) were added to the mixture in this order at 0 °C. After the reaction mixture was heated in an oil bath maintained at 50 °C for 5 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated NaHCO$_3$ solution and brine, dried over Na$_2$SO$_4$, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (22.0 mg, 91%) having a pure *cis* olefin as an oil.

^{1}H NMR δ 0.82 (t, *J* = 7.2 Hz, 3H, <u>CH$_3$</u>CH$_2$CH$_2$-), 1.04-1.20 (m, 2H, alkyl-H), 1.30-1.50 (m, 2H, alkyl-H), 1.57 (s, 3H, <u>Me</u>CSO$_2$Ph), 1.59 (s, 3H, <u>Me</u>CSO$_2$Ph), 3.66 (td, *J* = 6.6, 12.0 Hz, 1H, PrC<u>H</u>Ar), 3.77 (s, 6H, Ar-(O<u>Me</u>)$_2$), 5.32 (d, *J* = 12.0 Hz, 1H, -CH=C<u>H</u>CSO$_2$Ph), 5.72 (t, *J* = 12.0 Hz, 1H, -C<u>H</u>=CHCSO$_2$Ph), 6.27 (s, 3H, -C$_6$<u>H</u>$_3$(OMe)$_2$), 7.46 (t, *J* = 7.2 Hz, 2H, -SO$_2$<u>Ph</u>), 7.58 (t, *J* = 7.2 Hz, 1H, -SO$_2$<u>Ph</u>), 7.82 (d, *J* = 7.2 Hz, 2H, -SO$_2$<u>Ph</u>).

^{13}C NMR δ 14.00, 20.38, 23.75 (2 peaks), 39.71, 43.65, 55.24 (2 carbons), 66.81, 97.66, 105.51 (2 carbons), 135.79, 128.42 (2 carbons), 130.57 (2 carbons), 133.43, 136.41, 140.30, 146.82, 160.71 (2

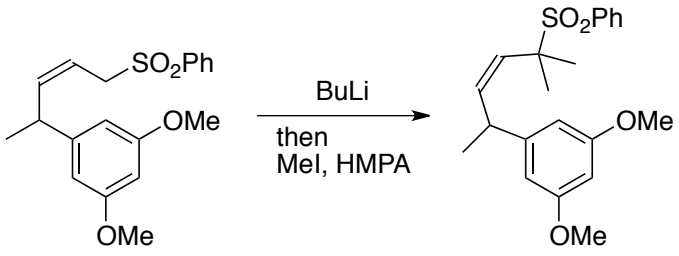
carbons).
IR (neat) 3062 (Ar and C=CH), 2956, 2931, 2870, 1655 (C=C), 1595, 1460, 1155, 1126, 1061, 806 cm^{-1}.
The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.

6,8-Dimethoxy-1,1-dimethyl-4-propyl-1,4-dihydronaphthalene (44). Friedel-Crafts reaction of 43.



To a suspension of $AlCl_3$ (14.7 mg, 0.110 mmol) in CH_2Cl_2 (1 mL) was added (*Z*)-5-(3,5-dimethoxyphenyl)-2-methyl-3-octen-2-yl phenyl sulfone (**43**) (22.0 mg, 0.055 mmol) in 1 mL of CH_2Cl_2 at 0 °C under argon. After the reaction mixture was stirred at 0 °C for 5 h, the reaction was terminated by the addition of aqueous saturated NH_4Cl solution (2 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (7.5 mg, 48%) as an oil.
^1H NMR δ 0.85 (t, *J* = 7.5 Hz, 3H, $\underline{CH_3}CH_2CH_2$-), 1.05-1.35 (m, 2H, alkyl-H), 1.37 (s, 3H, $(Me)_2C$-), 1.39 (s, 3H, $(Me)_2C$-), 1.50-1.70 (m, 2H, alkyl-H), 3.36 (td, *J* = 7.2, 3.9 Hz, 1H, PrC<u>H</u>-), 3.80 (s, 3H, -$C_6H_2(O\underline{Me})_2$), 3.81 (s, 3H, -$C_6H_2(O\underline{Me})_2$), 5.54 (d, *J* = 10.2 Hz, 1H, -CH=C<u>H</u>$C(Me)_2$), 5.61 (dd, *J* = 3.9, 10.2 Hz, 1H, -C<u>H</u>=CH$C(Me)_2$), 6.33 (d, *J* = 2.4 Hz, 1H, -$C_6\underline{H_2}(OMe)_2$), 6.35 (d, *J* = 2.4 Hz, 1H, -$C_6\underline{H_2}(OMe)_2$).
^{13}C NMR δ 14.29, 18.91, 28.74, 29.11, 34.84, 39.57, 41.75, 55.00, 55.18, 97.42, 104.12, 123.01, 124.49, 138.70, 140.23, 158.30, 159.22.
IR (neat) 3020 (Ar and C=CH), 2954, 2870, 1608, 1581, 1485, 1458, 1267, 1159, 1101, 1051, 831, 796, 755 cm^{-1}.

(*Z*)-5-(3,5-Dimethoxyphenyl)-2-methyl-3-hexen-2-yl phenyl sulfone (45) prepared by dilithiation and dimethylation of (*Z*)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (31).



To a solution of (*Z*)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (**31**) (278 mg, 0.800 mmol) in THF (2 mL) was added BuLi (1.12 mL, 1.57 M solution in hexane, 1.76 mmol) at 0 °C under argon. After the mixture was stirred at 0 °C for 30 min, iodomethane (0.498 mL, 8.00 mmol) and HMPA (1.39 mL, 8.00 mmol) were added to the reaction mixture in this order at 0 °C. After the reaction mixture was heated in an oil bath maintained at 50 °C for 5 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (15 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (215 mg, 72%) as an oil and as a pure *cis* olefin.

^{1}H NMR δ 1.22 (d, *J* = 6.6 Hz, 3H, MeCHAr), 1.57 (s, 3H, $MeCSO_2Ph$), 1.58 (s, 3H, $MeCSO_2Ph$), 3.77 (s, 6H, Ar-$(OMe)_2$), 3.94 (dq, *J* = 11.6, 6.6 Hz, 1H, MeCHAr), 5.24 (d, *J* = 11.6 Hz, 1H, -CH=CHCSO$_2$Ph), 5.71 (t, *J* = 11.6 Hz, 1H, -CH=CHCSO$_2$Ph), 6.30 (t, *J* = 2.4 Hz, 1H, -C_6H_3-$(OMe)_2$), 6.36 (d, *J* = 2.4 Hz, 2H, -C_6H_3-$(OMe)_2$), 7.49 (t, *J* = 7.2 Hz, 2H, -SO_2Ph), 7.61 (t, *J* = 7.2 Hz, 1H, -SO_2Ph), 7.85 (d, *J* = 7.2 Hz, 2H, -SO_2Ph).

NOESY experiments showed the correlation between the peaks at δ 1.58 ppm (Me_2CSO_2Ph) and at δ 3.94 ppm (MeCHAr), and at δ 5.24 ppm (-CH=CHCSO$_2$Ph) and at δ 5.71 ppm (-CH=CHCSO$_2$Ph). Thus, the stereochemistry of the olefin was assigned to *Z*.

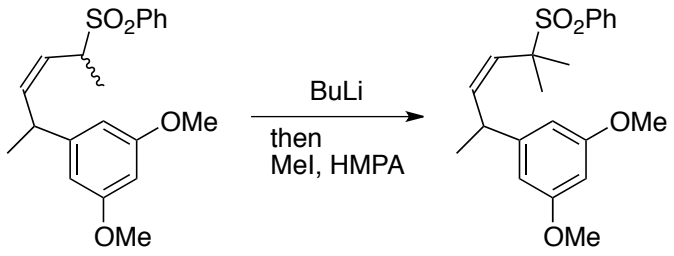
^{13}C NMR δ 22.26, 23.44, 24.07, 37.98, 55.23 (2 carbons), 64.98, 97.74, 105.01, 125.34, 128.47 (2 carbons), 130.58 (2 carbons), 133.49 (2 carbons), 135.84, 141.74, 147.88 160.78 (2 carbons).

IR (neat) 3068 (Ar and C=CH), 2968, 2837, 1596, 1458, 1300 (SO_2), 1156 (SO_2), 1077, 841, 691 cm^{-1}.

Anal. Calcd for $C_{21}H_{26}O_4S$: C, 67.35; H, 7.00. Found: C, 67.06; H, 6.98.

The *Z*-stereochemistry was confirmed by ^{1}H NMR NOESY experiments as well as ^{1}H NMR coupling constants.

(*Z*)-5-(3,5-Dimethoxyphenyl)-2-methyl-3-hexen-2-yl phenyl sulfone (45) prepared by lithiation and methylation of a 53:47 diastereomeric mixture of (*Z*)-5-(3,5-dimethoxyphenyl)-3-hexen-2-yl phenyl sulfones (32).

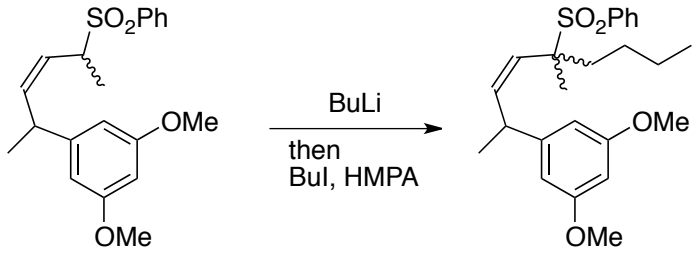


To a solution of a 53:47 diastereomeric mixture of (*Z*)-5-(3,5-dimethoxyphenyl)-3-hexen-2-yl phenyl sulfone (**32**) (72.1 mg, 0.200 mmol, prepared by aryl Grignard addition to sulfonyldiene **16**, followed by *in situ* methylation) in THF (1 mL) was added BuLi (0.144 mL, 1.67 M solution in hexane, 0.240 mmol) at 0 °C under argon. After the mixture was stirred at 0 °C for 30 min, iodomethane (0.062 mL, 1.00 mmol) and HMPA (0.350 mL, 2.00 mmol) were added to the mixture in this order at 0 °C. After the

reaction mixture was heated in an oil bath maintained at 50 °C for 5 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (69.7 mg, 93%) as an oil and as a pure *cis* olefin.

For spectral data, see: (*Z*)-5-(3,5-dimethoxyphenyl)-2-methyl-3-hexen-2-yl phenyl sulfone (**45**) shown above.

A 40:60 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-5-methyl-3-nonen-5-yl phenyl sulfone (46) prepared by lithiation and butylation of a 53:47 diastereomeric mixture of (*Z*)-5-(3,5-dimethoxyphenyl)-3-hexen-2-yl phenyl sulfone (32).



To a solution of a 53:47 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-3-hexen-2-yl phenyl sulfone (**32**) (144 mg, 0.400 mmol, prepared by aryl Grignard addition to sulfonyldiene **16**, followed by *in situ* methylation) in THF (1.5 mL) was added BuLi (0.290 mL, 1.67 M solution in hexane, 0.480 mmol) at 0 °C under argon. After the reaction mixture was stirred at 0 °C for 30 min, iodobutane (0.230 mL, 2.00 mmol) and HMPA (0.700 mL, 4.00 mmol) were added in this order at 0 °C. After the mixture was heated in an oil bath maintained at 60 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was 40:60. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (131 mg, 78%) as an oil and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^{1}H NMR δ 0.81 (t, *J* = 6.9 Hz, 3H, $C\underline{H}_3CH_2CH_2$-), 1.30 (d, *J* = 6.9 Hz, 3H, $\underline{Me}$CHAr), 1.14-1.33 (m, 4H, alkyl-H), 1.58 (s, 3H, -C($\underline{Me}$)SO_2Ph), 1.81-2.05 (m, 2H, alkyl-H), 3.76 (m, 1H, MeC$\underline{H}$Ar), 3.78 (s, 6H, Ar-(O$\underline{Me}$)$_2$), 5.05 (d, *J* = 11.4 Hz, 1H, -CH=C$\underline{H}$CSO$_2$Ph), 5.80 (t, *J* = 11.4 Hz, 1H, -C$\underline{H}$=CHCSO$_2$Ph), 6.29 (s, 1H, -C$_6\underline{H}_3$-(OMe)$_2$), 6.34 (s, 2H, -C$_6\underline{H}_3$-(OMe)$_2$), 7.43 (t, *J* = 7.5 Hz, 2H, -SO$_2$$\underline{Ph}$), 7.55 (t, *J* = 7.5 Hz, 1H, -SO$_2$$\underline{Ph}$), 7.80 (d, *J* = 7.5 Hz, 2H, -SO$_2$$\underline{Ph}$).

^{13}C NMR δ 13.87, 20.28, 22.62, 23.03, 26.17, 34.84, 38.04, 55.23 (2 carbons), 68.86, 97.84, 104.99 (2 carbons), 123.86, 128.35 (2 carbons), 130.60 (2 carbons), 133.37, 136.04, 142.80, 147.70, 160.72 (2 carbons).

Minor isomer: ^{1}H NMR (characteristic peaks are shown) δ 0.86 (t, *J* = 6.9 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$-), 1.09 (d, *J* = 6.9 Hz, 3H, <u>Me</u>CHAr), 1.57 (s, 3H, -C(<u>Me</u>)SO$_2$Ph), 3.76 (s, 6H, Ar-(O<u>Me</u>)$_2$), 3.97 (dq, *J* = 11.4, 6.9 Hz, 1H, MeC<u>H</u>Ar), 5.19 (d, *J* = 11.4 Hz, 1H, -CH=C<u>H</u>CSO$_2$Ph), 5.76 (t, *J* = 11.4 Hz, 1H, -C<u>H</u>=CHCSO$_2$Ph), 7.53 (t, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>), 7.64 (t, *J* = 7.5 Hz, 1H, -SO$_2$<u>Ph</u>), 7.87 (d, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>).

^{13}C NMR δ 13.87, 19.45, 22.12, 23.03, 26.10, 35.72, 37.75, 55.21 (2 carbons), 68.99, 97.78, 104.95 (2 carbons), 124.64, 128.42 (2 carbons), 130.80 (2 carbons), 133.43, 136.04, 146.69, 148.10, 160.78 (2 carbons).

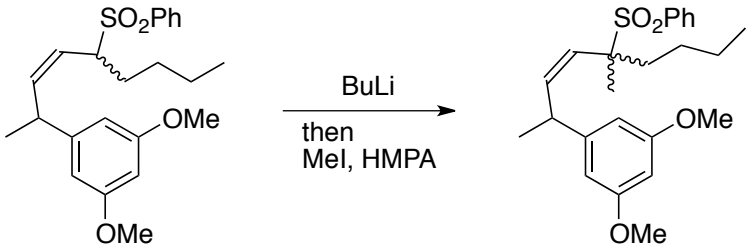
IR (neat) 3066 (Ar and C=CH), 2957, 1654 (C=C), 1596, 1458, 1299 (SO$_2$), 1149 (SO$_2$), 1068, 691 cm^{-1} for a 40:60 mixture of diastereoisomers.

These spectroscopic properties were in good agreement with those of a 57:43 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-5-methyl-3-nonen-5-yl phenyl sulfone (**46**) (*vide infra*).

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

These major and minor isomers were the opposite of those of **46** obtained by lithiation and methylation of a 61:39 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-3-nonen-5-yl phenyl sulfone (**33**) (*vide infra*).

A 57:43 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-5-methyl-3-nonen-5-yl phenyl sulfone (46) prepared by lithiation and methylation of a 61:39 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-3-nonen-5-yl phenyl sulfone (33).



To a solution of a 61:39 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-3-nonen-5-yl phenyl sulfone (**33**) (217 mg, 0.540 mmol, prepared by aryl Grignard addition to sulfonyldiene **16**, followed by *in situ* butylation) in THF (2 mL) was added BuLi (0.410 mL, 1.57 M solution in hexane, 0.650 mmol) at 0 °C under argon. After the mixture was stirred at 0 °C for 30 min, iodomethane (0.170 mL, 2.70 mmol) and HMPA (0.940 mL, 5.40 mmol) were added in this order to the reaction mixture at 0 °C. After the mixture was heated in an oil bath maintained at 50 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated NaHCO$_3$ solution and brine, dried over Na$_2$SO$_4$, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was 57:43. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (78.0 mg, 79%) as an oil and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^{1}H NMR δ 0.86 (t, *J* = 6.9 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$-), 1.09 (d, *J* = 6.9 Hz, 3H, <u>Me</u>CHAr), 1.14-1.38 (m, 4H, alkyl-H), 1.57 (s, 3H, -C(<u>Me</u>)SO$_2$Ph), 1.75-2.06 (m, 2H, alkyl-H), 3.76 (s, 6H, Ar-(O<u>Me</u>)$_2$), 3.97 (dq, *J* = 11.7, 6.9 Hz, 1H, MeC<u>H</u>Ar), 5.19 (d, *J* = 11.7 Hz, 1H, -CH=C<u>H</u>CSO$_2$Ph), 5.76 (t, *J* = 11.7 Hz, 1H, -C<u>H</u>=CHCSO$_2$Ph), 6.30 (s, 1H, -C$_6$<u>H</u>$_3$-(OMe)$_2$), 6.34 (s, 2H, -C$_6$<u>H</u>$_3$-(OMe)$_2$), 7.52 (t, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>), 7.64 (t, *J* = 7.5 Hz, 1H, -SO$_2$<u>Ph</u>), 7.87 (d, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>).

^{13}C NMR δ 13.87, 19.45, 22.11, 23.03, 26.09, 35.72, 37.74, 55.20 (2 carbons), 68.98, 97.76, 104.94 (2 carbons), 124.63, 128.42 (2 carbons), 130.79 (2 carbons), 133.43, 136.02, 142.69, 148.10, 160.77 (2 carbons).

Minor isomer: ^{1}H NMR (characteristic peaks are shown) δ 0.81 (t, *J* = 6.9 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$-), 1.30 (d, *J* = 6.9 Hz, 3H, <u>Me</u>CHAr), 1.58 (s, 3H, -C(<u>Me</u>)SO$_2$Ph), 3.76 (m, 1H, MeC<u>H</u>Ar), 3.78 (s, 6H, Ar-(O<u>Me</u>)$_2$), 5.05 (d, *J* = 11.7 Hz, 1H, -CH=C<u>H</u>CSO$_2$Ph), 5.81 (t, *J* = 11.7 Hz, 1H, -C<u>H</u>=CHCSO$_2$Ph), 7.43 (t, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>), 7.55 (t, *J* = 7.5 Hz, 1H, -SO$_2$<u>Ph</u>), 7.80 (d, *J* = 7.5 Hz, 2H, -SO$_2$<u>Ph</u>).

^{13}C NMR (characteristic peaks are shown) δ 20.28, 22.62, 26.17, 34.82, 38.04, 55.23 (2 carbons), 68.86, 97.83, 104.98 (2 carbons), 123.84, 128.35 (2 carbons), 130.59 (2 carbons), 133.37, 142.79, 147.69, 160.71 (2 carbons).

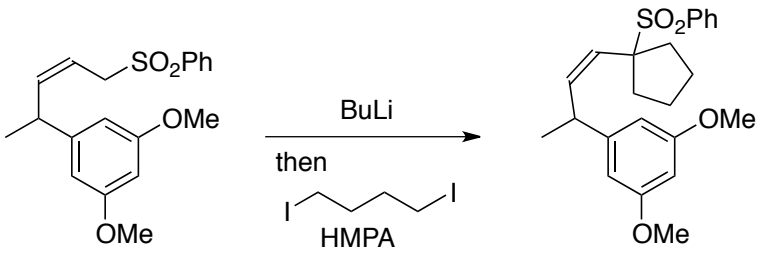
For full ^{1}H and ^{13}C NMR data for the minor isomer, see: the major isomer of (*Z*)-2-(3,5-dimethoxyphenyl)-5-methyl-3-nonen-5-yl phenyl sulfone (**46**).

IR (neat) 3065 (Ar), 3020 (Ar and C=CH), 2957, 1610, 1596, 1458, 1299 (SO$_2$), 1204, 1149 (SO$_2$), 1068, 758, 691 cm^{-1} for a 57:43 mixture of diastereoisomers.

Anal. Calcd for $C_{24}H_{32}O_4S$: C, 69.20; H, 7.74. Found: C, 69.29; H, 7.57 for a 57:43 mixture of diastereoisomers.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

(*Z*)-1,1-(1,4-Butylidene)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (47) prepared by dilithiation and dialkylation of (*Z*)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (31).



To a solution of (*Z*)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (**31**) (346 mg, 1.00 mmol) in THF (3 mL) was added BuLi (1.40 mL, 1.57 M solution in hexane, 2.20 mmol) at 0 °C under argon. After the reaction mixture was stirred at 0 °C for 30 min, 1,4-diiodobutane (0.659 mL, 5.00 mmol) and HMPA (1.74 mL, 10.0 mmol) were added in this order to the reaction mixture at 0 °C. After the reaction mixture was heated in an oil bath maintained at 60 °C for 8 h, the reaction was terminated by the addition of 1 N HCl solution (15 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated NaHCO$_3$ solution and brine, dried over Na$_2$SO$_4$, and concentrated *in vacuo* to give a crude oil,

which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (291 mg, 73%) as an oil and as a pure *cis* olefin.

^{1}H NMR δ 1.31 (d, *J* = 6.9 Hz, 3H, MeCHAr), 1.54-1.63 (m, 2H, alkyl-H), 1.78-1.97 (m, 4H, alkyl-H), 2.51-2.69 (m, 2H, alkyl-H), 3.79 (s, 6H, Ar-(OMe)$_2$), 4.01 (dq, *J* = 11.5, 6.9 Hz, 1H, MeCHAr), 5.05 (d, *J* = 11.5 Hz, 1H, -CH=CHCSO$_2$Ph), 5.76 (t, *J* = 11.5 Hz, 1H, -CH=CHCSO$_2$Ph), 6.31 (t, *J* = 2.4 Hz, 1H, -C$_6$H$_3$-(OMe)$_2$), 6.44 (d, *J* = 2.4 Hz, 2H, -C$_6$H$_3$-(OMe)$_2$), 7.49 (t, *J* = 7.8 Hz, 2H, -SO$_2$Ph), 7.60 (t, *J* = 7.8 Hz, 1H, -SO$_2$Ph), 7.84 (d, *J* = 7.8 Hz, 2H, -SO$_2$Ph).

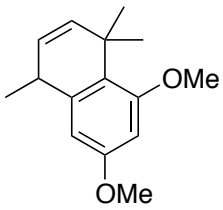
^{13}C NMR δ 22.43, 24.83, 25.59, 35.15, 37.11, 38.55, 55.22 (2 carbons), 74.22, 97.76, 105.03 (2 carbons), 127.09, 128.51 (2 carbons), 130.21 (2 carbons), 133.27, 137.60, 142.69, 147.97, 160.75 (2 carbons).

IR (neat) 3060 (Ar), 3014 (Ar and C=CH), 2961, 2872, 1596, 1458, 1299 (SO$_2$), 1204, 1141 (SO$_2$), 1084, 690 cm^{-1}.

Anal. Calcd for $C_{23}H_{28}O_4S$: C, 68.97; H, 7.05. Found: C, 69.02; H, 7.20.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

6,8-Dimethoxy-1,1,4-trimethyl-1,4-dihydronaphthalene (48). Friedel-Crafts reaction of 45.



To a suspension of $AlCl_3$ (80.0 mg, 0.600 mmol) in CH_2Cl_2 (1 mL) was added (*Z*)-5-(3,5-dimethoxyphenyl)-2-methyl-3-hexen-2-yl phenyl sulfone (**45**) (112 mg, 0.300 mmol) in 1 mL of CH_2Cl_2 at 0 °C under argon. After the reaction mixture was stirred at 0 °C for 5 h, the reaction was terminated by the addition of aqueous saturated NH_4Cl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (38.0 mg, 55%) as an oil.

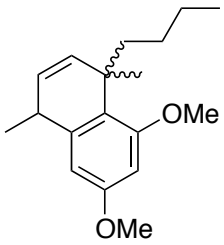
^{1}H NMR δ 1.28 (d, *J* = 6.9 Hz, 3H, MeCH-), 1.38 (s, 3H, (Me)$_2$C-), 1.40 (s, 3H, (Me)$_2$C-), 3.36 (dq, *J* = 3.9, 6.9 Hz, 1H, MeCH-), 3.80 (s, 3H, -C$_6$H$_2$-(OMe)$_2$), 3.81 (s, 3H, -C$_6$H$_2$-(OMe)$_2$), 5.49 (d, *J* = 10.2 Hz, 1H, -CH=CHC(Me)$_2$), 5.60 (dd, *J* = 3.9, 10.2 Hz, 1H, -CH=CHC(Me)$_2$), 6.35 (s, 2H, -C$_6$H$_2$-(OMe)$_2$).

^{13}C NMR δ 26.03, 28.87, 29.07, 34.74, 34.82, 55.01, 55.13, 97.43, 103.93, 123.58, 124.86, 137.68, 141.30, 158.27, 159.24.

IR (neat) 3020 (Ar and C=CH), 2999, 2956, 1609, 1582, 1458, 1119, 1049, 754 cm^{-1}.

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.85; H, 8.67.

A 77:23 diastereomeric mixture of 1-butyl-6,8-dimethoxy-1,4-dimethyl-1,4-dihydronaphthalene (49) prepared from a 57:43 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-5-methyl-3-nonen-5-yl phenyl sulfone (46).



To a suspension of $AlCl_3$ (66.7 mg, 0.500 mmol) in CH_2Cl_2 (1 mL) was added a 57:43 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-5-methyl-3-nonen-5-yl phenyl sulfone (**46**) (104 mg, 0.250 mmol, prepared by lithiation and methylation of a 61:39 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-3-nonen-5-yl phenyl sulfone (**33**)) in 1 mL of CH_2Cl_2 at 0 °C under argon. After the mixture was stirred at 0 °C for 5 h, the reaction was terminated by the addition of aqueous saturated NH_4Cl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the diastereoselectivity of the product was 77:23. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (41.8 mg, 61%) as an oil and of the same diastereomeric composition observed for the crude sample.

Major isomer: ^{1}H NMR δ 0.79 (t, *J* = 6.9 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$-), 1.10-1.26 (m, 5H, alkyl-H), 1.29 (d, *J* = 7.2 Hz, 3H, <u>Me</u>CH-), 1.36 (s, 3H, <u>Me</u>C-), 2.32 (dt, *J* = 4.5, 12.9 Hz, 1H, alkyl-H), 3.36 (dq, *J* = 3.9, 6.9 Hz, 1H, MeC<u>H</u>-), 3.79 (s, 6H, Ar-(O<u>Me</u>)$_2$), 5.31 (d, *J* = 10.0 Hz, 1H, MeCHCH=C<u>H</u>C-), 5.65 (dd, *J* = 3.9, 10.0 Hz, 1H, MeCHC<u>H</u>=CHC-), 6.33 (m, 2H, -C$_6$<u>H</u>$_2$-(OMe)$_2$).

^{13}C NMR δ 14.00, 23.14, 25.59, 28.53, 28.89, 34.48, 39.01, 39.54, 55.05 (2 peaks), 97.28, 103.87, 126.20 (2 peaks), 136.12 (2 peaks), 142.09, 158.17.

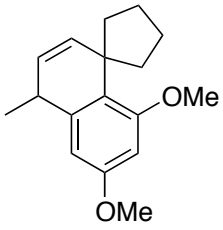
Minor isomer: ^{1}H NMR (characteristic peaks are shown) δ 0.76 (t, *J* = 6.9 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$-), 1.28 (d, *J* = 7.2 Hz, 3H, <u>Me</u>C-), 2.45 (dt, *J* = 4.5, 12.6 Hz, 1H, alkyl-H), 3.80 (s, 6H, Ar-(O<u>Me</u>)$_2$), 5.35 (d, *J* = 10.0 Hz, 1H, MeCHCH=C<u>H</u>C-), 5.69 (dd, *J* = 3.9, 10.0 Hz, 1H, MeCHC<u>H</u>=CHC-), 6.33 (m, 2H, -C$_6$<u>H</u>$_2$-(OMe)$_2$).

^{13}C NMR (characteristic peaks are shown) δ 14.03, 26.07, 28.06, 29.07, 34.84, 38.92, 40.39, 54.98 (2 peaks), 97.04, 121.82, 126.82 (2 peaks), 136.69, 142.42, 159.21.

IR (neat) 3020 (Ar and C=CH), 2956, 2926, 1608, 1584, 1465, 1160, 1052, 831 cm^{-1} for a 77:23 mixture of diastereoisomers.

Anal. Calcd for $C_{18}H_{26}O_2S$: C, 78.79; H, 9.55. Found: C, 78.49; H, 9.54 for a 77:23 mixture of diastereoisomers.

1,1-(1,4-Butylidene)-6,8-dimethoxy-4-methyl-1,4-dihydronaphthalene (50). Friedel-Crafts reaction of 47.



To a suspension of $AlCl_3$ (80.0 mg, 0.600 mmol) in CH_2Cl_2 (1 mL) was added (*Z*)-1,1-(1,4-butylidene)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (**47**) (120 mg, 0.300 mmol) in 1 mL of CH_2Cl_2 at 0 °C under argon. After the reaction mixture was stirred for 5 h at 0 °C, the reaction was terminated by the addition of aqueous saturated NH_4Cl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (57.2 mg, 74%) as a white solid.

^{1}H NMR δ 1.28 (d, *J* = 6.9 Hz, 3H, MeCH-), 1.46-1.59 (m, 2H alkyl-H), 1.70-1.98 (m, 4H, alkyl-H), 2.16-2.34 (m, 2H, alkyl-H), 3.35 (dq, *J* = 4.2, 6.9 Hz, 1H, MeCH-), 3.79 (s, 6H, Ar-(OMe)$_2$), 5.51 (dd, *J* = 4.2, 10.0 Hz, 1H, MeCHCH=CH-), 5.72 (d, *J* = 10.0 Hz, 1H, MeCHCH=CH-), 6.35 (s, 2H, -C$_6$H$_2$-(OMe)$_2$).

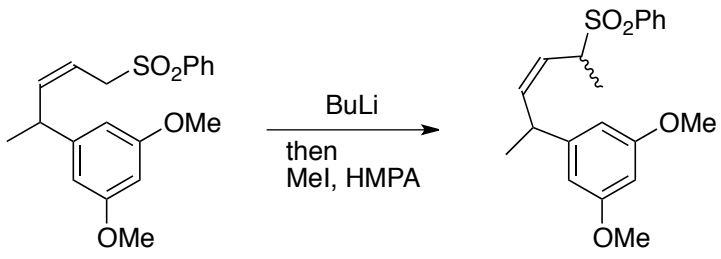
^{13}C NMR δ 25.77, 27.15, 27.21, 34.31, 41.12, 41.55, 43.96, 54.88, 55.15, 97.34, 103.59, 122.57, 123.21, 135.74, 141.88, 158.13, 158.45.

IR (KBr) 3018 (Ar and C=CH), 2934, 2862, 1608, 1585, 1448, 1351, 1199, 1162, 1058, 940, 827, 754, 637 cm^{-1}.

Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.33; H, 8.69.

M.p. 47-48 ºC.

A 45:55 diastereomeric mixture of (*Z*)-5-(3,5-dimethoxyphenyl)-3-hexen-2-yl phenyl sulfone (32) prepared by lithiation and methylation of (*Z*)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (31).



To a solution of (*Z*)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (**31**) (69.3 mg, 0.200 mmol)

in THF (2 mL) was added BuLi (0.153 mL, 1.57 M solution in hexane, 0.240 mmol) at 0 °C under argon. After the mixture was stirred at 0 °C for 30 min, iodomethane (0.062 mL, 1.00 mmol) and HMPA (0.173 mL, 1.00 mmol) were added in this order at 0 °C. After the reaction mixture was heated in an oil bath maintained at 50 °C for 4 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (5 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was 45:55. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (65 mg, 90%) as an oil and of the same diastereomerc composition observed for the crude sample.

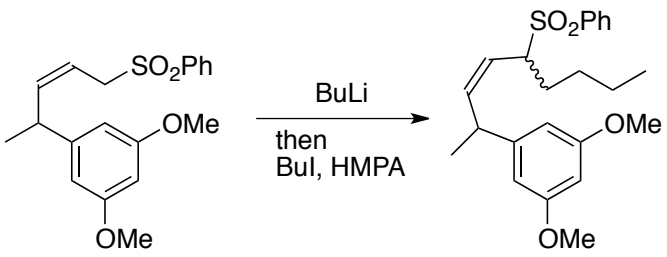
Major isomer: ^{1}H NMR δ 0.93 (d, *J* = 6.9 Hz, 3H, MeCHAr), 1.39 (d, *J* = 6.9 Hz, 3H, -CH(Me)SO_2Ph), 3.29 (dq, *J* = 10.4, 6.9 Hz, 1H, MeCHAr), 3.75 (s, 6H, Ar-(OMe)$_2$), 4.09 (m, 1H, -CH=CHCH(Me)SO_2Ph), 5.26 (t, *J* = 10.4 Hz, 1H, -CH=CHCHSO_2Ph), 5.70 (t, *J* = 10.4 Hz, 1H, -CH=CHCHSO_2Ph), 6.24 (d, *J* = 2.4 Hz, 2H, -C_6H_3-(OMe)$_2$), 6.28 (t, *J* = 2.4 Hz, 1H, -C_6H_3-(OMe)$_2$), 7.50 (t, *J* = 7.2 Hz, 2H, -SO_2Ph), 7.66 (t, *J* = 7.2 Hz, 1H, -SO_2Ph), 7.90 (d, *J* = 7.2 Hz, 2H, -SO_2Ph).

Minor isomer: ^{1}H NMR (characteristic peaks are shown) δ 1.22 (d, *J* = 6.9 Hz, 3H, MeCHAr), 1.48 (d, *J* = 6.9 Hz, 3H, -CH(Me)SO_2Ph), 3.44 (dq, *J* = 10.4, 6.9 Hz, 1H, MeCHAr), 3.76 (s, 6H, Ar-(OMe)$_2$), 5.27 (t, *J* = 10.4 Hz, 1H, -CH=CHCHSO_2Ph), 5.73 (t, *J* = 10.4 Hz, 1H, -CH=CHCHSO_2Ph), 6.16 (d, *J* = 2.4 Hz, 2H, -C_6H_3-(OMe)$_2$), 6.27 (t, *J* = 2.4 Hz, 1H, -C_6H_3-(OMe)$_2$), 7.39 (t, *J* = 7.2 Hz, 2H, -SO_2Ph), 7.57 (t, *J* = 7.2 Hz, 1H, -SO_2Ph), 7.76 (d, *J* = 7.2 Hz, 2H, -SO_2Ph).

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

These major and minor isomers were the opposite of those obtained by the aryl Grignard addition to sulfonyldiene **16**, followed by *in situ* methylation (*vide supra*). For full spectral data, see: the (*Z*)-5-(3,5-dimethoxyphenyl)-3-hexen-2-yl phenyl sulfone (**32**) prepared by aryl Grignard addition to sulfonyldiene **16**, followed by *in situ* methylation.

A 63:37 diastereomeric mixture of (*Z*)-2-(3,5-dimethoxyphenyl)-3-nonen-5-yl phenyl sulfone (33) prepared by lithiation and butylation of (*Z*)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (31).



To a solution of (*Z*)-4-(3,5-dimethoxyphenyl)-2-pentenyl phenyl sulfone (**31**) (346 mg, 1.00 mmol) in THF (5 mL) was added BuLi (0.760 mL, 1.57 M solution in hexane, 1.20 mmol) at 0 °C under argon. After the mixture was stirred at 0 °C for 30 min, iodobutane (0.570 mL, 5.00 mmol) and HMPA (1.74

mL, 10.0 mmol) were added in this order to the reaction mixture at 0 °C. After the reaction mixture was heated in an oil bath maintained at 60 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was 63:37. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (275 mg, 68%) as an oil and of the same diastereomeric composition observed for the crude sample.

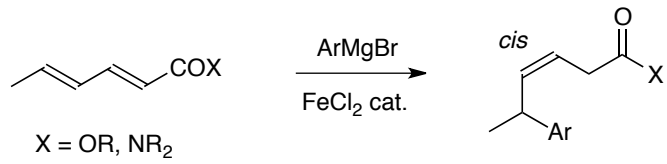
The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.

For spectral data, see: (*Z*)-2-(3,5-dimethoxyphenyl)-3-nonen-5-yl phenyl sulfone (**33**) prepared by aryl Grignard addition to sulfonyldiene **16**, followed by *in situ* butylation. These major and minor isomers were identical to those obtained by aryl Grignard addition to sulfonyldiene **16**, followed by *in situ* butylation.

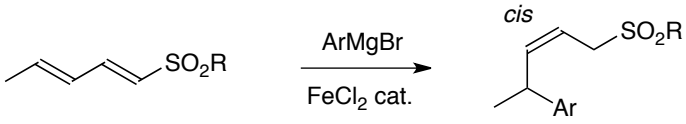
Chapter 3. Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Phosphine Oxides and Its Synthetic Application

Introduction

In the previous chapters, we discussed the iron-catalyzed selective conjugate addition of aryl Grignard reagents to α,β,γ,δ-unsaturated carbonyl compounds (eq 1)[1] and sulfones (eq 2).[2,3] In these reactions, δ-addition of aryl Grignard reagents and the *cis*-stereochemistry of the resultant olefin are always characteristic features.



(1)

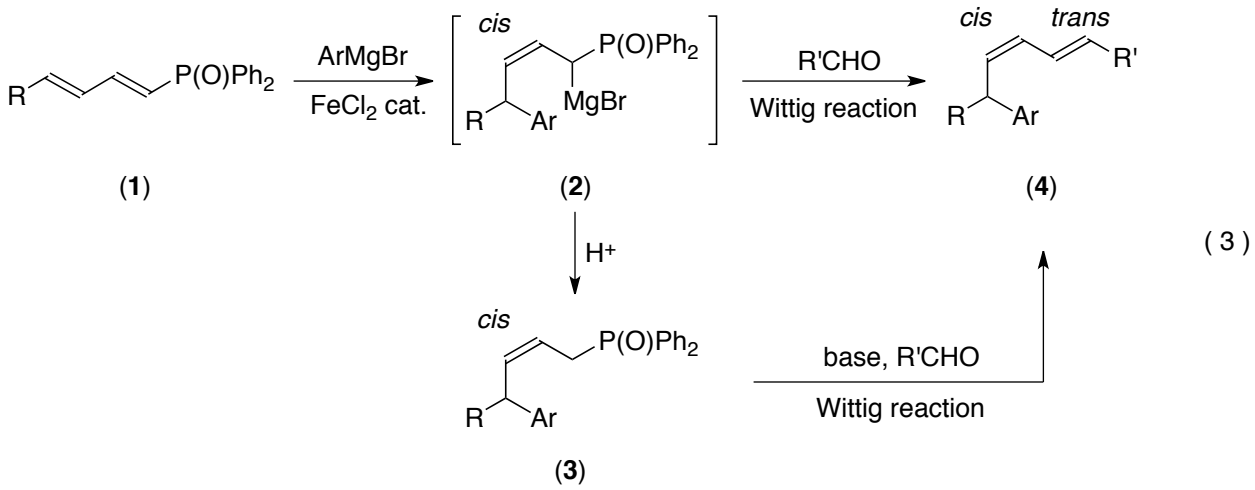


(2)

The successful iron-catalyzed conjugated addition of aryl Grignard reagents to α,β,γ,δ-unsaturated sulfones and its synthetic application as described above prompted us to search for other electron-deficient dienes as substrates for the iron-catalyzed conjugate addition. It is well known that vinyl phosphorus compounds are good Michael acceptors.[4] However, the study of the Michael addition to dienyl phosphorus compounds is rare, perhaps for the same reason of α,β,γ,δ-unsaturated carbonyl compounds described in Chapter 1. Thus, we began our study on the iron-catalyzed conjugate addition to α,β,γ,δ-unsaturated phosphorus compounds, choosing phosphine oxide as the phosphorus moiety. The transformation is illustrated in Scheme 1, where [(*E*,*E*)-1,3-pentadienyl]diphenylphosphine oxide (**1**) was treated with PhMgBr in the presence of the iron-catalyst and under the similar reaction conditions described in Chapter 2 to give exclusively *cis*-olefinic product **3** after hydrolytic work up. It should be noted that the product **3** is a stereo-defined precursor of the Wittig reagent. Thus the utility of the product obtained here may be found in the synthesis of stereo-defined 1-aryl-2,4-dienes **4** after the reaction with an aldehyde as shown in Scheme 1. The δ-addition of a Grignard reagent (from **1** to **2**) and the Wittig reaction of the resulting Wittig reagent (from **2** to **4**) in one pot were also possible to give diene **4.** The aryl-substituted dienes like **4** are found in naturally occurring products

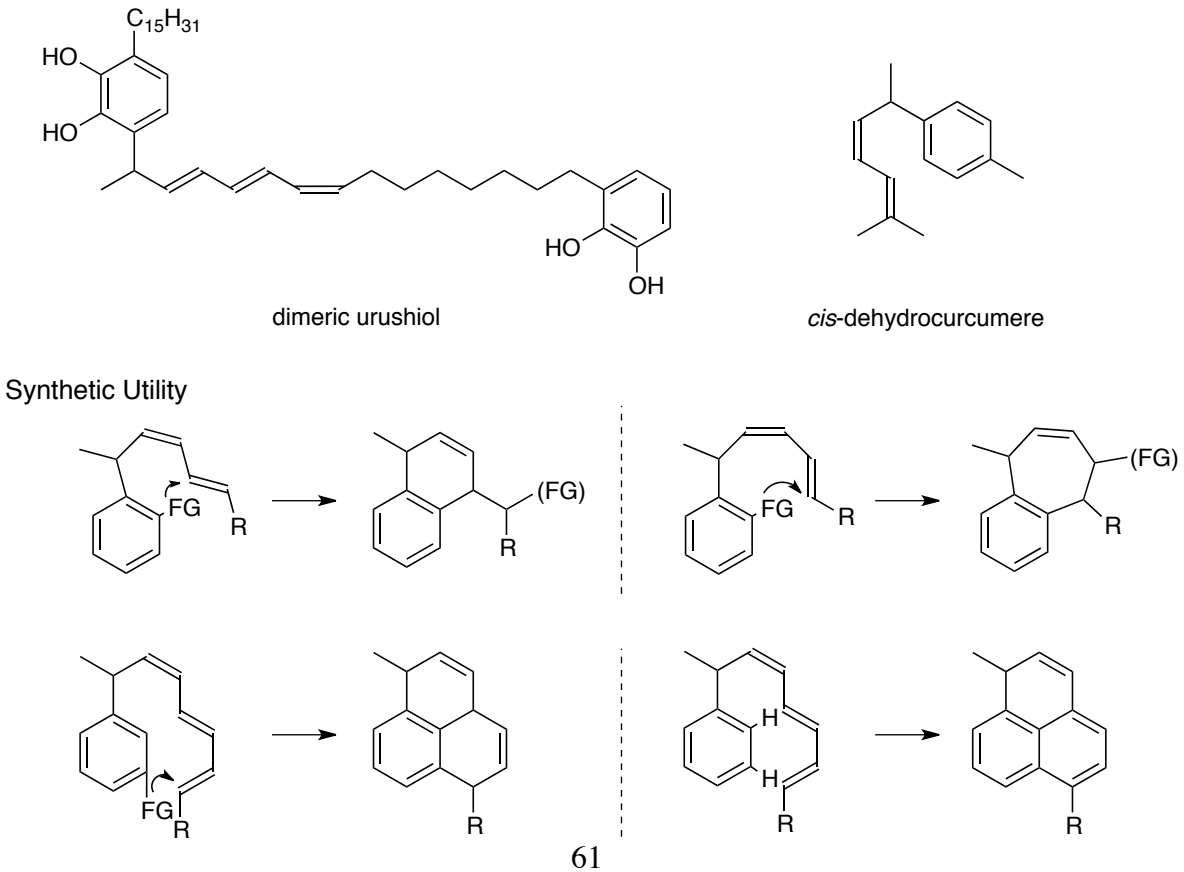
and their derivatives, and useful synthetic intermediates for the preparation of cyclic compounds as shown in Chart 1.

Scheme 1. Iron-catalyzed Addition to α,β,γ,δ-Unsaturated Phosphine Oxides and Its Synthetic Application.



(3)

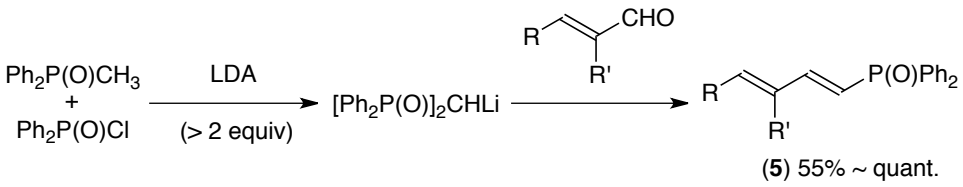
Chart 1. Naturally Occurring Products and Some Synthetic Utility.



Results and Disscussion

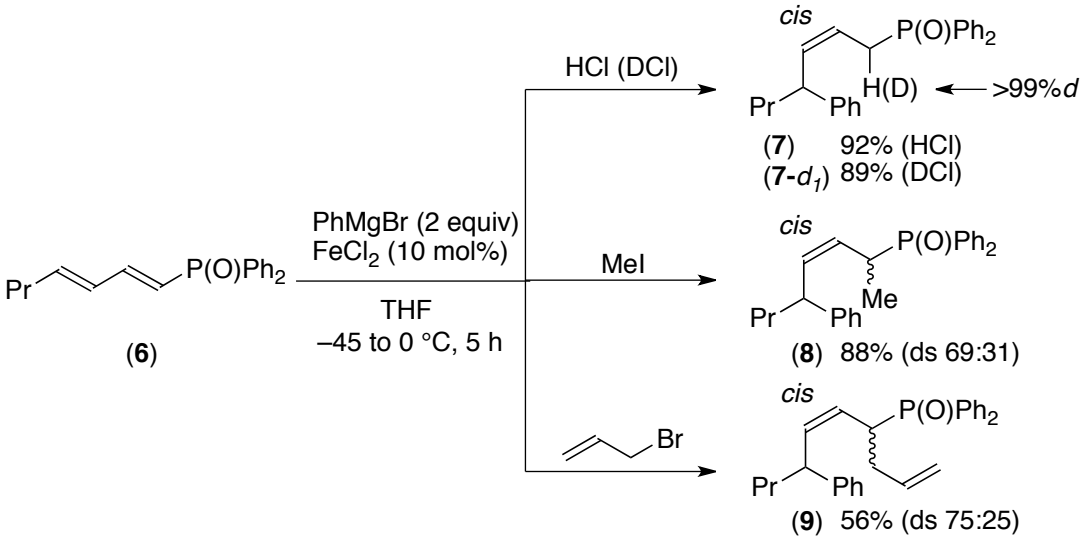
The requisite α,β,γ,δ-unsaturated phosphine oxides **5** were readily prepared from α,β-unsaturated aldehydes as shown in Scheme 2.[5]

Scheme 2. Preparation of α,β,γ,δ-Unsaturated Phosphine Oxides



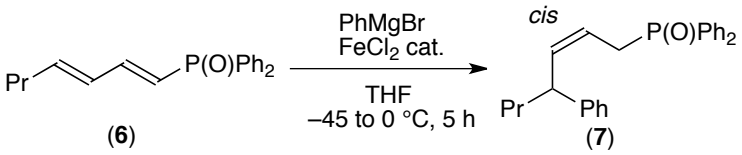
The iron-catalyzed addition to α,β,γ,δ-unsaturated phosphine oxides was carried out under the conditions adopted from those of the reactions of α,β,γ,δ-unsaturated carbonyl compounds and sulfones. Thus, [(*E*,*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) was treated with PhMgBr (2 equiv) in the presence of 10 mol% of $FeCl_2$ to afford virtually single *cis*-allylphosphine oxide **7** in high yield after hydrolysis. Alternatively, deuteriolysis and the treatment with alkyl halides gave deuterated product **7-***d*$_1$ with high deuterium incorporation and alkylated products **8** and **9** with *cis*-olefinic stereochemistry exclusively preserved (Scheme 3). This clearly shows that the magnesiated intermediate such as **2** in Scheme 1 could be used for further carbon-carbon bond formation or the introduction of functional groups.

Scheme 3. Iron-catalyzed Selective δ-Addition of PhMgBr to [(1*E*,3*E*)-1,3-Heptadienyl]diphenylphosphine Oxide.



As far as the catalyst load and the amount of the Grignard reagent are concerned, we examined them at the outset as shown in Table 1. Among the several combinations, 10 mol% of $FeCl_2$ p and 2 equiv of the Grignard reagent proved the Grignard reagent essential to complete the reaction, giving **7** in high yield.

Table 1. Optimum Amount of the Iron Catalyst and Grignard Reagent.

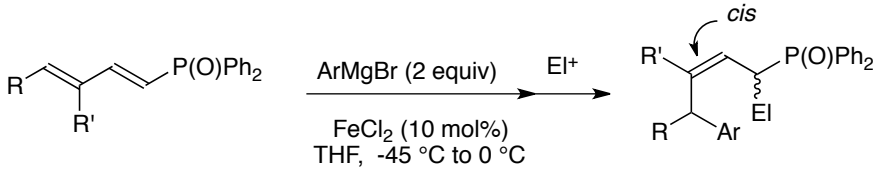


$FeCl_2$ (mol%)	PhMgBr (equiv)	**7** (%)	**6** (%)	determined by
3	2	trace	~quant.	^{1}H NMR
5	2	46	49	^{1}H NMR
10	**2**	**92**	-	isolated
10	1.5	71	29	^{1}H NMR
10	1.1	32	68	^{1}H NMR

As we found the iron-catalyzed addition to α,β,γ,δ-unsaturated phosphine oxides was again successful, we then investigated its generality as shown in Table 2. Besides [(*E*,*E*)-1,3-

heptadienyl]diphenylphosphine oxide (**6**), α,β,γ,δ-unsaturated phosphine oxides **12**-**15** having a different side chain produced the expected products **18**-**21** in good yields (entries 7-10). α,β,γ,δ-Unsaturated phosphine oxides **16** and **17** with different substitution patterns also afforded desired products **22** and **23** without any difficulty (entries 11-12). Aryl Grignard reagents such as tolyl-, anisyl-, and 3,5-dimethoxyphenylmagnesium bromides afforded exclusively *cis*-allylphosphine oxides **24**-**26** in good yields (entries 13-15).

Table 2. Preparation of Various *cis*-Allylphosphine Oxides.



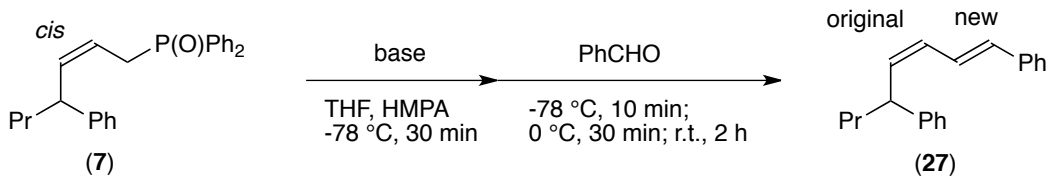
	substrate				product				
entry	R	R'		ArMgBr	El+	El	yield (%)		ds
1	Pr	H	(**6**)	PhMgBr	HCl	H	92	(**7**)	
2	Pr	H	(**6**)		DCl	D	89 (>99% *d*)	(**7**-d_1)	n.d.[a]
3	Pr	H	(**6**)		MeI	Me	88	(**8**)	69:31
4	Pr	H	(**6**)		CH_2=$CHCH_2$Br	CH_2=$CHCH_2$-	56	(**9**)	75:25
5	Pr	H	(**6**)		$PhCH_2$Br	$PhCH_2$-	66	(**10**)	78:22
6	Pr	H	(**6**)		$MeOCH_2Cl$	$MeOCH_2$-	71	(**11**)	60:40
7	Me	H	(**12**)		HCl	H	92	(**18**)	
8	$Ph(CH_2)_2$-	H	(**13**)		HCl	H	72	(**19**)	
9	CH_2=$CH(CH_2)_8$-	H	(**14**)		HCl	H	95	(**20**)	
10	*c*-C_6H_{11}-	H	(**15**)		HCl	H	95	(**21**)	
11	H	Me	(**16**)		HCl	H	49	(**22**)	
12	Pr	Et	(**17**)		HCl	H	82	(**23**)	
13	Pr	H	(**6**)	4-MeC_6H_4MgBr	HCl	H	63	(**24**)	
14	Pr	H	(**6**)	4-$(MeO)C_6H_4MgBr$	HCl	H	92	(**25**)	
15	Pr	H	(**6**)	3,5-$(MeO)_2C_6H_3MgBr$	HCl	H	60	(**26**)	

[a] The diastereoselectivity was hardly determined by ^{1}H NMR spectroscopy.

Having established the iron-catalyzed preparation of *cis*-allylphosphine oxides, we started investigating their utility in the Wittig reaction.[4] Table 3 summarizes its results, starting from **7** and benzaldehyde as representative substrates and yielding **27**. Although, the product yields and the diene

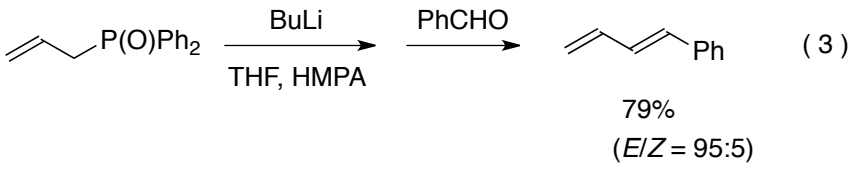
stereoselectivities vary a little, BuLi proved to be the base of choice. The addition of HMPA (hexamethylphosphoramide) was necessary (entry 5). This selection of base is in accord with a precedent of the Wittig reaction using just allyl(diphenyl)phosphine oxide itself as shown in eq 3.[6]

Table 3. Optimum Conditions for the Wittig Reaction of [(*Z*)-4-Phenyl-2-heptenyl]diphenylphosphine Oxide and Benzaldehyde.



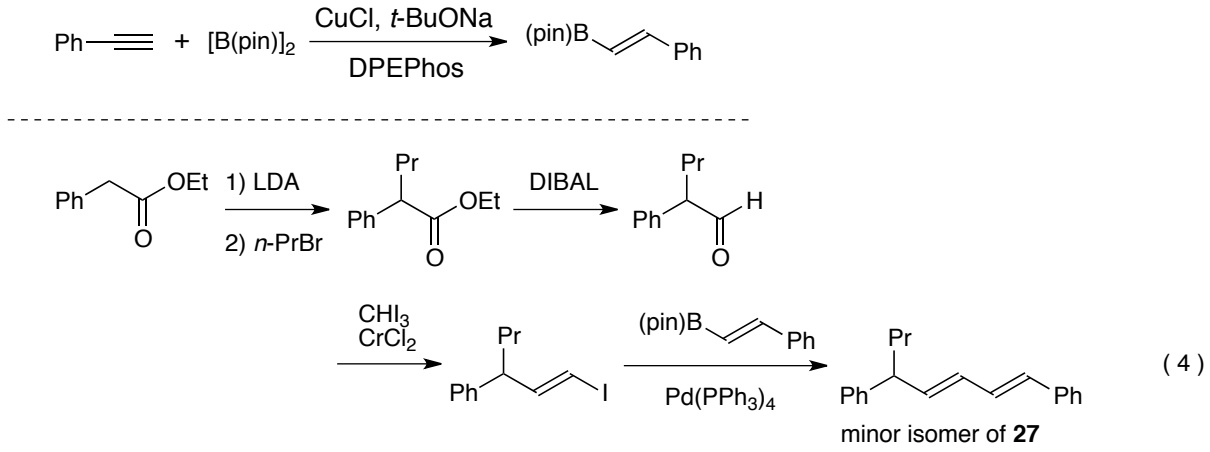
entry	base (equiv)	HMPA[a]	PhCHO (equiv)	isolated yield (%)	original *cis*:*trans*	new *cis*:*trans*
1	**BuLi (1.2)**	**+**	**1.2**	**72**	**93: 7**	***trans* only**
2	NaHMDS (1.2)	+	1.2	64	96: 4	*trans* only
3	KHMDS (1.2)	+	1.2	68	93: 7	*trans* only
4	**BuLi (1.2)**	**+**	**1.5**	**71**	**96: 4**	***trans* only**
5	BuLi (1.2)	-	1.5	23	89:11	*trans* only

[a] + : added, - : omitted.



(3)

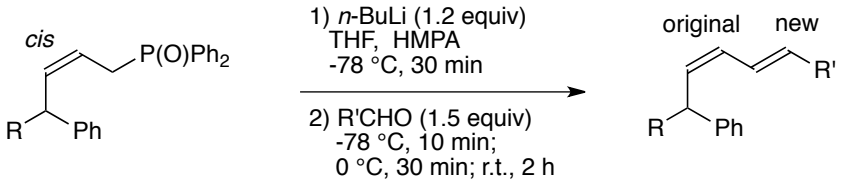
It is interesting to note that the original *cis*-olefin in **7** isomerized a little in the product **27**, while the newly generated olefin was exclusively controlled to be *trans*. The major isomer of **27**, (1*E*,3*Z*)-1,5-diphenyl-1,3-octadiene, was firmly characterized by the ^{1}H NMR spectroscopy. On the other hand, the structure of the minor isomer, (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene, was unambiguously identified by the comparison with an authentic sample prepared according to eq 4.[7a] The other two possible minor olefinic stereoisomers have not been detected in a crude reaction mixture.



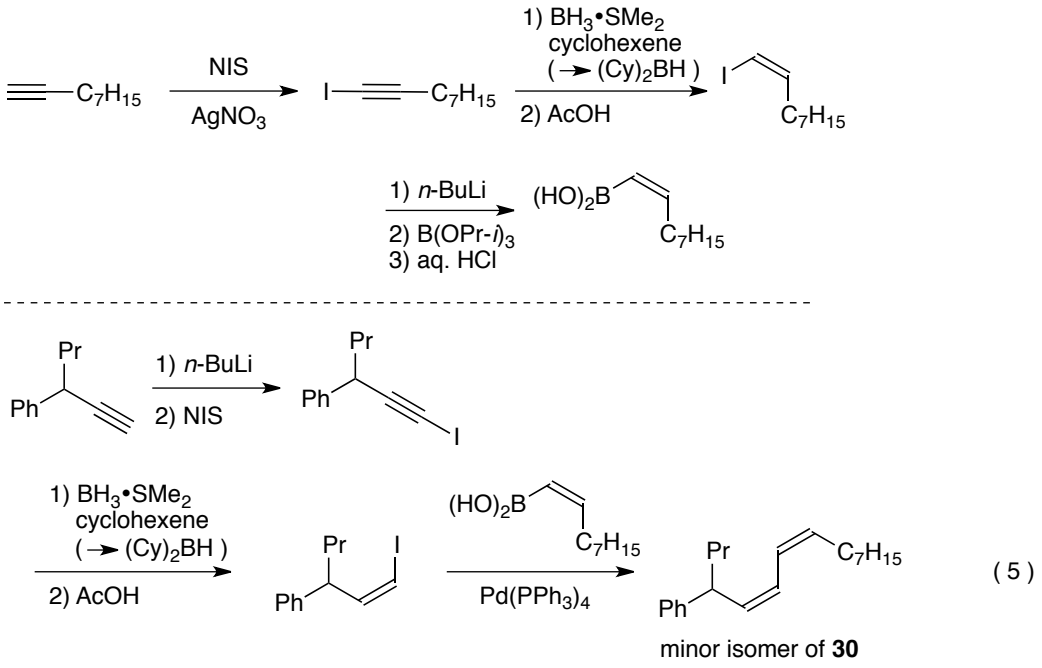
(4)

Under the optimal conditions using BuLi as base, other results of the Wittig reaction are summarized in Table 4. In the case of reaction with aromatic aldehydes, when an allylic substitutent (R) becomes smaller (Me vs. Pr, cf. entries 1 and 2), the stereochemistry of the original *cis*-olefin tends to be less retained. The reason for this phenomenon is unclear for now. To our surprise, when the Wittig reagent generated from **7** reacted with *aliphatic* aldehydes (entries 4-6), the original *cis*-olefin in **7** was completely retained, but the newly formed olefin was no longer exclusively *trans*. This stereochemistry of the diene was unambiguously confirmed for product **30** (entry 4). While the major isomer, (5*Z*,7*E*)-4-phenyl-5,7-pentadecadiene, was easily characterized by ^{1}H NMR spectroscopy, the minor isomer, (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene, was identified with an authentic sample prepared according to eq 5.[7b] The other two possible minor isomers were not seen by ^{1}H NMR analysis of the crude sample (entry 4). This change in stereochemistry of the dienes resulted from aromatic to aliphatic aldehydes appears unusual and should be quite interesting. In the case of reactions with aliphatic aldehydes (entries 4-6), that the *trans* selectivity of the newly formed olefin increases, as the steric hindrance of the aldehydes increases, may be an expected observation.

Table 4. Results of Wittig Reaction Starting from *cis*-Allylphosphine Oxide.

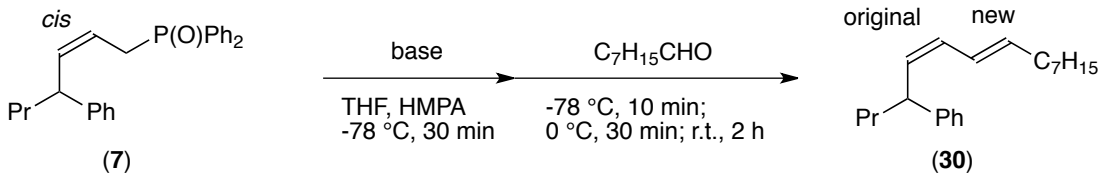


entry	R		R'CHO		yield (%)	original *cis*:*trans*	new *trans*:*cis*
1	Pr	(**7**)	PhCHO	(**27**)	71	96: 4	*trans* only
2	Me	(**18**)	PhCHO	(**28**)	64	89:11	*trans* only
3	Pr	(**7**)	*p*-$MeOC_6H_4CHO$	(**29**)	68	95: 5	*trans* only
4	Pr	(**7**)	$C_7H_{15}CHO$	(**30**)	64	*cis* only	86:14
5	Pr	(**7**)	*c*-$C_6H_{11}CHO$	(**31**)	72	*cis* only	89:11
6	Pr	(**7**)	*t*-BuCHO	(**32**)	61	*cis* only	93: 7



For supplementary data to entry 4 in Table 4, the selection of base is summarized in Table 5, where BuLi in the presence of HMPA was found optimum, as observed for benzaldehyde in Table 3.

Table 5. Supplementary Data to Entry 4 in Table 4.



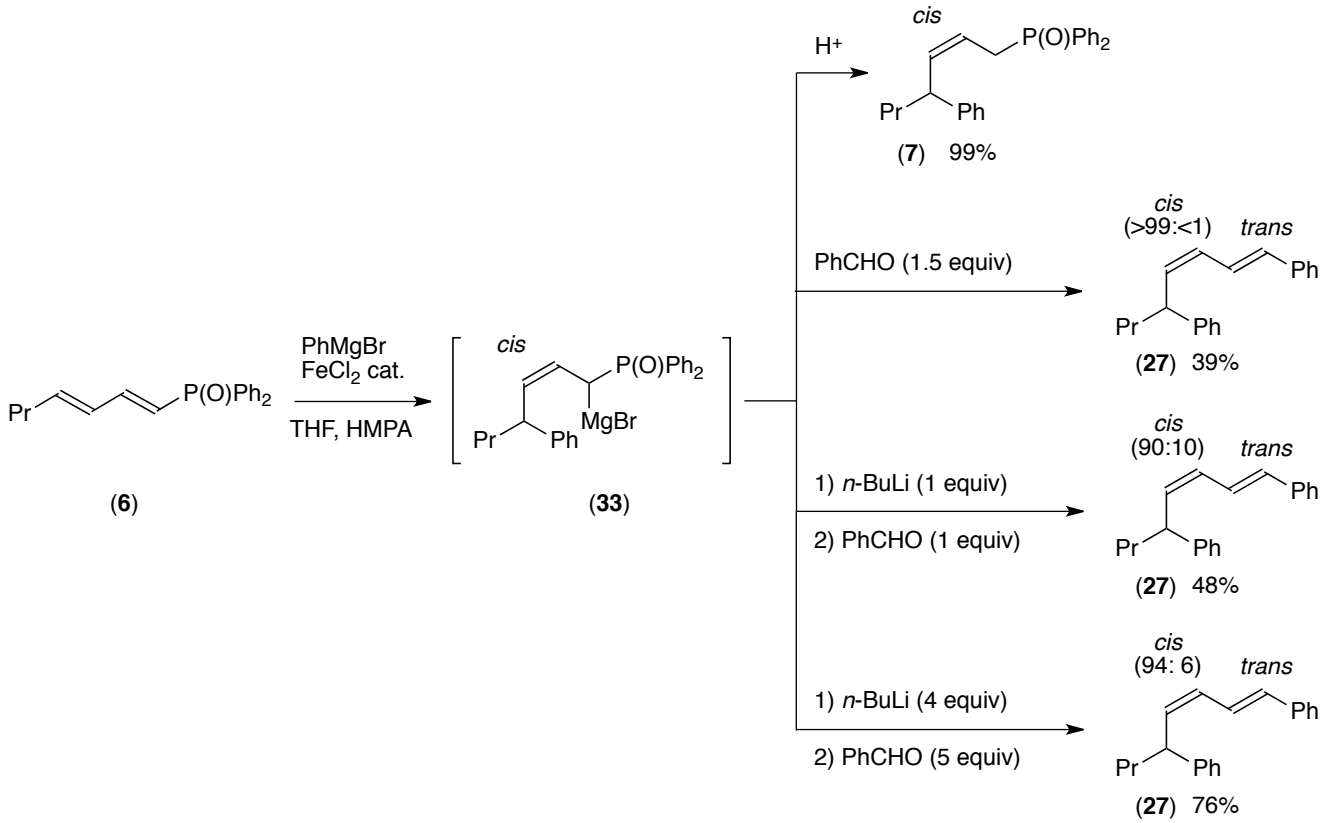
(**7**) (**30**)

entry	base (equiv)	HMPA[a]	$C_7H_{15}CHO$ (equiv)	isolated yield (%)	original *cis*:*trans*	new *cis*:*trans*
1	**BuLi (1.2)**	**+**	**1.2**	**53**	***cis* only**	**86:14**
2	NaHMDS (1.2)	+	1.2	69	*cis* only	69:31
3	KHMDS (1.2)	+	1.2	69	*cis* only	50:50
4	**BuLi (1.2)**	**+**	**1.5**	**64**	***cis* only**	**86:14**
5	BuLi (1.2)	-	1.5	35	*cis* only	78:22

[a] + : added, - : omitted.

Finally, we attempted a one-pot reaction throughout the iron-catalyzed δ-addition and the Wittig reaction, some results of which are summarized in Scheme 4. The role of BuLi is interesting to increase the product yields. This phenomenon may be attributable to the formation of an ate complex between allylmagesium species and BuLi, which increases the reactivity of the Wittig reagents. As the yield is higher than those of the two-step reactions described above, this *trans* formation is a convenient and selective one-pot preparation of arylated dienes.

Scheme 4. An Attempted One-pot δ-Addition and Wittig Reaction.



Conclusion

In conclusion, we developed the iron-catalyzed selective δ-addition of aryl Grignard reagents to α,β,γ,δ-unsaturated phosphine oxides to give *cis*-allylphosphine oxides, which could be used as precursors for the Wittig reaction giving stereo-defined arylated dienes. Further investigation on these reactions and their applications is now in progress.

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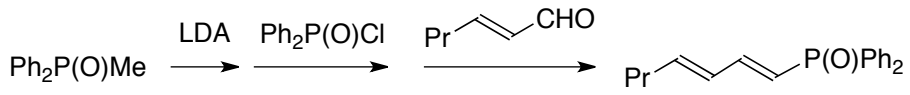
7. (a) Jung, H.-Y.; Feng, X.; Kim, H.; Yun, J. *Tetrahedron* **2012**, *68*, 3444-3449. (b) Fotsop, D. F.; Roussi, F.; Leverrier, A.; Bretéché, A.; Guéritte, F. *J. Org. Chem.* **2010**, *75*, 7412-7415.

Experimental section (Chapter 3)

General. ^{1}H and ^{13}C NMR spectra were taken on an Agilent 400-MR spectromer at 400 and 100 MHz, respectively. $CDCl_3$ and C_6D_6 were used as the solvent. Unless otherwise specified in spectral data, the former was always used. Chemical shifts are reported in parts per million shift (δ value) from Me_4Si (δ 0 ppm for ^{1}H) or based on the middle peak of the solvent ($CDCl_3$) (δ 77.00 ppm for ^{13}C NMR) as an internal standard. Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in Hertz. Infrared (IR) spectra were recorded on a JASCO FT/IR-4100 spectrometer and are reported in wave numbers (cm^{-1}). High resolution mass spectra (HRMS) were obtained on a Bruker micrOTOF II in positive electrospray ionization (ESI) method calibrated with sodium formate at the Suzukake-dai Material Analysis Center, Technical Department, Tokyo Institute of Technology. For recycling preparative HPLC, a Model LC-9201R/U equipped with a JAIGEL-H column (length: 600 mm × 2 cycles, bore: 20 mm) purchased from Japan Analytical Industry Co., Ltd. (Japan) was used. All reactions were carried out under argon. Dry solvents (THF, diethyl ether, and CH_2Cl_2) were purchased from Kanto Chemicals Co. (Japan). Chemicals were purified or dried in a standard manner, if necessary.

[(1*E*,3*E*)-1,3-Heptadienyl]diphenylphosphine oxide (6).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a solution of diisopropylamine (1.29 mL, 9.18 mmol) in THF (12 mL) was added *n*-BuLi (5.90 mL, 9.68 M solution in hexane, 12.0 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and methyl(diphenyl)phosphine oxide (1.04 g, 6.00 mmol) in THF (10 mL) was added. The mixture was stirred at –78 °C for 15 min and diphenylphosphinic chloride (1.14 mL, 6.00 mmol) was added at that temperature. After stirring for 10 min, (*E*)-2-hexenal (0.450 mL, 5.00 mmol) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of aqueous saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (1.21 g, 81%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 0.90 (t, *J* = 7.2 Hz, 3H, alkyl-H), 1.43 (sextet, *J* = 7.2 Hz, 2H, alkyl-H), 2.12 (q, *J* = 7.2 Hz, 2H, alkyl-H), 6.03 (dt, *J* = 15.2, 7.2 Hz, 1H, -C<u>H</u>=CH-CH=CH-P(O)Ph_2), 6.17 (dd, *J* = 17.2, 23.2 Hz, 1H, -CH=CH-CH=C<u>H</u>-P(O)Ph_2), 6.24 (dd, *J* = 10.4, 15.2 Hz, 1H, -CH=C<u>H</u>-CH=CH-P(O)Ph_2), 7.02 (dt, *J* =

10.4, 17.2 Hz, 1H, -CH=CH-C<u>H</u>=CH-P(O)Ph_2), 7.43-7.52 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.69-7.73 (m, 4H, -P(O)<u>Ph</u>$_2$).

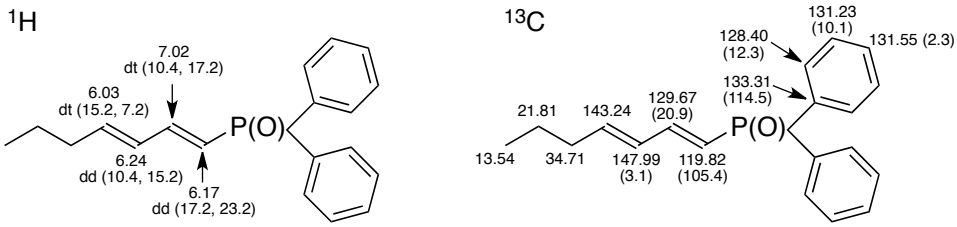
^{13}C NMR δ 13.54, 21.81, 34.71, 119.82 (d, *J* = 105.4 Hz, -C=C-C=<u>C</u>-P(O)Ph_2), 128.40 (d, *J* = 12.3 Hz, 4 carbons, *o*-P(O)Ph_2), 129.67 (d, *J* = 20.9 Hz, -C=C-<u>C</u>=C-P(O)Ph_2), 131.23 (d, *J* = 10.1 Hz, 4 carbons, *m*-P(O)Ph_2), 131.55 (d, *J* = 2.3 Hz, 2 carbons, *p*-P(O)Ph_2), 133.31 (d, *J* = 114.5 Hz, 2 carbons, *ipso*-P(O)Ph_2), 143.24 (-<u>C</u>=C-C=C-P(O)Ph_2), 147.99 (d, *J* = 3.1 Hz, -C=<u>C</u>-C=C-P(O)Ph_2).

IR (KBr) 3055 (Ar), 3027 (Ar and C=CH), 2983, 2930, 1642 (C=C-C=C), 1584 (C=C-C=C), 1437, 1182 (P=O), 1120, 1102, 1012, 809, 750, 722, 693, 530 cm^{-1}.

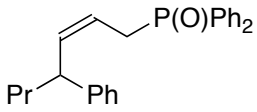
HRMS (ESI) Calcd for $C_{19}H_{21}PONa$ [M+Na]$^+$: 319.1222. Found: 319.1224.

M.p. 102-103 °C.

The *E*,*E*-diene stereochemistry was confirmed by ^{1}H NMR coupling constants.



[(*Z*)-4-Phenyl-2-heptenyl]diphenylphosphine oxide (7).



To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (59.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.460 mL, 0.870 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (69.0 mg, 92%) as an oil and as a single olefinic isomer.

^{1}H NMR δ 0.81 (t, *J* = 7.2 Hz, 3H, alkyl-H), 1.12 (m, 2H, alkyl-H), 1.42 (m, 1H, alkyl-H), 1.58 (m, 1H, alkyl-H), 3.16 (dd, *J* = 7.6, 14.8 Hz, 2H, -CH=CHC<u>H</u>$_2$P(O)Ph_2), 3.39 (dt, *J* = 10.8, 7.6 Hz, 1H, PhC<u>H</u>), 5.54 (dq, *J* = 10.8, 7.6 Hz, 1H, -CH=C<u>H</u>CH$_2$P(O)Ph_2), 5.75 (br t, *J* = 10.8 Hz, 1H, -C<u>H</u>=CHCH$_2$P(O)Ph_2), 7.07 (d, *J* = 7.2 Hz, 2H, Ph-H), 7.17 (t, *J* = 7.2 Hz, 1H, Ph-H), 7.25 (t, *J* = 7.2 Hz, 2H, Ph-H), 7.36-7.53 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.63-7.73 (m, 4H, -P(O)<u>Ph</u>$_2$).

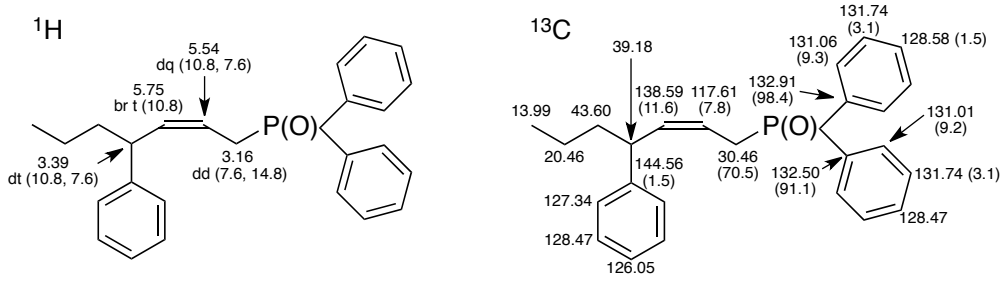
^{13}C NMR δ 13.99, 20.46, 30.46 (d, *J* = 70.5 Hz, -C=C-<u>C</u>-P(O)Ph_2), 39.18, 43.60, 117.61 (d, *J* = 7.8 Hz, -C=<u>C</u>-C-P(O)Ph_2), 126.05 (*p*-Ph), 127.34 (2 carbons, *o*-Ph), 128.47 (2 peaks consisting of 2 carbons and 1

carbon, *m*-Ph and *p*-P(O)Ph_2), 128.58 (d, *J* = 1.5 Hz, *p*-P(O)Ph_2), 131.01 (d, *J* = 9.2 Hz, 2 carbons, *o*-P(O)Ph_2), 131.06 (d, *J* = 9.3 Hz, 2 carbons, *o*-P(O)Ph_2), 131.74 (d, *J* = 3.1 Hz, 2 peaks of 2 carbons each, *m*-P(O)Ph_2), 132.50 (d, *J* = 91.1 Hz, *ipso*-P(O)Ph_2), 132.91 (d, *J* = 98.4 Hz, *ipso*-P(O)Ph_2), 138.59 (d, *J* = 11.6 Hz, -C=C-C-P(O)Ph_2), 144.56 (d, *J* = 1.5 Hz, *ipso*-Ph).

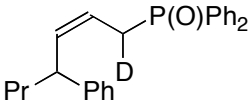
IR (neat) 3076 (Ar), 3056 (Ar), 3021 (Ar and C=CH), 2955, 2870, 1643 (C=C), 1591, 1437, 1194 (P=O), 1120, 843, 719, 697, 539, 510 cm^{-1}.

HRMS (ESI) Calcd for $C_{25}H_{27}PONa$ $[M+Na]^+$: 397.1692. Found: 397.1691.

The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.



A diastereomeric mixture of [(*Z*)-1-deuterio-4-phenyl-2-heptenyl]diphenylphosphine oxide (7-d_1).

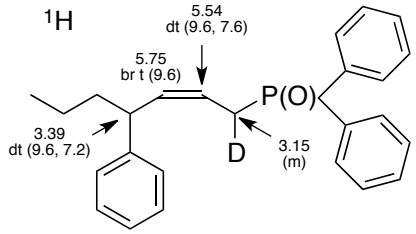


To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (59.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.339 mL, 1.18 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N DCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity was hardly determined. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (66.8 mg, 89%) as an oil. Its diastereoselectivity was again hardly determined by ^1H NMR spectroscopy.

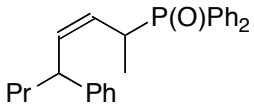
^1H NMR δ 0.81 (t, *J* = 7.2 Hz, 3H, alkyl-H), 1.12 (m, 2H, alkyl-H), 1.42 (m, 1H, alkyl-H), 1.58 (m, 1H, alkyl-H), 3.15 (m, 1H, -CH=CHC<u>H</u>DP(O)Ph_2), 3.39 (dt, *J* = 9.6, 7.2 Hz, 1H, PhC<u>H</u>), 5.54 (dt, *J* = 9.6, 7.6 Hz, 1H, -CH=C<u>H</u>CHDP(O)Ph_2), 5.75 (br t, *J* = 9.6 Hz, 1H, -C<u>H</u>=CHCHDP(O)Ph_2), 7.07 (d, *J* = 7.2 Hz, 2H, Ph-H), 7.17 (t, *J* = 7.2 Hz, 1H, Ph-H), 7.25 (t, *J* = 7.2 Hz, 2H, Ph-H), 7.36-7.53 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.63-7.73 (m, 4H, -P(O)<u>Ph</u>$_2$).

The integration of peak area at δ 3.15 ppm (-CH=CHC<u>H</u>DP(O)Ph_2) decreased its original value (2 H) to total 1.0 H to show >99% deuterium incorporation.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



A 69:31 diastereomeric mixture of [(*Z*)-5-phenyl-3-octen-2-yl]diphenylphosphine oxide (8).



To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (59.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.460 mL, 0.870 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, methyl iodide (0.075 mL, 1.0 mmol) was added. After the reaction mixture was heated in an oil bath maintained at 50 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity was 69:31. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (68.2 mg, 88%) as a white solid oil and of the same diastereomeric composition as observed for a crude sample.

Major isomer: ^{1}H NMR δ 0.89 (t, *J* = 7.2 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.15-1.80 (m, 4H, alkyl-H), 1.30 (dd, *J* = 7.2, 15.6 Hz, 3H, -CH(<u>Me</u>)P(O)Ph$_2$), 3.35-3.51 (m, 2H, -C<u>H</u>(Me)P(O)Ph$_2$ and PhC<u>H</u>), 5.55 (dt, *J* = 6.8, 10.8 Hz, 1H, -CH=C<u>H</u>-CH-P(O)Ph$_2$), 5.66 (dt, *J* = 2.0, 10.8 Hz, 1H, -C<u>H</u>=CH-CH-P(O)Ph$_2$), 6.88-7.58 (m, 11H, Ph-H and P(O)Ph$_2$), 7.62-7.95 (m, 4H, P(O)Ph$_2$).

^{13}C NMR δ 13.95, 13.99, 20.72, 33.37 (d, *J* = 71.2 Hz, -C=C-<u>C</u>-P(O)Ph$_2$), 40.10, 43.60, 125.96 (d, *J* = 7.0 Hz, -C=<u>C</u>-C-P(O)Ph$_2$), 125.99 (*p*-Ph), 127.29 (2 carbons, *o*-Ph), 128.03 (*p*-P(O)Ph$_2$), 128.14 (*p*-P(O)Ph$_2$), 128.49 (2 carbons, *m*-Ph), 131.17 (d, *J* = 8.5 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.24 (d, *J* = 6.9 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.46 (2 peaks of 2 carbons each, *m*-P(O)Ph$_2$), 132.31 (d, *J* = 94.5 Hz, 2 peaks, *ipso*-P(O)Ph$_2$), 135.66 (d, *J* = 11.6 Hz, -<u>C</u>=C-C-P(O)Ph$_2$), 144.54 (*ipso*-Ph).

Minor isomer: ^{1}H NMR (only characteristic peaks are shown) δ 0.73 (t, *J* = 7.2 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.07 (dd, *J* = 7.2, 16.0 Hz, 3H, -CH(<u>Me</u>)P(O)Ph$_2$), 5.68 (dt, *J* = 2.0, 10.8 Hz, 1H, -C<u>H</u>=CH-CH-POPh$_2$).

^{13}C NMR (only characteristic peaks are shown) δ 14.44, 14.49, 20.36, 34.08 (d, *J* = 71.3 Hz, -C=C-<u>C</u>-P(O)Ph$_2$), 38.95, 43.84, 125.34 (d, *J* = 6.2 Hz, -C=<u>C</u>-C-P(O)Ph$_2$), 126.07 (*p*-Ph), 127.18 (2 carbons, *o*-Ph), 128.37 (2 carbons, *m*-Ph), 131.09 (d, *J* = 8.5 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.31 (d, *J* = 8.5 Hz, 2 carbons,

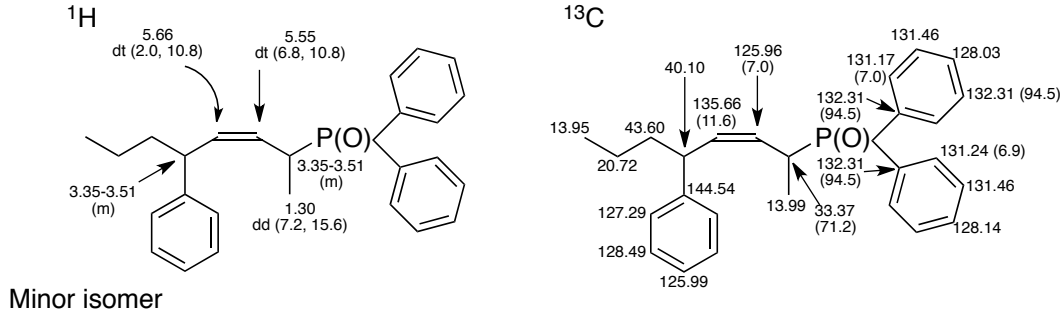
o-P(O)Ph_2), 131.62 (2 peaks of 2 carbons each, *m*-P(O)Ph_2), 132.44 (d, J = 94.5 Hz, 2 peaks, *ipso*-P(O)Ph_2), 136.79 (d, J = 11.6 Hz, -C=C-C-P(O)Ph_2), 144.94 (*ipso*-Ph).

IR (KBr) 3057 (Ar), 3026 (Ar), 2955, 2928, 2871, 1600 (C=C), 1492, 1453, 1438, 1177 (P=O), 1120, 1028, 999, 721, 697, 627 cm^{-1} for a 69:31 mixture of diastereoisomers.

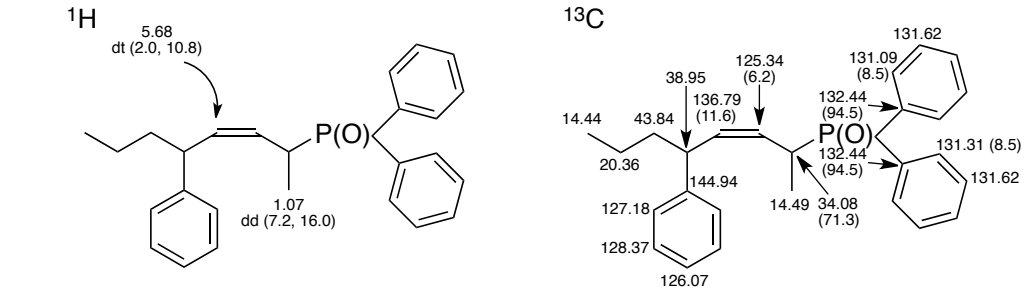
HRMS (ESI) Calcd for $C_{26}H_{29}PONa$ $[M+Na]^+$: 411.1848. Found: 411.1846 for a 69:31 mixture of diastereoisomers.

The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.

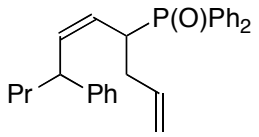
Major isomer



Minor isomer



A 75:25 diastereomeric mixture of [(*Z*)-7-phenyl-1,5-decadien-4-yl]diphenylphosphine oxide (9).



To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (59.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.330 mL, 1.22 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, allyl bromide (0.025 mL, 0.300 mmol) was added. After the reaction mixture was heated in an oil bath maintained at 50 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity was 75:25. The crude oil

was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (45.1 mg, 56%) as an oil and of the same diastereomeric composition observed for a crude sample.

Major isomer: ^{1}H NMR δ 0.85 (t, *J* = 7.2 Hz, 3H, alkyl-H), 1.25 (m, 2H, alkyl-H), 1.61 (m, 2H, alkyl-H), 2.36 (m, 2H, -C$\underline{H}_2$CH=CH_2), 3.22-3.46 (m, 2H, -C$\underline{H}$(Me)P(O)Ph_2 and PhC$\underline{H}$), 5.01 (d, *J* = 9.6 Hz, 1H, -CH=C$\underline{H}_2$), 5.03 (d, *J* = 16.8 Hz, 1H, -CH=C$\underline{H}_2$), 5.48 (dt, *J* = 8.0, 10.8 Hz, 1H, -CH=C$\underline{H}$-CH-P(O)Ph_2), 5.76 (m, 1H, -C$\underline{H}$=CH_2), 5.83 (dt, *J* = 3.2, 10.8 Hz, 1H, -C$\underline{H}$=CH-CH-P(O)Ph_2), 6.93-7.93 (m, 15H, Ph-H).

^{13}C NMR δ 14.05, 20.39, 33.13, 39.65 (*J* = 69.6 Hz, -C=C-$\underline{C}$-P(O)Ph_2), 40.47, 43.70, 117.07 ($H_2\underline{C}$=CH-), 123.32 (d, *J* = 5.4 Hz, -C=$\underline{C}$-C-P(O)Ph_2), 125.98 (*p*-Ph), 127.47 (2 carbons, *o*-Ph), 128.01 (*p*-P(O)Ph_2), 128.13 (*p*-P(O)Ph_2), 128.52 (2 carbons, *m*-Ph), 131.14 (d, *J* = 8.5 Hz, 2 carbons, *o*-P(O)Ph_2), 131.34 (d, *J* = 8.6 Hz, 2 carbons, *o*-P(O)Ph_2), 131.38 (2 carbons, *m*-P(O)Ph_2), 131.54 (2 carbons, *m*-P(O)Ph_2), 132.28 (d, *J* = 94.4 Hz, 2 peaks, *ipso*-P(O)Ph_2), 137.58 (d, *J* = 11.6 Hz, -$\underline{C}$=C-C-P(O)Ph_2), 138.70 (H_2C=$\underline{C}$H-), 144.32 (*ipso*-Ph).

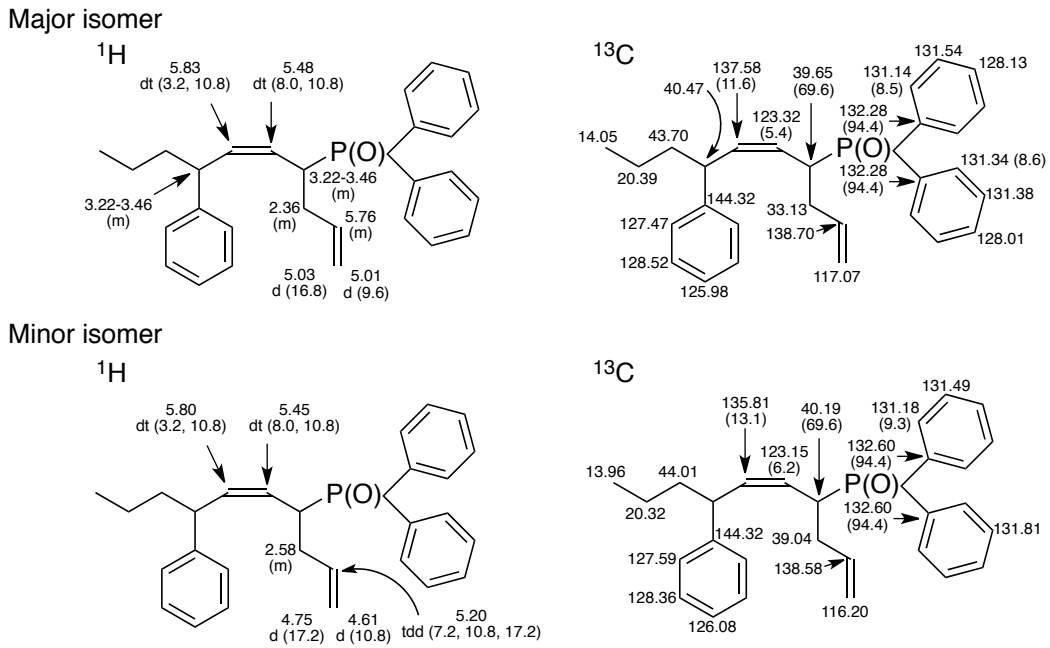
Minor isomer: ^{1}H NMR (only characteristic peaks are shown) δ 0.68 (t, *J* = 7.2 Hz, 3H, alkyl-H), 2.58 (m, 2H, -C$\underline{H}_2$CH=CH_2), 4.61 (d, *J* = 10.8 Hz, 1H, -CH=C$\underline{H}_2$), 4.75 (d, *J* = 17.2 Hz, 1H, -CH=C$\underline{H}_2$), 5.20 (tdd, *J* = 7.2, 10.8, 17.2 Hz, 1H, -C$\underline{H}$=CH_2), 5.45 (dt, *J* = 8.0, 10.8 Hz, 1H, -CH=C$\underline{H}$-CH-P(O)Ph_2), 5.80 (dt, *J* = 3.2, 10.8 Hz, 1H, -C$\underline{H}$=CH-CH-P(O)Ph_2).

^{13}C NMR (only characteristic peaks are shown) δ 13.96, 20.32, 39.04, 40.19 (*J* = 69.6 Hz, -C=C-$\underline{C}$-P(O)Ph_2), 44.01, 116.20 ($H_2\underline{C}$=CH-), 123.15 (d, *J* = 6.2 Hz, -C=$\underline{C}$-C-P(O)Ph_2), 126.08 (*p*-Ph), 127.59 (2 carbon, *o*-Ph), 128.36 (2 carbons, *m*-Ph), 131.18 (d, *J* = 9.3 Hz, 2 carbons, *o*-P(O)Ph_2), 131.49 (2 carbons, *m*-P(O)Ph_2), 131.81 (2 carbons, *m*-P(O)Ph_2), 132.60 (d, *J* = 94.4 Hz, 2 peaks, *ipso*-P(O)Ph_2), 135.81 (d, *J* = 13.1 Hz, -$\underline{C}$=C-C-P(O)Ph_2), 138.58 (H_2C=$\underline{C}$H-), 144.32 (*ipso*-Ph).

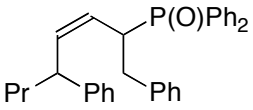
IR (neat) 3079 (Ar), 3061(Ar), 3013 (Ar), 2960, 2930, 2872, 1600 (C=C), 1493, 1438, 1216, 1184 (P=O), 1119, 1102, 919, 756 cm^{-1} for a 75:25 mixture of diastereoisomers.

HRMS (ESI) Calcd for $C_{28}H_{31}PONa$ $[M+Na]^+$: 447.2013. Found: 437.2005 for a 75:25 mixture of diastereoisomers.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



A 78:22 diastereomeric mixture of [(*Z*)-1,5-diphenyl-3-octen-2-yl]diphenylphosphine oxide (10).



To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (59.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.330 mL, 1.22 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, benzyl bromide (0.036 mL, 0.300 mmol) was added. After the reaction mixture was heated in an oil bath maintained at 50 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity was 78:22. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (60.9 mg, 66%) as an oil and of the same diastereomeric composition observed for a crude sample.

Major isomer: ^{1}H NMR δ 0.56 (t, *J* = 7.2 Hz, 3H, alkyl-Me), 0.85 (m, 2H, $CH_3C\underline{H}_2CH_2$), 1.05 (m, 2H, $CH_3CH_2C\underline{H}_2$), 2.70 (m, 2H, $C\underline{H}_2Ph$), 3.21 (ddd, *J* = 2.4, 8.8, 13.2 Hz, 1H, CH=CH-C<u>H</u>(Bn)-P(O)Ph_2), 3.56 (m, 1H, C<u>H</u>Ph), 5.50 (dt, *J* = 7.6, 10.4 Hz, 1H, CH=C<u>H</u>-CH(Bn)-P(O)Ph_2), 5.69 (dt, *J* = 2.4, 10.4 Hz, 1H, C<u>H</u>=CH-CH(Bn)-P(O)Ph_2), 6.90 (m, 2H, Ph-H), 7.04-7.20 (m, 6H, Ph-H), 7.23-7.30 (m, 2H, Ph-H), 7.35-7.50 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.75-7.99 (m, 4H, -P(O)<u>Ph</u>$_2$).

^{13}C NMR δ 13.81, 19.84, 34.78, 39.41, 42.42 (d, *J* = 68.1 Hz, -C=C-<u>C</u>-P(O)Ph_2), 43.96, 122.25 (d, *J* = 4.7 Hz, -C=<u>C</u>-C-P(O)Ph_2), 125.87 (*p*-Ph), 126.36 (*p*-Ph), 127.49 (2 carbons, *o*-Ph), 128.15 (*p*-P(O)Ph_2), 128.55 (*p*-P(O)Ph_2), 128.31 (2 carbons, *o*-Ph), 128.40 (2 carbons, *m*-Ph), 129.53 (2 carbons, *m*-Ph), 131.15 (d, *J* =

8.5 Hz, 2 carbons, *o*-P(O)Ph_2), 131.20 (d, *J* = 8.5 Hz, 2 carbons, *o*-P(O)Ph_2), 131.31 (d, *J* = 2.4 Hz, 2 carbons, *m*-P(O)Ph_2), 131.64 (d, *J* = 2.4 Hz, 2 carbons, *m*-P(O)Ph_2), 132.20 (d, *J* = 94.7 Hz, 2 peaks, *ipso*-P(O)Ph_2), 138.28 (d, *J* = 12.4 Hz, -C=C-C-P(O)Ph_2), 144.09 (2 peaks, *ipso*-Ph).

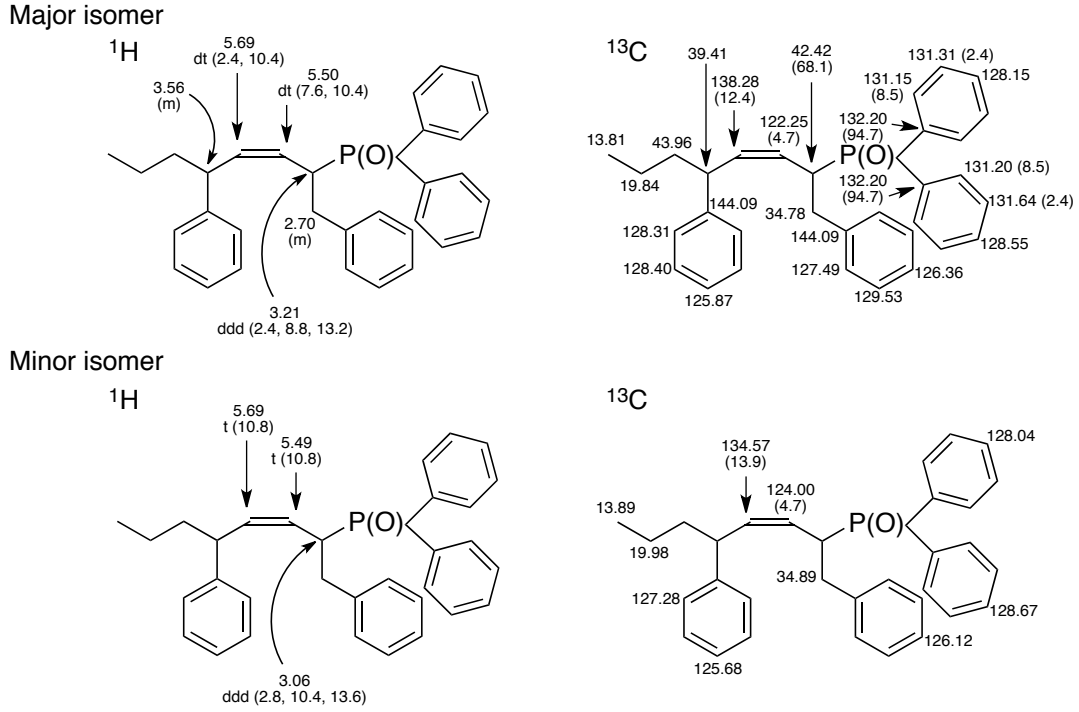
Minor isomer: ^{1}H NMR (only characteristic peaks are shown) δ 0.81-0.88 (m, 2H, alkyl-H), 3.06 (ddd, *J* = 2.8, 10.4, 13.6 Hz, 1H, CH=CH-CH(Bn)-P(O)Ph_2), 5.49 (t, *J* = 10.8 Hz, 1H, CH=CH-CH(Bn)-P(O)Ph_2), 5.69 (t, *J* = 10.8 Hz, 1H, CH=CH-CH(Bn)-P(O)Ph_2).

^{13}C NMR (only characteristic peaks are shown) δ 13.89, 19.98, 34.89, 124.00 (d, *J* = 4.7 Hz, -C=C-C-P(O)Ph_2), 125.68 (*p*-Ph), 126.12 (*p*-Ph), 127.28 (2 carbons, *o*-Ph), 128.04 (*p*-P(O)Ph_2), 128.67 (*p*-P(O)Ph_2), 134.57 (d, *J* = 13.9 Hz, -C=C-C-P(O)Ph_2).

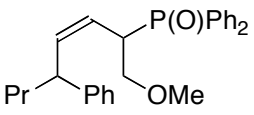
IR (neat) 3081 (Ar), 3058 (Ar), 3026 (Ar), 2953, 2927, 2867, 1601 (C=C), 1493, 1452, 1438, 1176 (P=O), 1118, 1103, 744, 722, 695 cm^{-1} for a 78:22 mixture of diastereoisomers.

HRMS (ESI) Calcd for $C_{32}H_{33}OPNa$ $[M+Na]^+$: 487.2161. Found: 487.2162 for a 78:22 mixture of diastereoisomers.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



A 60:40 diastereomeric mixture of [(*Z*)-1-methoxy-5-phenyl-3-octen-2-yl]diphenylphosphine oxide (11).



To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (59.3 mg, 0.200 mmol) and

$FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.330 mL, 1.20 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, chloromethyl methyl ether (0.075 mL, 1.00 mmol) and HMPA (0.330 mL, 2.00 mmol) were added. After the reaction mixture was heated in an oil bath maintained at 50 °C for 12 h, the reaction was terminated at room temperature by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity was 60:40. The crude oil was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (59.6 mg, 71%) as an oil and of the same diastereomeric composition observed for a crude sample.

Major isomer: ^{1}H NMR δ 0.87 (t, *J* = 7.2 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$), 1.25 (m, 2H, alkyl-H), 1.61 (m, 2H, alkyl-H), 2.70 (br d, *J* = 10.8 Hz, 1H, -C$\underline{H}$-CH$_2$-OMe), 3.24 (s, 3H, OC$\underline{H}_3$), 3.45-3.82 (m, 3H, -C$\underline{H}_2$-OMe and C$\underline{H}$Ph), 5.57 (dt, *J* = 8.0, 10.4 Hz, 1H, -CH=C$\underline{H}$-CH-P(O)Ph$_2$), 5.83 (br t, *J* = 10.4 Hz, 1H, -C$\underline{H}$=CH-CH-P(O)Ph$_2$), 7.02-7.92 (m, 15H, Ph-H).

^{13}C NMR δ 14.02, 20.44, 38.56, 41.25 (d, *J* = 64.3 Hz, -C=C-$\underline{C}$-P(O)Ph$_2$), 43.63, 58.85, 71.36, 122.15 (d, *J* = 5.5 Hz, -C=$\underline{C}$-C-P(O)Ph$_2$), 125.98 (*p*-Ph), 127.49 (2 carbon, *o*-Ph), 128.38 (*p*-P(O)Ph$_2$), 128.48 (*p*-P(O)Ph$_2$), 128.52 (2 carbons, *m*-Ph), 130.95 (d, *J* = 13.9 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.08 (d, *J* = 13.9 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.48 (d, *J* = 3.1 Hz, 2 carbons, *m*-P(O)Ph$_2$), 131.50 (d, *J* = 2.3 Hz, 2 carbons, *m*-P(O)Ph$_2$), 132.60 (d, *J* = 95.0 Hz, 2 peaks, *ipso*-P(O)Ph$_2$), 138.48 (d, *J* = 11.6 Hz, -$\underline{C}$=C-C-P(O)Ph$_2$), 144.66 (*ipso*-Ph).

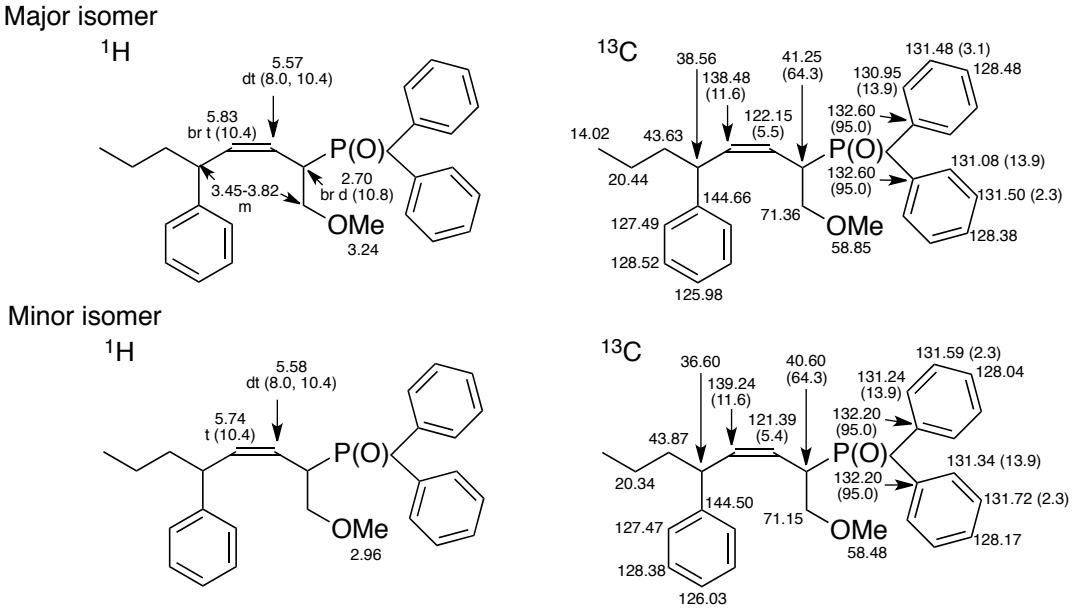
Minor isomer: ^{1}H NMR (only characteristic peaks are shown) δ 0.73 (t, *J* = 7.2 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$), 1.04 (m, 2H, alkyl-H), 1.42 (m, 2H, alkyl-H), 2.96 (s, 3H, OC$\underline{H}_3$), 5.58 (dt, *J* = 8.0, 10.4 Hz, 1H, -CH=C$\underline{H}$-CH-P(O)Ph$_2$), 5.74 (t, *J* = 10.4 Hz, 1H, -C$\underline{H}$=CH-CH-P(O)Ph$_2$).

^{13}C NMR (only characteristic peaks are shown) δ 20.34, 36.60, 40.60 (d, *J* = 64.3 Hz, -C=C-$\underline{C}$-P(O)Ph$_2$), 43.87, 58.48, 71.15, 121.39 (d, *J* = 5.4 Hz, -C=$\underline{C}$-C-P(O)Ph$_2$), 126.03 (*p*-Ph), 127.47 (2 carbons, *o*-Ph), 128.04 (*p*-P(O)Ph$_2$), 128.17 (*p*-P(O)Ph$_2$), 128.38 (2 carbons, *m*-Ph), 131.24 (d, *J* = 13.9 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.34 (d, *J* = 13.9 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.59 (d, *J* = 2.3 Hz, 2 carbons, *m*-P(O)Ph$_2$), 131.72 (d, *J* = 2.3 Hz, 2 carbons, *m*-P(O)Ph$_2$), 132.20 (d, *J* = 95.0 Hz, 2 peaks, *ipso*-P(O)Ph$_2$), 139.24 (d, *J* = 11.6 Hz, -$\underline{C}$=C-C-P(O)Ph$_2$), 144.50 (*ipso*-Ph).

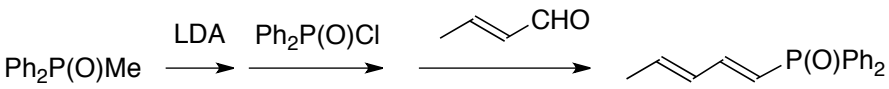
IR (neat) 3077 (Ar), 3058 (Ar), 3025 (Ar), 2955, 2928, 2871, 1600 (C=C), 1492, 1453, 1438, 1309, 1187 (P=O), 1117, 750, 722, 699, 664 cm^{-1} for a 60:40 mixture of diastereoisomers.

HRMS (ESI) Calcd for $C_{27}H_{31}PO_2Na$ $[M+Na]^+$: 441.1954. Found: 441.1957 for a 60:40 mixture of diastereoisomers.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



[(1*E*,3*E*)-1,3-Pentadienyl]diphenylphosphine oxide (12).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a solution of diisopropylamine (1.40 mL, 9.96 mmol) in THF (12 mL) was added *n*-BuLi (5.90 mL, 1.64 M in hexane, 9.68 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and methyl(diphenyl)phosphine oxide (1.04 g, 4.81 mmol) in THF (3 mL) was added. The mixture was stirred at –78 °C for 15 min and diphenylphosphinic chloride (0.900 mL, 4.84 mmol) was added at that temperature. After stirring for 10 min, (*E*)-2-butenal (0.360 mL, 4.04 mmol) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of aqueous saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (1.08 g, quant.) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 1.83 (d, *J* = 6.8 Hz, 3H, alkyl-Me), 6.06 (dq, *J* = 14.8, 6.8 Hz, 1H, -C<u>H</u>=CH-CH=CH-P(O)Ph_2), 6.15 (dd, *J* = 16.4, 23.2 Hz, 1H, -CH=CH-CH=C<u>H</u>-P(O)Ph_2), 6.23 (dd, *J* = 10.4, 14.8 Hz, 1H, -CH=C<u>H</u>-CH=CH-P(O)Ph_2), 7.03 (dt, *J* = 10.4, 16.4 Hz, 1H, -CH=CH-C<u>H</u>=CH-P(O)Ph_2), 7.42-7.54 (m, 6H, Ph-H), 7.70 (dd, *J* = 7.6, 12.0 Hz, 4H, Ph-H).

^{13}C NMR δ 18.40, 119.74 (d, *J* = 105.3 Hz, -C=C-C=<u>C</u>-P(O)Ph_2), 128.50 (d, *J* = 11.6 Hz, 4 carbons, *o*-P(O)Ph_2), 131.07 (d, *J* = 20.9 Hz, -C=C-<u>C</u>=C-P(O)Ph_2), 131.34 (d, *J* = 9.3 Hz, 4 carbons, *m*-P(O)Ph_2),

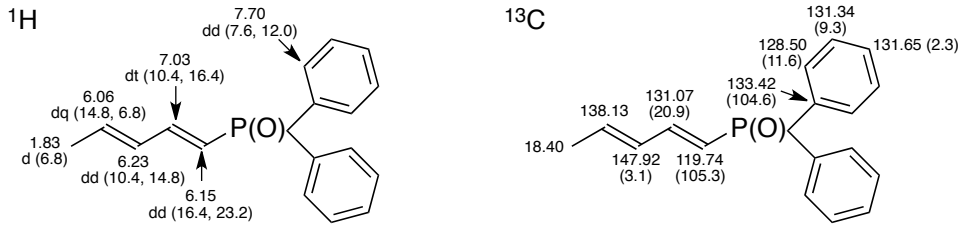
131.65 (d, J = 2.3 Hz, 2 carbons, *p*-P(O)Ph_2), 133.42 (d, J = 104.6 Hz, 2 carbons, *ipso*-P(O)Ph_2), 138.13 (-C=C-C=C-P(O)Ph_2), 147.92 (d, J = 3.1 Hz, -C=C-C=C-P(O)Ph_2).

IR (KBr) 3075 (Ar), 3055 (Ar), 3014 (Ar, C=C-H), 2987, 2956, 1646 (C=C-C=C), 1585 (C=C-C=C), 1439, 1183 (P=O), 1012, 816, 693, 530, 507 cm^{-1}.

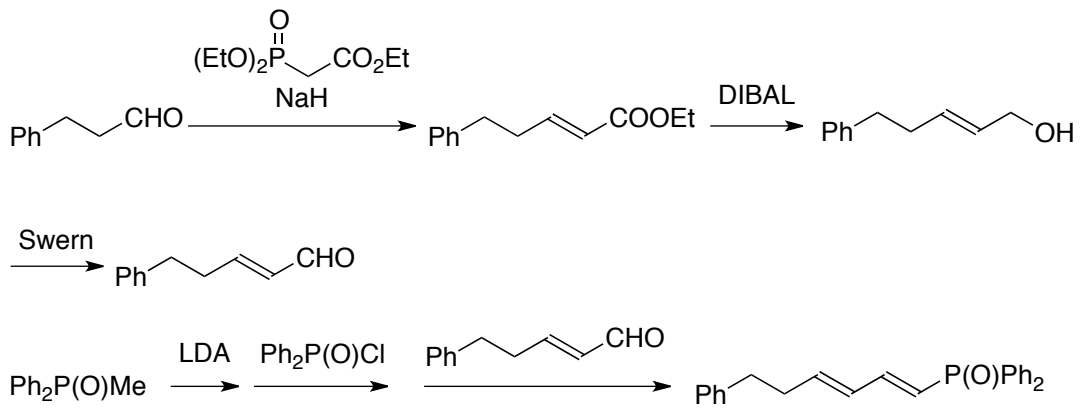
HRMS (ESI) Calcd for $C_{17}H_{17}NaOP$ $[M+Na]^+$: 291.0909. Found : 291.0908.

M.p. 162-163 °C.

The *E*,*E*-diene stereochemistry was confirmed by ^1H NMR coupling constants.



[(1*E*,3*E*)-6-Phenyl-1,3-hexadienyl]diphenylphosphine oxide (13).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a suspension of NaH (520 mg of a 60% suspension in mineral oil, 13.0 mmol) in THF (20 mL) was added triethyl phosphonoacetate (2.40 mL, 12.0 mmol) at 0 °C under argon. After the reaction mixture was stirred at room temperature for 10 min, it was cooled to 0 °C and 3-phenylpropanal (1.32 mL, 10.0 mmol) in THF (10 mL) was added dropwise. The reaction mixture was allowed to warm up to room temperature over 1 h and quenched with water (50 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford ethyl (*E*)-5-phenyl-2-pentenoate (1.60 g, 78%) as an oil and as a single olefinic isomer.

To a solution of ethyl (*E*)-5-phenyl-2-pentenoate (1.60 g, 7.84 mmol) in CH_2Cl_2 (15 mL) was added DIBAL (22.6 mL, 1.04 M solution in hexane, 23.5 mmol) at –78 °C under argan. The reaction mixture was allowed to warm up to 0 °C over 5 h and quenched with 1 N HCl solution. The organic layer was

separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with saturated aqueous $NaHCO_3$ solution, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford (*E*)-5-phenyl-2-penten-1-ol (1.16 g, 91%) as an oil.

To a solution of oxalyl chloride (0.860 mL, 10.0 mmol) in CH_2Cl_2 (20 mL) was added DMSO (0.960 mL, 13.5 mmol) in CH_2Cl_2 (5 mL) dropwise at –78 °C. After the solution was stirred at –78 °C for 20 min, (*E*)-5-phenyl-2-penten-1-ol (811 mg, 5.00 mmol) in CH_2Cl_2 (5 mL) was added dropwise and the reaction mixture was stirred at –78 °C for 1 h. Then, Et_3N (5.10 mL, 36.5 mmol) was added and the reaction mixture was allowed to warm up to 0 °C. After the reaction mixture was stirred at 0 °C for 20 min, aqueous saturated NH_4Cl solution was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give (*E*)-5-phenyl-2-pentenal (832 mg, 100%) as a yellow oil, which was essentially pure by ^{1}H NMR analysis and was used in the next step without purification.

To a solution of diisopropylamine (0.640 mL, 4.55 mmol) in THF (7 mL) was added *n*-BuLi (3.65 mL, 1.64 M solution in hexane, 5.98 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and methyl(diphenyl)phosphine oxide (629 mg, 2.91 mmol) in THF (2 mL) was added. The mixture was stirred at –78 °C for 15 min and diphenylphosphinic chloride (0.560 mL, 2.91 mmol) was added at that temperature. After stirring for 10 min, the above (*E*)-5-phenyl-2-pentenal (398 mg, 2.49 mmol) in THF (3 mL) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of aqueous saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (739 mg, 83%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 2.46 (dt, *J* = 6.8, 7.6 Hz, 2H, alkyl-H), 2.71 (t, *J* = 7.6 Hz, 2H, benzyl-H), 6.04 (dt, *J* = 15.2, 6.8 Hz, 1H, -C<u>H</u>=CH-CH=CH-P(O)Ph_2), 6.17 (dd, *J* = 16.8, 22.8 Hz, 1H, -CH=CH-CH=C<u>H</u>-P(O)Ph_2), 6.25 (dd, *J* = 11.2, 15.2 Hz, 1H, -CH=C<u>H</u>-CH=CH-P(O)Ph_2), 7.03 (dt, *J* = 11.2, 16.8 Hz, 1H, -CH=CH-C<u>H</u>=CH-P(O)Ph_2), 7.11-7.21 (m, 3H, Ph-H), 7.26 (t, *J* = 7.6 Hz, 2H, Ph-H), 7.38-7.53 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.64-7.76 (m, 4H, -P(O)<u>Ph</u>$_2$).

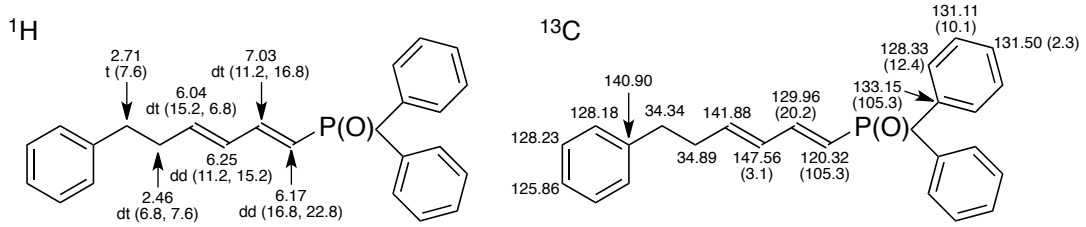
^{13}C NMR δ 34.34, 34.89, 120.32 (d, *J* = 105.3 Hz, -C=C-C=<u>C</u>-P(O)Ph_2), 125.86 (*p*-Ph), 128.18 (2 carbons, *o*-Ph), 128.23 (2 carbons, *m*-Ph), 128.33 (d, *J* = 12.4 Hz, 4 carbons, *o*-P(O)Ph_2), 129.96 (d, *J* = 20.2 Hz, -C=C-<u>C</u>=C-P(O)Ph_2), 131.11 (d, *J* = 10.1 Hz, 4 carbons, *m*-P(O)Ph_2), 131.50 (d, *J* = 2.3 Hz, 2 carbons, *p*-P(O)Ph_2), 133.15 (d, *J* = 105.3 Hz, 2 carbons, *ipso*-P(O)Ph_2), 140.90 (*ipso*-Ph), 141.88 (-<u>C</u>=C-C=C-P(O)Ph_2), 147.56 (d, *J* = 3.1 Hz, -C=<u>C</u>-C=C-P(O)Ph_2).

IR (KBr) 3076 (Ar), 3056 (Ar), 3021 (Ar and C=CH), 2988, 2846, 1644 (C=C-C=C), 1584 (C=C-C=C), 1310, 1179 (P=O), 1009, 812, 710, 694, 518 cm^{-1}.

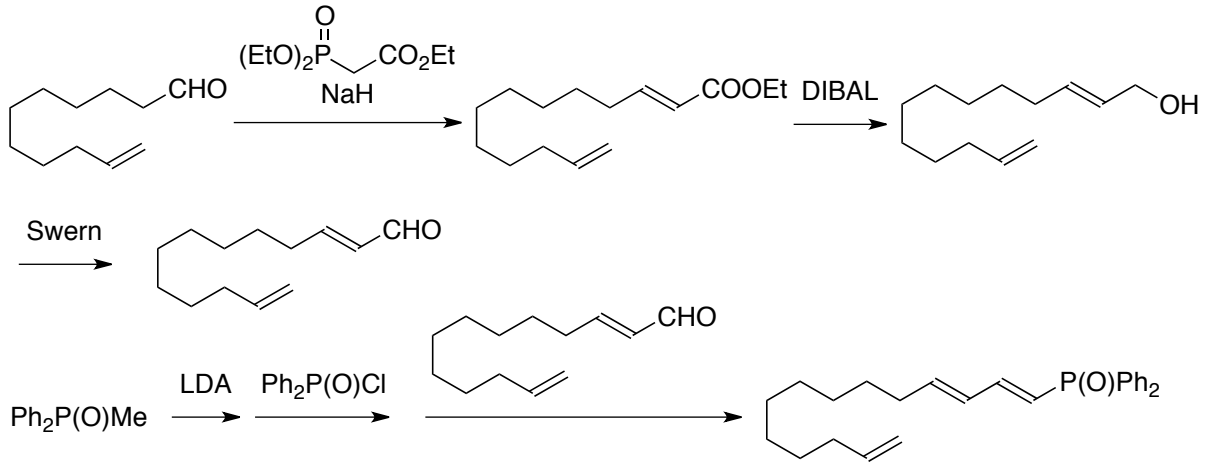
HRMS (ESI) Calcd for $C_{24}H_{23}PONa$ $[M+Na]^+$: 381.1379. Found: 381.1389.

M.p. 89-90 °C.

The *E*,*E*-diene stereochemistry was confirmed by ^{1}H NMR coupling constants.



[(1*E*,3*E*)-1,3,13-Tetradecatrienyl]diphenylphosphine oxide (14).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a suspension of NaH (520 mg of a 60% suspension in mineral oil, 13.0 mmol) in THF (20 mL) was added triethyl phosphonoacetate (2.40 mL, 12.0 mmol) at 0 °C under argon. After the reaction mixture was stirred at room temperature for 10 min, it was cooled to 0 °C and 10-undecanal (1.98 mL, 10.0 mmol) in THF (20 mL) was added dropwise. The reaction mixture was allowed to warm up to room temperature over 1 h and quenched with water (50 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford ethyl (*E*)-2,12-tridecadienoate (1.06 g, 45%) as an oil and as a single olefinic isomer.

To a solution of ethyl (*E*)-2,12-tridecadienoate (1.06 g, 4.46 mmol) in CH_2Cl_2 (20 mL) was added DIBAL (12.9 mL, 1.04 M solution in hexane, 13.4 mmol) at –78 °C under argon. The reaction mixture was allowed to warm up to 0 °C over 5 h and quenched with 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with saturated aqueous $NaHCO_3$ solution, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford (*E*)-2,12-tridecadien-1-ol (1.23 g, 100%) as an oil and as a single olefinic isomer.

To a solution of oxalyl chloride (1.08 mL, 12.6 mmol) in CH_2Cl_2 (13 mL) was added DMSO (1.96 g,

25.1 mmol) in CH_2Cl_2 (2 mL) dropwise at –78 °C. After the solution was stirred at –78 °C for 20 min, (*E*)-2,12-tridecadien-1-ol (1.23 g, 6.28 mmol) in CH_2Cl_2 (5 mL) was added dropwise and the reaction mixture was stirred at –78 ºC for 1 h. Then, Et_3N (5.23 mL, 37.7 mmol) was added and the reaction was allowed to warm up to 0 °C. After the reaction mixture was stirred at 0 ºC for 20 min, aqueous saturated NH_4Cl solution was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give (*E*)-trideca-2,12-dienal (1.09 g, 89%) as a yellowish oil, which was essentially pure by ^{1}H NMR analysis and was used in the next step without purification.

To a solution of diisopropylamine (1.45 mL, 10.3 mmol) in THF (15 mL) was added *n*-BuLi (8.23 mL 1.64 M solution in hexane, 13.5 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and methyl(diphenyl)phosphine oxide (1.46 g, 6.73 mmol) in THF (5 mL) was added. The mixture was stirred at –78 °C for 15 min and diphenylphosphinic chloride (1.28 mL, 6.73 mmol) was added at that temperature. After stirring for 10 min, the above (*E*)-trideca-2,12-dienal (1.09 g, 5.61 mmol) in THF (3 mL) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of aqueous saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (1.70 g, 81%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 1.28-1.40 (m, 12H, -CH_2=CHCH_2C$_6$H$_{12}$CH_2), 2.04 (q, *J* = 7.2 Hz, 2H, allylic-H), 2.15 (q, *J* = 7.2 Hz, 2H, allylic-H), 4.92 (d, *J* = 10.4 Hz, 1H, CH_2=CH-), 4.98 (d, *J* = 17.2 Hz, 1H, CH_2=CH-), 5.80 (ddt, *J* = 10.4, 17.2, 7.2 Hz, 1H, CH_2=CH-), 6.03 (dt, *J* = 15.2, 7.2 Hz, 1H, -CH=CH-CH=CHP(O)Ph_2), 6.16 (dd, *J* = 16.8, 22.8 Hz, 1H, -CH=CH-CH=CHP(O)Ph_2), 6.23 (dd, *J* = 10.8, 15.2 Hz, 1H, -CH=CH-CH=CHP(O)Ph_2), 7.03 (dt, *J* = 10.8, 16.8 Hz, 1H, -CH=CH-CH=CHP(O)Ph_2), 7.42-7.52 (m, 6H, -P(O)Ph_2), 7.70 (dd, *J* = 7.2, 12.0 Hz, 4H, -P(O)Ph_2).

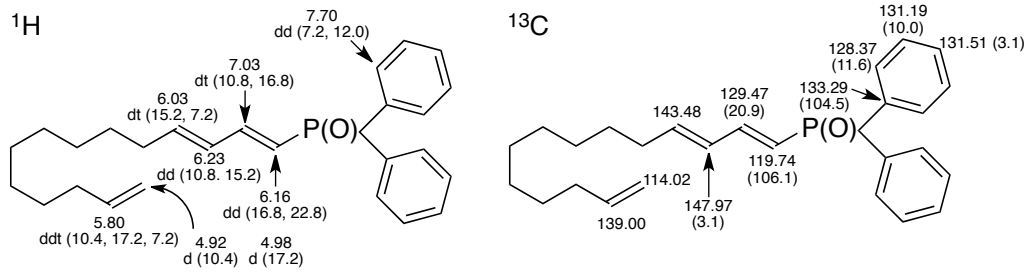
^{13}C NMR δ 28.56, 28.77, 28.94, 29.00, 29.22 (2 peaks), 32.66, 33.63, 114.02 (H_2C=CH-), 119.74 (d, *J* = 106.1 Hz, -C=C-C=C-P(O)Ph_2), 128.37 (d, *J* = 11.6 Hz, 4 carbons, *o*-P(O)Ph_2), 129.47 (d, *J* = 20.9 Hz, -C=C-C=C-P(O)Ph_2), 131.19 (d, *J* = 10.0 Hz, 4 carbons, *m*-P(O)Ph_2), 131.51 (d, *J* = 3.1 Hz, 2 carbons, *p*-P(O)Ph_2), 133.29 (d, *J* = 104.5 Hz, 2 carbons, *ipso*-P(O)Ph_2), 139.00 (H_2C=CH-), 143.48 (-C=C-C=C-P(O)Ph_2), 147.97 (d, *J* = 3.1 Hz, -C=C-C=C-P(O)Ph_2).

IR (KBr) 3076 (Ar), 3057 (Ar and C=CH), 2980, 2851, 1643 (C=C-C=C), 1585 (C=C-C=C), 1439, 1183 (P=O), 1099, 919, 824, 568, 529, 500 cm^{-1}.

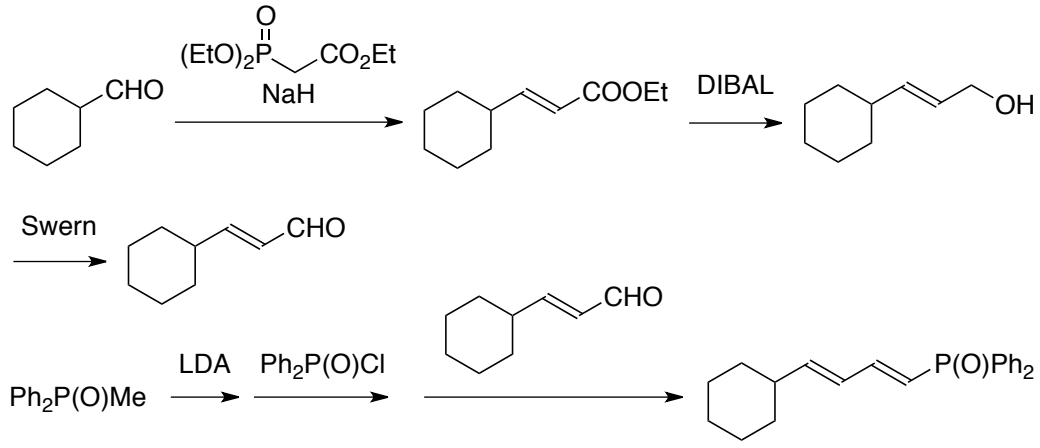
HRMS (ESI) Calcd for $C_{26}H_{33}PONa$ $[M+Na]^+$: 415.2161. Found: 415.2163.

M.p. 73-75 °C.

The *E*,*E*-diene stereochemistry was confirmed by ^{1}H NMR coupling constants.



[(1*E*,3*E*)-4-Cyclohexyl-1,3-butadienyl]diphenylphosphine oxide (15).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a suspension of NaH (780 mg of a 60% suspension in mineral oil, 19.5 mmol) in THF (50 mL) was added triethyl phosphonoacetate (3.60 mL, 18.0 mmol) at 0 °C under argon. After the reaction mixture was stirred at room temperature for 10 min, it was cooled to 0 °C and cyclohexanecarbaldehyde (1.68 g, 15.0 mmol) in THF (10 mL) was added dropwise. The reaction mixture was allowed to warm up to room temperature over 1 h and quenched with water (50 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford ethyl (*E*)-3-cyclohexyl-2-propenoate (3.12 g, 100%) as an oil and as a single olefinic isomer.

To a solution of ethyl (*E*)-3-cyclohexyl-2-propenoate (2.73 g, 15.0 mmol) in CH_2Cl_2 (50 mL) was added DIBAL (43.7 mL, 1.03 M solution in hexane, 45.0 mmol) at –78 °C under argon. The reaction mixture was allowed to warm up to 0 °C over 5 h and quenched with 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with saturated aqueous $NaHCO_3$ solution, water, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford (*E*)-3-cyclohexyl-2-propen-1-ol (1.88 g, 89%) as an oil.

To a solution of oxalyl chloride (0.515 mL, 6.00 mmol) in CH_2Cl_2 (20 mL) was added DMSO (630 mg,

8.10 mmol) in CH_2Cl_2 (2 mL) dropwise at –78 °C. After the solution was stirred at –78 °C for 20 min, (*E*)-3-cyclohexyl-2-propen-1-ol (420 mg, 3.00 mmol) in CH_2Cl_2 (2 mL) was added dropwise and the reaction mixture was stirred at –78 °C for 1 h. Then, Et_3N (3.04 mL, 22.0 mmol) was added and the reaction mixture was allowed to warm up to 0 °C. After the reaction mixture was stirred at 0 °C for 20 min, aqueous saturated NH_4Cl solution was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give (*E*)-3-cyclohexyl-2-propenal (551 mg, 100%) as a yellow oil, which was essentially pure by ^{1}H NMR analysis and was used in the next step without purification.

To a solution of diisopropylamine (0.300 mL, 2.13 mmol) in THF (10 mL) was added *n*-BuLi (1.70 mL, 1.64 M solution in hexane, 2.76 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and methyl(diphenyl)phosphine oxide (298 mg, 1.38 mmol) in THF (3 mL) was added. The mixture was stirred at –78 °C for 15 min and diphenylphosphinic chloride (0.262 mL, 1.38 mmol) was added at that temperature. After stirring for 10 min, the above (*E*)-3-cyclohexyl-2-propenal (159 mg, 1.15 mmol) in THF (2.0 mL) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of aqueous saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (261 mg, 68%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 1.05-1.34 (m, 5H, alkyl-H), 1.64-1.74 (m, 5H, alkyl-H), 2.04 (m, 1H, alkyl-H), 5.94 (dd, *J* = 6.8, 15.2 Hz, 1H, -C<u>H</u>=CH-CH=CH-P(O)Ph_2), 6.18 (dd, *J* = 17.2, 20.4 Hz, 1H, -CH=CH-CH=C<u>H</u>-P(O)Ph_2), 6.19 (dd, *J* = 10.4, 15.2 Hz, 1H, -CH=C<u>H</u>-CH=CH-P(O)Ph_2), 7.00 (dt, *J* = 10.4, 17.2 Hz, 1H, -CH=CH-C<u>H</u>=CH-P(O)Ph_2), 7.45-7.52 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.69-7.73 (m, 4H, -P(O)<u>Ph</u>$_2$).

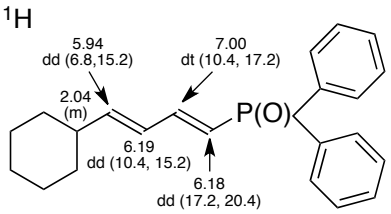
^{13}C NMR δ 25.72 (2 carbons), 25.93, 32.18 (2 carbons), 40.79, 119.96 (d, *J* = 105.3 Hz, -C=C-C=<u>C</u>-P(O)Ph_2), 127.04 (d, *J* = 20.9 Hz, -C=C-<u>C</u>=C-P(O)Ph_2), 128.40 (d, *J* = 11.6 Hz, 4 carbons, *o*-P(O)Ph_2), 131.27 (d, *J* = 9.3 Hz, 4 carbons, *m*-P(O)Ph_2), 131.55 (2 carbons, *p*-P(O)Ph_2), 133.37 (d, *J* = 105.3 Hz, 2 carbons, *ipso*-P(O)Ph_2), 148.39 (-<u>C</u>=C-C=C-P(O)Ph_2), 148.85 (-C=<u>C</u>-C=C-P(O)Ph_2).

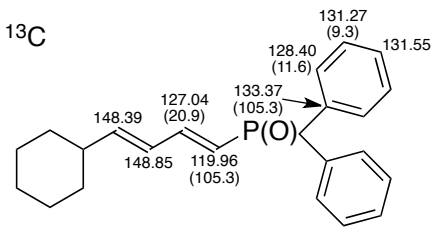
IR (KBr) 3077 (Ar), 3053 (Ar), 3026 (Ar and C=CH), 2990, 2921, 2848, 1639 (C=C-C=C), 1574 (C=C-C=C), 1439, 1181 (P=O), 1013, 699, 554, 504 cm^{-1}.

HRMS (ESI) Calcd for $C_{22}H_{25}PONa$ $[M+Na]^+$: 359.1535. Found: 359.1543.

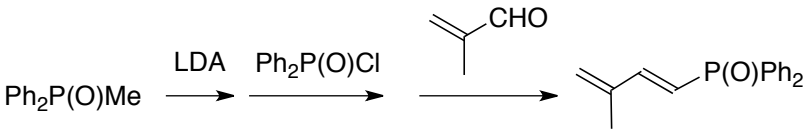
M.p. 124-125 °C.

The *E*,*E*-diene stereochemistry was confirmed by ^{1}H NMR coupling constants.





[(*E*)-3-Methyl-1,3-butadienyl]diphenylphosphine oxide (16).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a solution of diisopropylamine (0.514 mL, 3.66 mmol) in THF (9 mL) was added *n*-BuLi (2.91 mL 1.64 M solution in hexane, 4.80 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and methyl(diphenyl)phosphine oxide (519 mg, 2.40 mmol) in THF (3 mL) was added. The mixture was stirred at –78 °C for 15 min and diphenylphosphinic chloride (0.450 mL, 2.40 mmol) was added at that temperature. After stirring for 10 min, methacrolein (0.170 mL, 2.00 mmol) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of aqueous saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (326 mg, 61%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 1.93 (s, 3H, Me), 5.27 (s, 1H, H_2C=C(Me)-), 5.31 (s, 1H, H_2C=C(Me)-), 6.27 (dd, *J* = 17.6, 21.6 Hz, 1H, -CH=CHP(O)Ph_2), 7.16 (br t, *J* = 17.6 Hz, 1H, -CH=CHP(O)Ph_2), 7.45-7.52 (m, 6H, -P(O)Ph_2), 7.70-7.75 (m, 4H, -P(O)Ph_2).

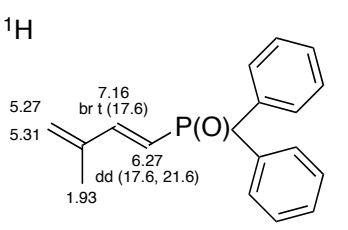
^{13}C NMR δ 17.84, 119.47 (d, *J* = 103.0 Hz, -C=C-C=C-P(O)Ph_2), 123.34 (-C=C-C=C-P(O)Ph_2), 128.39 (d, *J* = 12.4 Hz, 4 carbons, *o*-P(O)Ph_2), 131.17 (d, *J* = 10.0 Hz, 4 carbons, *m*-P(O)Ph_2), 131.60 (d, *J* = 2.3 Hz, 2 carbons, *p*-P(O)Ph_2), 132.97 (d, *J* = 104.6 Hz, 2 carbons, *ipso*-P(O)Ph_2), 140.71 (d, *J* = 17.8 Hz, -C=C-C=C-P(O)Ph_2), 149.89 (d, *J* = 3.1 Hz, -C=C-C=C-P(O)Ph_2).

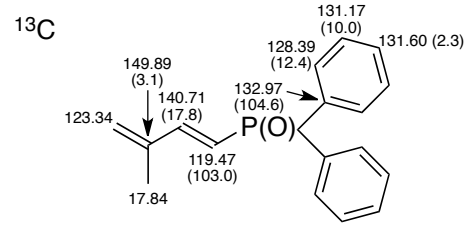
IR (KBr) 3052 (Ar and C=CH), 2918, 2950, 1621 (C=C-C=C), 1582 (C=C-C=C), 1439, 1181 (P=O), 933, 820, 720, 556 cm^{-1}.

HRMS (ESI) Calcd for $C_{17}H_{17}PONa$ $[M+Na]^+$: 291.0909. Found: 291.0918.

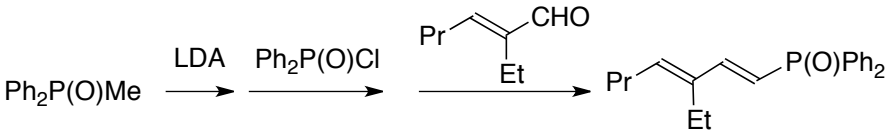
M.p. 164-166 °C.

The *E*-stereochemistry was confirmed by ^{1}H NMR coupling constants.





[(1*E*,3*E*)-3-Ethyl-1,3-heptadienyl]diphenylphosphine oxide (17).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a solution of diisopropylamine (0.514 mL, 3.66 mmol) in THF (10 mL) was added *n*-BuLi (2.91 mL 1.65 M solution in hexane, 4.80 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and methyl(diphenyl)phosphine oxide (519 mg, 2.40 mmol) in THF (3 mL) was added. The mixture was stirred at –78 °C for 15 min and diphenylphosphinic chloride (0.450 mL, 2.40 mmol) was added at that temperature. After stirring for 10 min, (*E*)-2-ethyl-2-hexenal (0.300 mL, 2.00 mmol) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of aqueous saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na_2SO_4, and concentrated *in vacuo* to a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (355 mg, 55%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 0.91 (t, *J* = 7.2 Hz, 3H, alkyl-Me), 1.03 (t, *J* = 7.2 Hz, 3H, alkyl-Me), 1.42 (sextet, *J* = 7.2 Hz, 2H, alkyl-H), 2.15 (q, *J* = 7.2 Hz, 2H, alkyl-H), 2.31 (q, *J* = 7.2 Hz, 2H, alkyl-H), 5.75 (t, *J* = 7.2 Hz, 1H, PrC<u>H</u>=C(Et)-), 6.17 (dd, *J* = 17.6, 22.0 Hz, 1H, -CH=C<u>H</u>-P(O)Ph_2), 6.98 (br t, *J* = 17.6 Hz, 1H, -C<u>H</u>=CH-P(O)Ph_2), 7.44-7.51 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.64-7.78 (m, 4H, -P(O)<u>Ph</u>$_2$).

Irradiation of the proton at δ 5.75 ppm (PrC<u>H</u>=C(Et)-) showed 2.7% NOE enhancement to that at δ 6.98 ppm (-C<u>H</u>=CH-P(O)Ph_2).

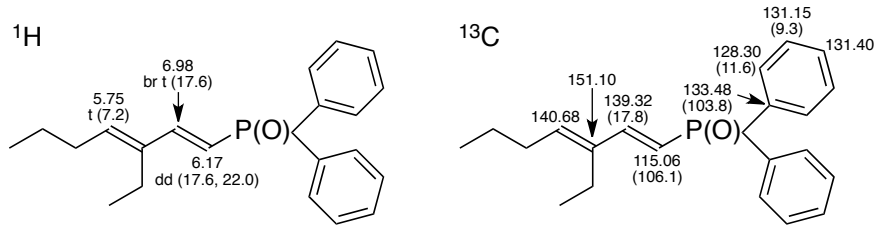
^{13}C NMR δ 13.25, 19.42, 22.22, 30.31, 33.67, 115.06 (d, *J* = 106.1 Hz, -C=C-C=<u>C</u>-P(O)Ph_2), 128.30 (d, *J* = 11.6 Hz, 4 carbons, *o*-P(O)Ph_2), 131.15 (d, *J* = 9.3 Hz, 4 carbons, *m*-P(O)Ph_2), 131.40 (2 carbons, *p*-P(O)Ph_2), 133.48 (d, *J* = 103.8 Hz, 2 carbons, *ipso*-P(O)Ph_2), 139.32 (d, *J* = 17.8 Hz, -C=C-<u>C</u>=C-P(O)Ph_2), 140.68 (-<u>C</u>=C-C=C-P(O)Ph_2), 151.10 (-C=<u>C</u>-C=C-P(O)Ph_2).

IR (KBr) 3065 (Ar), 3051 (Ar and C=CH), 3002 (Ar), 2967, 2926, 2857, 1631 (C=C-C=C), 1588 (C=C-C=C), 1439, 1380, 1177 (P=O), 1071, 997, 692, 584, 516 cm^{-1}.

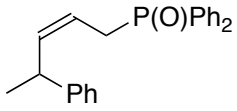
HRMS (ESI) Calcd for $C_{21}H_{25}PONa$ $[M+Na]^+$: 347.1535. Found: 347.1538.

M.p. 103-105 °C.

The *E*,*E*-diene stereochemistry was confirmed by ^{1}H NMR NOE experiments and ^{1}H NMR coupling constants.



[(*Z*)-4-Phenyl-2-pentenyl]diphenylphosphine oxide (18).



To a solution of [(1*E*,3*E*)-1,3-pentadienyl]diphenylphosphine oxide (**12**) (53.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.460 mL, 0.87 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (69.0 mg, 92%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 1.16 (d, *J* = 6.8 Hz, 3H, alkyl-Me), 3.06-3.30 (m, 2H, -CH=CHC<u>H</u>$_2$P(O)Ph$_2$), 3.61 (dq, *J* = 10.4, 6.8 Hz, 1H, C<u>H</u>Ph), 5.50 (dq, *J* = 10.4, 6.8 Hz, 1H, -CH=C<u>H</u>CH$_2$P(O)Ph$_2$), 5.72 (br t, *J* = 10.4 Hz, 1H, -C<u>H</u>=CHCH$_2$POPh$_2$), 7.11 (d, *J* = 7.2 Hz, 2H, Ph-H), 7.15 (t, *J* = 7.2 Hz, 1H, Ph-H), 7.24 (t, *J* = 7.2 Hz, 2H, Ph-H), 7.38-7.52 (m, 6H, -PO<u>Ph</u>$_2$), 7.68-7.76 (m, 4H, -PO<u>Ph</u>$_2$).

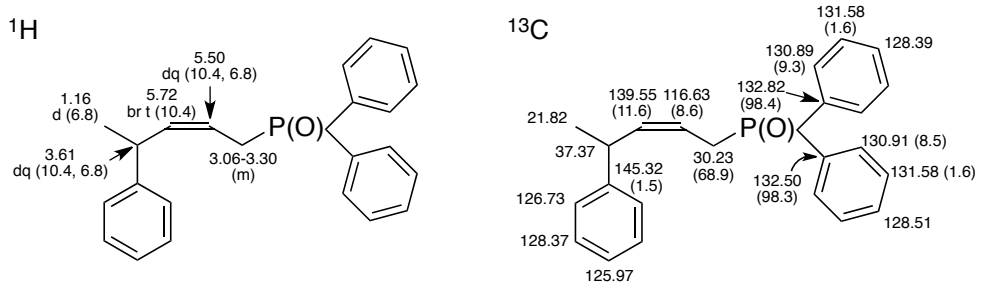
^{13}C NMR δ 21.82, 30.23 (d, *J* = 68.9 Hz, -C=C-<u>C</u>-P(O)Ph$_2$), 37.37, 116.63 (d, *J* = 8.6 Hz, -C=<u>C</u>-C-P(O)Ph$_2$), 125.97 (*p*-Ph), 126.73 (2 carbons, *o*-Ph), 128.37 (2 carbons, *m*-Ph), 128.39 (*p*-P(O)Ph$_2$), 128.51 (*p*-P(O)Ph$_2$), 130.89 (d, *J* = 9.3 Hz, 2 carbons, *o*-P(O)Ph$_2$), 130.91 (d, *J* = 8.5 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.58 (d, *J* = 1.6 Hz, 2 peaks of 2 carbons each, *m*-P(O)Ph$_2$), 132.50 (d, *J* = 98.3 Hz, *ipso*-P(O)Ph$_2$), 132.82 (d, *J* = 98.4 Hz, *ipso*-P(O)Ph$_2$), 139.55 (d, *J* = 11.6 Hz, -<u>C</u>=C-C-P(O)Ph$_2$), 145.32 (d, *J* = 1.5 Hz, *ipso*-Ph).

IR (KBr) 3077 (Ar), 3055 (Ar), 3021 (Ar and C=CH), 2965, 2873, 1591 (C=C), 1493, 1185 (P=O), 1120, 978, 848, 723, 555, 514 cm^{-1}.

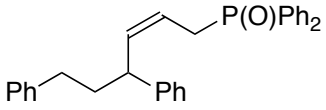
HRMS (ESI) Calcd for $C_{23}H_{23}PONa$ $[M+Na]^+$: 369.1384. Found: 369.1377.

M.p. 102-103 °C.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



[(*Z*)-4,6-Diphenyl-2-hexenyl]diphenylphosphine oxide (19).



To a solution of [(1*E*,3*E*)-6-phenyl-1,3-hexadienyl]diphenylphosphine oxide (**13**) (71.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.310 mL, 1.30 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (63.2 mg, 72%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 1.80 (dq, *J* = 13.2, 7.6 Hz, 1H, alkyl-H), 1.98 (dq, *J* = 13.2, 7.6 Hz, 1H, alkyl-H), 2.43 (t, *J* = 7.6 Hz, 2H, alkyl-H), 3.08 (dd, *J* = 7.6, 16.0 Hz, 2H, -CH=CHC<u>H</u>$_2$P(O)Ph$_2$), 3.40 (dt, *J* = 10.4, 7.6 Hz, 1H, C<u>H</u>Ph), 5.56 (dq, *J* = 10.4, 7.6 Hz, 1H, -CH=C<u>H</u>CH$_2$P(O)Ph$_2$), 5.79 (br t, *J* = 10.4 Hz, 1H, -C<u>H</u>=CHCH$_2$POPh$_2$), 7.08 (t, *J* = 7.2 Hz, 4H, *m*-Ph-H), 7.16 (t, *J* = 7.2 Hz, 1H, *p*-Ph-H), 7.18 (t, *J* = 7.2 Hz, 1H, *p*-Ph-H), 7.22-7.30 (m, 4H, *o*-Ph-H), 7.33-7.52 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.57-7.76 (m, 4H, -P(O)<u>Ph</u>$_2$).

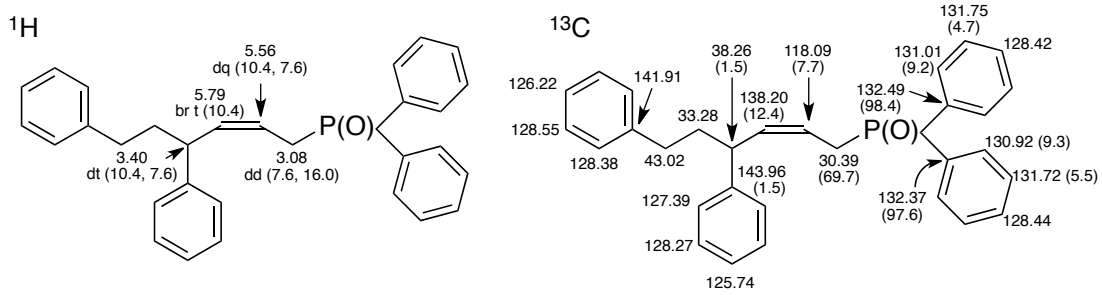
^{13}C NMR δ 30.39 (d, *J* = 69.7 Hz, -C=C-<u>C</u>-P(O)Ph$_2$), 33.28 (PhC-<u>C</u>), 38.26 (d, *J* = 1.5 Hz, -<u>C</u>-C=C-C-P(O)Ph$_2$), 43.02 (Ph<u>C</u>-C), 118.09 (d, *J* = 7.7 Hz, -C=<u>C</u>-C-P(O)Ph$_2$), 125.74 (*p*-Ph), 126.22 (*p*-Ph), 127.39 (2 carbons, *o*-Ph), 128.27 (2 carbons, *m*-Ph), 128.38 (2 carbons, *o*-Ph), 128.42 (*p*-P(O)Ph$_2$), 128.44 (*p*-P(O)Ph$_2$), 128.55 (2 carbons, *m*-Ph), 130.92 (d, *J* = 9.3 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.01 (d, *J* = 9.2 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.72 (d, *J* = 5.5 Hz, 2 carbons, *m*-P(O)Ph$_2$), 131.75 (d, *J* = 4.7 Hz, 2 carbons, *m*-P(O)Ph$_2$), 132.37 (d, *J* = 97.6 Hz, *ipso*-P(O)Ph$_2$), 132.49 (d, *J* = 98.4 Hz, *ipso*-P(O)Ph$_2$) 138.20 (d, *J* = 12.4 Hz, -<u>C</u>=C-C-P(O)Ph$_2$), 141.91 (*ipso*-Ph), 143.96 (d, *J* = 1.5 Hz, *ipso*-Ph at allylic position).

IR (KBr) 3080 (Ar), 3059 (Ar), 3025 (Ar and C=CH), 2938, 1592 (C=C), 1494, 1438, 1190 (P=O), 1120, 697, 663 cm^{-1}.

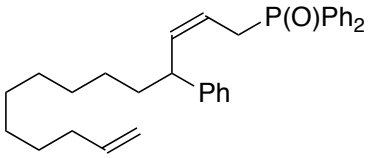
HRMS (ESI) Calcd for $C_{30}H_{29}PONa$ [M+Na]$^+$: 459.1848. Found: 459.1858.

M.p. 89-90 °C.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



[(*Z*)-4-Phenyl-2,13-tetradecadienyl]diphenylphosphine oxide (20).



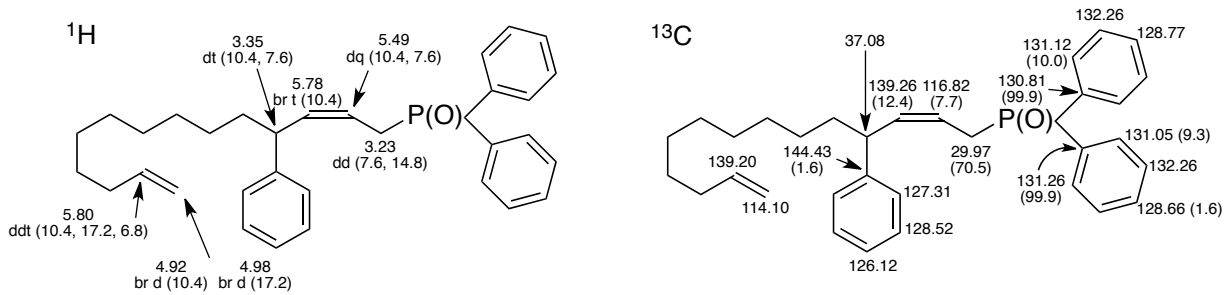
To a solution of [(1*E*,3*E*)-1,3,13-tetradecatrienyl]diphenylphosphine oxide (**14**) (78.5 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.350 mL, 1.30 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (89.3 mg, 95%) as an oil and as a single olefinic isomer.

^{1}H NMR δ 1.01-1.64 (m, 14H, alkyl-H), 2.03 (dt, *J* = 7.6, 6.8 Hz, 2H, CH_2=CHC$\underline{H}_2$-), 3.23 (dd, *J* = 7.6, 14.8 Hz, 2H, -CH=CHC$\underline{H}_2$P(O)Ph_2), 3.35 (dt, *J* = 10.4, 7.6 Hz, 1H, C$\underline{H}$Ph), 4.92 (br d, *J* = 10.4 Hz, 1H, C$\underline{H}_2$=CH-), 4.98 (br d, *J* = 17.2, 1H, C$\underline{H}_2$=CH-), 5.49 (dq, *J* = 10.4, 7.6 Hz, 1H, -CH=C$\underline{H}$CH$_2$P(O)Ph_2), 5.78 (br t, *J* = 10.4 Hz, 1H, -C$\underline{H}$=CHCH$_2$P(O)Ph_2), 5.80 (ddt, *J* = 10.4, 17.2, 6.8 Hz, 1H, CH_2=C$\underline{H}$-), 7.06 (d, *J* = 7.6 Hz, 2H, *o*-Ph-$\underline{H}$), 7.17 (t, *J* = 7.6 Hz, 1H, *p*-Ph-$\underline{H}$), 7.25 (t, *J* = 7.6 Hz, 2H, *m*-Ph-$\underline{H}$), 7.38-7.56 (m, 6H, -P(O)$\underline{Ph}_2$), 7.62-7.72 (m, 4H, -P(O)$\underline{Ph}_2$).

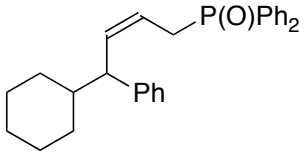
^{13}C NMR δ 27.30, 28.89, 29.07, 29.41 (2 peaks), 29.57, 29.97 (d, *J* = 70.5 Hz), 33.77, 37.08, 43.88, 114.10 (-CH=$\underline{C}$H$_2$), 116.82 (d, *J* = 7.7 Hz, -C=$\underline{C}$-C-P(O)Ph_2), 126.12 (*p*-Ph), 127.31 (2 carbons, *o*-Ph), 128.52 (2 carbons, *m*-Ph), 128.66 (d, *J* = 1.6 Hz, *p*-P(O)Ph_2), 128.77 (*p*-P(O)Ph_2), 130.81 (d, *J* = 99.9 Hz, *ipso*-P(O)Ph_2), 131.05 (d, *J* = 9.3 Hz, 2 carbons, *o*-P(O)Ph_2), 131.12 (d, *J* = 10.0 Hz, 2 carbons, *o*-P(O)Ph_2), 131.26 (d, *J* = 99.9 Hz, *ipso*-P(O)Ph_2), 132.26 (2 peaks of 2 carbons each, *m*-P(O)Ph_2), 139.20 (-$\underline{C}$H=CH$_2$), 139.26 (d, *J* = 12.4 Hz, -$\underline{C}$=C-C-P(O)Ph_2), 144.43 (d, *J* = 1.6 Hz, *ipso*-Ph).

IR (neat) 3079 (Ar), 3061 (Ar), 3014 (Ar and C=CH), 2927, 2855, 1639 (C=C), 1592, 1438, 1405, 1186 (P=O), 911, 756 cm^{-1}.

HRMS (ESI) Calcd for $C_{32}H_{39}PONa$ $[M+Na]^+$: 493.2631. Found: 493.2540.
The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.



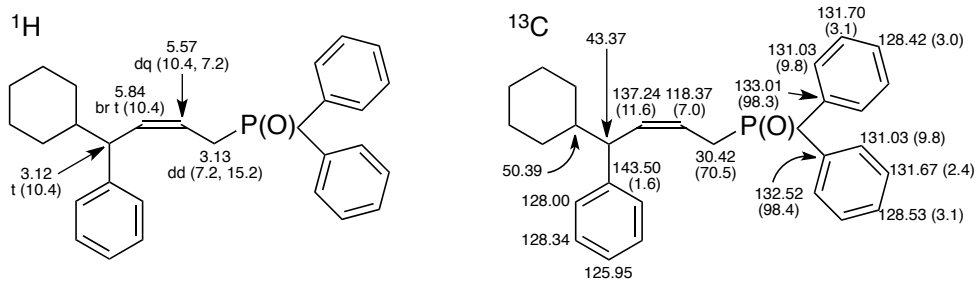
[(*Z*)-4-Cyclohexyl-4-phenyl-2-butenyl]diphenylphosphine oxide (21).



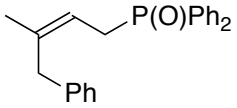
To a solution of [(1*E*,3*E*)-4-cyclohexyl-1,3-butadienyl]diphenylphosphine oxide (**15**) (67.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.350 mL, 1.16 M solution in THF, 0.400 mmol) at –45 °C under argon. After the reaction mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (78.5 mg, 95%) as a white solid and as a single olefinic isomer.
^1H NMR δ 0.64-0.77 (m, 2H, alkyl-H), 1.03-1.70 (m, 9H, alkyl-H), 3.12 (t, *J* = 10.4 Hz, 1H, C<u>H</u>Ph), 3.13 (dd, *J* = 7.2, 15.2 Hz, 2H, -CH=CHC<u>H</u>$_2$P(O)Ph$_2$), 5.57 (dq, *J* = 10.4, 7.2 Hz, 1H, -CH=C<u>H</u>CH$_2$P(O)Ph$_2$), 5.84 (br t, *J* = 10.4 Hz, 1H, -C<u>H</u>=CHCH$_2$P(O)Ph$_2$), 7.05 (d, *J* = 7.2 Hz, 2H, *o*-Ph-H), 7.17 (t, *J* = 7.2 Hz, 1H, *p*-Ph-H), 7.25 (t, *J* = 7.2 Hz, 2H, *m*-Ph-H), 7.31-7.53 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.57-7.71 (m, 4H, -P(O)<u>Ph</u>$_2$).
^{13}C NMR δ 26.31, 26.38, 26.60, 30.42 (d, *J* = 70.5 Hz, -C=C-<u>C</u>-P(O)<u>Ph</u>$_2$), 30.83, 31.11, 43.37, 50.39, 118.37 (d, *J* = 7.0 Hz, -C=<u>C</u>-C-P(O)<u>Ph</u>$_2$), 125.95 (*p*-Ph), 128.00 (2 carbons, *o*-Ph), 128.34 (2 carbons, *m*-Ph), 128.42 (d, *J* = 3.0 Hz, *p*-P(O)Ph$_2$), 128.53 (d, *J* = 3.1 Hz, *p*-P(O)Ph$_2$), 131.03 (d, *J* = 9.8 Hz, 2 peaks of 2 carbons each, *o*-P(O)Ph$_2$), 131.67 (d, *J* = 2.4 Hz, 2 carbons, *m*-P(O)Ph$_2$), 131.70 (d, *J* = 3.1 Hz, 2 carbons, *m*-P(O)Ph$_2$), 132.52 (d, *J* = 98.4 Hz, *ipso*-P(O)Ph$_2$), 133.01 (d, *J* = 98.3 Hz, *ipso*-P(O)Ph$_2$), 137.24 (d, *J* = 11.6 Hz, -<u>C</u>=C-C-P(O)Ph$_2$), 143.50 (d, *J* = 1.6 Hz, *ipso*-Ph).
IR (KBr) 3055 (Ar), 3026 (Ar and C=CH), 2919, 2848, 1599 (C=C), 1491, 1438, 1393, 1261, 1177 (P=O), 648, 512, 504, 430 cm^{-1}.
HRMS (ESI) Calcd for $C_{28}H_{31}OPNa$ $[M+Na]^+$: 437.2005. Found: 437.2016.

M.p. 100-101 °C.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



[(*Z*)-3-Methyl-4-phenyl-2-butenyl]diphenylphosphine oxide (22).



To a solution of [(*E*)-3-methyl-1,3-butadienyl]diphenylphosphine oxide (**16**) (53.7 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.440 mL, 0.90 M solution in THF, 0.400 mmol) at –45 °C under argon. After the reaction mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (33.8 mg, 49%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 1.60 (d, *J* = 2.8 Hz, 3H, alkyl-Me), 3.20 (dd, *J* = 7.2, 14.4 Hz, 2H, -C=CHC$\underline{H}_2$P(O)Ph_2), 3.24 (s, 2H, -CC$\underline{H}_2$-Ph), 5.43 (br q, *J* = 7.2 Hz, 1H, -C=C$\underline{H}$CH$_2$P(O)Ph_2), 7.00 (d, *J* = 7.2 Hz, 2H, *o*-Ph-H), 7.16 (t, *J* = 7.2 Hz, 1H, *p*-Ph-H), 7.22 (t, *J* = 7.2 Hz, 2H, *m*-Ph-H), 7.45-7.55 (m, 6H, -P(O)$\underline{Ph}_2$), 7.72-7.77 (m, 4H, -P(O)$\underline{Ph}_2$).

Irradiation of the proton at δ 5.43 ppm (-C=C$\underline{H}$CH$_2$P(O)Ph_2) showed 1.4% NOE enhancement to that at δ 1.60 ppm (allylic-Me).

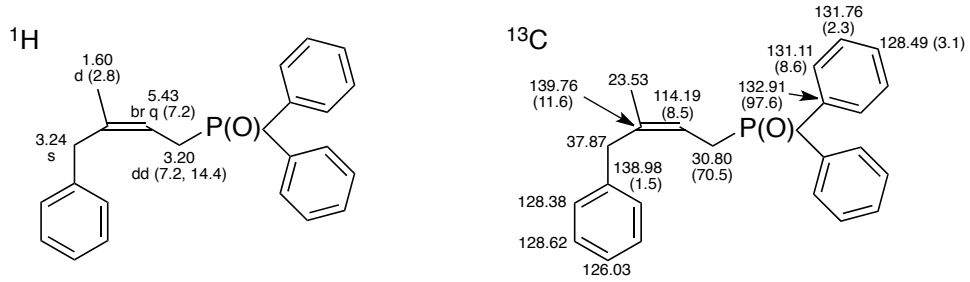
^{13}C NMR δ 23.53 (Me), 30.80 (d, *J* = 70.5 Hz, -C=C-$\underline{C}$-P(O)Ph_2), 37.87 (CH_2), 114.19 (d, *J* = 8.5 Hz, -C=$\underline{C}$-C-P(O)Ph_2), 126.03 (*p*-Ph), 128.38 (2 carbons, *o*-Ph), 128.49 (d, *J* = 3.1 Hz, 2 carbons, *p*-P(O)Ph_2), 128.62 (2 carbons, *m*-Ph), 131.11 (d, *J* = 8.6 Hz, 4 carbons, *o*-P(O)Ph_2), 131.76 (d, *J* = 2.3 Hz, 4 carbons, *m*-P(O)Ph_2), 132.91 (d, *J* = 97.6 Hz, 2 carbons, *ipso*-P(O)Ph_2), 138.98 (d, *J* = 1.5 Hz, *ipso*-Ph), 139.76 (d, *J* = 11.6 Hz, -$\underline{C}$=C-C-P(O)Ph_2).

IR (KBr) 3080 (Ar), 3058 (Ar), 3028 (Ar and C=CH), 2961, 2873, 1600 (C=C), 1493, 1450, 1437, 1178 (P=O), 1120, 1073, 745, 693, 551, 511 cm^{-1}.

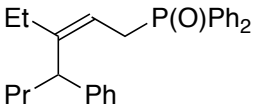
HRMS (ESI) Calcd for $C_{23}H_{23}NOPNa$ $[M+Na]^+$: 369.1379. Found: 369.1369.

M.p. 159-160 °C.

The *Z*-stereochemistry was confirmed by ^{1}H NMR NOE experiments.



[(*Z*)-3-Ethyl-4-phenyl-2-heptenyl]diphenylphosphine oxide (23).



To a solution of [(1*E*,3*E*)-3-ethyl-1,3-heptadienyl]diphenylphosphine oxide (**17**) (64.9 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.440 mL, 0.90 M solution in THF, 0.400 mmol) at –45 °C under argon. After the reaction mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (65.6 mg, 82%) as a white solid and as a single olefinic isomer.

^{1}H NMR δ 0.77 (t, *J* = 7.6 Hz, 3H, alkyl-Me), 0.87 (t, *J* = 7.6 Hz, 3H, alkyl-Me), 1.16 (sextet, *J* = 7.6 Hz, 2H, alkyl-H), 1.50 (m, 1H, alkyl-H), 1.63-1.96 (m, 3H, alkyl-H), 3.21-3.39 (m, 2H, -C=CHC$\underline{H}_2$P(O)Ph$_2$), 3.79 (t, *J* = 7.6 Hz, 1H, PhC$\underline{H}$), 5.37 (q, *J* = 7.6 Hz, 1H, -C=C$\underline{H}$CH$_2$P(O)Ph$_2$), 7.05 (d, *J* = 7.2 Hz, 2H, *o*-Ph-H), 7.14 (t, *J* = 7.2 Hz, 1H, *p*-Ph-H), 7.20 (t, *J* = 7.2 Hz, 2H, *m*-Ph-H), 7.44-7.55 (m, 6H, -P(O)$\underline{Ph}_2$), 7.73-7.78 (m, 4H, -P(O)$\underline{Ph}_2$).

Irradiation of the proton at δ 3.21-3.39 ppm (-C=CHC$\underline{H}_2$P(O)Ph$_2$) showed 3.3% NOE enhancement to that at δ 3.79 ppm (PhC$\underline{H}$), while irradiation of the proton at 3.79 ppm (PhC$\underline{H}$) showed 3.6% NOE enhancement to that at δ 3.21-3.39 ppm (-C=CHC$\underline{H}_2$P(O)Ph$_2$).

^{13}C NMR δ 12.75, 14.29, 20.90, 24.27, 30.55 (d, *J* = 70.5 Hz, -C=C-$\underline{C}$-P(O)Ph$_2$), 33.65, 45.52, 111.86 (d, *J* = 7.0 Hz,- C=$\underline{C}$-C-P(O)Ph$_2$), 125.89 (*p*-Ph), 127.79 (2 carbons, *o*-Ph), 128.08 (2 carbons, *m*-Ph), 128.46 (d, *J* = 3.9 Hz, *p*-P(O)Ph$_2$), 128.57 (d, *J* = 3.9 Hz, *p*-P(O)Ph$_2$), 131.14 (d, *J* = 8.5 Hz, 2 peaks of 2 carbons each, *o*-P(O)Ph$_2$), 131.71 (2 peaks of 2 carbons each, *m*-P(O)Ph$_2$), 132.93 (d, *J* = 97.6 Hz, *ipso*-P(O)Ph$_2$), 132.97 (d, *J* = 97.6 Hz, *ipso*-P(O)Ph$_2$), 142.90 (*ipso*-Ph), 148.40 (d, *J* = 11.6 Hz, -$\underline{C}$=C-C-P(O)Ph$_2$).

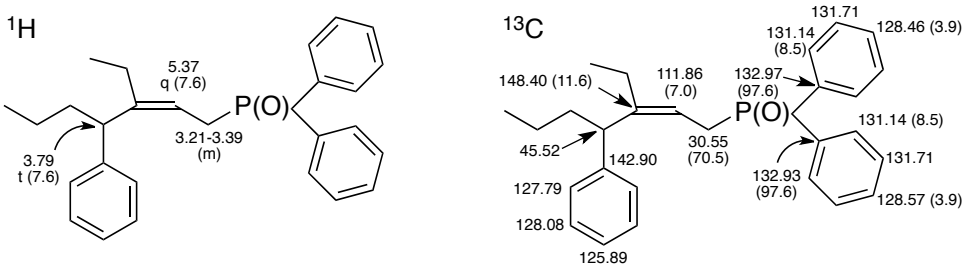
IR (KBr) 3051 (Ar), 3024 (Ar and C=CH), 2958, 2866, 1600 (C=C), 1437, 1172 (P=O), 1100, 743, 695,

535, 511 cm^{-1}.

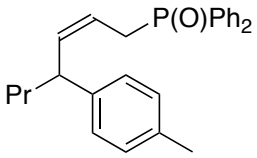
HRMS (ESI) Calcd for $C_{27}H_{31}NOPNa$ $[M+Na]^+$: 425.2015. Found: 425.2012.

M.p. 94-95 °C.

The *Z*-stereochemistry was confirmed by ^1H NMR NOE experiments.



[(*Z*)-4-(4-Methylphenyl)-2-heptenyl]diphenylphosphine oxide (24).



To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (59.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added (4-tolyl)magnesium bromide (0.640 mL, 0.630 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (48.8 mg, 63%) as an oil and as a single olefinic isomer.

^1H NMR δ 0.80 (t, *J* = 7.6 Hz, 3H, alkyl-Me), 1.12 (m, 2H, alkyl-H), 1.39 (m, 1H, alkyl-H), 1.55 (m, 1H, alkyl-H), 2.31 (s, 3H, -Ph-Me), 3.12-3.19 (m, 2H, -CH=CHC$\underline{H}_2$P(O)Ph_2), 3.35 (dt, *J* = 10.8, 7.6 Hz, 1H, C$\underline{H}$Ar), 5.49 (dq, *J* = 10.8, 7.6 Hz, 1H, -CH=C$\underline{H}$CH_2P(O)Ph_2), 5.73 (br t, *J* = 10.8 Hz, 1H, -C$\underline{H}$=CHCH_2P(O)Ph_2), 6.96 (d, *J* = 8.0 Hz, 2H, -$C_6\underline{H}_4$-Me), 7.05 (d, *J* = 8.0 Hz, 2H, -$C_6\underline{H}_4$-Me), 7.37-7.53 (m, 6H, -PO$\underline{Ph}_2$), 7.64-7.73 (m, 4H, -PO$\underline{Ph}_2$).

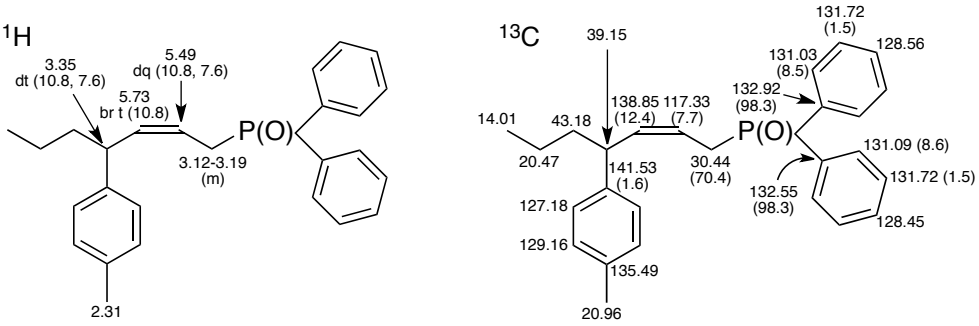
^{13}C NMR δ 14.01, 20.47, 20.96, 30.44 (d, *J* = 70.4 Hz, -C=C-$\underline{C}$-P(O)Ph_2), 39.15, 43.18, 117.33 (d, *J* = 7.7 Hz, -C=$\underline{C}$-C-P(O)Ph_2), 127.18 (2 carbons, *o*-Ph), 128.45 (*o*-P(O)Ph_2), 128.56 (*o*-P(O)Ph_2), 129.16 (2 carbons, *m*-Ph), 131.03 (d, *J* = 8.5 Hz, 2 carbons, *o*-P(O)Ph_2), 131.09 (d, *J* = 8.6 Hz, 2 carbons, *o*-P(O)Ph_2), 131.72 (d, *J* = 1.5 Hz, 2 peaks of 2 carbons each, *m*-P(O)Ph_2), 132.55 (d, *J* = 98.3 Hz, *ipso*-P(O)Ph_2), 132.92 (d, *J* = 98.3 Hz, *ipso*-P(O)Ph_2), 135.49 ($\underline{C}$-Me), 138.85 (d, *J* = 12.4 Hz, -$\underline{C}$=C-C-P(O)Ph_2), 141.53 (d, *J* = 1.6 Hz, $\underline{C}$=C-C-P(O)Ph_2).

IR (neat) 3077 (Ar), 3056 (Ar), 3013 (Ar and C=CH), 2957, 2871, 1658 (C=C), 1642, 1591 (C=C), 1438,

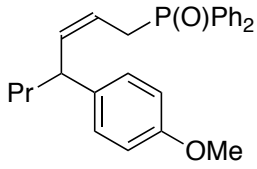
1186 (P=O), 1120, 1028, 814, 751, 695 cm^{-1}.

HRMS (ESI) Calcd for $C_{26}H_{29}PONa$ $[M+Na]^+$: 411.1848. Found: 411.1857.

The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.



[(*Z*)-4-(4-Methoxyphenyl)-2-heptenyl]diphenylphosphine oxide (25).



To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (59.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added (4-methoxyphenyl)magnesium bromide (0.400 mL, 1.00 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (74.7 mg, 92%) as an oil and as a single olefinic isomer.

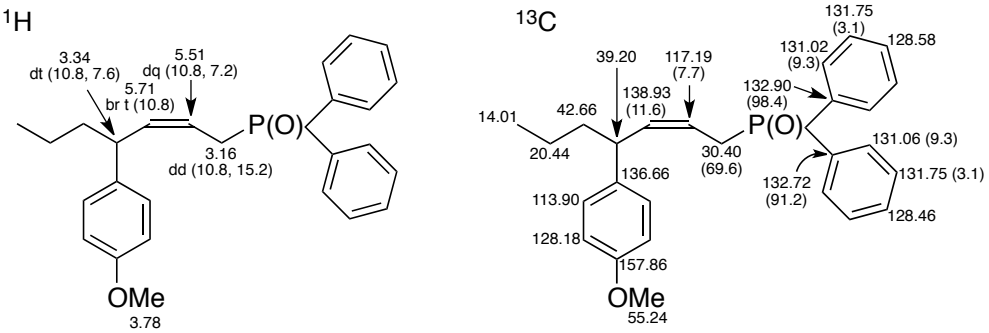
^1H NMR δ 0.81 (t, *J* = 7.2 Hz, 3H, alkyl-Me), 1.10 (m, 2H, alkyl-H), 1.35 (m, 1H, alkyl-H), 1.55 (m, 1H, alkyl-H), 3.16 (dd, *J* = 10.8, 15.2 Hz, 2H, -CH=CHC$\underline{H}_2$P(O)Ph_2), 3.34 (dt, *J* = 10.8, 7.6 Hz, 1H, C$\underline{H}$Ar), 3.78 (s, 3H, O$\underline{Me}$), 5.51 (dq, *J* = 10.8, 7.2 Hz, 1H, -CH=C$\underline{H}$CH$_2$P(O)Ph_2), 5.71 (br t, *J* = 10.8 Hz, 1H, -C$\underline{H}$=CHCH$_2$P(O)Ph_2), 6.78 (d, *J* = 8.8 Hz, 2H, -$C_6\underline{H}_4$-OMe), 6.99 (d, *J* = 8.8 Hz, 2H, -$C_6\underline{H}_4$-OMe), 7.36-7.54 (m, 6H, -PO$\underline{Ph}_2$), 7.64-7.74 (m, 4H, -PO$\underline{Ph}_2$).

^{13}C NMR δ 14.01, 20.44, 30.40 (d, *J* = 69.6 Hz, -C=C-$\underline{C}$-P(O)Ph_2), 39.20, 42.66, 55.24 (OMe), 113.90 (2 carbons, *o*-Ar), 117.19 (d, *J* = 7.7 Hz, -C=$\underline{C}$-C-P(O)Ph_2), 128.18 (2 carbons, *m*-Ar), 128.46 (*p*-P(O)Ph_2), 128.58 (*p*-P(O)Ph_2), 131.02 (d, *J* = 9.3 Hz, 2 carbons, *o*-P(O)Ph_2), 131.06 (d, *J* = 9.3 Hz, 2 carbons, *o*-P(O)Ph_2), 131.75 (d, *J* = 3.1 Hz, 2 peaks of 2 carbons each, *m*-P(O)Ph_2), 132.72 (d, *J* = 91.2 Hz, *ipso*-P(O)Ph_2), 132.90 (d, *J* = 98.4 Hz, *ipso*-P(O)Ph_2), 136.66 (*ipso*-Ar), 138.93 (d, *J* = 11.6 Hz, -$\underline{C}$=C-C-P(O)Ph_2), 157.86 ($\underline{C}$-OMe).

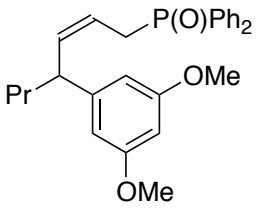
IR (neat) 3056 (Ar), 3010 (Ar and C=CH), 2955, 2929, 1609 (C=C), 1510, 1464, 1438, 1249, 1180 (P=O), 1034, 830, 748, 696, 430 cm^{-1}.

HRMS (ESI) Calcd for $C_{26}H_{29}PO_2Na$ $[M+Na]^+$: 427.1797. Found: 427.1795.

The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.



[(*Z*)-4-(3,5-Dimethoxyphenyl)-2-heptenyl]diphenylphosphine oxide (26).



To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (59.3 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added (3,5-dimethoxyphenyl)magnesium bromide (0.390 mL, 1.02 M solution in THF, 0.400 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (52.3 mg, 60%) as an oil and as a single olefinic isomer.

^1H NMR δ 0.81 (t, *J* = 7.2 Hz, 3H, alkyl-Me), 1.12 (m, 2H, alkyl-H), 1.37 (m, 1H, alkyl-H), 1.55 (m, 1H, alkyl-H), 3.15 (dd, *J* = 7.6, 14.8 Hz, 2H, -CH=CHC<u>H</u>$_2$POPh$_2$), 3.32 (dt, *J* = 10.4, 7.6 Hz, 1H, C<u>H</u>Ar), 3.76 (s, 6H, (O<u>Me</u>)$_2$), 5.53 (dq, *J* = 10.4, 7.6 Hz, 1H, -CH=C<u>H</u>CH$_2$P(O)Ph$_2$), 5.73 (br t, *J* = 10.4 Hz, 1H, -C<u>H</u>=CHCH$_2$P(O)Ph$_2$), 6.27 (d, *J* = 2.0 Hz, 2H, *o*-Ar), 6.29 (t, *J* = 2.0 Hz, 1H, *p*-Ar), 7.37-7.52 (m, 6H, -P(O)<u>Ph</u>$_2$), 7.63-7.73 (m, 4H, -P(O)<u>Ph</u>$_2$).

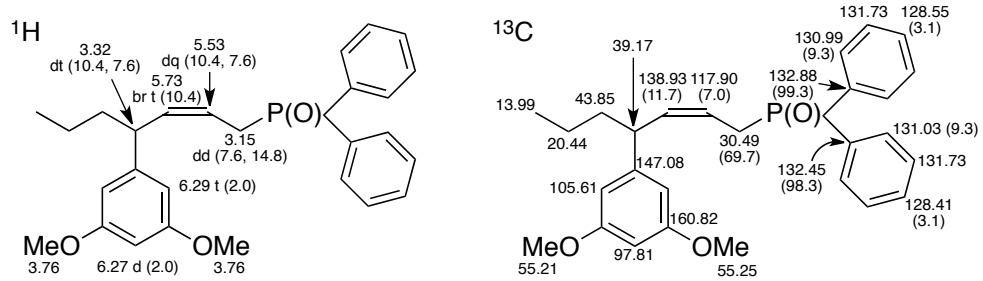
^{13}C NMR δ 13.99, 20.44, 30.49 (d, *J* = 69.7 Hz, -C=C-<u>C</u>-P(O)Ph$_2$), 39.17, 43.85, 55.21 (OMe), 55.25 (OMe), 97.81 (*p*-Ar), 105.61 (2 carbons, *o*-Ar), 117.90 (d, *J* = 7.0 Hz, -C=<u>C</u>-C-P(O)Ph$_2$), 128.41 (d, *J* = 3.1 Hz, *p*-P(O)Ph$_2$), 128.55 (d, *J* = 3.1 Hz, *p*-P(O)Ph$_2$), 130.99 (d, *J* = 9.3 Hz, 2 carbons, *o*-P(O)Ph$_2$), 131.03 (d,

J = 9.3 Hz, 2 carbons, *o*-P(O)Ph_2), 131.73 (2 peaks of 2 carbons each, *m*-P(O)Ph_2), 132.45 (d, J = 98.3 Hz, *ipso*-P(O)Ph_2), 132.88 (d, J = 99.3 Hz, *ipso*-P(O)Ph_2), 138.93 (d, J = 11.7 Hz, -C=C-C-P(O)Ph_2), 147.08 (*ipso*-Ar), 160.82 (2 carbons, -C-OMe).

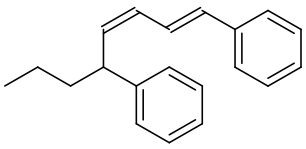
IR (neat) 3077 (Ar), 3057 (Ar), 2956, 2871, 1605, 1594 (C=C), 1461, 1437, 1203, 1154 (P=O), 1063, 839, 749, 456 cm^{-1}.

HRMS (ESI) Calcd for $C_{27}H_{31}PO_3Na$ $[M+Na]^+$: 457.1903. Found: 457.1897.

The *Z*-stereochemistry was confirmed by ^1H NMR coupling constants.



A 96:4 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene (27).



To a solution of [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide (**7**) (112 mg, 0.300 mmol) in THF (1.80 mL) and HMPA (0.520 mL, 2.99 mmol) was added *n*-BuLi (0.220 mL, 1.64 M solution in hexane, 0.360 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, benzaldehyde (0.046 mL, 0.450 mmol) was added at –78 °C. After the reaction was continued at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which was hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (56.2 mg, (1*E*,3*Z*)/(1*E*,3*E*) = 96:4, 71%) as a pale yellow oil.

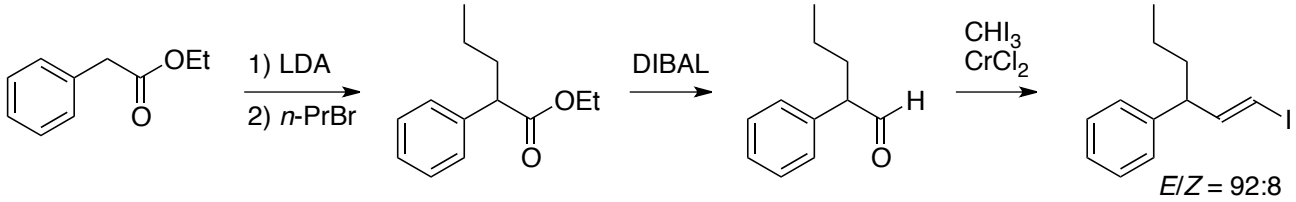
Major (1*E*,3*Z*)-isomer: ^1H NMR δ 0.92 (t, J = 7.6 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$), 1.33 (m, 2H, CH$_3$C$\underline{H}_2$CH$_2$), 1.73 (m, 2H, CH$_3$CH$_2$C$\underline{H}_2$), 3.85 (dt, J = 10.4, 8.0 Hz, 1H, C$\underline{H}$Ph), 5.63 (t, J = 10.4 Hz, 1H, C$\underline{H}$=CH-CH=CH-Ph), 6.19 (t, J = 10.4 Hz, 1H, CH=C$\underline{H}$-CH=CH-Ph), 6.54 (d, J = 15.6 Hz, 1H, CH=CH-CH=C$\underline{H}$-Ph), 7.13 (dd, J = 10.4, 15.6 Hz, 1H, CH=CH-C$\underline{H}$=CH-Ph), 7.16-7.42 (m, 10H, Ph-H).

^{13}C NMR δ 14.06, 20.75, 38.93, 43.82, 124.25, 126.05, 126.37 (2 carbons), 127.26 (2 carbons), 127.47, 128.22, 128.53 (2 carbons), 128.59 (2 carbons), 132.88, 136.53, 137.48 (*ispo*-Ph), 145.08 (*ispo*-Ph).

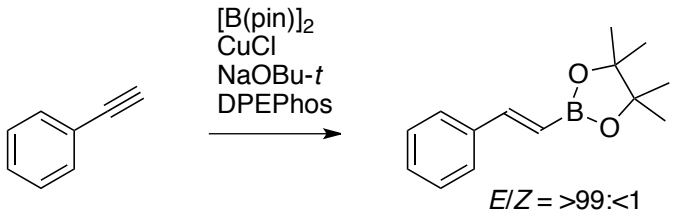
Minor (1*E*,3*E*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 3.35 (q, *J* = 7.6 Hz, 1H, PrC<u>H</u>Ph), 5.94 (dd, *J* = 7.6, 15.6 Hz, 1H, C<u>H</u>=CH-CH=CH-Ph), 6.45 (d, *J* = 15.6 Hz, 1H, CH=CH-CH=C<u>H</u>-Ph), 6.75 (dd, *J* = 10.0, 15.6 Hz, 1H, CH=CH-C<u>H</u>=CH-Ph).
^{13}C NMR (only characteristic peaks are shown) δ 38.04, 126.13, 127.26, 127.60.
IR (neat) 3080 (Ar), 3060 (Ar), 3026 (Ar, C=C-H), 3004 (Ar), 2956, 2927, 2870, 1680 (C=C-C=C), 1589 (C=C-C=C), 1575, 1451, 1029, 984, 945 cm^{-1} for a 96:4 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-isomers.
HRMS (APPI) Calcd for $C_{20}H_{22}$ $[M+H]^+$: 263.1794. Found: 263.1789 for a 96:4 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-isomers.
The 1*E*,3*Z*-diene stereochemistry of the major isomer was confirmed by ^{1}H NMR coupling constants.

An authentic sample of (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene.

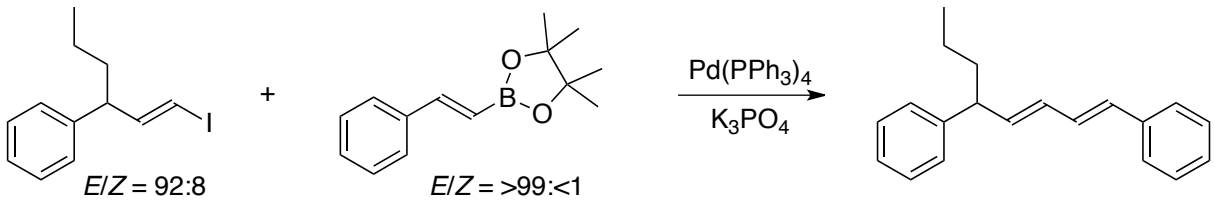
An authentic sample of the minor isomer, (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene, was prepared independently from (*E*)-1-iodo-3-phenyl-1-hexene and (*E*)-4,4,5,5-tetramethyl-2-(β-styryl)-1,3-dioxa-2-borolane as shown below. The above minor product of the Wittig reaction and the authentic sample prepared by the following palladium-catalyzed reaction were identical by ^{1}H and ^{13}C NMR spectroscopy.



Org. Biomol. Chem. **2003**, *1*, 3726-3737.



Tetrahedron **2012**, *68*, 3444-3449.



J. Org. Chem. **2010**, *75*, 7412-7415.

To a solution of diisopropylamine (2.60 mL, 18.6 mmol) in THF (20 mL) was added *n*-BuLi (11.0 mL, 1.64 M in hexane, 18.0 mmol) dropwise at 0 °C. After the mixture was stirred at that temperature for 15 min, it was cooled to –78 °C and ethyl phenylacetate (2.40 mL, 15.1 mmol) was added. After stirring at

–78 °C for 1 h, 1-bromopropane (1.65 mL, 18.2 mmol) was added to the mixture, which was then warmed to room temperature over 6 h. The reaction was terminated by the addition of ethyl acetate and 1 N HCl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford ethyl 2-phenylpentanoate (1.52 g, 49%) as an oil.

To a solution of ethyl 2-phenylpentanoate (1.83 g, 8.90 mmol) in CH_2Cl_2 (50 mL) was added DIBAL (11.0 mL, 1.02 M in hexane, 11.2 mmol) at –78 °C over 30 min under argon. After the mixture was stirred at that temperature for 2.5 h, the reaction was terminated by the successive addition of MeOH and 1 N HCl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers ware washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford 2-phenylpentanal (872 mg, 60%) as an oil.

To a solution of $CrCl_2$ (992 mg, 8.07 mmol) in THF (30 mL) were added CHI_3 (1.08 g, 2.73 mmol) and 2-phenylpentanal (120 mg, 0.738 mmol) in THF (3 mL) in this order at 0 °C. After the mixture was stirred at that temperature for 1 h and at room temperature for 2 h, the reaction was terminated by the addition of H_2O. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $Na_2S_2O_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford a mixture of (*E*)-1-iodo-3-phenyl-1-hexene (*E*/*Z* = 92:8) as an oil and CHI_3 as solids (total 129 mg, the exact yield of the vinyl iodide was not determined). Only the oil portion of this product was used in the next step.

Major (*E*)-isomer: ^{1}H NMR δ 0.89 (t, *J* = 7.2 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.28 (m, 2H, CH$_3$C<u>H</u>$_2$CH$_2$), 1.69 (m, 2H, CH$_3$CH$_2$C<u>H</u>$_2$), 3.28 (q, *J* = 7.6 Hz, 1H, PrC<u>H</u>Ph), 6.02 (d, *J* = 14.0 Hz, 1H, CH=C<u>H</u>-I), 6.65 (dd, *J* = 7.6, 14.0 Hz, 1H, C<u>H</u>=CH-I), 7.17-7.38 (m, 5H, Ar-H).

Minor (*Z*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 3.68 (q, *J* = 7.6 Hz, 1H, PrC<u>H</u>Ph), 6.23-6.31 (m, 2H, C<u>H</u>=C<u>H</u>I).

The *E*-stereochemistry of the major isomer was confirmed by the ^{1}H NMR coupling constant (*J* = 14.0 Hz), which is typical to *E*-alkenyl iodide [*Org*. *Biomol*. *Chem*. **2003**, *1*, 3726-3737].

After a mixture of CuCl (5.8 mg, 0.059 mmol), NaOBu-*t* (12.5 mg, 0.130 mmol), and DPEPhos (34.6 mg, 0.0642 mmol) in THF (1.2 mL) was stirred at room temperature for 30 min, $[B(pin)]_2$ (509 mg, 2.00 mmol) was added. After stirring for 10 min, phenylacetylene (0.220 mL, 2.00 mmol) and MeOH (0.165 mL, 4.08 mmol) were added successively. The reaction mixture was stirred at the same temperature for 24 h, filtered through Celite, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford (*E*)-4,4,5,5-tetramethyl-2-(β-styryl)-1,3-dioxa-2-borolane (421 mg, *E*/*Z* = >99:<1, 91%) as an oil.

^{1}H NMR δ 1.32 (s, 12H, Me), 6.17 (d, *J* = 18.4 Hz, Ph-C<u>H</u>=CH-B), 7.28-7.36 (m, 3H, Ar-H), 7.40 (d, *J* = 18.4 Hz, 1H, CH=C<u>H</u>-B), 7.49 (dd, *J* = 6.8 Hz, 8.4 Hz, 2H, Ar-H).

The *E*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

Peaks of the other olefinic isomers were not seen on ^{1}H NMR spectra of crude and purified samples. Thus the olefinic stereoselectivity was judged to be >99:<1 based on the limit of detection of NMR spectroscopy.

To a solution of (*E*)-1-iodo-3-phenyl-1-hexene (52.2 mg, 0.182 mmol, *E*/*Z* = 92:8) prepared above and (*E*)-4,4,5,5-tetramethyl-2-(β-styryl)-1,3-dioxa-2-borolane (48.6 mg, 0.211 mmol, *E*/*Z* = >99:<1) in THF (2 mL) and H_2O (1 mL) was added K_3PO_4 (256 mg, 1.20 mmol) under argon at room temperature. After vigorous stirring at that temperature for 15 min, $Pd(PPh_3)_4$ (23.8 mg, 0.0206 mmol) was added to the mixture, which was then covered with aluminum foil. After vigorous stirring at room temperature for 16 h, the reaction was terminated by the addition of aqueous 3 N NaOH solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were successively washed with aqueous saturated NH_4Cl solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford the title compound (29.8 mg, (1*E*,3*E*)/(1*E*,3*Z*)/(1*Z*,3*Z*) = 86:7:7, 63%) as a pale yellow oil.

Major (1*E*,3*E*)-isomer: ^{1}H NMR δ 0.91 (t, *J* = 7.6 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.30 (m, 2H, alkyl-H), 1.73 (q, *J* = 7.6 Hz, 2H, alkyl-H), 3.35 (q, *J* = 7.6 Hz, 1H, PrC<u>H</u>Ph), 5.94 (dd, *J* = 7.6, 15.2 Hz, 1H, C<u>H</u>=CH-CH=CH-Ph), 6.20 (dd, *J* = 10.4, 15.2 Hz, 1H, CH=C<u>H</u>-CH=CH-Ph), 6.45 (d, *J* = 15.6 Hz, 1H, CH=CH-CH=C<u>H</u>-Ph), 6.75 (dd, *J* = 10.4, 15.6 Hz, 1H, CH=CH-C<u>H</u>=CH-Ph), 7.15-7.45 (m, 10H, Ar-H).

^{13}C NMR δ 13.99, 20.73, 38.10, 48.75, 126.16 (2 peaks of 2 carbons), 126.29, 127.17, 127.63, 128.46 (2 carbons), 128.54 (2 carbons), 129.27, 129.93, 130.82, 139.09 (*ipso*-Ph), 144.65 (*ipso*-Ph).

Minor (1*E*,3*Z*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 3.85 (dt, *J* = 10.8, 8.0 Hz, 1H, PrC<u>H</u>Ph), 5.63 (t, *J* = 10.8 Hz, 1H, C<u>H</u>=CH-CH=CH-Ph), 6.54 (d, *J* = 15.6 Hz, 1H, CH=CH-CH=C<u>H</u>-Ph), 7.13 (dd, *J* = 10.8, 15.6 Hz, 1H, CH=CH-C<u>H</u>=CH-Ph).

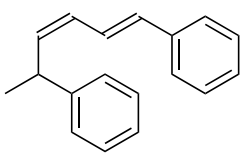
Second minor (1*Z*,3*Z*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 3.61 (q, *J* = 8.0 Hz, 1H, PrC<u>H</u>Ph), 5.71 (dd, *J* = 8.0, 10.8 Hz, 1H, C<u>H</u>=CH-CH=CH-Ph), 6.35 (d, *J* = 10.8 Hz, 1H, CH=CH-CH=C<u>H</u>-Ph).

IR (neat) 3080 (Ar), 3060 (Ar), 3024 (Ar, C=C-H), 2956, 2928, 2870, 1597 (C=C-C=C), 1666 (C=C-C=C), 1494, 1450, 987, 744, 698 cm^{-1} for an 86:7:7 mixture of (1*E*,3*E*)-, (1*E*,3*Z*)-, and (1*Z*,3*Z*)-isomers.

HRMS (APPI) Calcd for $C_{20}H_{22}$ $[M+H]^+$: 263.1794. Found: 263.1800 for an 86:7:7 mixture of (1*E*,3*E*)-, (1*E*,3*Z*)- and (1*Z*,3*Z*)-isomers.

The 1*E*,3*E*-diene stereochemistry of the major isomer was confirmed by ^{1}H NMR coupling constants.

An 89:11 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-1,5-diphenyl-1,3-hexadiene (28).



To a solution of [(*Z*)-4-phenyl-2-pentenyl]diphenylphosphine oxide (**18**) (104 mg, 0.299 mmol) in THF (1.80 mL) and HMPA (0.520 mL, 2.99 mmol) was added *n*-BuLi (0.220 mL, 1.64 M solution in hexane, 0.361 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that

temperature for 30 min, benzaldehyde (0.045 mL, 0.441 mmol) was added at –78 °C. After the reaction was continued at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (44.8 mg, (1*E*,3*Z*)/(1*E*,3*E*) = 89:11, 64%) as a pale yellow oil.

Major (1*E*,3*Z*)-isomer: ^{1}H NMR δ 1.43 (d, *J* = 7.2 Hz, 3H, Me), 4.07 (dq, *J* = 10.4, 7.2 Hz, 1H, MeC<u>H</u>Ph), 5.63 (t, *J* = 10.4 Hz, 1H, -C<u>H</u>=CH-CH=CH-Ph), 6.17 (t, *J* = 10.4 Hz, 1H, -CH=C<u>H</u>-CH=CH-Ph), 6.57 (d, *J* = 15.2 Hz, 1H, -CH=CH-CH=C<u>H</u>-Ph), 7.15 (dd, *J* = 10.4, 15.2 Hz, 1H, -CH=CH-C<u>H</u>=CH-Ph), 7.18-7.43 (m, 10H, Ar-H).

^{13}C NMR δ 21.98, 37.84, 124.13, 126.09, 126.41 (2 carbons), 126.90 (2 carbons), 127.49, 127.52, 128.52 (2 carbons), 128.59 (2 carbons), 133.03, 137.46, 137.49 (*ispo*-Ph), 145.83 (*ispo*-Ph).

Minor (1*E*,3*E*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 3.58 (quintet, *J* = 6.8 Hz, 1H, MeC<u>H</u>Ph), 6.00 (dd, *J* = 6.8, 15.6 Hz, 1H, -C<u>H</u>=CH-CH=CH-Ph), 6.48 (d, *J* = 15.6 Hz, -CH=CH-CH=C<u>H</u>-Ph), 6.77 (dd, *J* = 10.4, 15.6 Hz, 1H, -CH=C<u>H</u>-CH=CH-Ph), 7.07 (dd, *J* = 10.4, 15.6 Hz, 1H, -CH=CH-C<u>H</u>=CH-Ph).

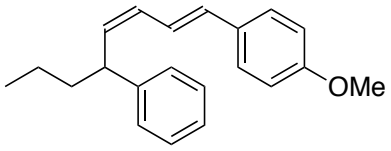
^{13}C NMR (only characteristic peaks are shown) δ 21.16, 123.37, 126.18 (2 carbons), 127.20, 127.26, 129.21, 130.96, 139.84.

IR (neat) 3102 (Ar), 3083 (Ar), 3060 (Ar), 3027 (Ar, C=C-H), 3003 (Ar), 2967, 2927, 1679 (C=C-C=C), 1602 (C=C-C=C), 1494, 1451, 1202, 1165, 1124, 1073, 973 cm^{-1} for an 89:11 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-isomers.

HRMS (EI) Calcd for $C_{18}H_{18}$ $[M]^+$: 234.1409. Found: 234.1409 for an 89:11 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-isomers.

The 1*E*,3*Z*-diene stereochemistry of the major isomer was confirmed by ^{1}H NMR coupling constants.

A 95:5 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-1-(4-methoxyphenyl)-5-phenyl-1,3-octadiene (29).



To a solution of [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide (**7**) (113 mg, 0.302 mmol) in THF (1.80 mL) and HMPA (0.525 mL, 3.02 mmol) was added *n*-BuLi (0.230 mL, 1.58 M solution in hexane, 0.363 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, 4-methoxybenzaldehyde (0.055 mL, 0.452 mmol) was added at –78 °C. After the reaction was continued at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted

with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (60.4 mg, (1*E*,3*Z*)/(1*E*,3*E*) = 95:5, 68%) as a yellow oil.

Major (1*E*,3*Z*)-isomer: ^{1}H NMR δ 0.92 (t, *J* = 7.2 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.33 (m, 2H, CH$_3$C<u>H</u>$_2$CH$_2$), 1.71 (m, 2H, CH$_3$CH$_2$C<u>H</u>$_2$), 3.80 (s, 3H, OMe), 3.84 (dt, *J* = 10.4, 8.0 Hz, 1H, C<u>H</u>Ph), 5.57 (t, *J* = 10.4 Hz, 1H, -C<u>H</u>=CH-CH=CH-Ar), 6.17 (t, *J* = 10.4 Hz, 1H, -CH=C<u>H</u>-CH=CH-Ar), 6.49 (d, *J* = 15.6 Hz, 1H, -CH=CH-CH=C<u>H</u>-Ar), 6.86 (d, *J* = 8.8 Hz, 2H, Ar-H), 7.00 (dd, *J* = 10.4, 15.6 Hz, 1H, -CH=CH-C<u>H</u>=CH-Ar), 7.14-7.30 (m, 5H, Ph-H), 7.34 (d, *J* = 8.8 Hz, 2H, Ar-H).

^{13}C NMR δ 14.05, 20.75, 39.04, 43.81, 55.32, 114.09 (2 carbons), 122.39, 126.00, 127.29 (2 carbons), 127.59 (2 carbons), 128.45 (*ispo*-Ph), 128.51 (2 carbons), 130.38, 132.46, 135.42, 145.29 (*ipso*-Ph), 159.23.

Minor (1*E*,3*E*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 5.88 (dd, *J* = 7.6, 15.6 Hz, 1H, -C<u>H</u>=CH-CH=CH-Ar), 6.40 (d, *J* = 15.6 Hz, 1H, -CH=CH-CH=C<u>H</u>-Ar), 6.62 (dd, *J* = 10.6, 15.6 Hz, 1H, -CH=C<u>H</u>-CH=CH-Ar), 6.93 (dd, *J* = 10.6, 15.6 Hz, 1H, -CH=CH-C<u>H</u>=CH-Ar).

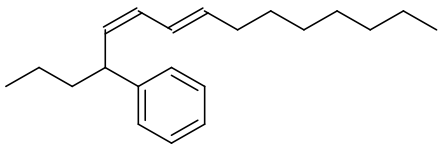
^{13}C NMR (only characteristic peaks are shown) δ 38.14, 48.73, 114.04, 130.07, 137.91, 144.81, 158.99.

IR (neat) 3061 (Ar), 3028 (Ar, C=C-H), 3003 (Ar), 2956, 2931, 2871, 1679 (C=C-C=C), 1603 (C=C-C=C), 1512, 1253, 1174, 1032 cm^{-1} for a 95:5 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-isomers.

HRMS (FAB, NBA) Calcd for $C_{21}H_{24}O$ [M]$^+$: 292.1827. Found: 292.1834 for a 95:5 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-isomers.

The 1*E*,3*Z*-diene stereochemistry of the major isomer was confirmed by ^{1}H NMR coupling constants.

An 86:14 mixture of (5*Z*,7*E*)- and (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene (30).



With 1.2 equiv of $C_7H_{15}CHO$

To a solution of [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide (**7**) (143.9 mg, 0.320 mmol) in THF (1.90 mL) and HMPA (0.557 mL, 3.20 mmol) was added *n*-BuLi (0.234 mL, 1.58 M solution in hexane, 0.384 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, octanal (0.060 mL, 0.384 mmol) was added at –78 °C. After the reaction was continued at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The

crude product was chromatographed on silica gel (hexane) to afford the title compound (48.3 mg, (5*Z*,7*E*)/(5*Z*,7*Z*) = 86:14, 53%) as an oil.

With 1.5 equiv of $C_7H_{15}CHO$

To a solution of [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide (**7**) (74.6 mg, 0.199 mmol) in THF (1.20 mL) and HMPA (0.350 mL, 2.01mmol) was added *n*-BuLi (0.150 mL, 1.64 M solution in hexane, 0.246 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, octanal (0.047 mL, 0.300 mmol) was added at –78 °C. After the reaction was continued at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (36.3 mg, (5*Z*,7*E*)/(5*Z*,7*Z*) = 86:14, 64%) as an oil.

Major (5*Z*,7*E*)-isomer: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 7.6 Hz, 3H, Me), 0.90 (t, *J* = 7.6 Hz, 3H, Me), 1.18-1.43 (m, 12H, Alkyl-H), 1.65 (m, 2H, $CH_3CH_2C\underline{H}_2CHPh$), 2.10 (m, 2H, CH=CH-C$\underline{H}_2$), 3.72 (dt, *J* = 10.8, 7.6 Hz, 1H, C$\underline{H}$Ph), 5.40 (t, *J* = 10.8 Hz, 1H, C$\underline{H}$=CH-CH=CH-C_7H_{15}), 5.68 (dt, *J* = 14.6, 7.2 Hz, 1H, CH=CH-CH=C$\underline{H}$-C_7H_{15}), 5.98 (t, *J* = 10.8 Hz, 1H, CH=C$\underline{H}$-CH=CH-C_7H_{15}), 6.38 (dd, *J* = 10.8, 14.6 Hz, 1H, CH=CH-C$\underline{H}$=CH-C_7H_{15}), 7.14-7.31 (m, 5H, Ph-H).

^{1}H NMR (C_6D_6) δ 0.84-0.91 (m, 6H, alkyl-Me), 1.19-1.40 (m, 12H, alkyl-H), 1.63 (m, 2H, $CH_3CH_2C\underline{H}_2CHPh$), 2.06 (q, *J* = 6.8 Hz, 2H, CH=CH-C$\underline{H}_2$), 3.81 (td, *J* = 7.2, 10.4 Hz, 1H, PrC$\underline{H}$Ph), 5.44 (t, *J* = 10.8 Hz, 1H, C$\underline{H}$=CH-CH=CH-C_7H_{15}), 5.66 (td, *J* = 6.8, 14.8 Hz, 1H, CH=CH-CH=C$\underline{H}$-C_7H_{15}), 6.10 (t, *J* = 10.8 Hz, 1H, CH=C$\underline{H}$-CH=CH-C_7H_{15}), 6.58 (dd, *J* = 10.8, 14.8 Hz, 1H, CH=CH-C$\underline{H}$=CH-C_7H_{15}), 7.16-7.19 (m, 5H, Ar-H).

^{13}C NMR δ 14.08, 14.14, 20.73, 22.70, 29.21 (2 peaks), 29.33, 31.90, 32.92, 39.07, 43.51, 125.47, 125.90, 127.27 (2 carbons), 128.30, 128.45 (2 carbons), 133.35, 135.79, 145.51 (*ipso*-Ph).

Minor (5*Z*,7*Z*)-isomer: ^{1}H NMR (only characteristic peaks are shown) ($CDCl_3$) δ 5.49 (m, 1H, CH=CH-CH=C$\underline{H}$-C_7H_{15}), 5.58 (m, 1H, C$\underline{H}$=CH-CH=CH-C_7H_{15}), 6.23-6.33 (m, 2H, CH=C$\underline{H}$-C$\underline{H}$=CH-C_7H_{15}).

^{1}H NMR (only characteristic peaks are shown) (C_6D_6) δ 2.13 (q, *J* = 7.2 Hz, 2H, CH=CH-C$\underline{H}_2$), 5.52 (td, *J* = 7.2, 10.4 Hz, 1H, CH=CH-CH=C$\underline{H}$-C_7H_{15}), 5.56 (t, *J* = 10.4 Hz, 1H, C$\underline{H}$=CH-CH=CH-C_7H_{15}), 6.40 (t, *J* = 10.4 Hz, 1H, CH=CH-C$\underline{H}$=CH-C_7H_{15}), 6.51 (t, *J* = 10.4 Hz, 1H, CH=C$\underline{H}$-CH=CH-C_7H_{15}).

^{13}C NMR (only characteristic peaks are shown) δ 14.00, 27.56, 29.63, 38.97, 43.25, 123.11, 123.47, 133.19, 135.35, 145.36.

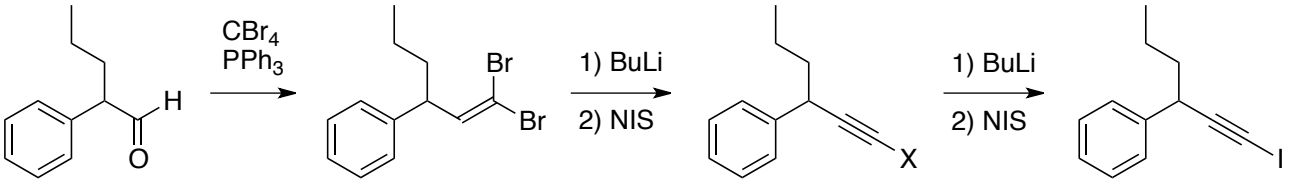
IR (neat) 3083 (Ar), 3061 (Ar), 3026 (Ar, C=C-H), 3003 (Ar), 2956, 2926, 2872, 2854, 1651 (C=C-C=C), 1600 (C=C-C=C), 1465, 1454, 982, 947 cm^{-1} for an 86:14 mixture of (5*Z*,7*E*)- and (5*Z*,7*Z*)-isomers.

HRMS (APPI) Calcd for $C_{21}H_{32}$ $[M+H]^+$: 285.2577. Found: 285.2572 for an 86:14 mixture of (5*Z*,7*E*)- and (5*Z*,7*Z*)-isomers.

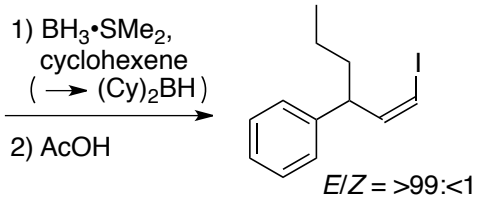
The 5*Z*,7*E*-diene stereochemistry of the major isomer was confirmed by ^{1}H NMR coupling constants.

An authentic sample of (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene.

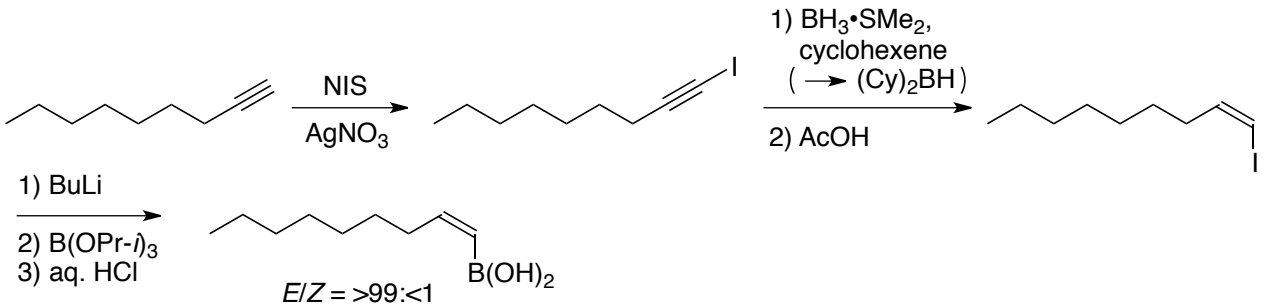
An authentic sample of the minor isomer, (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene, was prepared independently from (*Z*)-1-iodo-3-phenyl-1-hexene and (*Z*)-1-nonenylboronic acid as shown below. The above minor product of the Wittig reaction and the authentic sample prepared by the following palladium-catalyzed reaction were identical by ^{1}H and ^{13}C NMR spectroscopy.



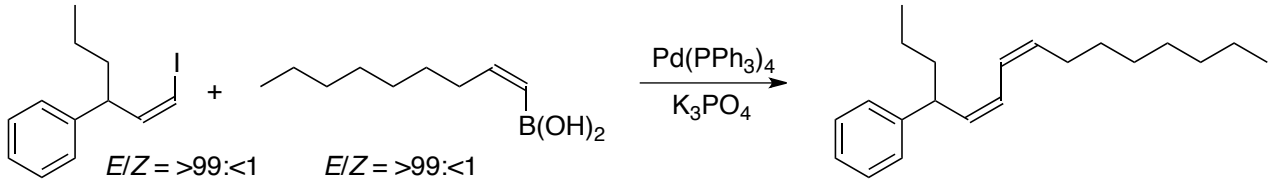
J. Org. Chem. **2004**, *69*, 3787-3793. X : I/H = 33:67 (inseprable)



J. Org. Chem. **1989**, *69*, 6064-6067.



Tetrahedron Lett. **2000**, *41*, 10357-10361.
J. Org. Chem. **2002**, *67*, 7110-7123.
Org. Lett. **2012**, *14*, 544-547.



J. Org. Chem. **2010**, *75*, 7412-7415.

To a solution of CBr_4 (3.35 g, 10.1 mmol) in CH_2Cl_2 (20 mL) was added PPh_3 (5.65 g, 21.5 mmol) at 0 °C. After stirring at 0 °C for 30 min, 2-phenylpentanal (872 mg, 5.38 mmol) was added at that temperature, and the stirring was continued for an additional 2 h at the same temperature. The reaction was terminated by the addition of H_2O. The organic layer was separated and the aqueous layer was extracted

with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude solid, which was chromatographed on silica gel (hexane) to afford 1,1-dibromo-3-phenyl-1-hexene (1.09 g, quant.) as an oil.

To a solution of 1,1-dibromo-3-phenyl-1-hexene (1.09 g, 6.73 mmol) in THF (10 mL) was added *n*-BuLi (7.80 mL, 1.64 M in hexane, 12.8 mmol) at –78 °C under argon. After stirring at that temperature for 1 h, *N*-iodosuccinimide (2.42 g, 10.8 mmol) was added. After the mixture was warmed to 0 °C over 1.5 h, the reaction was terminated by the addition of aqueous saturated $Na_2S_2O_3$ solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude mixture of 1-iodo-3-phenyl-1-hexyne and 3-phenyl-1-hexyne in a ratio of 33:67 by ^{1}H NMR analysis. This crude oil was chromatographed on silica gel (hexane) to afford a mixture of the iodoalkyne and alkyne (571 mg, 53%) of the same ratio as above.

To a solution of the 33:67 mixture of 1-iodo-3-phenyl-1-hexyne and 3-phenyl-1-hexyne (430 mg, ca. 2.72 mmol) in THF (9 mL) was added *n*-BuLi (2.60 mL, 1.58 M in hexane, 4.11 mmol) at –78 °C under argon. After stirring for 30 min, *N*-iodosuccinimide (915 mg, 4.07 mmol) was added. After the reaction mixture was warmed up to 0 °C over 1.5 h, the reaction was terminated by the addition of aqueous saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford 1-iodo-3-phenyl-1-hexyne (437 mg, 53% uncontaminated with the alkyne) as an oil.

To a solution of $BH_3 \cdot SMe_2$ (0.770 mL, 2.0 M in THF, 1.54 mmol) in THF (5 mL) was added cyclohexene (0.335 mL, 3.08 mmol) at 0 °C. The resulting solution was stirred at that temperature for 1 h and at room temperature for 1 h. Then, 1-iodo-3-phenyl-1-hexyne (437 mg, 1.54 mmol) was added and the mixture was stirred for 1 h. The reaction was terminated by the addition of glacial acetic acid (1 mL), diluted with hexane, and washed with brine 3 times, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford (*Z*)-1-iodo-3-phenyl-1-hexene (169 mg, 38%) as an oil and as a single olefinic isomer.

^{1}H NMR δ 0.93 (t, *J* = 7.2 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.31 (m, 2H, CH$_3$C<u>H</u>$_2$CH$_2$), 1.77 (m, 2H, CH$_3$CH$_2$C<u>H</u>$_2$), 3.68 (q, *J* = 7.6 Hz, 1H, PrC<u>H</u>Ph), 6.24 (d, *J* = 7.6 Hz, 1H, CH=C<u>H</u>I), 6.27 (t, *J* = 7.6 Hz, 1H, C<u>H</u>=CHI), 7.23-7.37 (m, 5H, Ar-H).

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

Peaks of the other olefinic isomers were not seen on ^{1}H NMR spectra of crude and purified samples. Thus the olefinic stereoselectivity was judged to be >99:<1 based on the limit of detection of NMR spectroscopy.

To a solution of 1-nonyne (0.320 mL, 1.96 mmol) in acetone (10 mL) were added $AgNO_3$ (105 mg, 0.616 mmol) and *N*-iodosuccinimide (626 mg, 2.78 mmol) in this order at room temperature. After stirred at room temperature overnight, the reaction mixture was concentrated *in vacuo* and diluted with H_2O and ethyl acetate. The organic layer was separated and washed successively with H_2O and brine until the precipitation of AgCl was no longer observed. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford 1-iodo-1-nonyne

(430 mg, 88%) as an oil.

To a solution of $BH_3 \cdot SMe_2$ (0.860 mL, 2.0 M in THF, 1.72 mmol) in THF (3 mL) was added cyclohexene (0.370 mL, 3.42 mmol) at 0 °C. After the mixture was stirred at that temperature for 1 h and at room temperature for 1 h, 1-iodo-1-nonyne (430 mg, 1.72 mmol) was added. After the mixture was stirred for 1 h, the reaction was terminated by the addition of glacial acetic acid (1 mL), diluted with hexane, and washed with brine 3 times, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford (*Z*)-1-iodo-1-nonene (223 mg, 54%) as an oil and with a *Z*/*E* ratio of >99:<1.

To a solution of (*Z*)-1-iodo-1-nonene (223 mg, 0.924 mmol, *Z*/*E* = >99:<1) in diethyl ether (6 mL) was added *n*-BuLi (0.680 mL, 1.64 M in hexane, 1.12 mmol) at –78 °C. After stirring at that temperature for 1 h, triisopropyl borate (0.257 mL, 1.11 mmol) was added. The mixture was warmed to room temperature and was stirred for an additional 16 h. Then, aqueous 1 N HCl (2 mL) was added and the mixture was stirred for 1 h. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford (*Z*)-1-nonenylboronic acid (98.1 mg, *Z*/*E* = >99:<1, 62%) as an oil.

^{1}H NMR δ 0.88 (t, *J* = 6.8 Hz, 3H, Alkyl-Me), 1.22-1.46 (br, 10H, alkyl-H), 2.55 (dq, *J* = 1.2, 7.6 Hz, 2H, C$\underline{H}_2$-CH=CH-B), 5.42 (d, *J* = 14.0 Hz, 1H, CH=C$\underline{H}$-B), 6.61 (dt, *J* = 14.0, 7.6 Hz, 1H, C$\underline{H}$=CH-B).

The *Z*-stereochemistry was confirmed by the ^{1}H NMR coupling constant (*J* = 14.0 Hz), which is typical to *Z*-alkenylboroic acid [*Org*. *Lett*. **2012**, *14*, 544-547; *Tetrahedron Lett*. **2000**, *41*, 10357-10361; *J*. *Org*. *Chem*. **2002**, *67*, 7110-7123].

To a solution of (*Z*)-1-iodo-3-phenyl-1-hexene (86.1 mg, 0.301 mmol, *Z*/*E* = >99:<1) and (*Z*)-1-nonenylboronic acid (61.6 mg, 0.362 mmol, *Z*/*E* = >99:<1) in THF (3 mL) and H_2O (1.50 mL) was added K_3PO_4 (389 mg, 1.83 mmol) under argon at room temperature. After vigorous stirring at that temperature for 15 min, $Pd(PPh_3)_4$ (34.8 mg, 0.0301 mmol) was added to the mixture, which was then covered with aluminum foil. After vigorous stirring at room temperature for 16 h, the reaction was terminated by the addition of aqueous 3 N NaOH solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were successively washed with aqueous saturated NH_4Cl solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford the title compound (48.6 mg, 57%) as an oil.

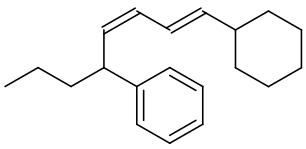
^{1}H NMR ($CDCl_3$) δ 0.79-0.93 (m, 6H, alkyl-Me), 1.18-1.42 (m, 12H, alkyl-H), 1.67 (m, 2H, $CH_3CH_2C\underline{H}_2$CHPh), 2.16 (m, 2H, CH=CH-C$\underline{H}_2$), 3.75 (dt, *J* = 9.6, 7.6 Hz, 1H, PrC$\underline{H}$Ph), 5.40-5.57 (m, 2H, C$\underline{H}$=CH-CH=C$\underline{H}$-C_7H_{15}), 6.22-6.38 (m, 2H, CH=C$\underline{H}$-C$\underline{H}$=CH-C_7H_{15}), 7.14-7.31 (m, 5H, Ar-H).

^{1}H NMR (C_6D_6) δ 0.82-1.00 (m, 6H, alkyl-Me), 1.17-1.44 (m, 12H, alkyl-H), 1.63 (m, 2H, $CH_3CH_2C\underline{H}_2$CHPh), 2.14 (q, *J* = 7.2 Hz, 2H, CH=CH-C$\underline{H}_2$), 3.80 (td, *J* = 7.2, 10.0 Hz, 1H, PrC$\underline{H}$Ph), 5.51 (td, *J* = 7.2, 10.0 Hz, 1H, CH=CH-CH=C$\underline{H}$-C_7H_{15}), 5.56 (t, *J* = 10.0 Hz, 1H, C$\underline{H}$=CH-CH=CH-C_7H_{15}), 6.40 (t, *J* = 10.0 Hz, 1H, CH=CH-C$\underline{H}$=CH-C_7H_{15}), 6.51 (t, *J* = 10.0 Hz, 1H, CH=C$\underline{H}$-CH=CH-C_7H_{15}), 7.14-7.21 (m, 5H, Ar-H).

^{13}C NMR δ 14.04, 20.67, 22.64, 27.54, 29.16, 29.24, 29.60, 29.70, 31.83, 38.99, 43.26, 123.11, 123.49,

125.91, 127.31 (2 carbons), 128.44 (2 carbons), 133.17, 135.35, 145.39 (*ipso*-Ph).
IR (neat) 3084 (Ar), 3061 (Ar), 3029 (Ar, C=C-H), 3002 (Ar), 2956, 2925, 2854, 1651 (C=C-C=C), 1600 (C=C-C=C), 1464, 1455, 1378, 698 cm^{-1}.
HRMS (APPI) Calcd for $C_{21}H_{32}$ $[M+H]^+$: 285.2577. Found: 285.2576.
The 5*Z*,7*Z*-diene stereochemistry of the major isomer was confirmed by ^1H NMR coupling constants.

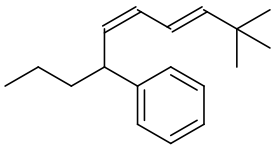
An 89:11 mixture of (1*E*,3*Z*)- and (1*Z*,3*Z*)-1-cyclohexyl-5-phenyl-1,3-octadiene (31).



To a solution of [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide (**7**) (113 mg, 0.303 mmol) in THF (1.80 mL) and HMPA (0.527 mL, 3.03 mmol) was added *n*-BuLi (0.230 mL, 1.58 M solution in hexane, 0.363 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, cyclohexanecarbaldehyde (0.055 mL, 0.454 mmol) was added at –78 °C. After the reaction was continued at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^1H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (58.4 mg, (1*E*,3*Z*)/(1*Z*,3*Z*) = 89:11, 72%) as an oil.
Major (1*E*,3*Z*)-isomer: ^1H NMR δ 0.90 (t, *J* = 7.2 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.00-1.40 (m, 9H, alkyl-H), 1.56-1.77 (m, 5H, alkyl-H), 2.01 (m, 1H, allylic cyclohexyl), 3.72 (dt, *J* = 10.4, 7.6 Hz, 1H, C<u>H</u>Ph), 5.41 (t, *J* = 10.4 Hz, 1H, C<u>H</u>=CH-CH=CH-Hex-*c*), 5.63 (dd, *J* = 6.8, 15.2 Hz, 1H, CH=CH-CH=C<u>H</u>-Hex-*c*), 5.97 (t, *J* = 10.4 Hz, 1H, CH=C<u>H</u>-CH=CH-Hex-*c*), 6.34 (dd, *J* = 10.4, 15.2 Hz, 1H, CH=CH-C<u>H</u>=CH-Hex-*c*), 7.14-7.31 (m, 5H, Ph-H).
^{13}C NMR δ 14.02, 20.67, 26.03 (2 peaks), 26.18, 32.90, 32.93, 39.11, 40.97, 43.52, 122.93, 125.87, 127.28 (2 carbons), 128.42 (2 carbons), 128.53, 133.50, 141.42, 145.55 (*ipso*-Ph).
Minor (1*Z*,3*Z*)-isomer: ^1H NMR (only characteristic peaks are shown) δ 0.89 (t, *J* = 7.2 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 2.43 (m, 1H, allylic cyclohexyl), 5.32 (t, *J* = 11.6 Hz, 1H, CH=CH-CH=C<u>H</u>-Hex-*c*), 5.52 (t, *J* = 11.6 Hz, 1H, C<u>H</u>=CH-CH=CH-Hex-*c*), 6.24 (t, *J* = 11.6 Hz, 1H, CH=C<u>H</u>-CH=CH-Hex-*c*), 6.26 (t, *J* = 11.6 Hz, 1H, CH=CH-C<u>H</u>=CH-Hex-*c*).
^{13}C NMR (only characteristic peaks are shown) δ 121.64, 123.26, 135.38, 138.93, 140.40.
IR (neat) 3084 (Ar), 3061 (Ar), 3026 (Ar, C=C-H), 3004 (Ar), 2955, 2925, 2850, 1649 (C=C-C=C), 1601 (C=C-C=C), 1493, 1449, 1380, 1030, 968, 947 cm^{-1} for an 89:11 mixture of (1*E*,3*Z*)- and (1*Z*,3*Z*)-isomers.
HRMS (FAB, NBA) Calcd for $C_{20}H_{28}$ $[M]^+$: 268.2191. Found: 268.2188 for an 89:11 mixture of (1*E*,3*Z*)- and (1*Z*,3*Z*)-isomers.

The 1*E*,3*Z*-diene stereochemistry of the major isomer was confirmed by ^{1}H NMR coupling constants.

A 93:7 mixture of (3*E*,5*Z*)- and (3*Z*,5*Z*)-2,2-dimethyl-7-phenyl-3,5-decadiene (32).



To a solution of [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide (**7**) (115 mg, 0.309 mmol) in THF (1.80 mL) and HMPA (0.535 mL, 3.08 mmol) was added *n*-BuLi (0.233 mL, 1.58 M solution in hexane, 0.368 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, pivalaldehyde (0.050 mL, 0.460 mmol) was added at –78 °C. After the reaction was continued at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (45.5 mg, (3*E*,5*Z*)/(3*Z*,5*Z*) = 93:7, 61%) as an oil.

Major (3*E*,5*Z*)-isomer: ^{1}H NMR δ 0.90 (t, *J* = 7.6 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$), 1.04 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.29 (m, 2H, CH$_3$C$\underline{H}_2$CH$_2$), 1.69 (m, 2H, CH$_3$CH$_2$C$\underline{H}_2$), 3.73 (dt, *J* = 10.4, 7.6 Hz, 1H, C$\underline{H}$Ph), 5.43 (t, *J* = 10.4 Hz, 1H, C$\underline{H}$=CH-CH=CH-C(CH$_3$)$_3$), 5.70 (d, *J* = 15.6 Hz, 1H, CH=CH-CH=C$\underline{H}$-C(CH$_3$)$_3$), 5.98 (t, *J* = 10.4 Hz, 1H, CH=C$\underline{H}$-CH=CH-C(CH$_3$)$_3$), 6.30 (dd, *J* = 10.4, 15.6 Hz, 1H, CH=CH-C$\underline{H}$=CH-C(CH$_3$)$_3$), 7.14-7.31 (m, 5H, Ph-H).

^{13}C NMR δ 14.02, 20.63, 29.53 (3 carbons), 33.31, 39.09, 43.50, 120.19, 125.87, 127.27 (2 carbons), 128.42 (2 carbons), 128.60, 133.57, 145.55 (*ipso*-Ph), 146.47.

Minor (3*Z*,5*Z*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 5.53 (t, *J* = 11.6 Hz, 1H, C$\underline{H}$=CH-CH=CH-C(CH$_3$)$_3$), 5.70 (d, *J* = 11.6 Hz, 1H, CH=CH-CH=C$\underline{H}$-C(CH$_3$)$_3$), 6.18 (t, *J* = 11.6 Hz, 1H, CH=C$\underline{H}$-CH=CH-C(CH$_3$)$_3$), 6.49 (t, *J* = 11.6 Hz, 1H, CH=CH-C$\underline{H}$=CH-C(CH$_3$)$_3$).

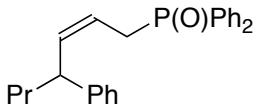
^{13}C NMR (only characteristic peaks are shown) δ 31.37 (3 carbons), 38.18, 38.93, 42.59, 121.86, 123.83, 125.04, 127.57 (2 carbons), 130.12 (2 carbons), 135.58, 142.38, 144.21.

IR (neat) 3084 (Ar), 3061 (Ar), 3027 (Ar, C=C-H), 3004 (Ar), 2958, 2930, 2866, 1650 (C=C-C=C), 1601 (C=C-C=C), 1494, 1475, 1463, 1453, 1362, 1030, 984, 949 cm^{-1} for a 93:7 mixture of (3*E*,5*Z*)- and (3*Z*,5*Z*)-isomers.

HRMS (FAB, NBA) Calcd for $C_{18}H_{26}$ [M]$^+$: 242.2035. Found: 242.2035 for a 93:7 mixture of (3*E*,5*Z*)- and (3*Z*,5*Z*)-isomers.

The 3*E*,5*Z*-diene stereochemistry of the major isomer was confirmed by ^{1}H NMR coupling constants.

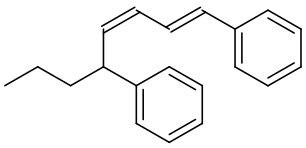
Confirmation of the formation of intermediate (33), in the one-pot reaction (Scheme 4). [(*Z*)-4-Phenyl-2-heptenyl]diphenylphosphine oxide (7).



To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (29.6 mg, 0.100 mmol) and $FeCl_2$ (1.27 mg, 0.010 mmol) in THF (1.00 mL) and HMPA (0.175 mL, 1.00 mmol) was added phenylmagnesium bromide (0.171 mL, 1.170 M solution in THF, 0.200 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (36.9 mg, 99%) as an oil and as a single olefinic isomer.

For spectral data, see: [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide (**7**).

One-pot procedure: An 94:6 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene (27).



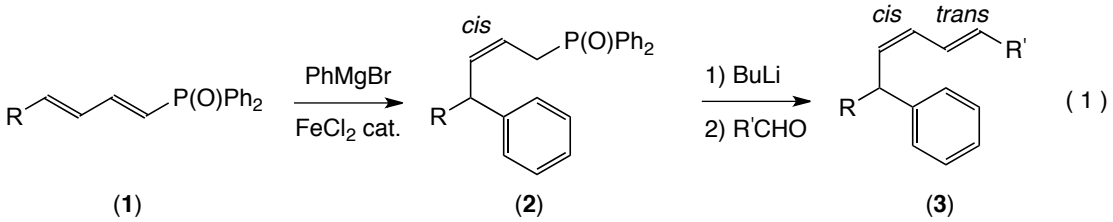
To a solution of [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide (**6**) (148.2 mg, 0.500 mmol) and $FeCl_2$ (6.3 mg, 0.050 mmol) in THF (1.00 mL) and HMPA (0.870 mL, 5.00 mmol) was added phenylmagnesium bromide (0.820 mL, 1.22 M solution in THF, 1.00 mmol) at –45 °C under argon. After the mixture was warmed up to 0 °C over 5 h, *n*-BuLi (1.27 mL, 1.58 M solution in hexane, 2.00 mmol) was added dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, benzaldehyde (0.255 mL, 2.50 mmol) was added at –78 °C. After the reaction was continued at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (99.8 mg, (1*E*,3*Z*)/(1*E*,3*E*) = 94:6, 76%) as a pale yellow oil.

For spectral data, see: a 96:4 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene (**27**).

Chapter 4. Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Phosphonates and Its Synthetic Application

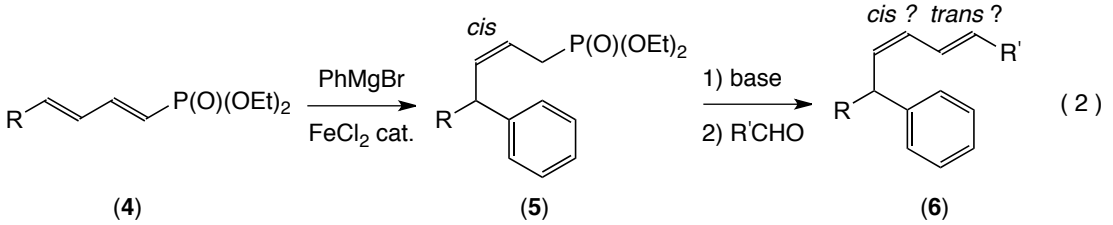
Introduction

In the preceding chapter, we described the iron-catalyzed selective δ-addition of aryl Grignard reagents to α,β,γ,δ-unsaturated phosphine oxides **1** as shown in eq 1. The utility of its products **2** in the Wittig reaction, giving stereo-defined arylated dienes **3**, was subsequently demonstrated.



(**1**) (**2**) (**3**) (1)

In this chapter, we would like to disclose the suitability of another representative phosphorus functional group, phosphonate formulated as $(RO)_2P(O)$-, in this selective conjugate addition in place of the phosphine oxides described in the preceding chapter.[1] The whole transformation can be formulated as in eq 2.

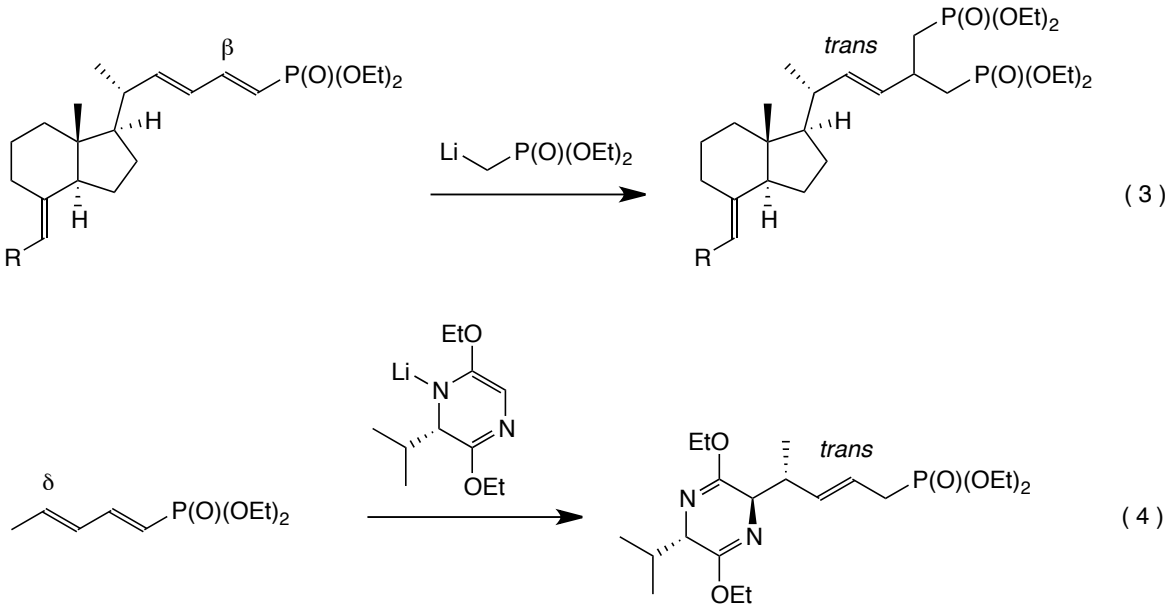


(**4**) (**5**) (**6**) (2)

As a phosphonate group is of less electron-withdrawing character than phosphine oxide, our initial concern was whether the addition to α,β,γ,δ-unsaturated phosphonates **4** smoothely took place or not. Despite such a negative expectation, we fortunately found that the transformation of eq 2 is in fact feasible to give **5**, and more importantly the high *cis*-selectivity in the resultant olefin **5** is again attained. The product **5** could be used for the Wittig reaction, giving dienes **6**, whose stereoselectivity will be compared with that described in Chapter 3.

As far as the conjugate addition to α,β,γ,δ-unsaturated phosphonates is concerned, a couple of related reactions are known (Scheme 1).[2] However, the first reaction is a β-addition of the nucleophile (eq 3)[2a] and the second is a δ-addition yet yielding the *trans*-olefinic product (eq 4).[2b] Thus, both reactions are different from our regio- and stereoselection so that these reactions could be used complementarily each other.

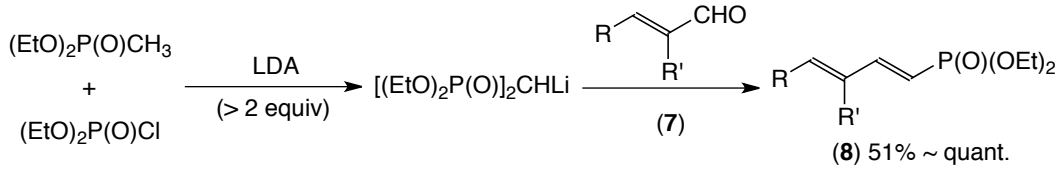
Scheme 1. Some Relevant Reactions.



Results and Discussion

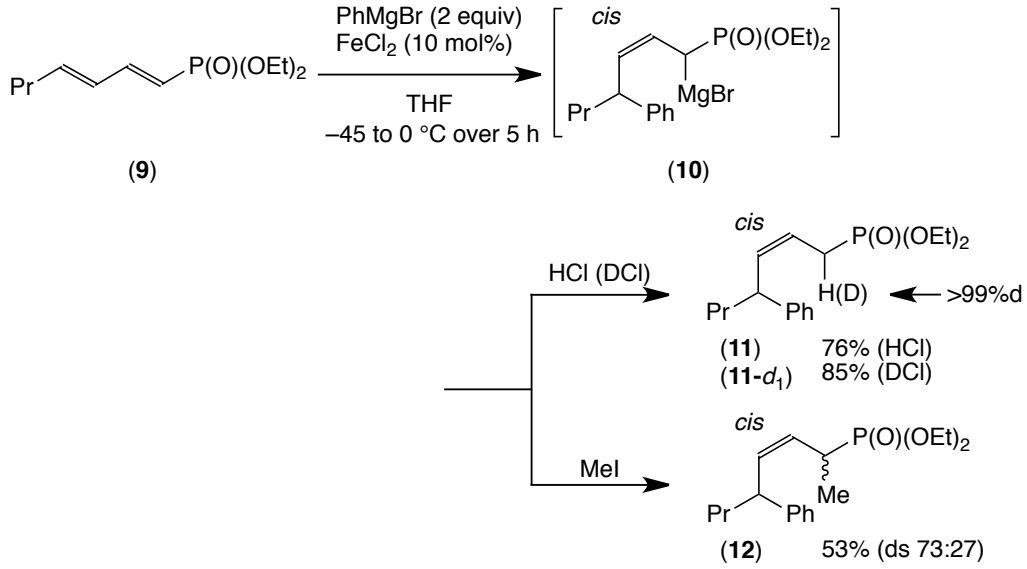
The preparation of requisite α,β,γ,δ-unsaturated phosphonates **8** was readily carried out with the same methodology shown in Chapter 3, starting from α,β-unsaturated aldehydes **7** as shown in Scheme 2.[3]

Scheme 2. Preparation of α,β,γ,δ-Unsaturated Phosphonates.



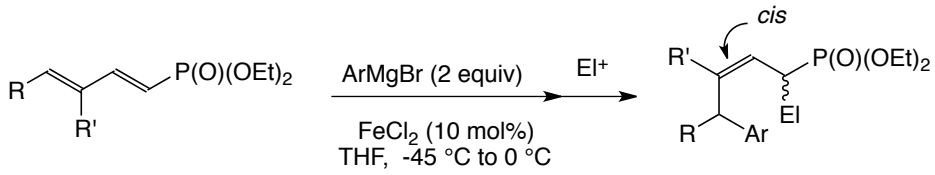
Diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate (**9**) was treated with 10 mol % of $FeCl_2$ and PhMgBr under the conditions similar to those in Chapter 3. After hydrolysis, *cis*-allylphosphonate **11** was obtained in good yields and with the exclusive olefinic stereoselectivity as shown in Scheme 3. Deuteriolysis gave **11**-d_1 with high deuterium incorporation, showing the presence of magnesiated intermediate **10**. This intermediate **10** was successfully utilized for further carbon-carbon bond formation such as methylation, giving **12** in good yield and with exclusive *cis*-olefinic stereochemistry.

Scheme 3. Iron-catalyzed Selective δ-Addition of PhMgBr to Diethyl (1*E*,3*E*)-1,3-Heptadienylphosphonate.



As we were able to establish the fundamental reaction, we proceeded to see the scope and limitation of this reaction. The results of the conjugated addition starting from various α,β,γ,δ-unsaturated phosphonates and Grignard reagents are summarized in Table 1. In addition to diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate (**9**), other α,β,γ,δ-unsaturated phosphonates **13** and **14** having a different side chain afforded the desired products **16** and **17** in good yields and with exclusively *cis*-olefinic selectivity (entries 4 and 5). Furthermore, phosphonate **15** of a different substitution pattern reacted smoothly with the Grignard reagent to produce allylphosphonate **18** in good yield as a single product (entry 6). On the other hand, aryl Grignard reagents like tolyl-, anisyl-, and 3,5-dimethoxyphenylmagnesium bromides afforded the single desired products with *cis*-olefin (**19**-**21**) in good yields (entries 7-9).

Table 1. Preparation of Various *cis*-Allylphosphonates.

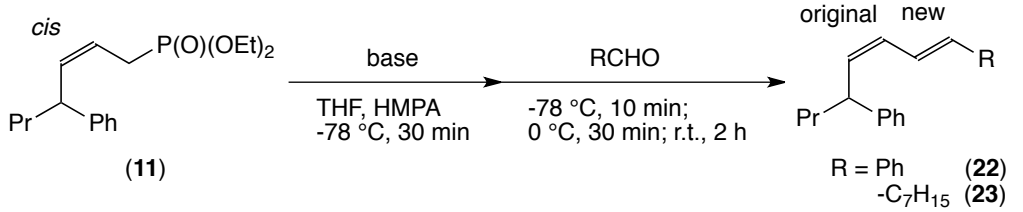


	substrate				product				
entry	R	R'		ArMgBr	El+	El	yield (%)		ds
1	Pr	H	(**9**)	PhMgBr	HCl	H	76	(**11**)	
2	Pr	H	(**9**)		DCl	D	85 (>99% *d*)	(**11**-d_1)	n.d.[a]
3	Pr	H	(**9**)		MeI	Me	53	(**12**)	73:27
4	$Ph(CH_2)_2$-	H	(**13**)		HCl	H	47	(**16**)	
5	*c*-C_6H_{11}-	H	(**14**)		HCl	H	94	(**17**)	
6[b]	Pr	Et	(**15**)		HCl	H	quant.	(**18**)	
7	Pr	H	(**9**)	4-MeC_6H_4MgBr	HCl	H	54	(**19**)	
8	Pr	H	(**9**)	4-$(MeO)C_6H_4MgBr$	HCl	H	60	(**20**)	
9	Pr	H	(**9**)	3,5-$(MeO)_2C_6H_3MgBr$	HCl	H	94	(**21**)	

[a] The diastereoselectivity was hardly determined by ^1H NMR spectroscopy.
[b] PhMgBr (3 equiv) and $FeCl_2$ (20 mol%) were used.

Having established the iron-catalyzed preparation of *cis*-allylphosphonates, we started to investigate the Wittig reaction by using these allylphosphonates. Table 2 summarizes its results, starting from **11** and benzaldehyde as representative substrates and yielding **22** (entries 1-8). Considering both product yields and diene stereoselectivities, we judged that NaHMDS (HMDS = hexamethyldisilazide, $(Me_3Si)_2N^-$) is the base of choice in place of BuLi used in Chapter 3. This tendency is also valid for an aliphatic aldehyde, octanal (entries 9-11). In both cases, the combined use of this base and HMPA was again essential (entry 6 vs. 7 and entry 9 vs. 10).

Table 2. Optimum Conditions for the Wittig Reaction with Diethyl (*Z*)-4-Phenyl-2-heptenylphosphonate.



(**11**)

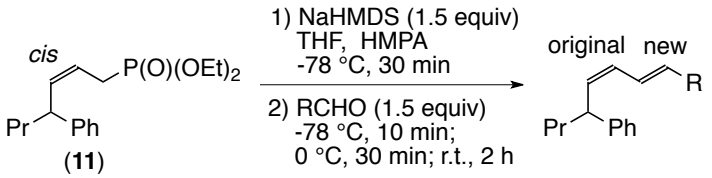
R = Ph (**22**)
$-C_7H_{15}$ (**23**)

entry	base (equiv)	HMPA[a]	RCHO (equiv)	isolated yield (%)	original *cis* : *trans*	new *trans* : *cis*
1	BuLi (1.2)	+	PhCHO (1.2)	39	95: 5	*trans* only
2	LiHMDS (1.2)	+	PhCHO (1.2)	42	97: 3	*trans* only
3	NaHMDS (1.2)	+	PhCHO (1.2)	54	96: 4	*trans* only
4	KHMDS (1.2)	+	PhCHO (1.2)	62	93: 7	*trans* only
5	LiHMDS (1.5)	+	PhCHO (1.5)	46	97: 3	*trans* only
6	**NaHMDS (1.5)**	**+**	**PhCHO (1.5)**	**71**	**93: 7**	***trans* only**
7	NaHMDS (1.5)	-	PhCHO (1.5)	33	97: 3	*trans* only
8	KHMDS (1.5)	+	PhCHO (1.5)	61	95: 5	*trans* only
9	**NaHMDS (1.5)**	**+**	**$C_7H_{15}CHO$ (1.5)**	**74**	***cis* only**	**83:17**
10	NaHMDS (1.5)	-	$C_7H_{15}CHO$ (1.5)	16	*cis* only	89:11
11	KHMDS (1.5)	+	$C_7H_{15}CHO$ (1.5)	67	*cis* only	60:40

[a] + : added, - : omitted.

Under the optimal conditions using NaHMDS as base, other results of Wittig reaction are summarized in Table 3. In the reaction with both aromatic and aliphatic aldehydes (**22** and **23**), the major isomer was readily characterized by ^{1}H NMR spectroscopy, and the structure of the minor isomer was unambiguously identified by the comparison with authentic samples, which are the same compound prepared in eqs 4 and 5 of Chapter 3.[4] The other two possible minor olefinic stereoisomers have not been detected in a crude reaction mixture in each case (entries 1 and 2). As the steric hindrance of the aliphatic aldehydes increases, the *trans* selectivity of the newly formed olefin increases (entries 2-4), which may be an expected observation.

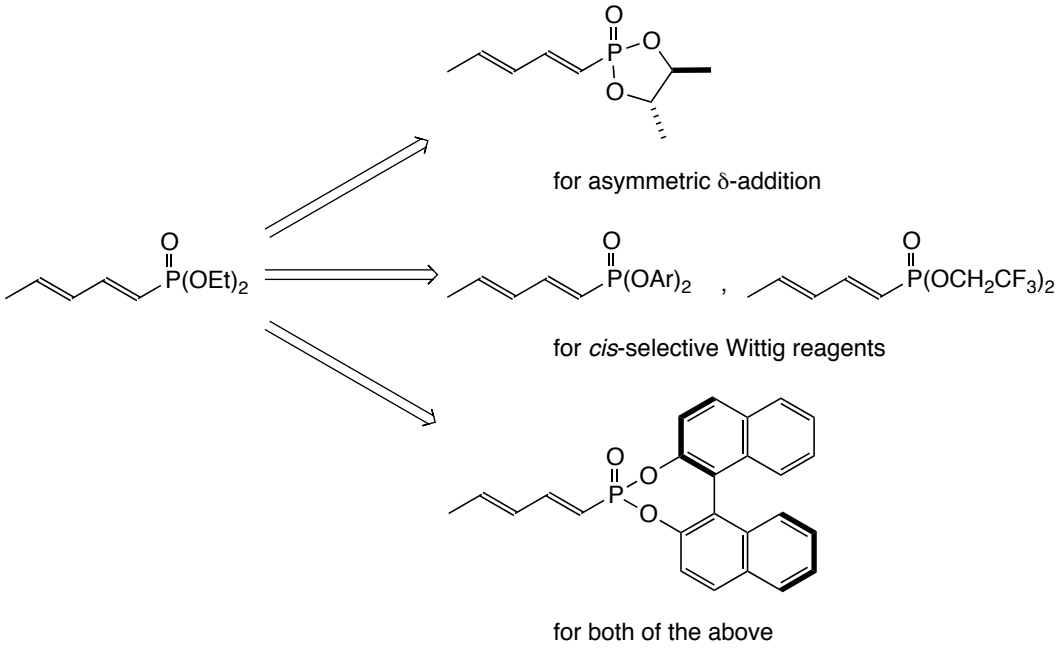
Table 3. *cis*-Allylphosphonates as Wittig Reagents.



entry	RCHO	product: isolated yield (%)	product: original (*cis* : *trans*)	product: new (*trans* : *cis*)
1	PhCHO	(**22**) 71	93: 7	*trans* only
2	$C_7H_{15}CHO$	(**23**) 74	*cis* only	83:17
3	*c*-$C_6H_{11}CHO$	(**24**) 72	*cis* only	81:19
4	*t*-BuCHO	(**25**) 76	*cis* only	92: 8

In general, there is little difference in both reactivity and selectivity of the iron-catalyzed addition and its subsequent Wittig reaction between α,β,γ,δ-unsaturated phosphine oxides and the corresponding phosphonates. However, the ligand modification on the P atom is much easier for phosphonates than phosphine oxides. Thus, the information obtained in this chapter appears more important, because it facilitates the extension of this reaction to the asymmetric conjugate addition as well as *cis*-selective Wittig reaction. A few examples of such idea are listed in Scheme 3 as perspective of this chapter.[1,5]

Scheme 3. Perspective of Conjugate Addition to α,β,γ,δ-Unsaturated Phosphonates.



Conclusion

In conclusion, we successfully extended the iron-catalyzed selective addition of aryl Grignard reagents to α,β,γ,δ-unsaturated phosphonates to give *cis*-allylphosphonates, which can be utilized as Wittig reagents to produce stereo-defined arylated dienes. Further investigation on these reactions and their applications is now in progress.

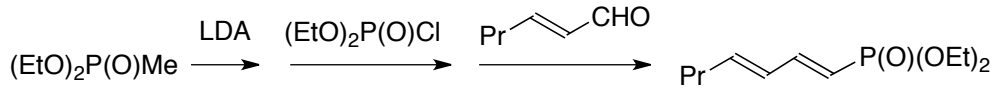
References and Notes

1. For reviews on organophosphorus chemistry, see: (a) Cadogan, J. I. G., Ed. *Organophosphorus Reagents in Organic Synthesis*; Academic Press: London, 1979. (b) Quin, L. D. *A Guide to Organophosphorus Chemistry*; John Wiley & Sons: New York, 2000. (c) Murphy, P. J., Ed. *Organophosphorus Reagents*; Academic Press: Oxford, 2004.
2. (a) Steinmeyer, A.; Schwarz, K.; Haberey, M.; Langer, G.; Wiesinger, H. *Steroids* **2001**, *66*, 257–266. (b) Ojea, V.; Conde, S.; Ruiz, M.; Fernández, M. C.; Quintela J. M. *Tetrahedron Lett*. **1997**, *38*, 4311–4314. See also: (c) Hornillos, V.; Pérez, M.; Fañanás-Mastral, M.; Feringa, B. L. *Chem. Eur. J*. **2013**, *19*, 5432-5441.
3. Ojea, V.; Conde, S.; Ruiz, M.; Fernández, M. C.; Quintela J. M. *Tetrahedron Lett*. **1997**, *38*, 4311–4314.
4. For preparation of authentic samples, see: (a) Jung, H.-Y.; Feng, X.; Kim, H.; Yun, J. *Tetrahedron* **2012**, *68*, 3444-3449. (b) Fotsop, D. F.; Roussi, F.; Leverrier, A.; Bretéché, A.; Guéritte, F. *J. Org. Chem*. **2010**, *75*, 7412-7415.
5. Ando, K.; Okumura, M.; Nagaya, S. *Tetrahedron Lett*. **2013**, *54*, 2026-2028.

Experimental section (Chapter 4)

General. ^{1}H and ^{13}C NMR spectra were taken on an Agilent 400-MR spectromer at 400 and 100 MHz, respectively. $CDCl_3$ and C_6D_6 were used as the solvent. Unless otherwise specified in spectral data, the former was always used. Chemical shifts are reported in parts per million shift (δ value) from Me_4Si (δ 0 ppm for ^{1}H) or based on the middle peak of the solvent ($CDCl_3$) (δ 77.00 ppm for ^{13}C NMR) as an internal standard. Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in Hertz. Infrared (IR) spectra were recorded on a JASCO FT/IR-4100 spectrometer and are reported in wave numbers (cm^{-1}). High resolution mass spectra (HRMS) were obtained on a Bruker micrOTOF II in positive electrospray ionization (ESI) method calibrated with sodium formate at the Suzukake-dai Material Analysis Center, Technical Department, Tokyo Institute of Technology. For recycling preparative HPLC, a Model LC-9201R/U equipped with a JAIGEL-H column (length: 600 mm × 2 cycles, bore: 20 mm) purchased from Japan Analytical Industry Co., Ltd. (Japan) was used. All reactions were carried out under argon. Dry solvents (THF, diethyl ether, and CH_2Cl_2) were purchased from Kanto Chemicals Co. (Japan). Chemicals were purified or dried in a standard manner, if necessary.

Diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate (9).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a solution of diisopropylamine (1.29 mL, 9.04 mmol) in THF (15 mL) was added *n*-BuLi (7.27 mL, 1.64 M solution in hexane, 12.0 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and diethyl methylphosphonate (0.870 mL, 6.00 mmol) was added. The mixture was stirred at –78 °C for 10 min and diethyl chlorophosphate (0.860 mL, 6.00 mmol) was added at that temperature. After stirring for 10 min, *trans*-2-hexenal (0.580 mL, 5.00 mmol) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (1.28 g, quant.) as an oil and as a single olefinic isomer.

^{1}H NMR δ 0.92 (t, *J* = 7.2 Hz, 3H, $C\underline{H}_3CH_2CH_2$), 1.33 (t, *J* = 7.2 Hz, 6H, $-P(O)(OCH_2C\underline{H}_3)_2$), 1.43 (sextet, *J* = 7.2 Hz, 2H, $CH_3C\underline{H}_2CH_2$), 2.13 (q, *J* = 7.2 Hz, 2H, $CH_3CH_2C\underline{H}_2$), 4.08 (quintet, *J* = 7.2 Hz, 4H, $-P(O)(OC\underline{H}_2CH_3)_2$), 5.57 (dd, *J* = 17.2, 19.6 Hz, 1H, $-CH=CH-CH=C\underline{H}-P(O)(OEt)_2$), 6.06 (dt, *J* = 15.2, 7.2 Hz, 1H, $-C\underline{H}=CH-CH=CH-P(O)(OEt)_2$), 6.14 (dd, *J* = 10.0, 15.2 Hz, 1H, $-CH=C\underline{H}-CH=CH-P(O)(OEt)_2$),

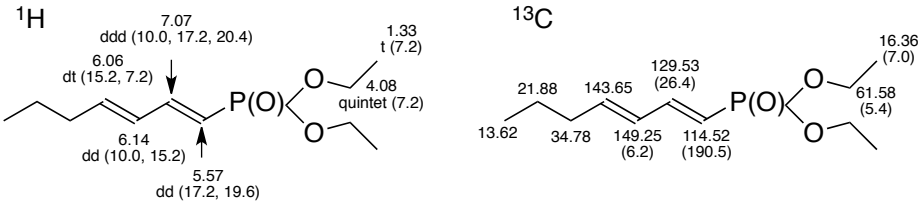
7.07 (ddd, J = 10.0, 17.2, 20.4 Hz, 1H, -CH=CH-C<u>H</u>=CH-P(O)(OEt)$_2$).

^{13}C NMR δ 13.62, 16.36 (d, J = 7.0 Hz, 2 carbons, -P(O)(OCH$_2$<u>C</u>H$_3$)$_2$), 21.88, 34.78, 61.58 (d, J = 5.4 Hz, 2 carbons, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 114.52 (d, J = 190.5 Hz, -CH=CH-CH=<u>C</u>H-P(O)(OEt)$_2$), 129.53 (d, J = 26.4 Hz, -CH=CH-<u>C</u>H=CH-P(O)(OEt)$_2$), 143.65 (-<u>C</u>H=CH-CH=CH-P(O)(OEt)$_2$), 149.25 (d, J = 6.2 Hz, -CH=<u>C</u>H-CH=CH-P(O)(OEt)$_2$).

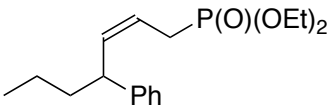
IR (neat) 3019 (C=C-H), 2980, 2961, 2931, 2907, 2873, 1644 (C=C-C=C), 1595 (C=C-C=C), 1247 (P=O), 1055, 1028, 963 cm^{-1}.

HRMS (ESI) Calcd for $C_{11}H_{21}O_3PNa$ [M+Na]$^+$: 255.1121. Found: 225.1121.

The (*E*,*E*)-stereochemistry was confirmed by ^{1}H NMR coupling constants.



Diethyl (*Z*)-4-phenyl-2-heptenylphosphonate (11).



To a solution of diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate (**9**) (46.5 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.345 mL, 1.16 M solution in THF, 0.400 mmol) dropwise at –45 °C under argon. After the solution was warmed to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (46.9 mg, 76%) as an oil and as a single olefinic isomer.

^{1}H NMR δ 0.89 (t, J = 7.6 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.25 (t, J = 7.2 Hz, 3H, -P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 1.27 (t, J = 7.2 Hz, 3H, -P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 1.29 (m, 2H, CH$_3$C<u>H</u>$_2$CH$_2$), 1.65 (m, 2H, CH$_3$CH$_2$C<u>H</u>$_2$), 2.60 (dt, J = 14.8, 7.6 Hz, 1H, -CH=CHC<u>H</u>$_2$P(O)(OEt)$_2$), 2.70 (dt, J = 14.8, 7.6 Hz, 1H, -CH=CHC<u>H</u>$_2$P(O)(OEt)$_2$), 3.52 (dt, J = 10.0, 7.6 Hz, 1H, PrC<u>H</u>Ph), 4.02 (m, 4H, -P(O)(OC<u>H</u>$_2$CH$_3$)$_2$) 5.46 (dq, J = 10.0, 7.6 Hz, 1H, -CH=C<u>H</u>CH$_2$P(O)(OEt)$_2$), 5.77 (br t, J = 10.0 Hz, 1H, -C<u>H</u>=CHCH$_2$P(O)(OEt)$_2$), 7.16 (t, J = 7.2 Hz, 1H, Ph-H), 7.19 (d, J = 7.2 Hz, 2H, Ph-H), 7.27 (t, J = 7.2 Hz, 2H, Ph-H).

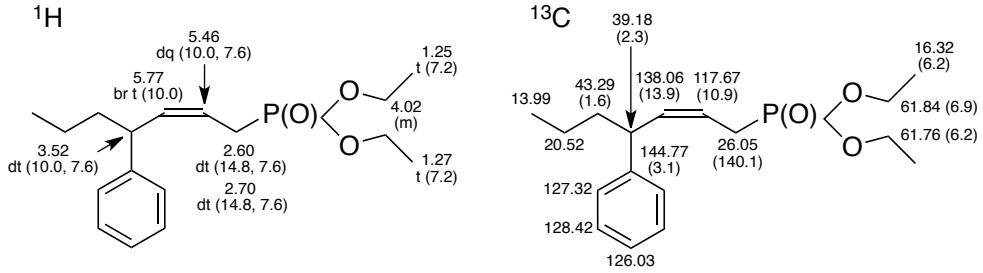
^{13}C NMR δ 13.99, 16.32 (d, J = 6.2 Hz, 2 peaks, -P(O)(OCH$_2$<u>C</u>H$_3$)$_2$), 20.52, 26.05 (d, J = 140.1 Hz, -C=C-<u>C</u>-P(O)(OEt)$_2$), 39.18 (d, J = 2.3 Hz, Pr<u>C</u>H), 43.29 (d, J = 1.6 Hz, CH$_3$CH$_2$<u>C</u>H$_2$-), 61.76 (d, J = 6.2 Hz, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 61.84 (d, J = 6.9 Hz, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 117.67 (d, J = 10.9 Hz, -C=<u>C</u>-C-P(O)(OEt)$_2$),

126.03 (*p*-Ph), 127.32 (2 carbons, *o*-Ph), 128.42 (2 carbons, *m*-Ph), 138.06 (d, J = 13.9 Hz, -C=C-C-P(O)(OEt)$_2$), 144.77 (d, J = 3.1 Hz, *ipso*-Ph).

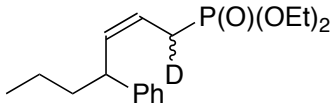
IR (neat) 3083 (Ar), 3061 (Ar), 3029 (Ar, C=C-H), 2969, 2933, 2875, 1627, 1595 (C=C), 1216 (P=O), 1029, 864, 754, 666 cm^{-1}.

HRMS (ESI) Calcd for $C_{17}H_{27}O_3PNa$ [M+Na]$^+$: 333.1590. Found: 333.1590.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



A diastereomeric mixture of diethyl (*Z*)-1-deuterio-4-phenyl-2-heptenylphosphonate (11-d_1).

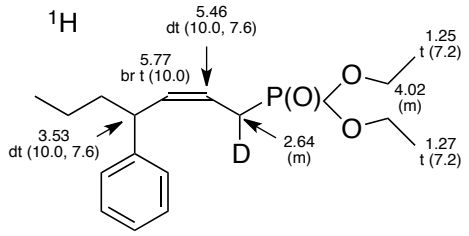


To a solution of diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate (**9**) (46.4 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.333 mL, 1.20 M solution in THF, 0.400 mmol) dropwise at –45 °C under argon. After the solution was warmed to 0 °C over 5 h, the reaction was terminated by addition of 1 N DCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity of the product was hardly determined. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (52.9 mg, 85%) as an oil. The diastereoselectivity of this product was hardly determined by ^{1}H NMR spectroscopy.

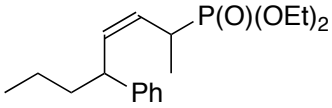
^{1}H NMR δ 0.89 (t, J = 7.6 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$), 1.25 (t, J = 7.2 Hz, 3H, -P(O)(OCH$_2$C$\underline{H}_3$)$_2$), 1.27 (t, J = 7.2 Hz, 3H, -P(O)(OCH$_2$C$\underline{H}_3$)$_2$), 1.29 (m, 2H, CH$_3$C$\underline{H}_2$CH$_2$), 1.65 (m, 2H, CH$_3$CH$_2$C$\underline{H}_2$), 2.64 (m, 1H, -CH=CHC$\underline{H}$DP(O)(OEt)$_2$), 3.53 (dt, J = 10.0, 7.6 Hz, 1H, PrC$\underline{H}$Ph), 4.02 (m, 4H, -P(O)(OC$\underline{H}_2$CH$_3$)$_2$), 5.46 (dt, J = 10.0, 7.6 Hz, 1H, -CH=C$\underline{H}$CHDP(O)(OEt)$_2$), 5.77 (br t, J = 10.0 Hz, 1H, -C$\underline{H}$=CHCHDP(O)(OEt)$_2$), 7.17 (t, J = 7.2 Hz, 1H, Ph-H), 7.19 (d, J = 7.2 Hz, 2H, Ph-H), 7.28 (t, J = 7.2 Hz, 2H, Ph-H).

The integration of peak area at δ 2.64 (-CH=CHC$\underline{H}$D-P(OEt)$_2$) decreased its original value (2 H) to total 1.0 H to show >99% deuterium incorporation at this position.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



A 73:27 diastereomeric mixture of diethyl (*Z*)-5-phenyl-3-octen-2-ylphosphonate (12).



To a solution of diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate (**9**) (46.5 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.330 mL, 1.22 M solution in THF, 0.400 mmol) dropwise at –45 °C under argon. After the mixture was warmed to 0 °C over 5 h, methyl iodide (0.060 mL, 1.00 mmol) and HMPA (0.330 mL, 2.00 mmol) were added in this order. After the reaction mixture was heated in an oil bath maintained at 50 °C for 12 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which revealed that the olefinic bond was exclusively *cis* and the diastereoselectivity was 73:27. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (34.5 mg, 53%) as an oil and of the same diastereomeric composition as observed for a crude sample.

Major isomer: ^{1}H NMR δ 0.90 (t, *J* = 7.6 Hz, 3H, $C\underline{H}_3CH_2CH_2$), 1.12 (t, *J* = 7.2 Hz, 3H, -P(O)($OCH_2C\underline{H}_3$)$_2$), 1.18 (t, *J* = 7.2 Hz, 3H, -P(O)($OCH_2C\underline{H}_3$)$_2$), 1.28 (m, 2H, $CH_3C\underline{H}_2CH_2$), 1.30 (dd, *J* = 7.2, 18.8 Hz, 3H, -CH(<u>Me</u>)P(O)$(OEt)_2$), 1.58 (m, 2H, $CH_3CH_2C\underline{H}_2$), 3.00 (m, 1H, -C<u>H</u>(Me)P(O)$(OEt)_2$), 3.52 (dt, *J* = 10.4, 7.2 Hz, 1H, -C<u>H</u>Ph), 3.95 (m, 2H, -P(O)($OC\underline{H}_2CH_3$)$_2$), 4.13 (m, 2H, -P(O)($OC\underline{H}_2CH_3$)$_2$), 5.38 (dt, *J* = 7.2, 10.4 Hz, 1H, -CH=C<u>H</u>-CH(Me)P(O)$(OEt)_2$), 5.67 (dt, *J* = 3.6, 10.4 Hz, 1H, -C<u>H</u>=CH-CH(Me)P(O)$(OEt)_2$), 7.13-7.30 (m, 5H, Ph-H).

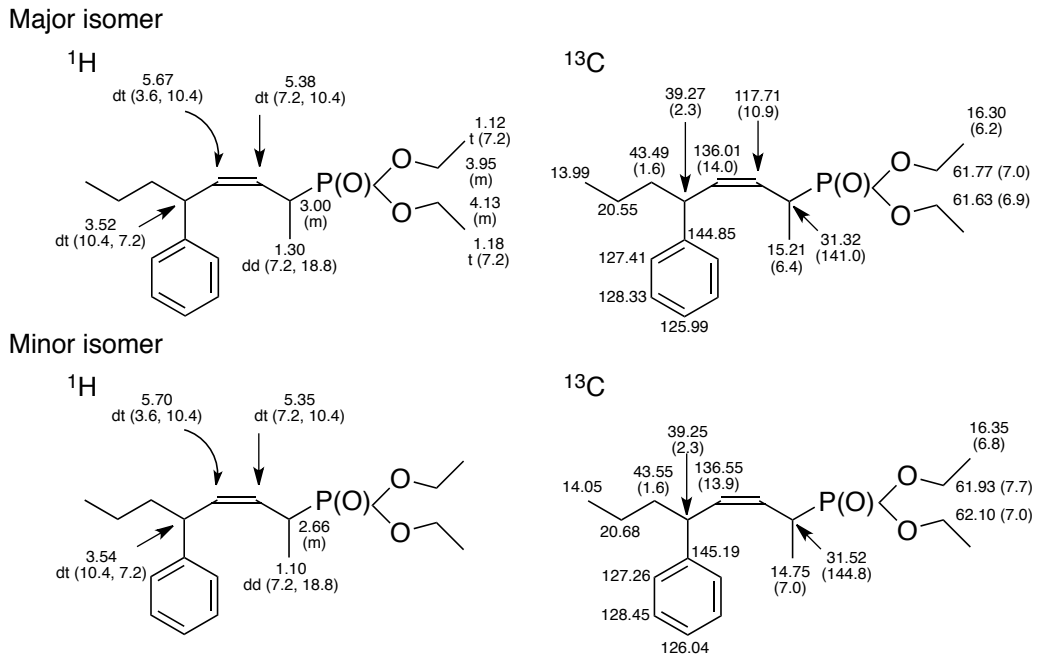
^{13}C NMR δ 13.99, 15.21 (d, *J* = 6.4 Hz, -CH(<u>Me</u>)), 16.30 (d, *J* = 6.2 Hz, 2 peaks, -P(O)($OCH_2\underline{C}H_3$)$_2$), 20.55, 31.32 (d, *J* = 141.0 Hz, -C=C-<u>C</u>-P(O)$(OEt)_2$), 39.27 (d, *J* = 2.3 Hz, Pr<u>C</u>H), 43.49 (d, *J* = 1.6 Hz, $CH_3CH_2\underline{C}H_2$-), 61.63 (d, *J* = 6.9 Hz, -P(O)($O\underline{C}H_2CH_3$)$_2$), 61.77 (d, *J* = 7.0 Hz, -P(O)($O\underline{C}H_2CH_3$)$_2$), 117.71 (d, *J* = 10.9 Hz, -C=<u>C</u>-C-P(O)$(OEt)_2$), 125.99 (*p*-Ph), 127.41 (2 carbons, *o*-Ph), 128.33 (2 carbons, *m*-Ph), 136.01 (d, *J* = 14.0 Hz, -<u>C</u>=C-C-P(O)$(OEt)_2$), 144.85 (*ipso*-Ph).

Minor isomer: ^{1}H NMR (only characteristic peaks are shown) δ 0.88 (t, *J* = 7.2 Hz, 3H, alkyl-Me), 1.10 (dd, *J* = 7.2, 18.8 Hz, 3H, -CH(<u>Me</u>)P(O)$(OEt)_2$), 2.66 (m, 1H -C<u>H</u>(Me)P(O)$(OEt)_2$), 3.54 (dt, *J* = 10.4, 7.2 Hz, 1H, -C<u>H</u>Ph), 5.35 (dt, *J* = 7.2, 10.4 Hz, 1H, -CH=C<u>H</u>-CH(Me)P(O)$(OEt)_2$), 5.70 (dt, *J* = 3.6, 10.4 Hz, 1H, -C<u>H</u>=CH-CH(Me)P(O)$(OEt)_2$), 7.14-7.29 (m, 5H, Ph-H).

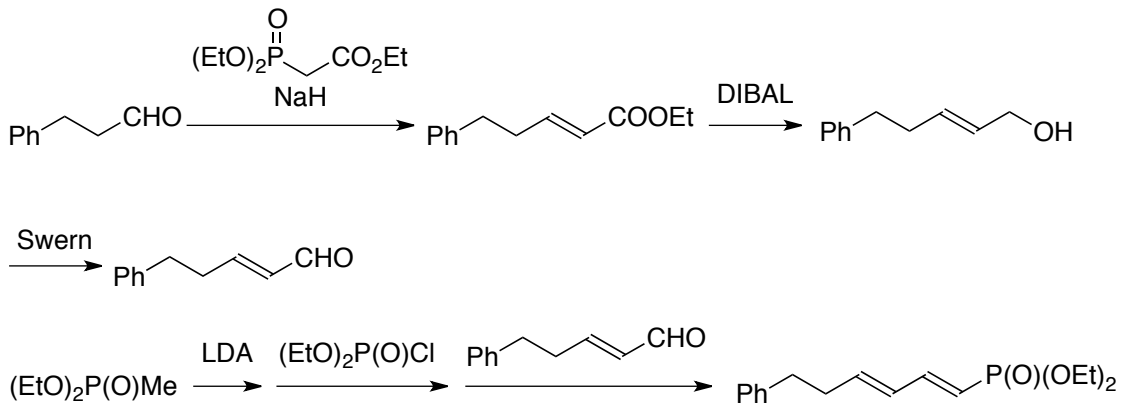
^{13}C NMR (only characteristic peaks are shown) δ 14.05, 14.75 (d, *J* = 7.0 Hz, -CH(Me)), 16.35 (d, *J* = 6.8 Hz, 2 peaks, -P(O)(OCH$_2$CH$_3$)$_2$), 20.68, 31.52 (d, *J* = 144.8 Hz, -C=C-C-P(O)(OEt)$_2$), 39.25 (d, *J* = 2.3 Hz, PrCH), 43.55 (d, *J* = 1.6 Hz, CH$_3$CH$_2$CH$_2$-), 61.93 (d, *J* = 7.7 Hz, -P(O)(OCH$_2$CH$_3$)$_2$), 62.10 (d, *J* = 7.0 Hz, -P(O)(OCH$_2$CH$_3$)$_2$), 126.04 (*p*-Ph), 127.26 (2 carbons, *o*-Ph), 128.45 (2 carbons, *m*-Ph), 136.55 (d, *J* = 13.9 Hz, -C=C-C-P(O)(OEt)$_2$), 145.19 (*ipso*-Ph).

IR (neat) 3083 (Ar), 3061 (Ar), 3026 (Ar, C=C-H), 2958, 2931, 2873, 1601 (C=C), 1455, 1247 (P=O), 1163, 1058, 1025, 964, 752, 700 cm^{-1} for a 73:27 diastereomeric mixture of diethyl (*Z*)-5-phenyl-3-octen-2-ylphosphonate.

HRMS (ESI) Calcd for $C_{18}H_{29}O_3PNa$ $[M+Na]^+$: 347.1747. Found: 347.1742 for a 73:27 diastereomeric mixture of diethyl (*Z*)-5-phenyl-3-octen-2-ylphosphonate.



Diethyl (1*E*,3*E*)-6-phenyl-1,3-hexadienylphosphonate (13).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.;

Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a solution of diisopropylamine (1.24 mL, 8.25 mmol) in THF (20 mL) was added *n*-BuLi (7.04 mL, 1.64 M solution in hexane, 11.5 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and and diethyl methylphosphonate (0.840 mL, 5.77 mmol) was added. The mixture was stirred at –78 °C for 10 min and diethyl chlorophosphate (0.830 mL, 5.77 mmol) was added at that temperature. After stirring for 10 min, (*E*)-5-phenyl-2-pentenal (771 mg, 4.81 mmol) in THF (5 mL) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (771 mg, 54%) as an oil and as a single olefinic isomer.

^{1}H NMR δ 1.32 (t, *J* = 7.2 Hz, 6H, -P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 2.46 (dt, *J* = 6.8, 7.6 Hz, 2H, PhCH$_2$C<u>H</u>$_2$), 2.73 (t, *J* = 7.6 Hz, 2H, PhC<u>H</u>$_2$CH$_2$), 4.06 (quintet, *J* = 7.2 Hz, 4H, -P(O)(OC<u>H</u>$_2$CH$_3$)$_2$), 5.57 (dd, *J* = 17.2, 19.2 Hz, 1H, -CH=CH-CH=C<u>H</u>-P(O)(OEt)$_2$), 6.08 (dt, *J* = 15.2, 6.8 Hz, 1H, -C<u>H</u>=CH-CH=CH-P(O)(OEt)$_2$), 6.15 (dd, *J* = 10.0, 15.2 Hz, 1H, -CH=C<u>H</u>-CH=CH-P(O)(OEt)$_2$), 7.05 (ddd, *J* = 10.0, 17.2, 20.8 Hz, 1H, -CH=CH-C<u>H</u>=CH-P(O)(OEt)$_2$), 7.15 (d, *J* = 7.2 Hz, 2H, Ph-H), 7.19 (t, *J* = 7.2 Hz, 1H, Ph-H), 7.28 (t, *J* = 7.2 Hz, 2H, Ph-H).

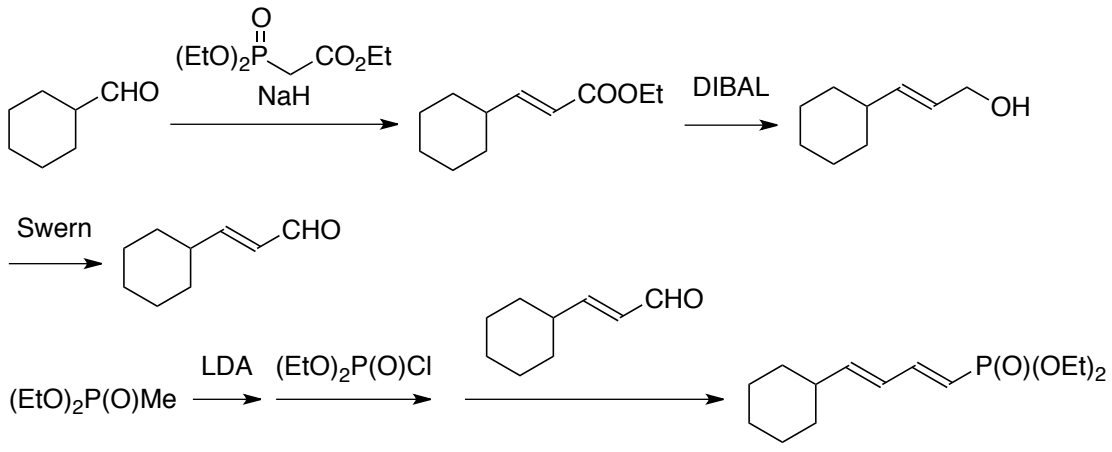
^{13}C NMR δ 16.24 (d, *J* = 6.2 Hz, 2 carbons, -P(O)(OCH$_2$<u>C</u>H$_3$)$_2$), 34.36, 34.94, 61.51 (d, *J* = 5.3 Hz, 2 carbons, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 114.98 (d, *J* = 190.5 Hz, -CH=CH-CH=<u>C</u>H-P(O)(OEt)$_2$), 125.94 (*p*-Ph), 128.24 (2 carbons, *o*-Ph), 128.29 (2 carbons, *m*-Ph), 129.81 (d, *J* = 26.3 Hz, -CH=CH-<u>C</u>H=CH-P(O)(OEt)$_2$), 140.94 (*ipso*-Ph), 142.28 (-<u>C</u>H=CH-CH=CH-P(O)(OEt)$_2$), 148.83 (d, *J* = 5.4 Hz, -CH=<u>C</u>H-CH=CH-P(O)(OEt)$_2$).

IR (neat) 3086 (Ar), 3063 (Ar, C=C-H), 2991, 1644 (C=C-C=C), 1595 (C=C-C=C), 1454, 1238, 1217 (P=O), 1029, 755, 667 cm^{-1}.

HRMS (ESI) Calcd for $C_{16}H_{23}O_3PNa$ [M+Na]$^+$: 317.1286. Found: 317.1277.

The (*E*,*E*)-diene stereochemistry was confirmed by ^{1}H NMR coupling constants.

Diethyl (1*E*,3*E*)-4-cyclohexyl-1,3-butadienylphosphonate (14).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a solution of diisopropylamine (1.78 mL, 12.7 mmol) in THF (25 mL) was added *n*-BuLi (10.1 mL, 1.64 M solution in hexane, 16.6 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and diethyl methylphosphonate (1.20 mL, 8.30 mmol) was added. The mixture was stirred at –78 °C for 10 min and diethyl chlorophosphate (1.20 mL, 8.30 mmol) was added at that temperature. After stirring for 10 min, (*E*)-3-cyclohexyl-2-propenal (956 mg, 6.92 mmol) in THF (5 mL) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (956 mg, 51%) as an oil and as a single olefinic isomer.

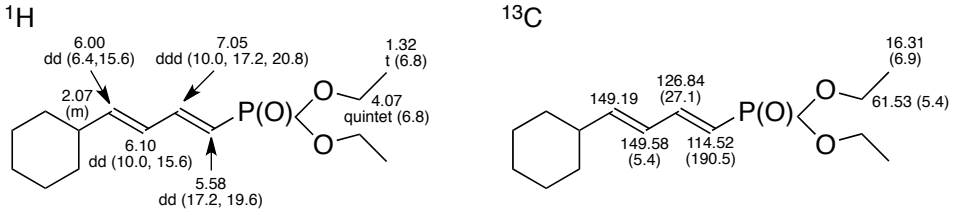
^{1}H NMR δ 1.06-1.37 (m, 6H, alkyl-H), 1.32 (t, J = 6.8 Hz, 6H, -P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 1.62-1.78 (m, 4H, alkyl-H), 2.07 (m, 1H, alkyl-H), 4.07 (quintet, J = 6.8 Hz, 4H, -P(O)(OC<u>H</u>$_2$CH$_3$)$_2$), 5.58 (dd, J = 17.2, 19.6 Hz, 1H, -CH=CH-CH=C<u>H</u>-P(O)(OEt)$_2$), 6.00 (dd, J = 6.4, 15.6 Hz, 1H, -C<u>H</u>=CH-CH=CH-P(O)(OEt)$_2$), 6.10 (dd, J = 10.0, 15.6 Hz, 1H, -CH=C<u>H</u>-CH=CH-P(O)(OEt)$_2$), 7.05 (ddd, J = 10.0, 17.2, 20.8 Hz, 1H, -CH=CH-C<u>H</u>=CH-P(O)(OEt)$_2$).

^{13}C NMR δ 16.31 (d, J = 6.9 Hz, 2 carbons, -P(O)(OCH$_2$<u>C</u>H$_3$)$_2$), 25.75 (2 carbons), 25.96, 32.20 (2 carbons), 40.81, 61.53 (d, J = 5.4 Hz, 2 carbons, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 114.52 (d, J = 190.5 Hz, -CH=CH-CH=<u>C</u>H-P(O)(OEt)$_2$), 126.84 (d, J = 27.1 Hz, -CH=CH-<u>C</u>H=CH-P(O)(OEt)$_2$), 149.19 (-<u>C</u>H=CH-CH=CH-P(O)(OEt)$_2$), 149.58 (d, J = 5.4 Hz, -CH=<u>C</u>H-CH=CH-P(O)(OEt)$_2$).

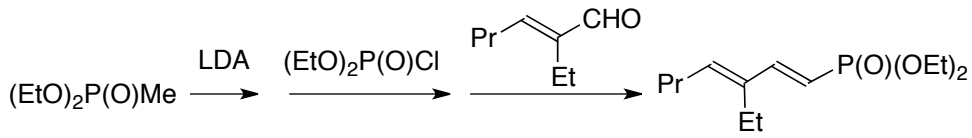
IR (neat) 3035 (C=C-H), 2983, 2926, 2852, 1642 (C=C-C=C), 1593 (C=C-C=C), 1448, 1242 (P=O), 1028, 851, 800, 753 cm^{-1}.

HRMS (ESI) Calcd for $C_{14}H_{25}O_3PNa$ [M+Na]$^+$: 295.1434. Found: 295.1433.

The (*E*,*E*)-stereochemistry was confirmed by ^{1}H NMR coupling constants.



Diethyl (1*E*,3*E*)-3-ethyl-1,3-heptadienylphosphonate (15).



The Horner-Emmons reagent was prepared by a literature method [Ashburn, B. O.; Rathbone, L. K.; Camp, E. H.; Carter, R. G. *Tetrahedron* **2008**, *64*, 856-865].

To a solution of diisopropylamine (0.520 mL, 3.70 mmol) in THF (15 mL) was added *n*-BuLi (4.40 mL, 1.64 M solution in hexane, 4.80 mmol) at 0 °C under argon. After the reaction was stirred at 0 °C for 15 min, the mixture was cooled to –78 °C and diethyl methylphosphonate (0.520 mL, 2.40 mmol) was added. The mixture was stirred at –78 °C for 10 min and diethyl chlorophosphate (0.520 mL, 2.40 mmol) was added at that temperature. After stirring for 10 min, (*E*)-2-ethyl-2-hexenal (0.450 mL, 2.00 mmol) was added and the mixture was warmed to room temperature over 5 h. The reaction was terminated by the addition of 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (487 mg, 94%) as an oil and as a single olefinic isomer.

^{1}H NMR δ 0.94 (t, *J* = 7.6 Hz, 3H, alkyl-Me), 1.01 (t, *J* = 7.6 Hz, 3H, alkyl-Me), 1.34 (m, 6H, -P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 1.46 (quintet, *J* = 7.6 Hz, 2H, CH$_3$C<u>H</u>$_2$CH$_2$CH=C), 2.17 (q, *J* = 7.6 Hz, 2H, CH$_3$CH$_2$C<u>H</u>$_2$CH=C), 2.27 (q, *J* = 7.6 Hz, 2H, PrCH=C(C<u>H</u>$_2$CH$_3$)-CH), 4.08 (m, 4H, -P(O)(OC<u>H</u>$_2$CH$_3$)$_2$), 5.59 (t, *J* = 18.0 Hz, 1H, Pr-CH=C(Et)-CH=C<u>H</u>-), 5.74 (t, *J* = 7.6 Hz, 1H, Pr-C<u>H</u>=C(Et)-CH=CH-P(O)(OEt)$_2$), 7.02 (dd, *J* = 18.0, 22.0 Hz, 1H, Pr-CH=C(Et)-C<u>H</u>=CH-P(O)(OEt)$_2$).

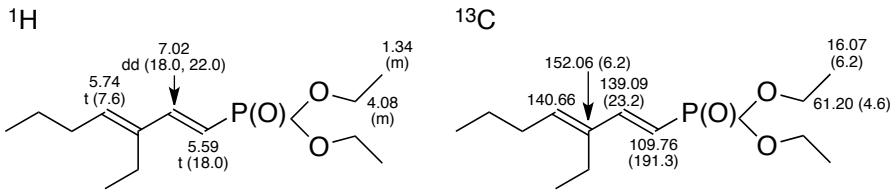
Irradiation of the proton at δ 5.74 ppm (PrC<u>H</u>=C(Et)-) showed 4.1% NOE enhancement to that at δ 7.02 (-C<u>H</u>=CH-P(O)(OEt)$_2$), while irradiation of the proton at δ 7.02 (-C<u>H</u>=CH-P(O)(OEt)$_2$) showed 3.8% NOE enhancement to that at δ 5.74 ppm (PrC<u>H</u>=C(Et)-).

^{13}C NMR δ 12.94, 13.51, 16.07 (d, *J* = 6.2 Hz, 2 carbons, -P(O)(OCH$_2$<u>C</u>H$_3$)$_2$), 19.07, 22.11, 30.16, 61.20 (d, *J* = 4.6 Hz, 2 carbons, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 109.76 (d, *J* = 191.3 Hz, -CH=C(Et)-CH=<u>C</u>H-P(O)(OEt)$_2$), 139.09 (d, *J* = 23.2 Hz, -CH=C(Et)-<u>C</u>H=CH-P(O)(OEt)$_2$), 140.66 (-<u>C</u>H=C(Et)-CH=CH-P(O)(OEt)$_2$), 152.06 (d, *J* = 6.2 Hz, -CH=<u>C</u>(Et)-CH=CH-P(O)(OEt)$_2$).

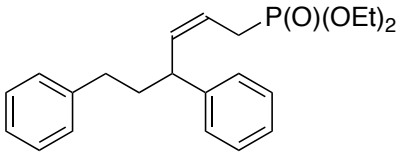
IR (neat) 3030 (C=C-H), 2969, 2933, 2875, 1627 (C=C-C=C), 1595 (C=C-C=C), 1216 (P=O), 1029, 864, 754, 666 cm^{-1}.

HRMS (ESI) Calcd for $C_{13}H_{25}O_3PNa$ [M+Na]$^+$: 283.1433. Found: 283.1434.

The *E*,*E*-diene stereochemistry was confirmed by ^{1}H NMR NOE experiments.



Diethyl (*Z*)-4,6-diphenyl-2-hexenylphosphonate (16).



To a solution of diethyl (1*E*,3*E*)-6-phenyl-1,3-hexadienylphosphonate (**13**) (58.9 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.328 mL, 1.22 M solution in THF, 0.400 mmol) dropwise at –45 °C under argon. After the solution was warmed to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (35.2 mg, 47%) as an oil and as a single olefinic isomer.

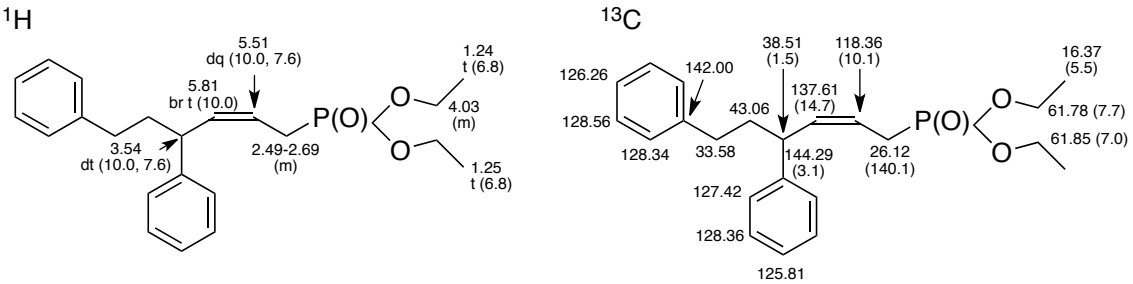
^{1}H NMR δ 1.24 (t, *J* = 6.8 Hz, 3H, P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 1.25 (t, *J* = 6.8 Hz, 3H, P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 2.02 (m, 2H, PhCH$_2$C<u>H</u>$_2$), 2.49-2.69 (m, 4H, PhC<u>H</u>$_2$CH$_2$ and -CH=CHC<u>H</u>$_2$P(O)(OEt)$_2$), 3.54 (dt, *J* = 10.0, 7.6 Hz, 1H, C<u>H</u>Ph), 4.03 (m, 4H, P(O)(OC<u>H</u>$_2$CH$_3$)$_2$), 5.51 (dq, *J* = 10.0, 7.6 Hz, 1H, -CH=C<u>H</u>CH$_2$P(O)(OEt)$_2$), 5.81 (br t, *J* = 10.0 Hz, 1H, C<u>H</u>=CH-CH$_2$P(O)(OEt)$_2$), 7.12-7.32 (m, 10H, Ar-H).

^{13}C NMR δ 16.37 (d, *J* = 5.5 Hz, 2 peaks, -P(O)(OCH$_2$<u>C</u>H$_3$)$_2$), 26.12 (d, *J* = 140.1 Hz, -C=C-<u>C</u>-P(O)(OEt)$_2$), 33.58, 38.51 (d, *J* = 1.5 Hz, -<u>C</u>HPh(C=C)), 43.06, 61.78 (d, *J* = 7.7 Hz, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 61.85 (d, *J* = 7.0 Hz, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 118.36 (d, *J* = 10.1 Hz, -C=<u>C</u>-C-P(O)(OEt)$_2$), 125.81 (*p*-Ph), 126.26 (*p*-Ph), 127.42 (2 carbons, *o*-Ph), 128.34 (2 carbons, *o*-Ph), 128.36 (2 carbons, *m*-Ph), 128.56 (2 carbon, *m*-Ph), 137.61 (d, *J* = 14.7 Hz, -<u>C</u>=C-C-P(O)(OEt)$_2$), 142.00 (*ipso*-Ph), 144.29 (d, *J* = 3.1 Hz, *ipso*-Ph at allylic position).

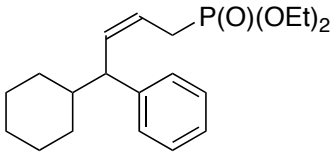
IR (neat) 3061 (Ar), 3026 (Ar, C=C-H), 2981, 2926, 2857, 1602 (C=C), 1495, 1454, 1251 (P=O), 1055, 1028, 963, 748, 700 cm^{-1}.

HRMS (ESI) Calcd for $C_{22}H_{29}O_3PNa$ $[M+Na]^+$: 395.1747. Found: 395.1752.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



Diethyl (*Z*)-4-cyclohexyl-4-phenyl-2-heptenylphosphonate (17).



To a solution of diethyl (1*E*,3*E*)-4-cyclohexyl-1,3-butadienylphosphonate (**14**) (54.5 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.328 mL, 1.22 M solution in THF, 0.400 mmol) dropwise at –45 °C under argon. After the solution was warmed to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (65.7 mg, 94%) as an oil and as a single olefinic isomer.

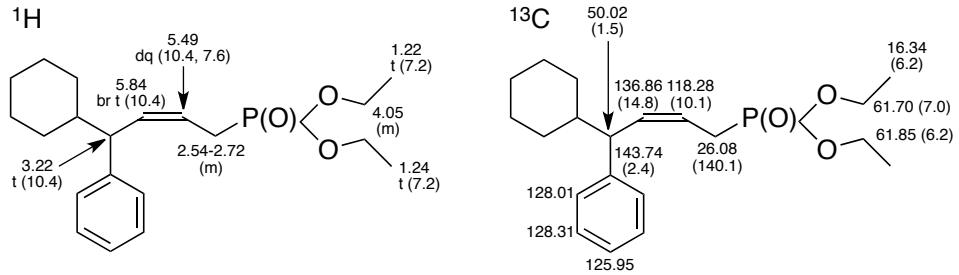
^{1}H NMR δ 0.78-1.90 (m, 11H, alkyl-H), 1.22 (t, *J* = 7.2 Hz, 3H, -P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 1.24 (t, *J* = 7.2 Hz, 3H, -P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 2.54-2.72 (m, 2H, -CH=CHC<u>H</u>$_2$P(O)(OEt)$_2$), 3.22 (t, *J* = 10.4 Hz, 1H, C<u>H</u>Ph), 4.05 (m, 4H, -P(O)(OC<u>H</u>$_2$CH$_3$)$_2$), 5.49 (dq, *J* = 10.4, 7.6 Hz, 1H, -CH=C<u>H</u>CH$_2$P(O)(OEt)$_2$), 5.84 (br t, *J* = 10.4 Hz, 1H, -C<u>H</u>=CHCH$_2$P(O)(OEt)$_2$), 7.15 (d, *J* = 7.6 Hz, 2H, Ph-H), 7.16 (t, *J* = 7.6 Hz, 1H, Ph-H), 7.26 (t, *J* = 7.6 Hz, 2H, Ph-H).

^{13}C NMR δ 16.34 (d, *J* = 6.2 Hz, 2 peaks, -P(O)(OCH$_2$<u>C</u>H$_3$)$_2$), 26.08 (d, *J* = 140.1 Hz, -C=C-<u>C</u>-P(O)(OEt)$_2$), 26.34, 26.42, 26.50, 31.04, 31.24, 43.34, 50.20 (d, *J* = 1.5 Hz, -<u>C</u>HPh(C=C)), 61.70 (d, *J* = 7.0 Hz, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 61.85 (d, *J* = 6.2 Hz, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 118.28 (d, *J* = 10.1 Hz, -C=<u>C</u>-C-P(O)(OEt)$_2$), 125.95 (*p*-Ph), 128.01 (2 carbons, *o*-Ph), 128.31 (2 carbons, *m*-Ph), 136.86 (d, *J* = 14.8 Hz, -<u>C</u>=C-C-P(O)(OEt)$_2$), 143.74 (d, *J* = 2.4 Hz, *ipso*-Ph).

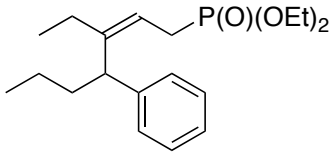
IR (neat) 3083 (Ar), 3061 (Ar), 3025 (Ar, C=C-H), 2981, 2927, 2852, 1600 (C=C), 1449, 1392, 1251 (P=O), 1055, 1027, 965, 757, 702 cm^{-1}.

HRMS (ESI) Calcd for $C_{20}H_{31}O_3PNa$ [M+Na]$^+$: 373.1903. Found: 373.1902

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



Diethyl (*Z*)-3-ethyl-4-phenyl-2-heptenylphosphonate (18).



To a solution of diethyl (1*E*,3*E*)-3-ethyl-1,3-heptadienylphosphonate (**15**) (52.1 mg, 0.200 mmol) and $FeCl_2$ (5.1 mg, 0.040 mmol) in 1 mL of THF was added phenylmagnesium bromide (0.328 mL, 1.22 M solution in THF, 0.600 mmol) dropwise at –45 °C under argon. After the solution was warmed to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (71.4 mg, quant.) as an oil and as a single olefinic isomer.

^{1}H NMR δ 0.88 (t, *J* = 7.2 Hz, 3H, alkyl-Me), 0.94 (t, *J* = 7.2 Hz, 3H, alkyl-Me), 1.31 (m, 2H, $CH_3C\underline{H}_2CH_2$), 1.330 (t, *J* = 7.2 Hz, 3H, -P(O)($OCH_2C\underline{H}_3$)$_2$), 1.334 (t, *J* = 7.2 Hz, 3H, -P(O)($OCH_2C\underline{H}_3$)$_2$), 1.74 (m, 2H, alkyl-H), 1.92 (m, 2H, $CH_3C\underline{H}_2C$=CH), 2.69-2.91 (m, 2H, -CH=CH-$C\underline{H}_2$P(O)(OEt)$_2$), 3.88 (t, *J* = 7.2 Hz, 1H, C<u>H</u>Ph), 4.12 (quintet, *J* = 7.2 Hz, 2H, -P(O)($OC\underline{H}_2CH_3$)$_2$), 4.13 (quintet, *J* = 7.2 Hz, 2H, P(O)($OC\underline{H}_2CH_3$)$_2$), 5.29 (q, *J* = 7.6 Hz, 1H, -C=C<u>H</u>-CH_2P(O)(OEt)$_2$), 7.14-7.29 (m, 5H, Ar-H).

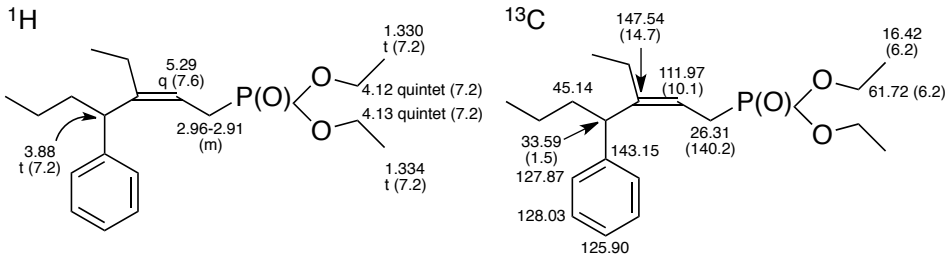
Irradiation of the proton at δ 2.69-2.91 ppm (-CH=CH-$C\underline{H}_2$P(O)(OEt)$_2$) showed 3.7% NOE enhancement to that at δ 3.88 ppm (C<u>H</u>Ph).

^{13}C NMR δ 12.62, 14.25, 16.42 (d, *J* = 6.2 Hz, 2 peaks, -P(O)($OCH_2\underline{C}H_3$)$_2$), 20.88, 23.90, 26.31 (d, *J* = 140.2 Hz, -C=C-<u>C</u>-P(O)(OEt)$_2$), 33.59 (d, *J* = 1.5 Hz, -<u>C</u>HPh(C=C)), 45.14, 61.72 (d, *J* = 6.2 Hz, 2 peaks, -P(O)($O\underline{C}H_2CH_3$)$_2$), 111.97 (d, *J* = 10.1 Hz, -C=<u>C</u>-C-P(O)(OEt)$_2$), 125.90 (*p*-Ph), 127.87 (2 carbons, *o*-Ph), 128.03 (2 carbons, *m*-Ph), 143.15 (*ipso*-Ph), 147.54 (d, *J* = 14.7 Hz, -<u>C</u>=C-C-P(O)(OEt)$_2$).

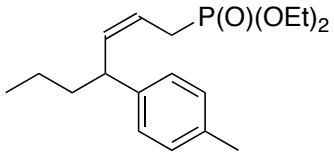
IR (neat) 3061 (Ar), 2990, 2932, 2873, 1600 (C=C), 1392, 1243, 1216 (P=O), 1057, 1030, 757, 667 cm^{-1}.

HRMS (ESI) Calcd for $C_{19}H_{31}O_3PNa$ $[M+Na]^+$: 361.1903. Found: 361.1903.

The *Z*-stereochemistry was confirmed by ^{1}H NMR NOE experiments.



Diethyl (*Z*)-4-(4-methylphenyl)-2-heptenylphosphonate (19)



To a solution of diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate (**9**) (46.4 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added 4-methyphenylmagnesium bromide (0.330 mL, 0.817 M solution in THF, 0.400 mmol) dropwise at –45 °C under argon. After the solution was warmed to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (34.7 mg, 54%) as an oil and as a single olefinic isomer.

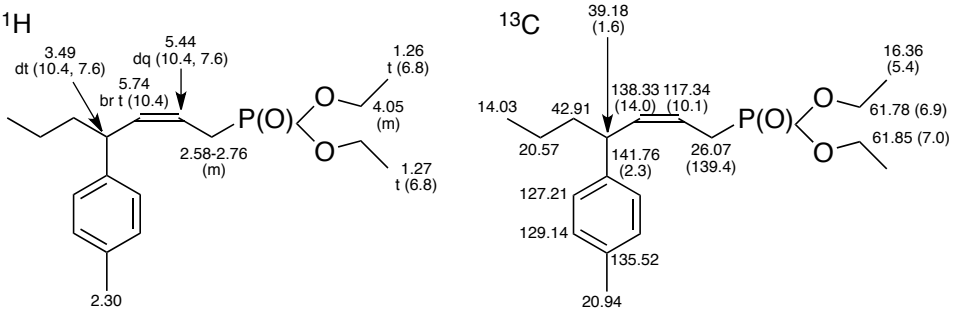
^{1}H NMR δ 0.88 (t, *J* = 7.2 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$), 1.26 (t, *J* = 6.8 Hz, 3H, -P(O)(OCH$_2$C$\underline{H}_3$)$_2$), 1.27 (t, *J* = 6.8 Hz, 3H, -P(O)(OCH$_2$C$\underline{H}_3$)$_2$), 1.30 (m, 2H, CH$_3$C$\underline{H}_2$CH$_2$), 1.63 (m, 2H, CH$_3$CH$_2$C$\underline{H}_2$), 2.30 (s, 3H, Ph-C$\underline{H}_3$), 2.58-2.76 (m, 2H, -CH=CHC$\underline{H}_2$P(O)(OEt)$_2$), 3.49 (dt, *J* = 10.4, 7.6 Hz, 1H, PrC$\underline{H}$Ar), 4.05 (m, 4H, P(OC$\underline{H}_2$CH$_3$)$_2$), 5.44 (dq *J* = 10.4, 7.6 Hz, 1H, -CH=C$\underline{H}$-CH$_2$P(O)(OEt)$_2$), 5.74 (br t, *J* = 10.4 Hz, 1H, -C$\underline{H}$=CH-CH$_2$P(O)(OEt)$_2$), 7.08 (s, 4H, Ar-H).

^{13}C NMR δ 14.03, 16.36 (d, *J* = 5.4 Hz, 2 peaks, -P(O)(OCH$_2$C$\underline{H}_3$)$_2$), 20.57, 20.94, 26.07 (d, *J* = 139.4 Hz, -C=C-C-P(O)(OEt)$_2$), 39.18 (d, *J* = 1.6 Hz, -CHPh), 42.91, 61.78 (d, *J* = 6.9 Hz, -P(O)(OCH$_2$CH$_3$)$_2$), 61.85 (d, *J* = 7.0 Hz, -P(O)(OCH$_2$CH$_3$)$_2$), 117.34 (d, *J* = 10.1 Hz, -C=C-C-P(O)(OEt)$_2$), 127.21 (2 carbons, *o*-Ph), 129.14 (2 carbons, *m*-Ph), 135.52 (C-Me), 138.33 (d, *J* = 14.0 Hz, -C=C-C-P(O)(OEt)$_2$), 141.76 (d, *J* = 2.3 Hz, *ipso*-Ph).

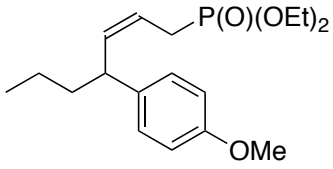
IR (neat) 3019 (Ar), 2994 (Ar), 2961, 2930, 2873, 1619 (C=C), 1512, 1216 (P=O), 1030, 968, 761, 668, 418 cm^{-1}.

HRMS (ESI) Calcd for $C_{18}H_{29}O_3PNa$ $[M+Na]^+$: 347.1747. Found: 347.1739.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



Diethyl (*Z*)-4-(4-methoxyphenyl)-2-heptenylphosphonate (20).



To a solution of diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate (**9**) (46.4 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.200 mmol) in 1 mL of THF was added 4-methoxyphenylmagnesium bromide (0.444 mL, 0.900 M solution in THF, 0.400 mmol) dropwise at –45 °C under argon. After the solution was warmed to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (40.7 mg, 60%) as an oil and as a single olefinic isomer.

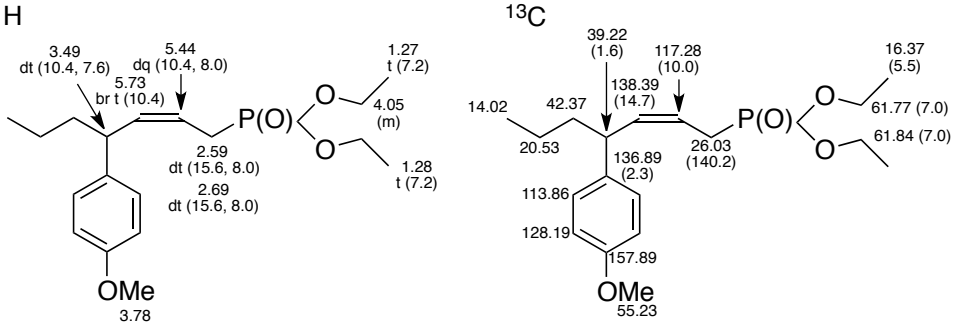
^{1}H NMR δ 0.89 (t, *J* = 7.6 Hz, 3H, alkyl-Me), 1.27 (t, *J* = 7.2 Hz, 3H, -P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 1.28 (t, *J* = 7.2 Hz, 3H, -P(O)(OCH$_2$C<u>H</u>$_3$)$_2$), 1.29 (m, 2H, CH$_3$C<u>H</u>$_2$CH$_2$), 1.62 (m, 2H, CH$_3$CH$_2$C<u>H</u>$_2$), 2.59 (dt, *J* = 15.6, 8.0 Hz, 1H, -CH=CH-C<u>H</u>$_2$P(O)(OEt)$_2$), 2.69 (dt, *J* = 15.6, 8.0 Hz, 1H, CH=CH-C<u>H</u>$_2$P(O)(OEt)$_2$), 3.49 (dt, *J* = 10.4, 7.6 Hz, 1H, PrC<u>H</u>Ar), 3.78 (s, 3H, O<u>Me</u>), 4.05 (m, 4H, -P(O)(OC<u>H</u>$_2$CH$_3$)$_2$), 5.44 (dq, *J* = 10.4, 8.0 Hz, 1H, -CH=C<u>H</u>-CH$_2$P(O)(OEt)$_2$), 5.73 (br t, *J* = 10.4 Hz, 1H, -C<u>H</u>=CH-CH$_2$P(O)(OEt)$_2$), 6.82 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.11 (d, *J* = 8.4 Hz, 2H, Ar-H).

^{13}C NMR δ 14.02, 16.37 (d, *J* = 5.5 Hz, 2 peaks, -P(O)(OCH$_2$<u>C</u>H$_3$)$_2$), 20.53, 26.03 (d, *J* = 140.2 Hz, -C=C-<u>C</u>-P(O)(OEt)$_2$), 39.22 (d, *J* = 1.6 Hz, -<u>C</u>HAr), 42.37, 55.23, 61.77 (d, *J* = 7.0 Hz, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 61.84 (d, *J* = 7.0 Hz, -P(O)(O<u>C</u>H$_2$CH$_3$)$_2$), 113.86 (2 carbons, *o*-Ar), 117.28 (d, *J* = 10.0 Hz, -C=<u>C</u>-C-P(O)(OEt)$_2$), 128.19 (2 carbons, *m*-Ar), 136.89 (d, *J* = 2.3 Hz, *ipso*-Ar), 138.39 (d, *J* = 14.7 Hz, -<u>C</u>=C-C-P(O)(OEt)$_2$), 157.89 (<u>C</u>-OMe).

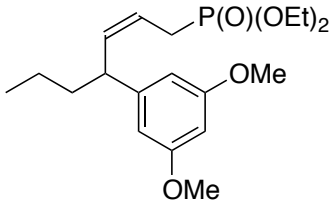
IR (neat) 3061 (Ar, C=C-H), 3017 (Ar), 2957, 2930, 1609 (C=C), 1511, 1465, 1250 (P=O), 1029, 964, 831, 784, 696 cm^{-1}.

HRMS (ESI) Calcd for $C_{18}H_{29}PO_4Na$ [M+Na]$^+$: 363.1696. Found: 363.1706.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



Diethyl (*Z*)-4-(3,5-dimethoxyphenyl)-2-heptenylphosphonate (21).



To a solution of diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate (**9**) (46.4 mg, 0.200 mmol) and $FeCl_2$ (2.5 mg, 0.020 mmol) in 1 mL of THF was added 3,5-dimethoxyphenylmagnesium bromide (0.481 mL, 0.831 M solution in THF, 0.400 mmol) dropwise at –45 °C under argon. After the solution was warmed to 0 °C over 5 h, the reaction was terminated by the addition of 1 N HCl solution (1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which did not show the presence of regio- and olefinic stereoisomers. The crude product was chromatographed on silica gel (hexane-ethyl acetate) to afford the title compound (69.7 mg, 94%) as an oil and as a single olefinic isomer.

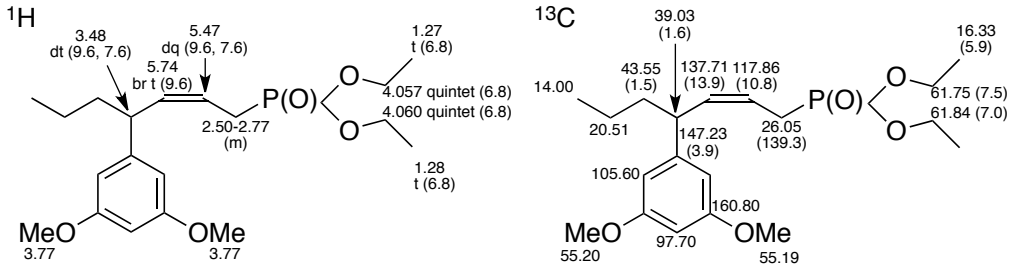
^{1}H NMR δ 0.89 (t, *J* = 7.2 Hz, 3H, C$\underline{H}_3$CH$_2$CH$_2$), 1.27 (t, *J* = 6.8 Hz, 3H, -P(O)(OCH$_2$C$\underline{H}_3$)$_2$), 1.28 (t, *J* = 6.8 Hz, 3H, -P(O)(OCH$_2$C$\underline{H}_3$)$_2$), 1.30 (m, 2H, CH$_3$C$\underline{H}_2$CH$_2$), 1.63 (m, 2H, CH$_3$CH$_2$C$\underline{H}_2$), 2.50-2.77 (m, 2H, -CH=CH-C$\underline{H}_2$P(O)(OEt)$_2$), 3.48 (dt, *J* = 9.6, 7.6 Hz, 1H, PrC$\underline{H}$Ar), 3.77 (s, 6H, Ar-OC$\underline{H}_3$), 4.057 (quintet, *J* = 6.8 Hz, 2H, -P(O)(OC$\underline{H}_2$CH$_3$)$_2$), 4.060 (quintet, *J* = 6.8 Hz, 2H, -P(O)(OC$\underline{H}_2$CH$_3$)$_2$), 5.47 (dq, *J* = 9.6, 7.6 Hz, 1H, CH=C$\underline{H}$-CH$_2$P(O)(OEt)$_2$), 5.74 (br t, *J* = 9.6 Hz, 1H, C$\underline{H}$=CH-CH$_2$P(O)(OEt)$_2$), 6.29 (t, *J* = 2.0 Hz, 1H, Ar-H), 6.36 (d, *J* = 2.0 Hz, 2H, Ar-H).

^{13}C NMR δ 14.00, 16.33 (d, *J* = 5.9 Hz, 2 peaks, -P(O)(OCH$_2$C$\underline{H}_3$)$_2$), 20.51, 26.05 (d, *J* = 139.3 Hz, -C=C-C-P(O)(OEt)$_2$), 39.03 (d, *J* = 1.6 Hz, -C$\underline{H}$Ar), 43.55 (d, *J* = 1.5 Hz, CH$_3$CH$_2$C$\underline{H}_2$), 55.19 (OMe), 55.20 (OMe), 61.75 (d, *J* = 7.5 Hz, -P(O)(OC$\underline{H}_2$CH$_3$)$_2$), 61.84 (d, *J* = 7.0 Hz, -P(O)(OC$\underline{H}_2$CH$_3$)$_2$), 97.70 (*p*-Ar), 105.60 (2 carbons, *o*-Ar), 117.86 (d, *J* = 10.8 Hz, -C=C-C-P(O)(OEt)$_2$), 137.71 (d, *J* = 13.9 Hz, -C=C-C-P(O)(OEt)$_2$), 147.23 (d, *J* = 3.9 Hz, *ipso*-Ar), 160.80 (2 carbons, C-OMe).

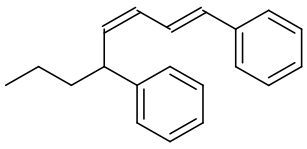
IR (neat) 3025 (Ar, C=C-H), 2957, 2931, 1605 (C=C), 1596, 1461, 1251, 1204 (P=O), 1155, 936, 835, 745, 695 cm^{-1}.

HRMS (ESI) Calcd for $C_{19}H_{31}O_5PNa$ $[M+Na]^+$: 393.1804. Found: 393.1801.

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.



A 93:7 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene (22).

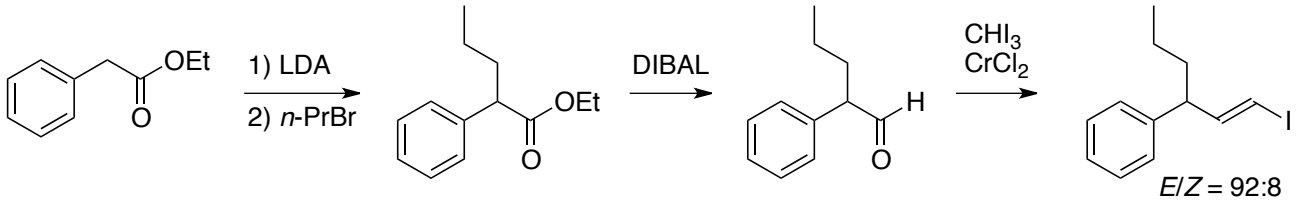


To a solution of diethyl (*Z*)-4-phenyl-2-heptenylphosphonate (**11**) (91.6 mg, 0.295 mmol) in THF (1.80 mL) and HMPA (0.515 mL, 2.96 mmol) was added NaHMDS (0.441 mL, 1.0 M solution in THF, 0.441 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, benzaldehyde (0.045 mL, 0.441 mmol) was added at –78 °C. After the reaction mixture was stirred at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was quenched with an aqueous 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (55.1 mg, (1*E*,3*Z*)/(1*E*,3*E*) = 93:7, 71%) as a pale yellow oil.

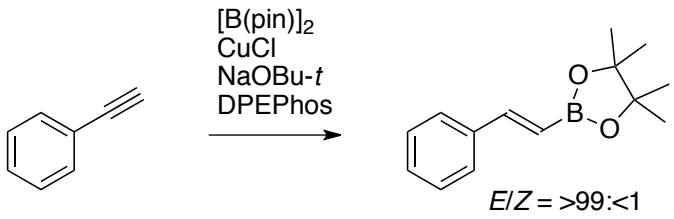
For spectral data, see: a 96:4 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene (**27**) in Chapter 3.

An authentic sample of (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene.

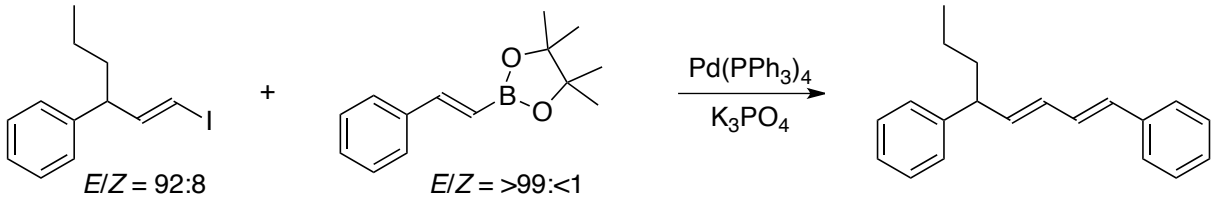
An authentic sample of the minor isomer, (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene, was prepared independently from (*E*)-1-iodo-3-phenyl-1-hexene and (*E*)-4,4,5,5-tetramethyl-2-(β-styryl)-1,3-dioxa-2-borolane as shown below. The above minor product of the Wittig reaction and the authentic sample prepared by the following palladium-catalyzed reaction were identical by ^{1}H and ^{13}C NMR spectroscopy.



Org. Biomol. Chem. **2003**, *1*, 3726-3737.



Tetrahedron **2012**, *68*, 3444-3449.



J. Org. Chem. **2010**, *75*, 7412-7415.

To a solution of diisopropylamine (2.60 mL, 18.6 mmol) in THF (20 mL) was added *n*-BuLi (11.0 mL, 1.64 M in hexane, 18.0 mmol) dropwise at 0 °C. After the mixture was stirred at that temperature for 15 min, it was cooled to –78 °C and ethyl phenylacetate (2.40 mL, 15.1 mmol) was added. After stirring at –78 °C for 1 h, 1-bromopropane (1.65 mL, 18.2 mmol) was added to the mixture, which was then warmed to room temperature over 6 h. The reaction was terminated by the addition of ethyl acetate and 1 N HCl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford ethyl 2-phenylpentanoate (1.52 g, 49%) as an oil.

To a solution of ethyl 2-phenylpentanoate (1.83 g, 8.90 mmol) in CH_2Cl_2 (50 mL) was added DIBAL (11.0 mL, 1.02 M in hexane, 11.2 mmol) at –78 °C over 30 min under argon. After the mixture was stirred at that temperature for 2.5 h, the reaction was terminated by the successive addition of MeOH and 1 N HCl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers ware washed successively with aqueous saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford 2-phenylpentanal (872 mg, 60%) as an oil.

To a solution of $CrCl_2$ (992 mg, 8.07 mmol) in THF (30 mL) were added CHI_3 (1.08 g, 2.73 mmol) and 2-phenylpentanal (120 mg, 0.738 mmol) in THF (3 mL) in this order at 0 °C. After the mixture was stirred at that temperature for 1 h and at room temperature for 2 h, the reaction was terminated by the addition of H_2O. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with aqueous saturated $Na_2S_2O_3$ solution and brine,

dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford a mixture of (*E*)-1-iodo-3-phenyl-1-hexene (*E*/*Z* = 92:8) as an oil and CHI_3 as solids (total 129 mg, the exact yield of the vinyl iodide was not determined). Only the oil portion of this product was used in the next step.

Major (*E*)-isomer: ^{1}H NMR δ 0.89 (t, *J* = 7.2 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.28 (m, 2H, CH$_3$C<u>H</u>$_2$CH$_2$), 1.69 (m, 2H, CH$_3$CH$_2$C<u>H</u>$_2$), 3.28 (q, *J* = 7.6 Hz, 1H, PrC<u>H</u>Ph), 6.02 (d, *J* = 14.0 Hz, 1H, CH=C<u>H</u>-I), 6.65 (dd, *J* = 7.6, 14.0 Hz, 1H, C<u>H</u>=CH-I), 7.17-7.38 (m, 5H, Ar-H).

Minor (*Z*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 3.68 (q, *J* = 7.6 Hz, 1H, PrC<u>H</u>Ph), 6.23-6.31 (m, 2H, C<u>H</u>=C<u>H</u>I).

The *E*-stereochemistry of the major isomer was confirmed by the ^{1}H NMR coupling constant (*J* = 14.0 Hz), which is typical to *E*-alkenyl iodide [*Org*. *Biomol*. *Chem*. **2003**, *1*, 3726-3737].

After a mixture of CuCl (5.8 mg, 0.059 mmol), NaOBu-*t* (12.5 mg, 0.130 mmol), and DPEPhos (34.6 mg, 0.0642 mmol) in THF (1.2 mL) was stirred at room temperature for 30 min, $[B(pin)]_2$ (509 mg, 2.00 mmol) was added. After stirring for 10 min, phenylacetylene (0.220 mL, 2.00 mmol) and MeOH (0.165 mL, 4.08 mmol) were added successively. The reaction mixture was stirred at the same temperature for 24 h, filtered through Celite, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford (*E*)-4,4,5,5-tetramethyl-2-(β-styryl)-1,3-dioxa-2-borolane (421 mg, *E*/*Z* = >99:<1, 91%) as an oil.

^{1}H NMR δ 1.32 (s, 12H, Me), 6.17 (d, *J* = 18.4 Hz, Ph-C<u>H</u>=CH-B), 7.28-7.36 (m, 3H, Ar-H), 7.40 (d, *J* = 18.4 Hz, 1H, CH=C<u>H</u>-B), 7.49 (dd, *J* = 6.8 Hz, 8.4 Hz, 2H, Ar-H).

The *E*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

Peaks of the other olefinic isomers were not seen on ^{1}H NMR spectra of crude and purified samples. Thus the olefinic stereoselectivity was judged to be >99:<1 based on the limit of detection of NMR spectroscopy.

To a solution of (*E*)-1-iodo-3-phenyl-1-hexene (52.2 mg, 0.182 mmol, *E*/*Z* = 92:8) prepared above and (*E*)-4,4,5,5-tetramethyl-2-(β-styryl)-1,3-dioxa-2-borolane (48.6 mg, 0.211 mmol, *E*/*Z* = >99:<1) in THF (2 mL) and H_2O (1 mL) was added K_3PO_4 (256 mg, 1.20 mmol) under argon at room temperature. After vigorous stirring at that temperature for 15 min, $Pd(PPh_3)_4$ (23.8 mg, 0.0206 mmol) was added to the mixture, which was then covered with aluminum foil. After vigorous stirring at room temperature for 16 h, the reaction was terminated by the addition of aqueous 3 N NaOH solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were successively washed with aqueous saturated NH_4Cl solution and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford the title compound (29.8 mg, (1*E*,3*E*)/(1*E*,3*Z*)/(1*Z*,3*Z*) = 86:7:7, 63%) as a pale yellow oil.

Major (1*E*,3*E*)-isomer: ^{1}H NMR δ 0.91 (t, *J* = 7.6 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.30 (m, 2H, alkyl-H), 1.73 (q, *J* = 7.6 Hz, 2H, alkyl-H), 3.35 (q, *J* = 7.6 Hz, 1H, PrC<u>H</u>Ph), 5.94 (dd, *J* = 7.6, 15.2 Hz, 1H, C<u>H</u>=CH-CH=CH-Ph), 6.20 (dd, *J* = 10.4, 15.2 Hz, 1H, CH=C<u>H</u>-CH=CH-Ph), 6.45 (d, *J* = 15.6 Hz, 1H, CH=CH-CH=C<u>H</u>-Ph), 6.75 (dd, *J* = 10.4, 15.6 Hz, 1H, CH=CH-C<u>H</u>=CH-Ph), 7.15-7.45 (m, 10H, Ar-H).

^{13}C NMR δ 13.99, 20.73, 38.10, 48.75, 126.16 (2 peaks of 2 carbons), 126.29, 127.17, 127.63, 128.46 (2 carbons), 128.54 (2 carbons), 129.27, 129.93, 130.82, 139.09 (*ipso*-Ph), 144.65 (*ipso*-Ph).

Minor (1*E*,3*Z*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 3.85 (dt, *J* = 10.8, 8.0 Hz, 1H,

PrC<u>H</u>Ph), 5.63 (t, *J* = 10.8 Hz, 1H, C<u>H</u>=CH-CH=CH-Ph), 6.54 (d, *J* = 15.6 Hz, 1H, CH=CH-CH=C<u>H</u>-Ph), 7.13 (dd, *J* = 10.8, 15.6 Hz, 1H, CH=CH-C<u>H</u>=CH-Ph).

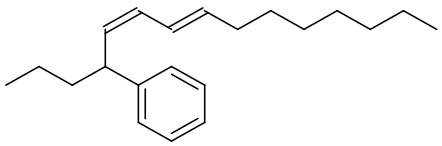
Second minor (1*Z*,3*Z*)-isomer: ^{1}H NMR (only characteristic peaks are shown) δ 3.61 (q, *J* = 8.0 Hz, 1H, PrC<u>H</u>Ph), 5.71 (dd, *J* = 8.0, 10.8 Hz, 1H, C<u>H</u>=CH-CH=CH-Ph), 6.35 (d, *J* = 10.8 Hz, 1H, CH=CH-CH=C<u>H</u>-Ph).

IR (neat) 3080 (Ar), 3060 (Ar), 3024 (Ar, C=C-H), 2956, 2928, 2870, 1597 (C=C-C=C), 1666 (C=C-C=C), 1494, 1450, 987, 744, 698 cm^{-1} for an 86:7:7 mixture of (1*E*,3*E*)-, (1*E*,3*Z*)-, and (1*Z*,3*Z*)-isomers.

HRMS (APPI) Calcd for $C_{20}H_{22}$ $[M+H]^+$: 263.1794. Found: 263.1800 for an 86:7:7 mixture of (1*E*,3*E*)-, (1*E*,3*Z*)- and (1*Z*,3*Z*)-isomers.

The 1*E*,3*E*-diene stereochemistry of the major isomer was confirmed by ^{1}H NMR coupling constants.

An 83:17 mixture of (5*Z*,7*E*)- and (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene (23).

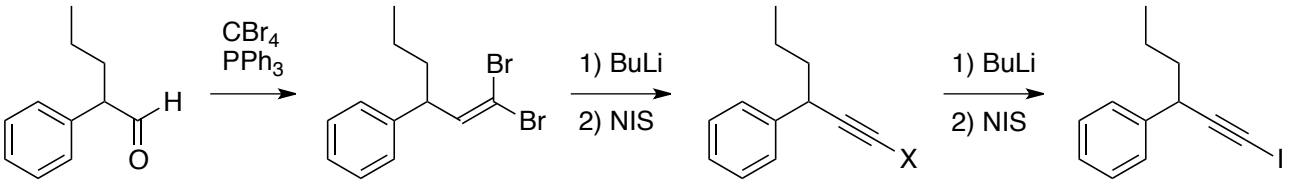


To a solution of diethyl (*Z*)-4-phenyl-2-heptenylphosphonate (**11**) (92.7 mg, 0.299 mmol) in THF (1.80 mL) and HMPA (0.520 mL, 2.99 mmol) was added NaHMDS (0.450 mL, 1.0 M solution in THF, 0.450 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, octanal (0.070 mL, 0.449 mmol) was added at –78 °C. After the reaction mixture was stirred at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was quenched with an aqueous 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (62.7 mg, (5*Z*,7*E*)/(5*Z*,7*Z*) = 83:17, 74%) as an oil.

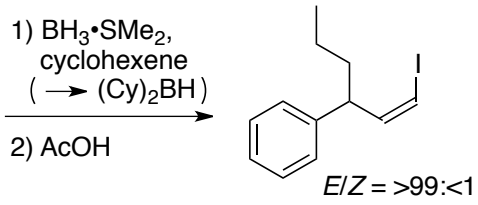
For spectral data, see: an 86:14 mixture of (5*Z*,7*E*)- and (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene (**30**) in Chapter 3.

An authentic sample of (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene.

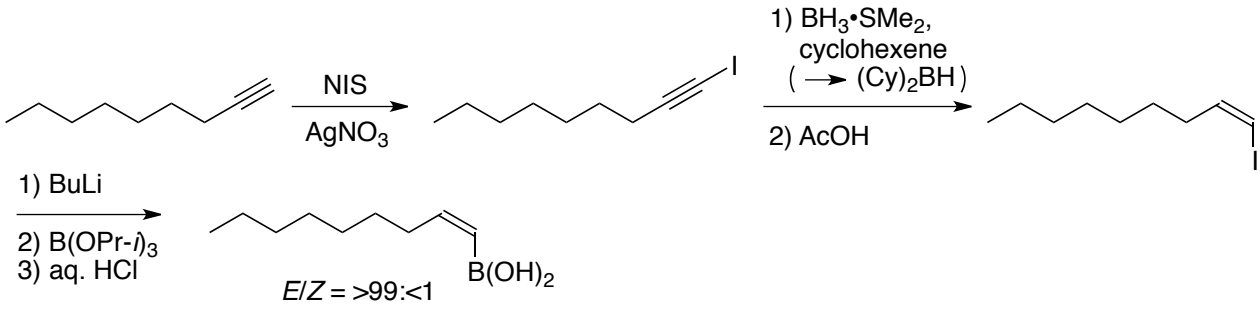
An authentic sample of the minor isomer, (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene, was prepared independently from (*Z*)-1-iodo-3-phenyl-1-hexene and (*Z*)-1-nonenylboronic acid as shown below. The above minor product of the Wittig reaction and the authentic sample prepared by the following palladium-catalyzed reaction were identical by ^{1}H and ^{13}C NMR spectroscopy.



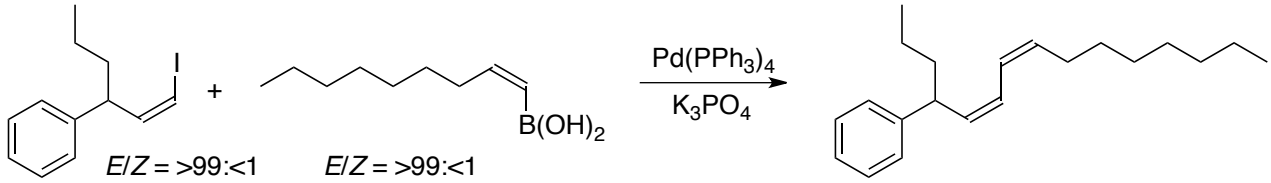
J. Org. Chem. **2004**, *69*, 3787-3793. X : I/H = 33:67 (inseprable)



J. Org. Chem. **1989**, *69*, 6064-6067.



Tetrahedron Lett. **2000**, *41*, 10357-10361.
J. Org. Chem. **2002**, *67*, 7110-7123.
Org. Lett. **2012**, *14*, 544-547.



J. Org. Chem. **2010**, *75*, 7412-7415.

To a solution of CBr_4 (3.35 g, 10.1 mmol) in CH_2Cl_2 (20 mL) was added PPh_3 (5.65 g, 21.5 mmol) at 0 °C. After stirring at 0 °C for 30 min, 2-phenylpentanal (872 mg, 5.38 mmol) was added at that temperature, and the stirring was continued for an additional 2 h at the same temperature. The reaction was terminated by the addition of H_2O. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude solid, which was chromatographed on silica gel (hexane) to afford 1,1-dibromo-3-phenyl-1-hexene (1.09 g, quant.) as an oil.

To a solution of 1,1-dibromo-3-phenyl-1-hexene (1.09 g, 6.73 mmol) in THF (10 mL) was added *n*-BuLi (7.80 mL, 1.64 M in hexane, 12.8 mmol) at –78 °C under argon. After stirring at that temperature for 1 h, *N*-iodosuccinimide (2.42 g, 10.8 mmol) was added. After the mixture was warmed to 0 °C over 1.5 h, the reaction was terminated by the addition of aqueous saturated $Na_2S_2O_3$ solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were

washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude mixture of 1-iodo-3-phenyl-1-hexyne and 3-phenyl-1-hexyne in a ratio of 33:67 by ^{1}H NMR analysis. This crude oil was chromatographed on silica gel (hexane) to afford a mixture of the iodoalkyne and alkyne (571 mg, 53%) of the same ratio as above.

To a solution of the 33:67 mixture of 1-iodo-3-phenyl-1-hexyne and 3-phenyl-1-hexyne (430 mg, ca. 2.72 mmol) in THF (9 mL) was added *n*-BuLi (2.60 mL, 1.58 M in hexane, 4.11 mmol) at –78 °C under argon. After stirring for 30 min, *N*-iodosuccinimide (915 mg, 4.07 mmol) was added. After the reaction mixture was warmed up to 0 °C over 1.5 h, the reaction was terminated by the addition of aqueous saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford 1-iodo-3-phenyl-1-hexyne (437 mg, 53% uncontaminated with the alkyne) as an oil.

To a solution of $BH_3 \cdot SMe_2$ (0.770 mL, 2.0 M in THF, 1.54 mmol) in THF (5 mL) was added cyclohexene (0.335 mL, 3.08 mmol) at 0 °C. The resulting solution was stirred at that temperature for 1 h and at room temperature for 1 h. Then, 1-iodo-3-phenyl-1-hexyne (437 mg, 1.54 mmol) was added and the mixture was stirred for 1 h. The reaction was terminated by the addition of glacial acetic acid (1 mL), diluted with hexane, and washed with brine 3 times, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford (*Z*)-1-iodo-3-phenyl-1-hexene (169 mg, 38%) as an oil and as a single olefinic isomer.

^{1}H NMR δ 0.93 (t, *J* = 7.2 Hz, 3H, C<u>H</u>$_3$CH$_2$CH$_2$), 1.31 (m, 2H, CH$_3$C<u>H</u>$_2$CH$_2$), 1.77 (m, 2H, CH$_3$CH$_2$C<u>H</u>$_2$), 3.68 (q, *J* = 7.6 Hz, 1H, PrC<u>H</u>Ph), 6.24 (d, *J* = 7.6 Hz, 1H, CH=C<u>H</u>I), 6.27 (t, *J* = 7.6 Hz, 1H, C<u>H</u>=CHI), 7.23-7.37 (m, 5H, Ar-H).

The *Z*-stereochemistry was confirmed by ^{1}H NMR coupling constants.

Peaks of the other olefinic isomers were not seen on ^{1}H NMR spectra of crude and purified samples. Thus the olefinic stereoselectivity was judged to be >99:<1 based on the limit of detection of NMR spectroscopy.

To a solution of 1-nonyne (0.320 mL, 1.96 mmol) in acetone (10 mL) were added $AgNO_3$ (105 mg, 0.616 mmol) and *N*-iodosuccinimide (626 mg, 2.78 mmol) in this order at room temperature. After stirred at room temperature overnight, the reaction mixture was concentrated *in vacuo* and diluted with H_2O and ethyl acetate. The organic layer was separated and washed successively with H_2O and brine until the precipitation of AgCl was no longer observed. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford 1-iodo-1-nonyne (430 mg, 88%) as an oil.

To a solution of $BH_3 \cdot SMe_2$ (0.860 mL, 2.0 M in THF, 1.72 mmol) in THF (3 mL) was added cyclohexene (0.370 mL, 3.42 mmol) at 0 °C. After the mixture was stirred at that temperature for 1 h and at room temperature for 1 h, 1-iodo-1-nonyne (430 mg, 1.72 mmol) was added. After the mixture was stirred for 1 h, the reaction was terminated by the addition of glacial acetic acid (1 mL), diluted with hexane, and washed with brine 3 times, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford (*Z*)-1-iodo-1-nonene (223 mg, 54%) as an oil and with a *Z*/*E* ratio of >99:<1.

To a solution of (*Z*)-1-iodo-1-nonene (223 mg, 0.924 mmol, *Z*/*E* = >99:<1) in diethyl ether (6 mL)

was added *n*-BuLi (0.680 mL, 1.64 M in hexane, 1.12 mmol) at –78 °C. After stirring at that temperature for 1 h, triisopropyl borate (0.257 mL, 1.11 mmol) was added. The mixture was warmed to room temperature and was stirred for an additional 16 h. Then, aqueous 1 N HCl (2 mL) was added and the mixture was stirred for 1 h. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane-ethyl acetate) to afford (*Z*)-1-nonenylboronic acid (98.1 mg, *Z*/*E* = >99:<1, 62%) as an oil.

^{1}H NMR δ 0.88 (t, *J* = 6.8 Hz, 3H, Alkyl-Me), 1.22-1.46 (br, 10H, alkyl-H), 2.55 (dq, *J* = 1.2, 7.6 Hz, 2H, C$\underline{H}_2$-CH=CH-B), 5.42 (d, *J* = 14.0 Hz, 1H, CH=C$\underline{H}$-B), 6.61 (dt, *J* = 14.0, 7.6 Hz, 1H, C$\underline{H}$=CH-B).

The *Z*-stereochemistry was confirmed by the ^{1}H NMR coupling constant (*J* = 14.0 Hz), which is typical to *Z*-alkenylboroic acid [*Org*. *Lett*. **2012**, *14*, 544-547; *Tetrahedron Lett*. **2000**, *41*, 10357-10361; *J*. *Org*. *Chem*. **2002**, *67*, 7110-7123].

To a solution of (*Z*)-1-iodo-3-phenyl-1-hexene (86.1 mg, 0.301 mmol, *Z*/*E* = >99:<1) and (*Z*)-1-nonenylboronic acid (61.6 mg, 0.362 mmol, *Z*/*E* = >99:<1) in THF (3 mL) and H_2O (1.50 mL) was added K_3PO_4 (389 mg, 1.83 mmol) under argon at room temperature. After vigorous stirring at that temperature for 15 min, $Pd(PPh_3)_4$ (34.8 mg, 0.0301 mmol) was added to the mixture, which was then covered with aluminum foil. After vigorous stirring at room temperature for 16 h, the reaction was terminated by the addition of aqueous 3 N NaOH solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were successively washed with aqueous saturated NH_4Cl solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was chromatographed on silica gel (hexane) to afford the title compound (48.6 mg, 57%) as an oil.

^{1}H NMR ($CDCl_3$) δ 0.79-0.93 (m, 6H, alkyl-Me), 1.18-1.42 (m, 12H, alkyl-H), 1.67 (m, 2H, $CH_3CH_2C\underline{H}_2$CHPh), 2.16 (m, 2H, CH=CH-C$\underline{H}_2$), 3.75 (dt, *J* = 9.6, 7.6 Hz, 1H, PrC$\underline{H}$Ph), 5.40-5.57 (m, 2H, C$\underline{H}$=CH-CH=C$\underline{H}$-C_7H_{15}), 6.22-6.38 (m, 2H, CH=C$\underline{H}$-C$\underline{H}$=CH-C_7H_{15}), 7.14-7.31 (m, 5H, Ar-H).

^{1}H NMR (C_6D_6) δ 0.82-1.00 (m, 6H, alkyl-Me), 1.17-1.44 (m, 12H, alkyl-H), 1.63 (m, 2H, $CH_3CH_2C\underline{H}_2$CHPh), 2.14 (q, *J* = 7.2 Hz, 2H, CH=CH-C$\underline{H}_2$), 3.80 (td, *J* = 7.2, 10.0 Hz, 1H, PrC$\underline{H}$Ph), 5.51 (td, *J* = 7.2, 10.0 Hz, 1H, CH=CH-CH=C$\underline{H}$-C_7H_{15}), 5.56 (t, *J* = 10.0 Hz, 1H, C$\underline{H}$=CH-CH=CH-C_7H_{15}), 6.40 (t, *J* = 10.0 Hz, 1H, CH=CH-C$\underline{H}$=CH-C_7H_{15}), 6.51 (t, *J* = 10.0 Hz, 1H, CH=C$\underline{H}$-CH=CH-C_7H_{15}), 7.14-7.21 (m, 5H, Ar-H).

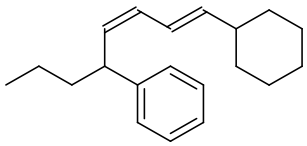
^{13}C NMR δ 14.04, 20.67, 22.64, 27.54, 29.16, 29.24, 29.60, 29.70, 31.83, 38.99, 43.26, 123.11, 123.49, 125.91, 127.31 (2 carbons), 128.44 (2 carbons), 133.17, 135.35, 145.39 (*ipso*-Ph).

IR (neat) 3084 (Ar), 3061 (Ar), 3029 (Ar, C=C-H), 3002 (Ar), 2956, 2925, 2854, 1651 (C=C-C=C), 1600 (C=C-C=C), 1464, 1455, 1378, 698 cm^{-1}.

HRMS (APPI) Calcd for $C_{21}H_{32}$ $[M+H]^+$: 285.2577. Found: 285.2576.

The 5*Z*,7*Z*-diene stereochemistry of the major isomer was confirmed by ^{1}H NMR coupling constants.

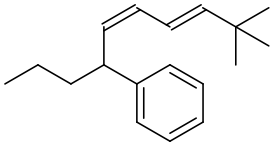
An 81:19 mixture of (1*E*,3*Z*)- and (1*Z*,3*Z*)-1-cyclohexyl-5-phenyl-1,3-octadiene (24).



To a solution of diethyl (*Z*)-4-phenyl-2-heptenylphosphonate (**11**) (93.3 mg, 0.301 mmol) in THF (1.80 mL) and HMPA (0.520 mL, 2.99 mmol) was added NaHMDS (0.450 mL, 1.0 M solution in THF, 0.450 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, cyclohexanecarbaldehyde (0.055 mL, 0.454 mmol) was added at –78 °C. After the reaction mixture was stirred at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was quenched with an aqueous 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (58.0 mg, (1*E*,3*Z*)/(1*Z*,3*Z*) = 81:19, 72%) as an oil.

For spectral data, see: an 89:11 mixture of (1*E*,3*Z*)- and (1*Z*,3*Z*)-1-cyclohexyl-5-phenyl-1,3-octadiene (**31**) in Chapter 3.

A 92:8 mixture of (3*E*,5*Z*)- and (3*Z*,5*Z*)-2,2-dimethyl-7-phenyl-3,5-decadiene (25).



To a solution of diethyl (*Z*)-4-phenyl-2-heptenylphosphonate (**11**) (93.5 mg, 0.301 mmol) in THF (1.80 mL) and HMPA (0.500 mL, 2.87 mmol) was added NaHMDS (0.450 mL, 1.0 M solution in THF, 0.450 mmol) dropwise at –78 °C under argon. After the reaction mixture was stirred at that temperature for 30 min, pivalaldehyde (0.050 mL, 0.460 mmol) was added at –78 °C. After the reaction mixture was stirred at –78 °C for 10 min, at 0 °C for 30 min, and at room temperature for 2 h, it was quenched with an aqueous 1 N HCl solution. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed successively with 1 N HCl solution, aqueous saturated $NaHCO_3$ solution, and brine, dried over Na_2SO_4, and concentrated *in vacuo* to give a crude oil, ^{1}H NMR analysis of which hardly determined the olefinic stereoselectivity at this stage. The crude product was chromatographed on silica gel (hexane) to afford the title compound (55.2 mg, (3*E*,5*Z*)/(3*Z*,5*Z*) = 92:8, 76%) as an oil.

For spectral data, see: a 93:7 mixture of (3*E*,5*Z*)- and (3*Z*,5*Z*)-2,2-dimethyl-7-phenyl-3,5-decadiene (**32**) in Chapter 3.

Chapter 5. Summary

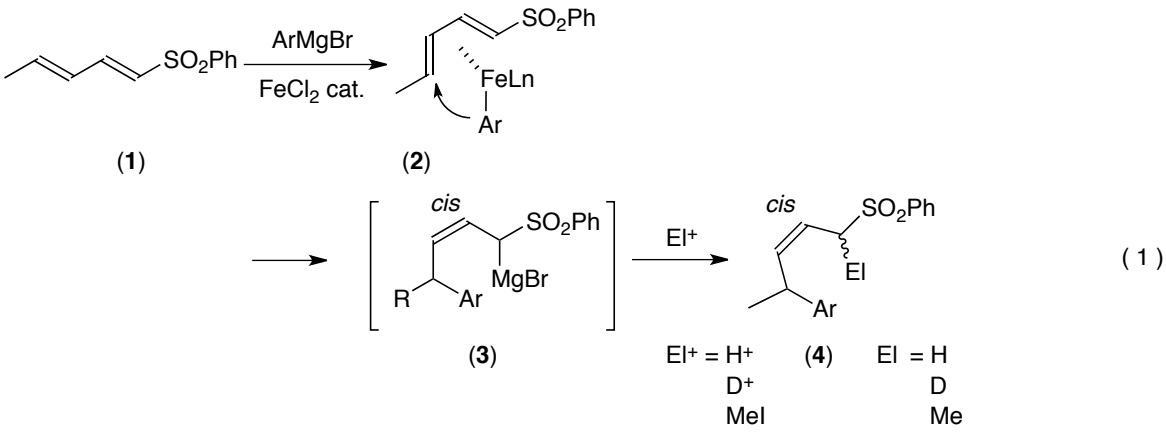
In this research, we focused our attention on the development of the new iron-catalyzed selective addition of aryl Grignard reagents to α,β,γ,δ-unsaturated sulfones, phosphine oxides, and phosphonates, and its synthetic application as shown below.

Chapter 1 Introduction.

The recent research in the field of conjugate addition in organic synthesis and the contribution from our laboratory are briefly summarized. In addition, the importance of this study from the scientific and practical point of view is discussed.

Chapter 2 Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Sulfones and Its Synthetic Application.

α,β,γ,δ-Unsaturated sulfones **1** were treated with aryl Grignard reagents in the presence of $FeCl_2$ to afford virtually single *cis*-allyl sulfones **3** after hydrolysis (eq 1). Deuteration and the treatment with alkyl halides gave the deuterated and alkylated products with the exclusive *cis*-olefinic stereochemistry, which clearly shows the presence of the magnesiated intermediate **3** resulting from the aryl delivery via the *s-cis*-diene-iron complex such as **2**. This *cis*-allyl slufones **4** were first bis-alkylated to give **5**, which then was subjected to the intramolecular Friedel-Crafts reaction to give bicyclic compounds **6** (eq 2).



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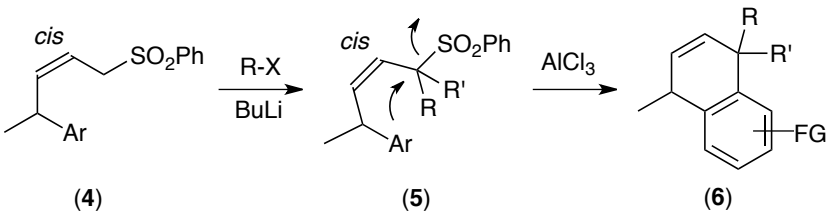
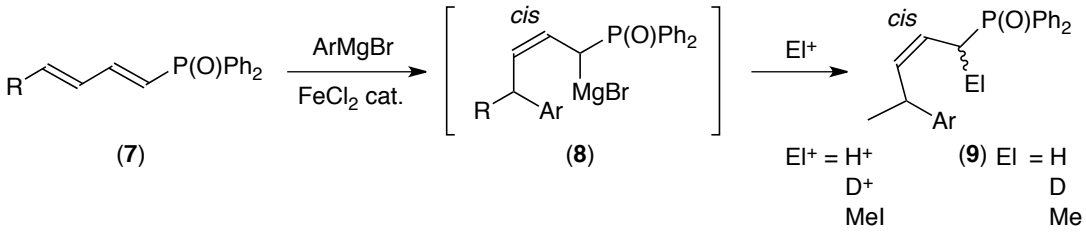


(2)

Chapter 3 Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Phosphine Oxides and Its Synthetic Application.

α,β,γ,δ-Unsaturated phosphine oxides **7** were treated with aryl Grignard reagents in the presence of $FeCl_2$ to afford virtually single *cis*-allylphosphine oxides **9** after hydrolysis (eq 3). Alternatively, deuteration and the treatment with alkyl halides gave the deuterated and alkylated products with the exclusive *cis*-olefinic stereochemistry, which clearly shows that the presence of the magnesiated intermediate such as **8**. The *cis*-allylphosphine oxides **9** obtained herein could be used as precursors for the Wittig reaction, giving stereo-defined arylated dienes **10** with high stereoselectivity (eq 4).



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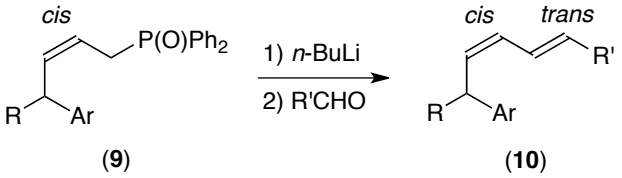
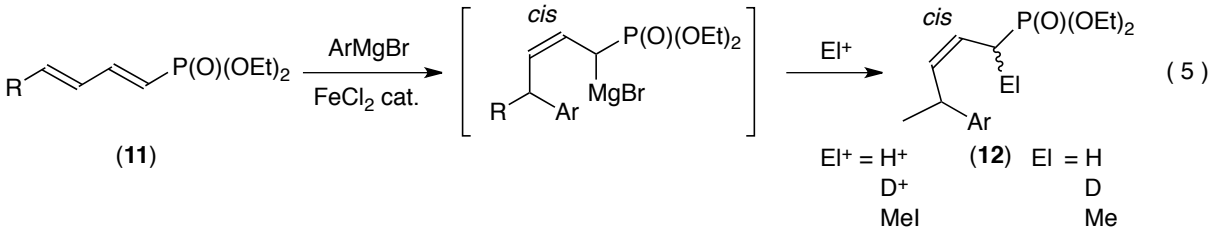


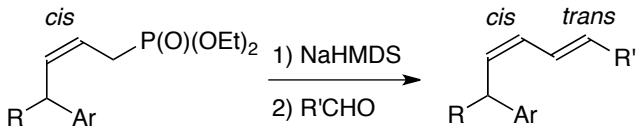
(4)

Chapter 4 Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Phosphonates and Its Synthetic Application.

α,β,γ,δ-Unsaturated phosphonates **11** were treated with aryl Grignard reagents in the presence of $FeCl_2$ to give *cis*-allylphosphonates **12** after hydrolysis (eq 5). In addition, deuteriolysis and methylation gave the deuterated and methylated products again with the exclusive *cis*-olefinic stereochemistry. The *cis*-allylphosphonate **12** could be used as precursors for the Wittig reaction with aldehydes, giving stereo-defined arylated dienes **10** with high stereoselectivity (eq 6). As the ligands on the P atom of phosphonates could be more easily modified than that in phosphine oxides (Chapter 3), this reaction would be more readily extended to the asymmetric conjugate addition as well as *cis*-selective Wittig reaction.



(**11**) (**12**) (5)



(**12**) (**10**) (6)

In summary, we have successfully developed the new iron-catalyzed selective δ-addition of aryl Grignard reagents to α,β,γ,δ-unsaturated sulfones, phosphine oxides, and phosphonates, affording virtually single arylated *cis*-olefinic products. Their synthetic applications have been also demonstrated, serving the construction of important structures of naturally occurring and artificially useful compounds.

Publication

Hata, T.; Nakada, T.; **Oh, Y. T.**; Hirone, N.; Urabe, H. "Iron-Catalyzed Regio- and Stereoselective Conjugate Addition of Aryl-Grignard Reagents to α,β,γ,δ-Unsaturated Sulfones and Its Synthetic Application," *Adv. Synth. Catal.* **2013**, *355*, 1736-1740.

Other Publication

Oh, Y. T.; Senda, K.; Hata, T.; Urabe, H. "Rh-Catalyzed Intramolecular Debenzylative Cyclization of Amines. Butyrolactams from Benzylamines Having a Chloroacteylene Moiety," *Tetrahedron Lett.* **2011**, *52*, 2458-2461.

Presentation

1) Hata, T.; Nakada, T.; **Oh, Y. T.**; Hirone, N.; Urabe, H.
"Iron-catalyzed Selective Conjugate Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Sulfones and Its Application"
57th Symposium on Organometallic Chemistry, Japan (September 16-18, 2010, Chuo University, O2-06) (Oral Presentation)

2) **Oh, Y. T.**; Sugano, G.; Hata, T.; Urabe, H.
"Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Organophosphorus Compounds"
93rd Annual Meeting of the Chemical Society of Japan (March 22-25, 2013, Ritsumeikan University, 2F-04) (Oral Presentation)

3) Nakagawa, K.; **Oh, Y. T.**; Hata, T.; Urabe, H.
"Iron-catalyst Selective Addition of Aryl Grignard Reagents to Electron-Deficient Dienes"
10th International Symposium on Carbanion Chemistry (September 23-26, 2013, Kyoto, P-96)
(Poster Presentation)

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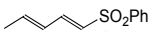
Thanks to Takuya Nakada, by collaborating the work in Chapter 2. And also special thanks for Goshi Sugano, by his collaboration with me on the contents of Chapters 3 and 4.

And to all those people who prayed for me, my friends and specially my family in Korea who are always praying and supporting me my abroad live. Thank you everybody who is reading this thesis.

Finally all thanks to my God, for everything.

Chapter 2. Supporting Information

Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Sulfones and Its Synthetic Application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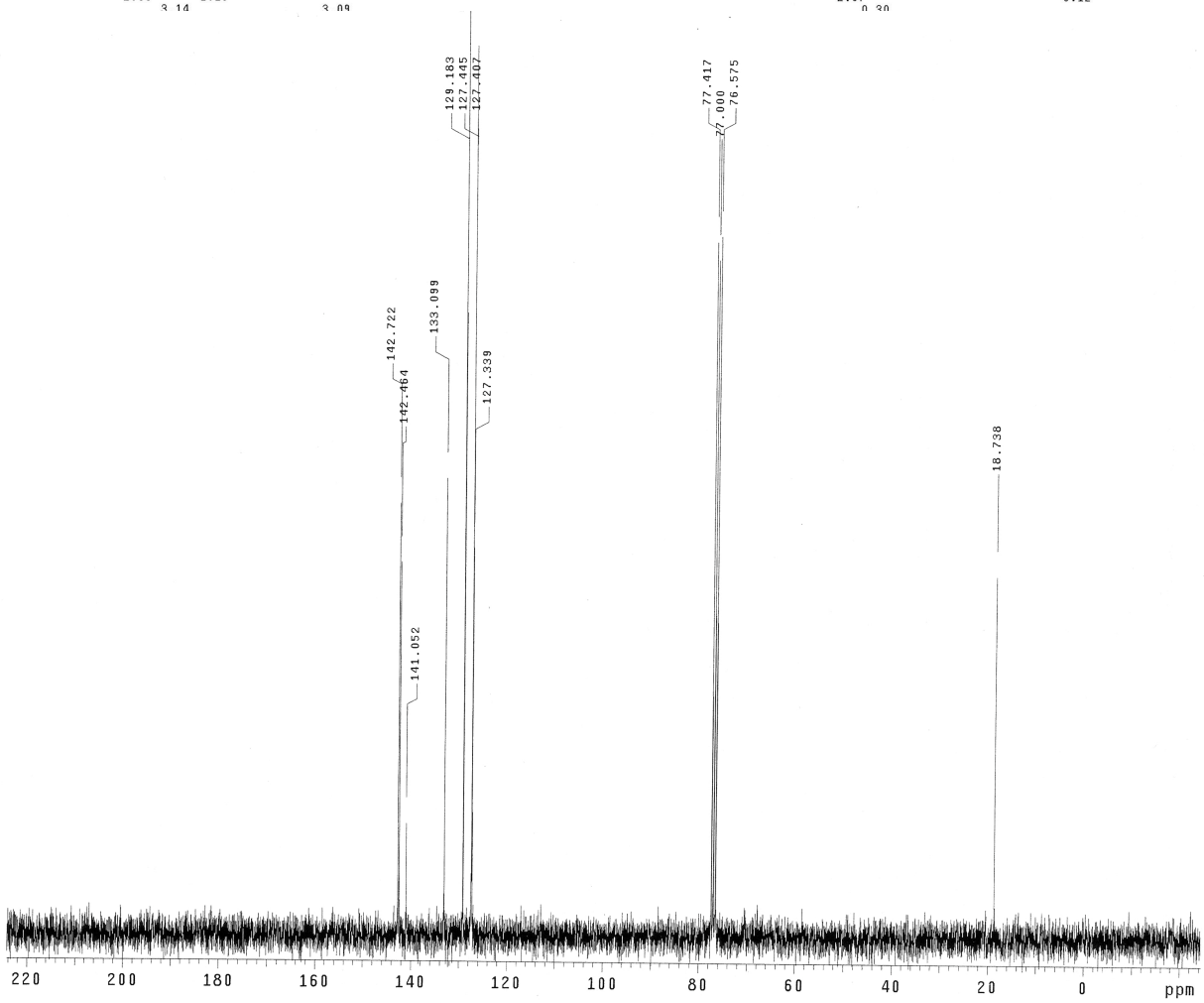
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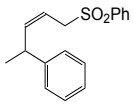
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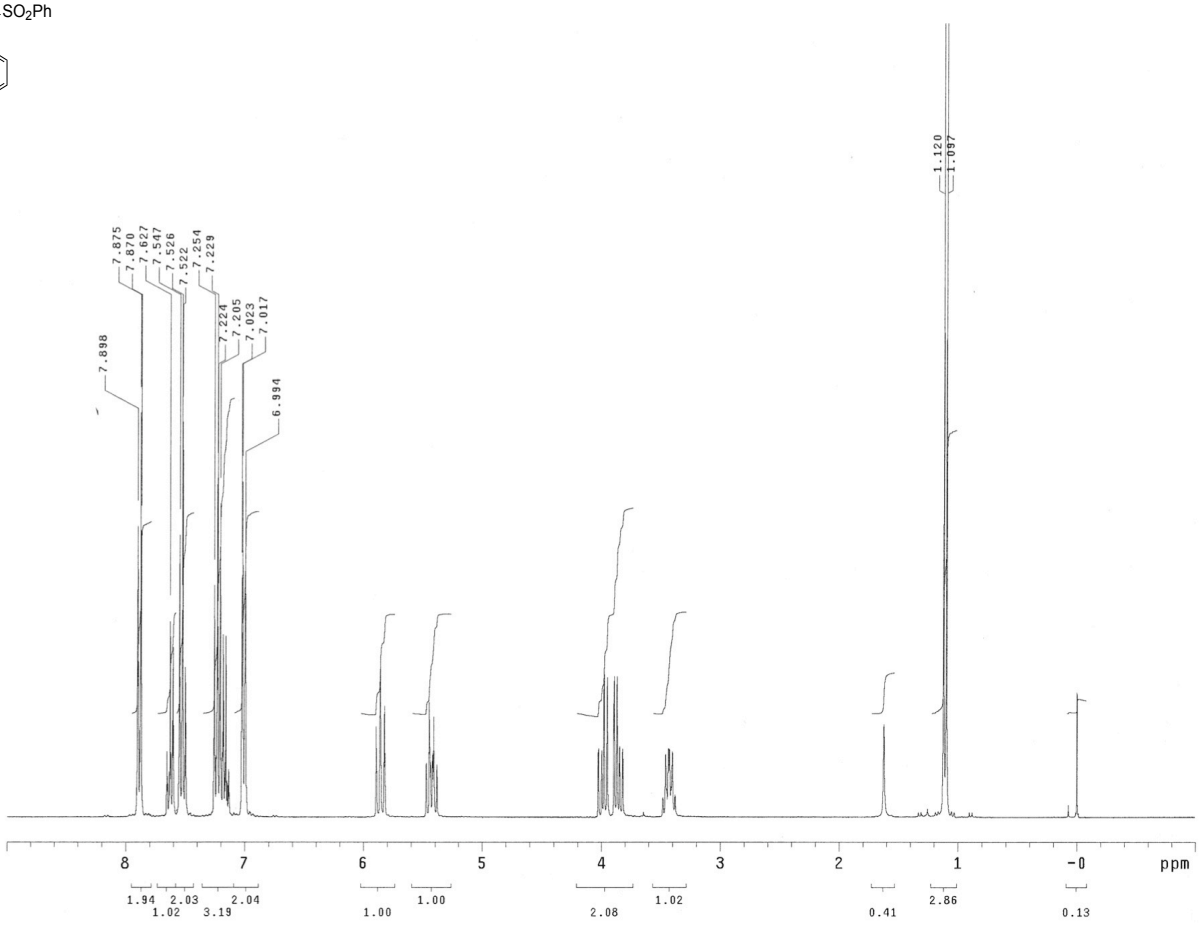
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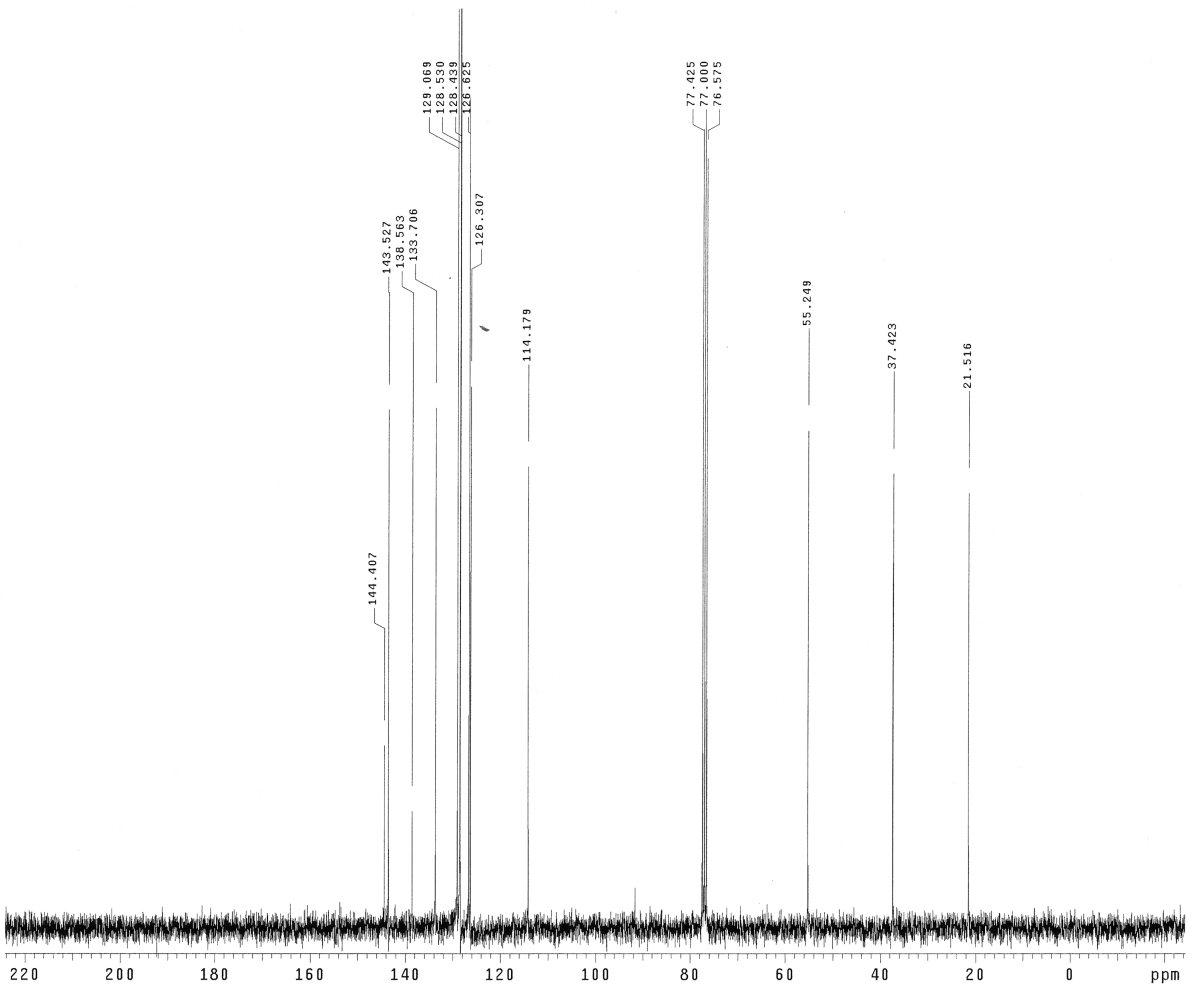
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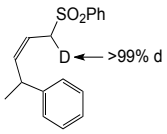
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D
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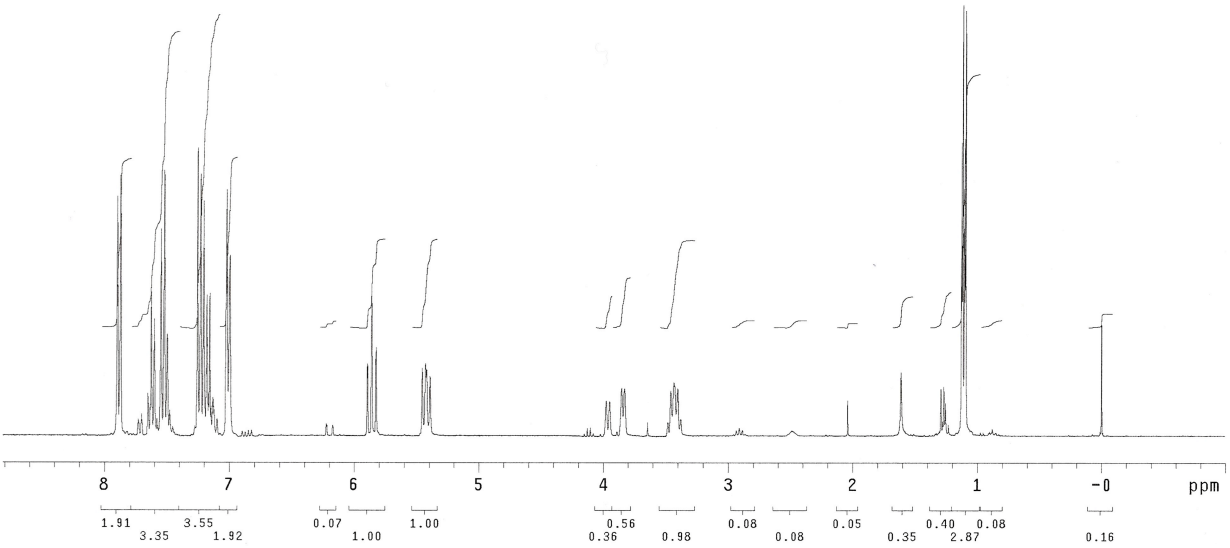
(**17**-d_1)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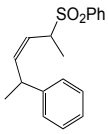
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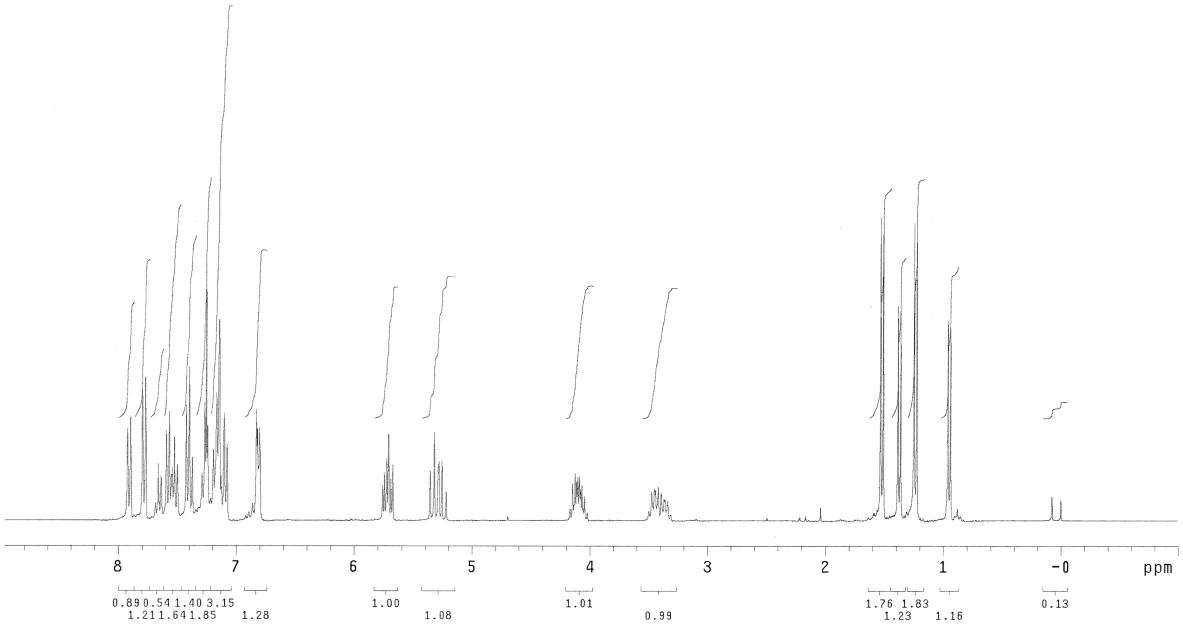
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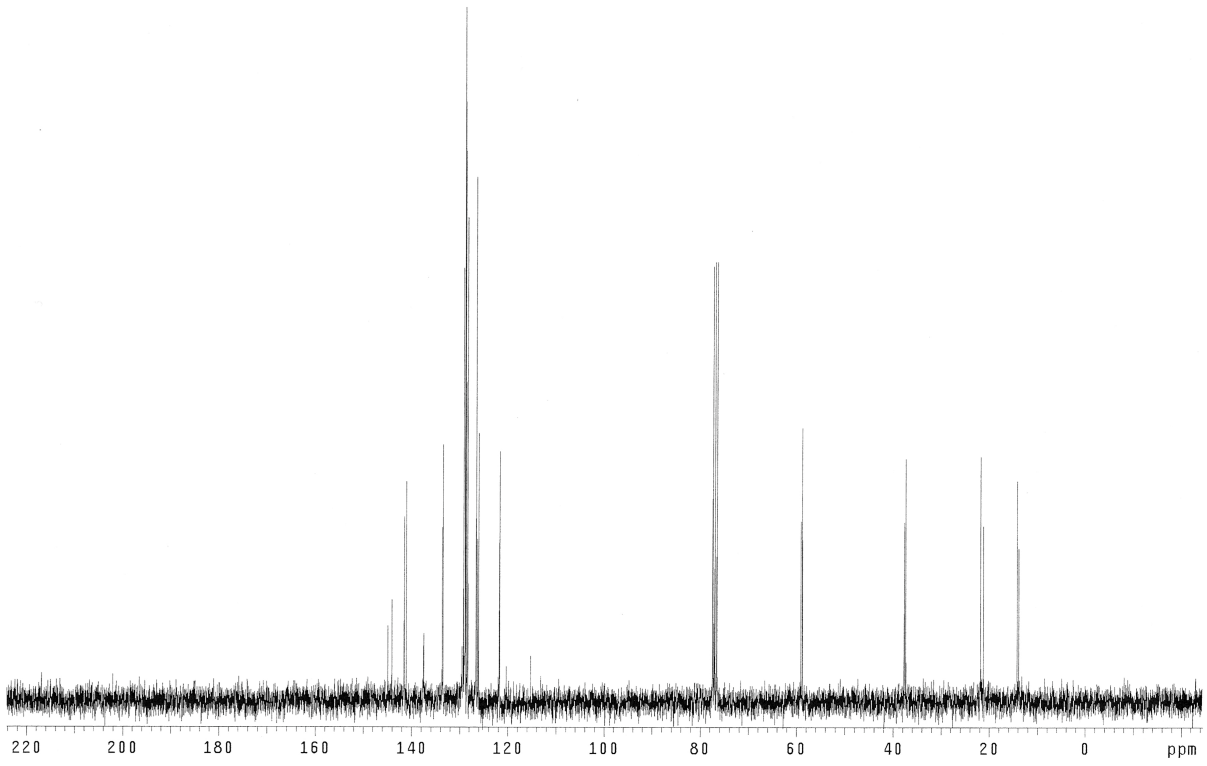
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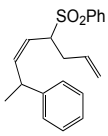
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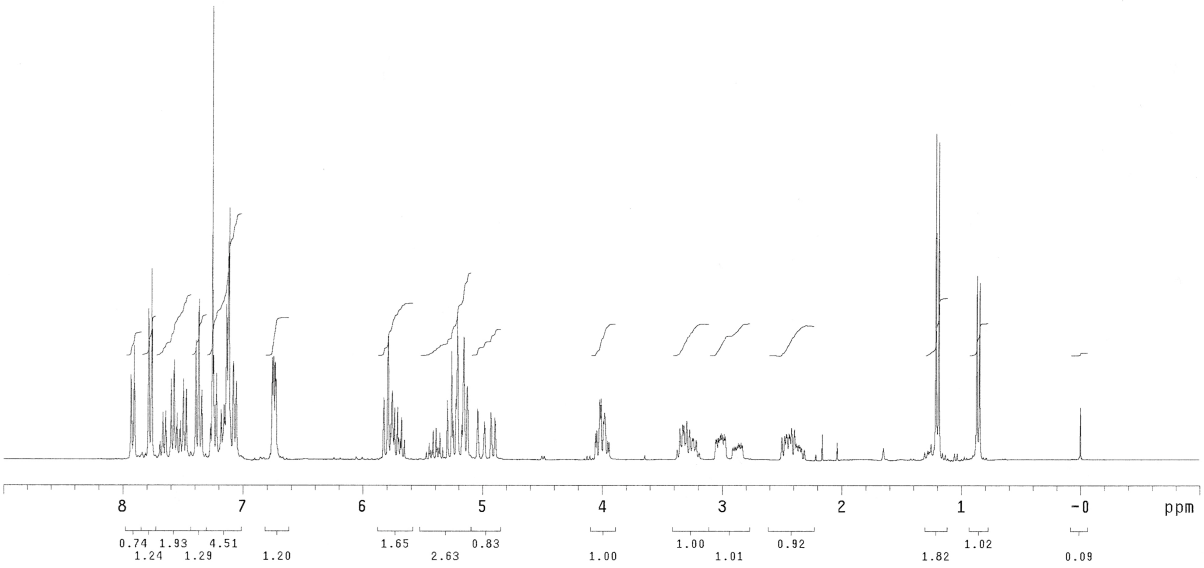
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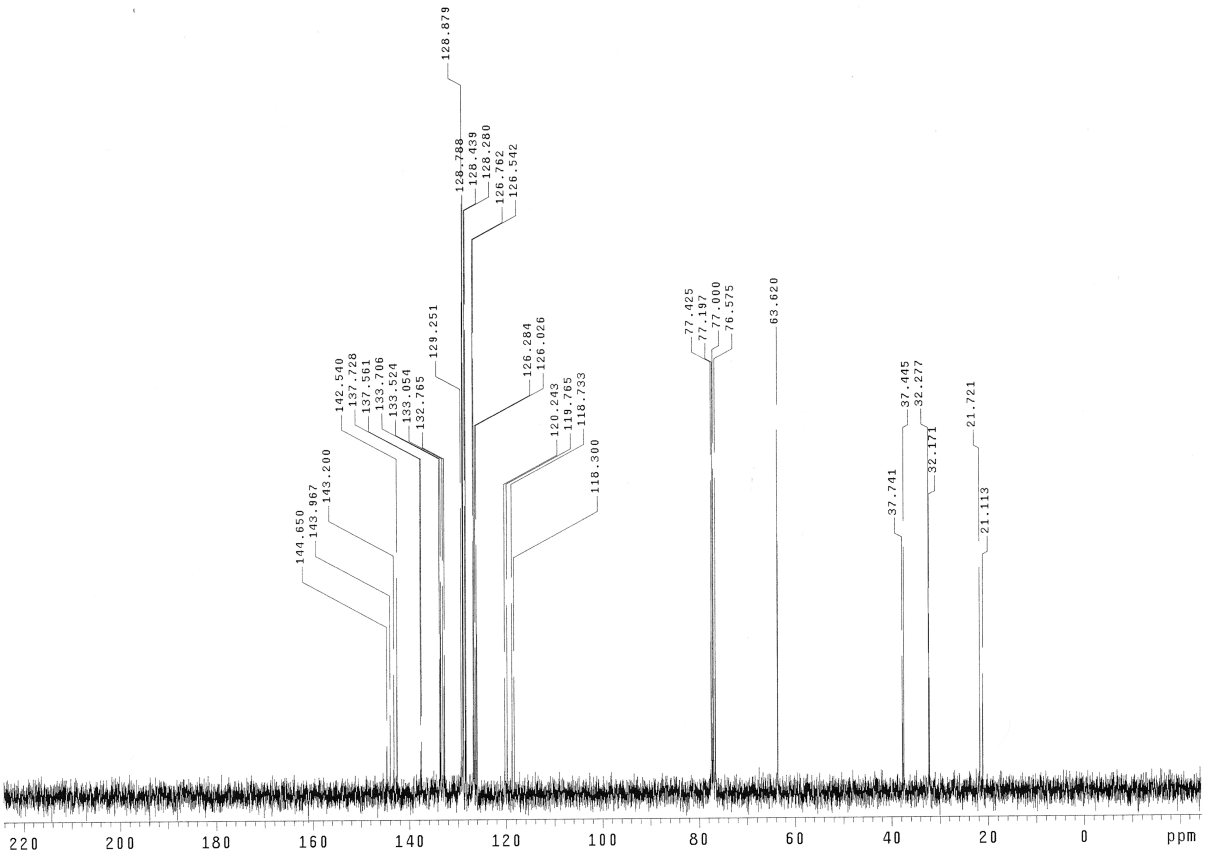
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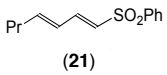
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SO2Ph

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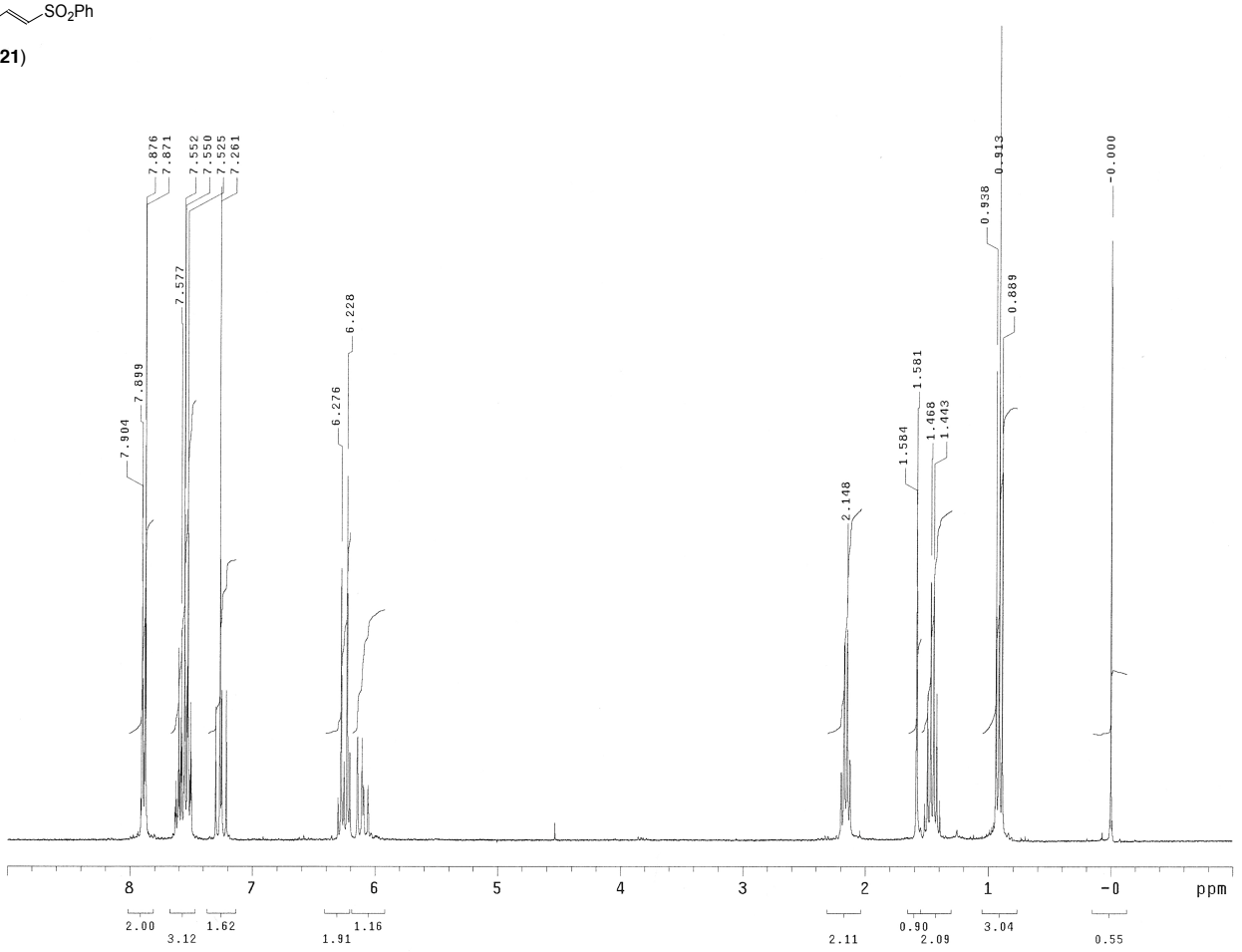
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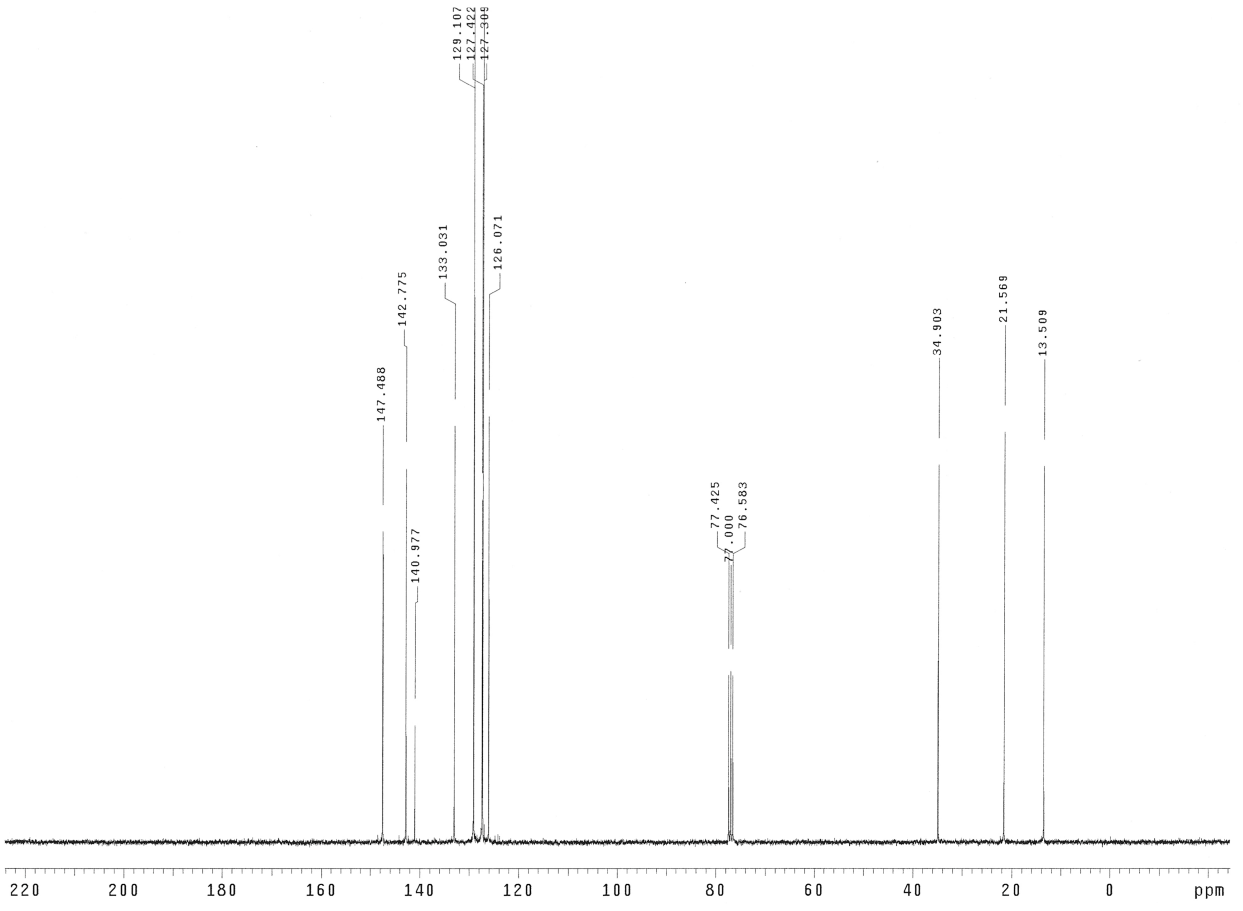
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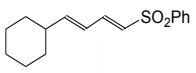
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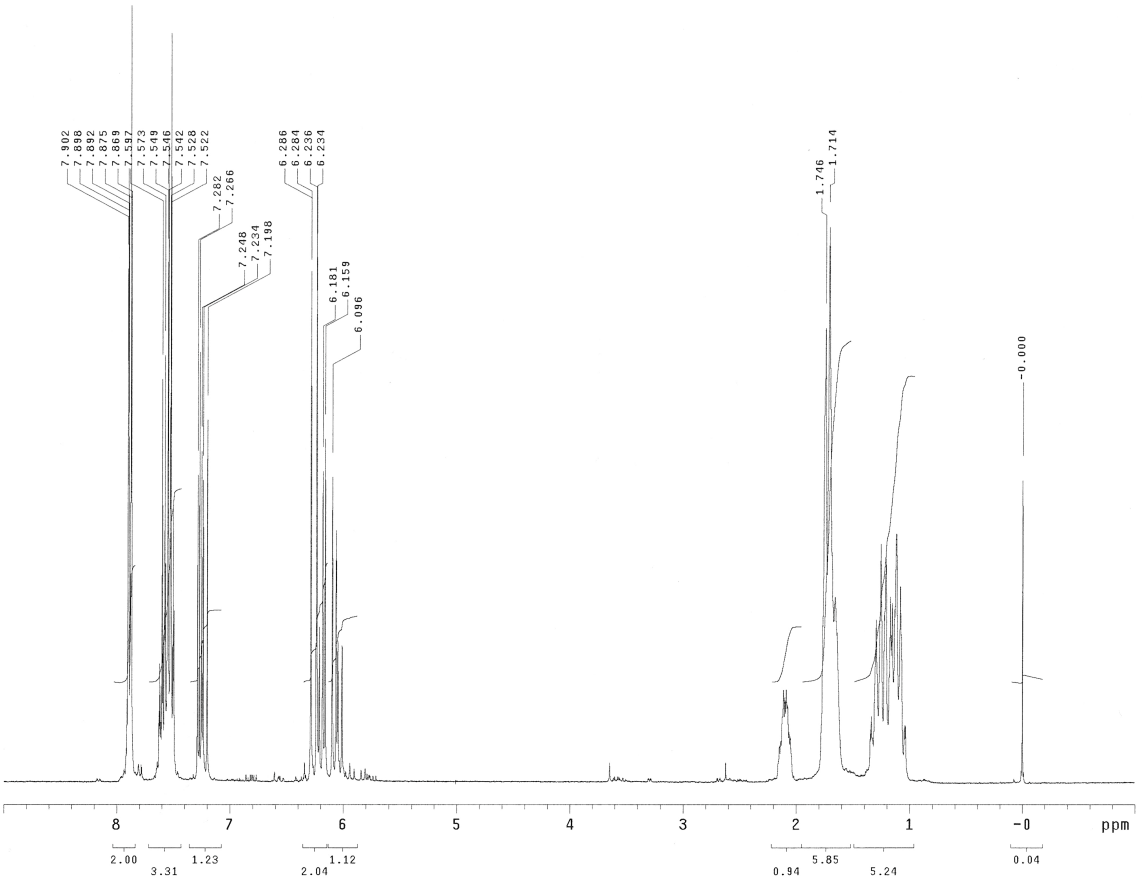
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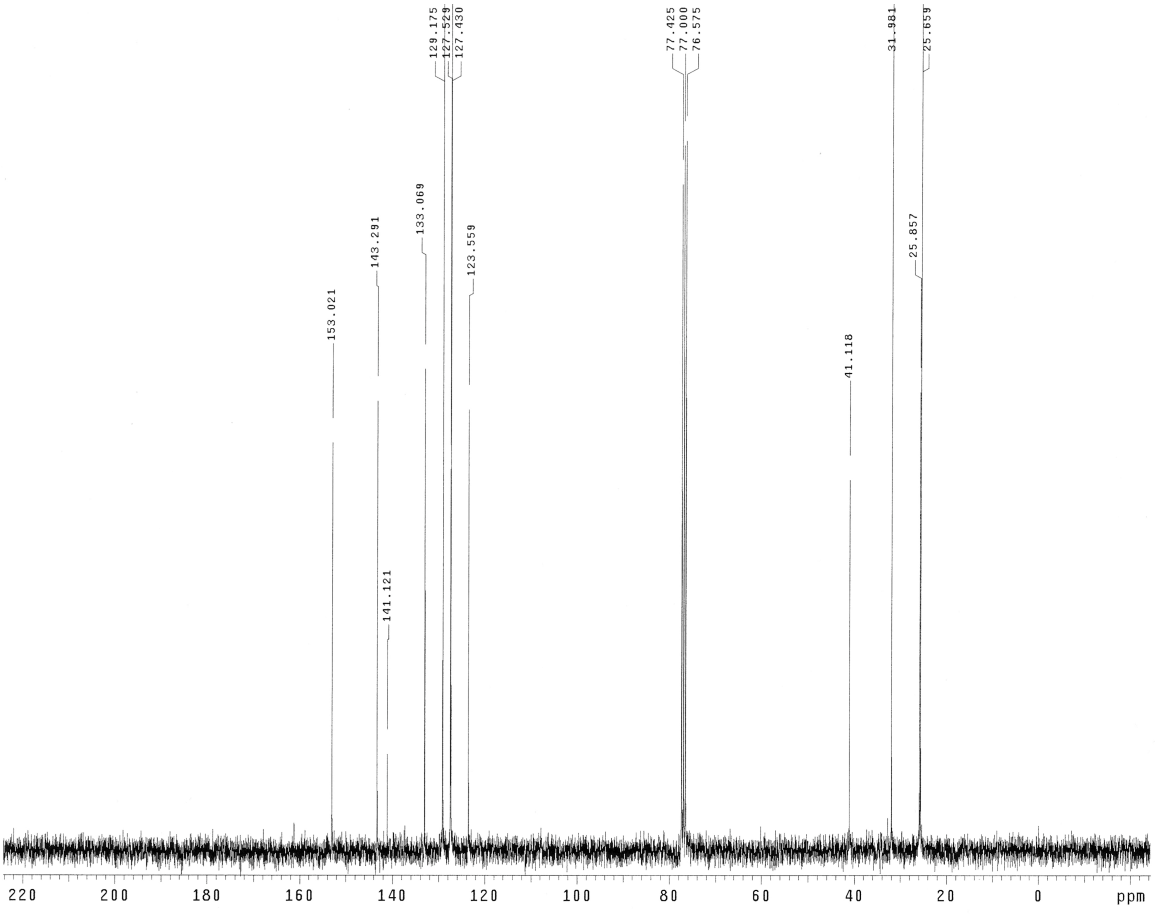
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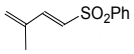
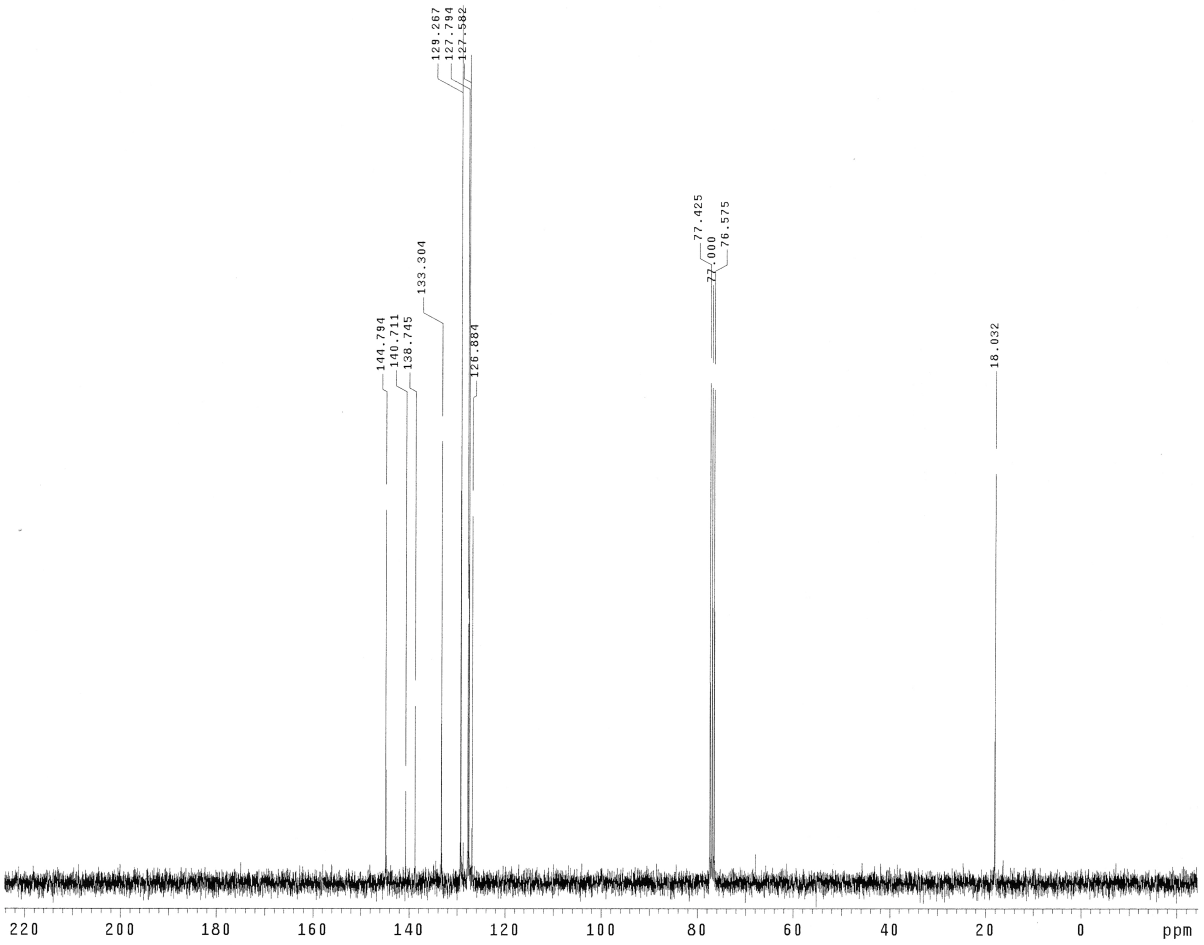
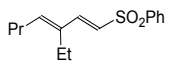
0
ppm


SO2Ph

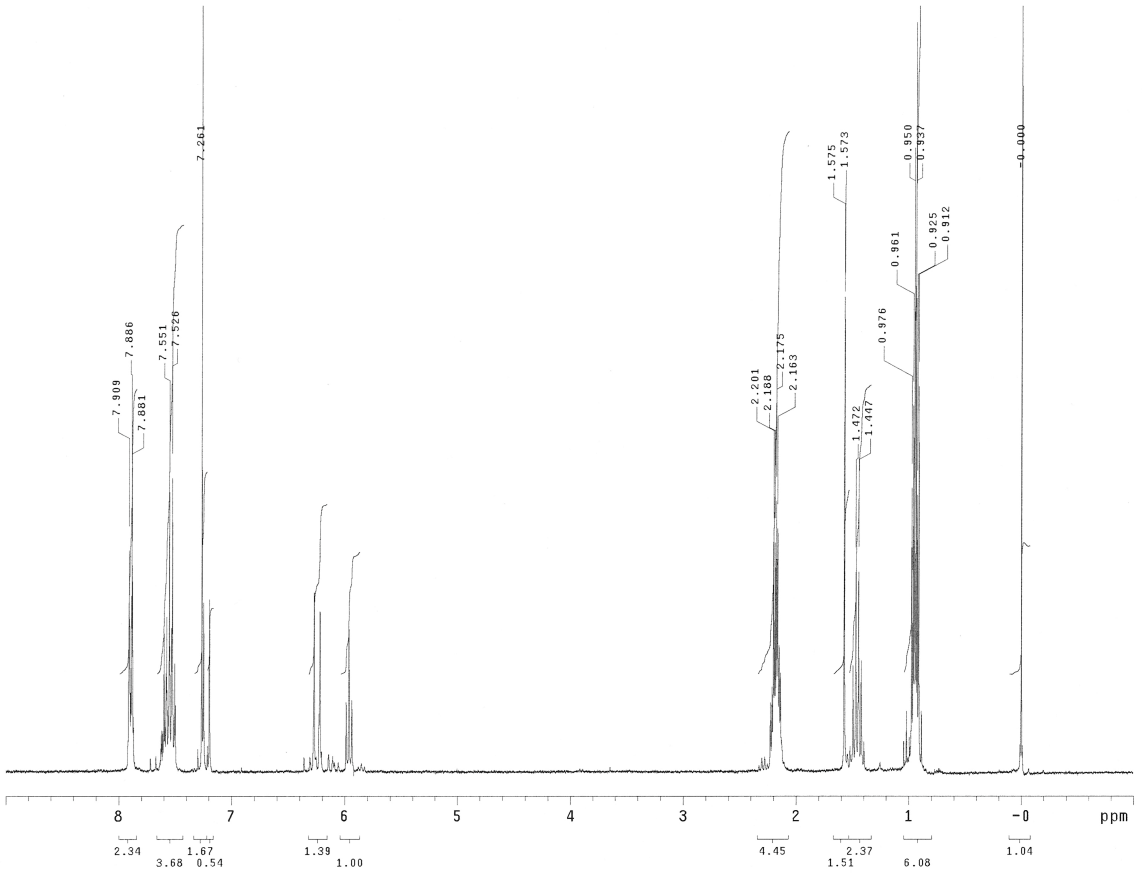
(**23**)

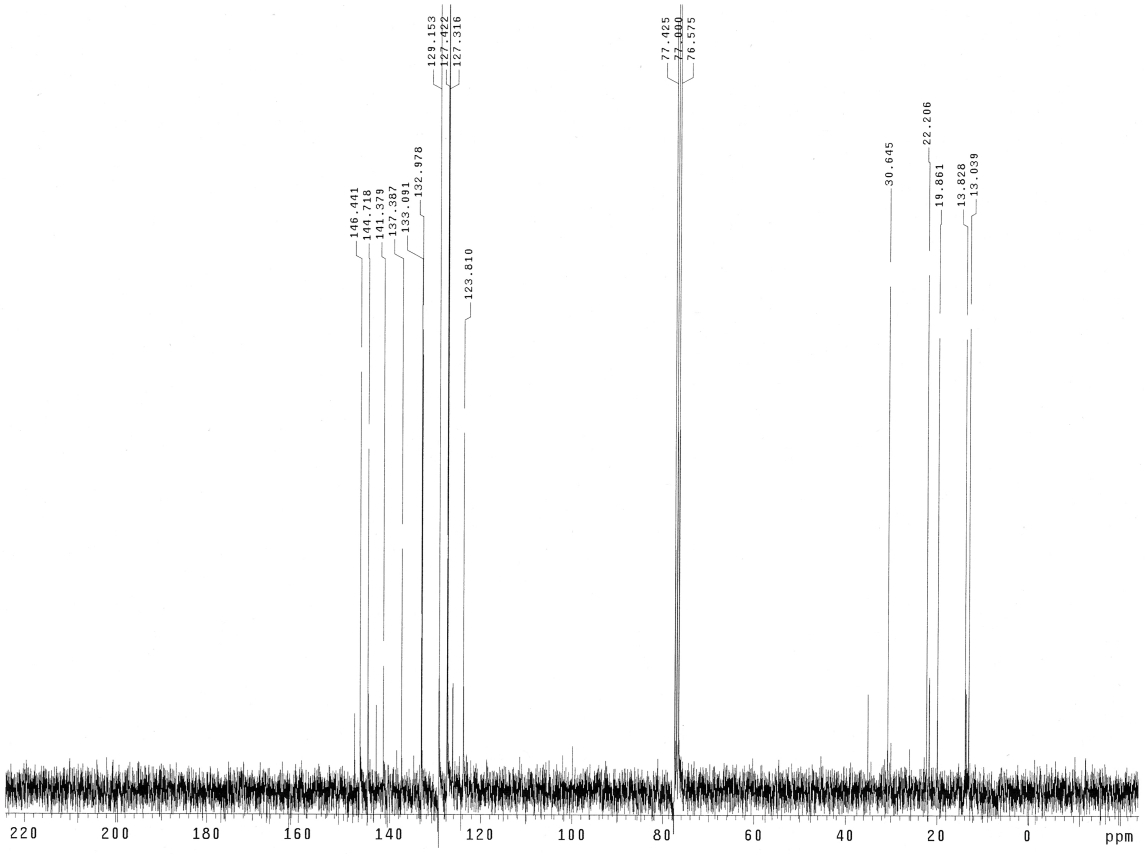
7.926
7.924
7.922
7.899
7.894
7.572
7.547
7.378
7.328
7.262
6.347
6.296
5.480
5.478
5.448
1.837
1.835
1.585
0.001
0.000
8
7
6
5
4
3
2
1
-0
ppm
2.29
1.07
3.63
0.72
1.00
2.32
3.23
1.24
0.67

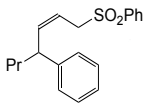

144.794
140.711
138.745
133.304
129.267
127.794
127.582
126.884
77.425
77.000
76.575
18.032
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Pr
SO2Ph
Et

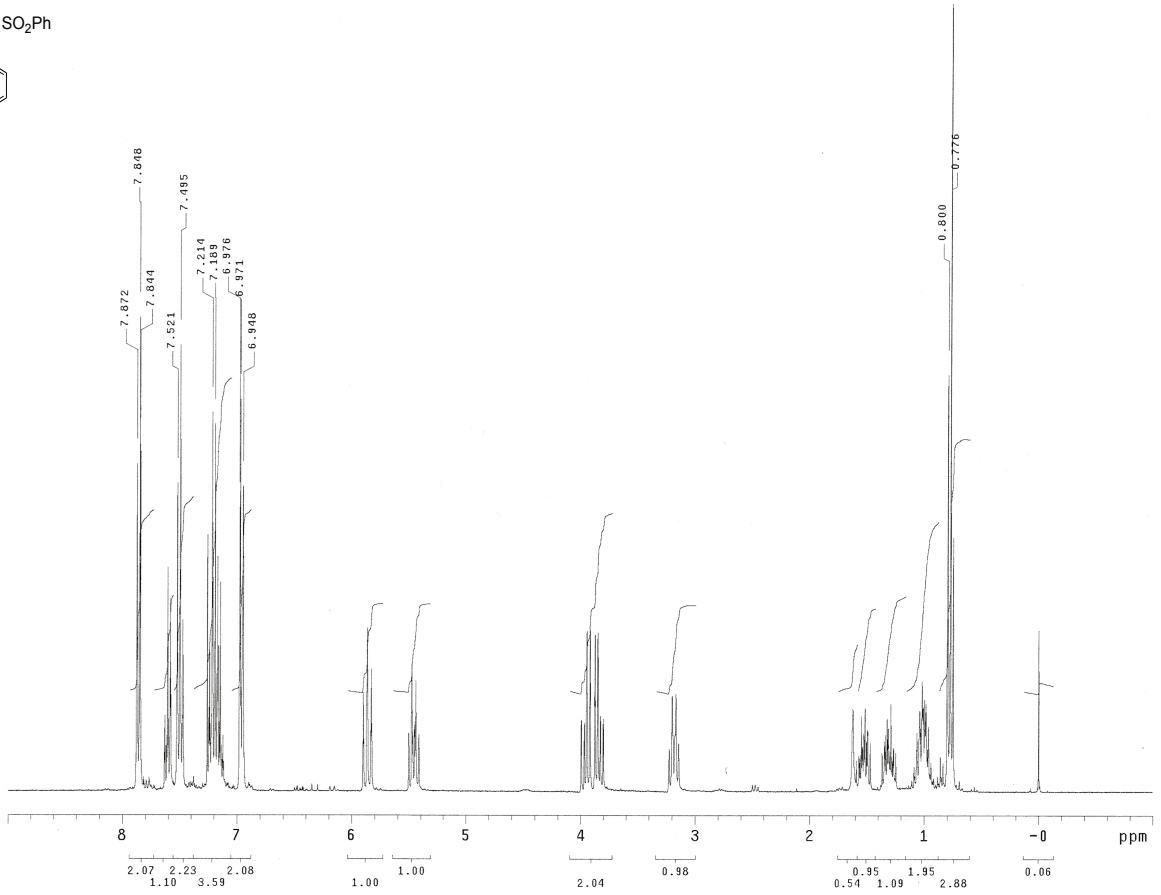
(**24**)

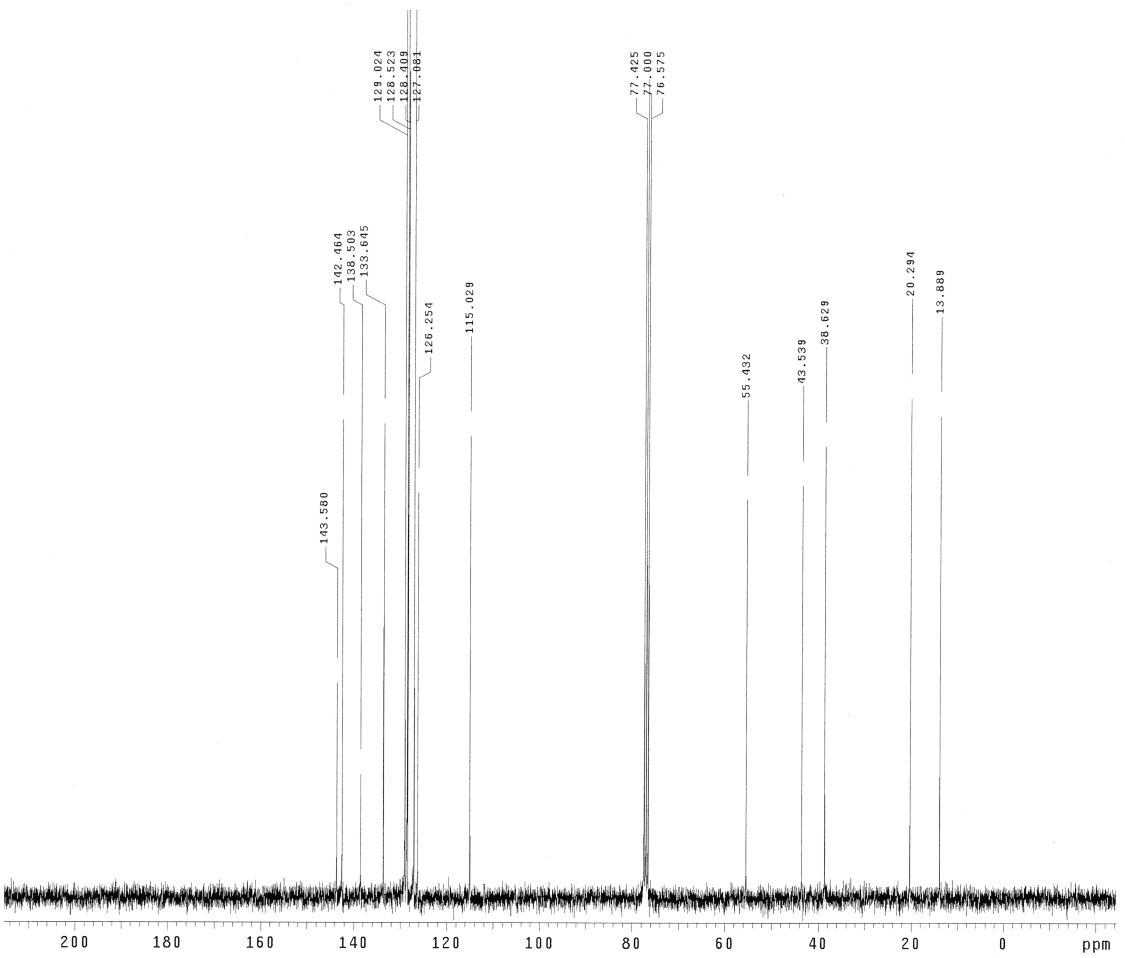

7.909
7.886
7.881
7.551
7.526
7.261
2.201
2.188
2.175
2.163
1.575
1.573
1.472
1.447
0.976
0.961
0.950
0.937
0.925
0.912
0.000
8
7
6
5
4
3
2
1
-0
ppm
2.34
3.68
1.67
0.54
1.39
1.00
4.45
1.51
2.37
6.08
1.04

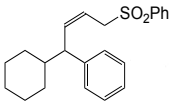

146.441
144.718
141.379
137.387
133.091
132.978
129.153
127.422
127.316
123.810
77.425
77.000
76.575
30.645
22.206
19.861
13.828
13.039
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
Pr

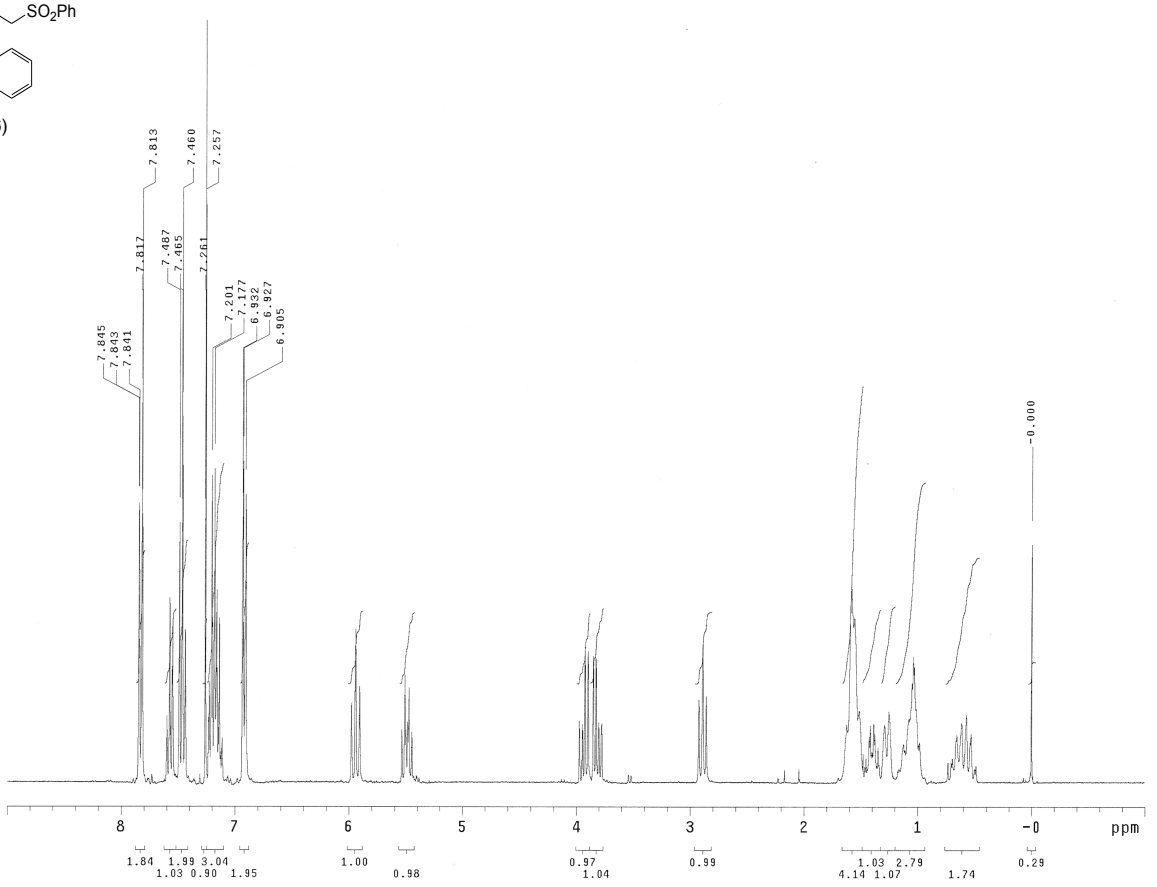
(**25**)

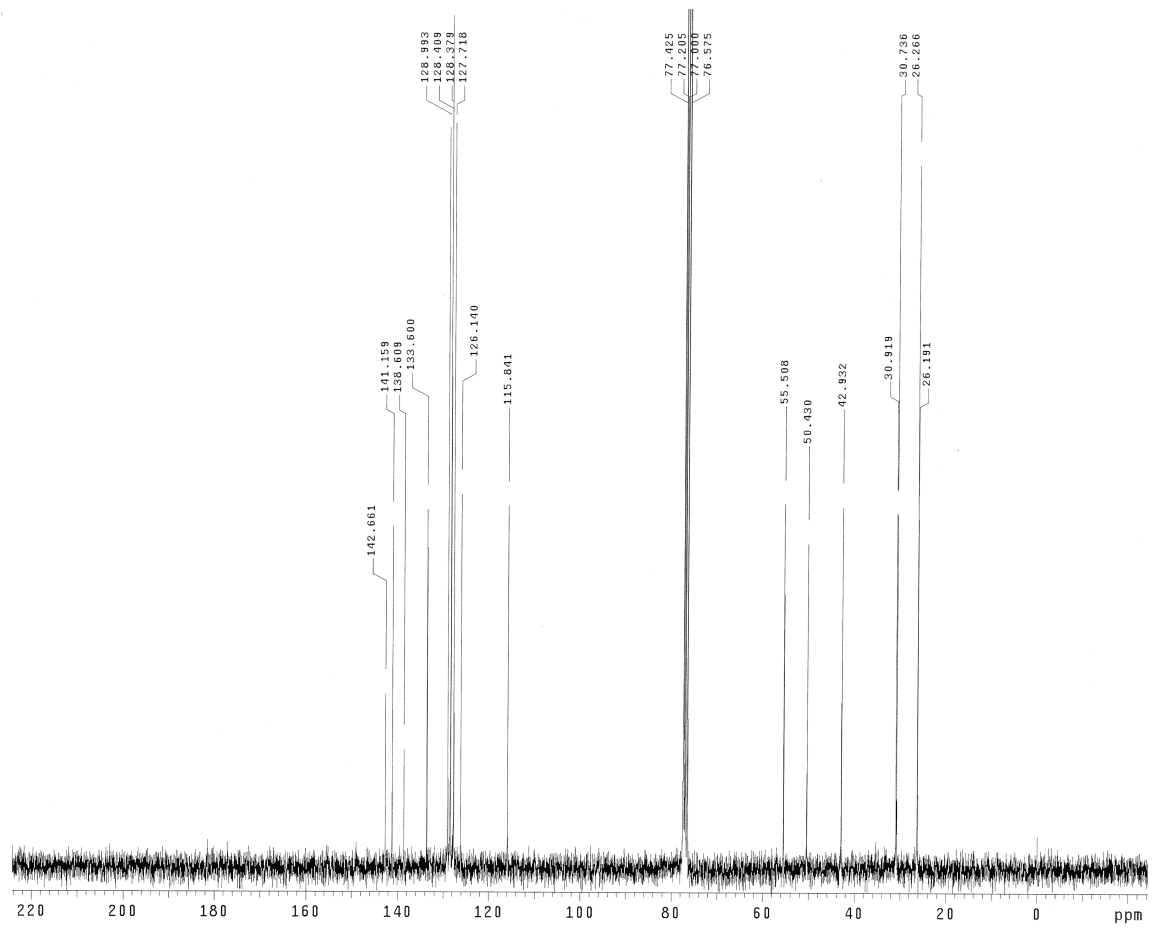

7.872
7.848
7.844
7.521
7.495
7.214
7.189
6.976
6.971
6.948
0.800
0.776
8
7
6
5
4
3
2
1
-0
ppm
2.07 2.23 2.08
1.10 3.59
1.00
1.00
2.04
0.98
0.95 1.95
0.54 1.09 2.88
0.06

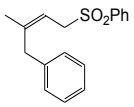

142.464
138.503
133.645
129.024
128.523
128.409
127.081
126.254
115.029
77.425
77.000
76.575
143.580
55.432
43.539
38.629
20.294
13.889
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph

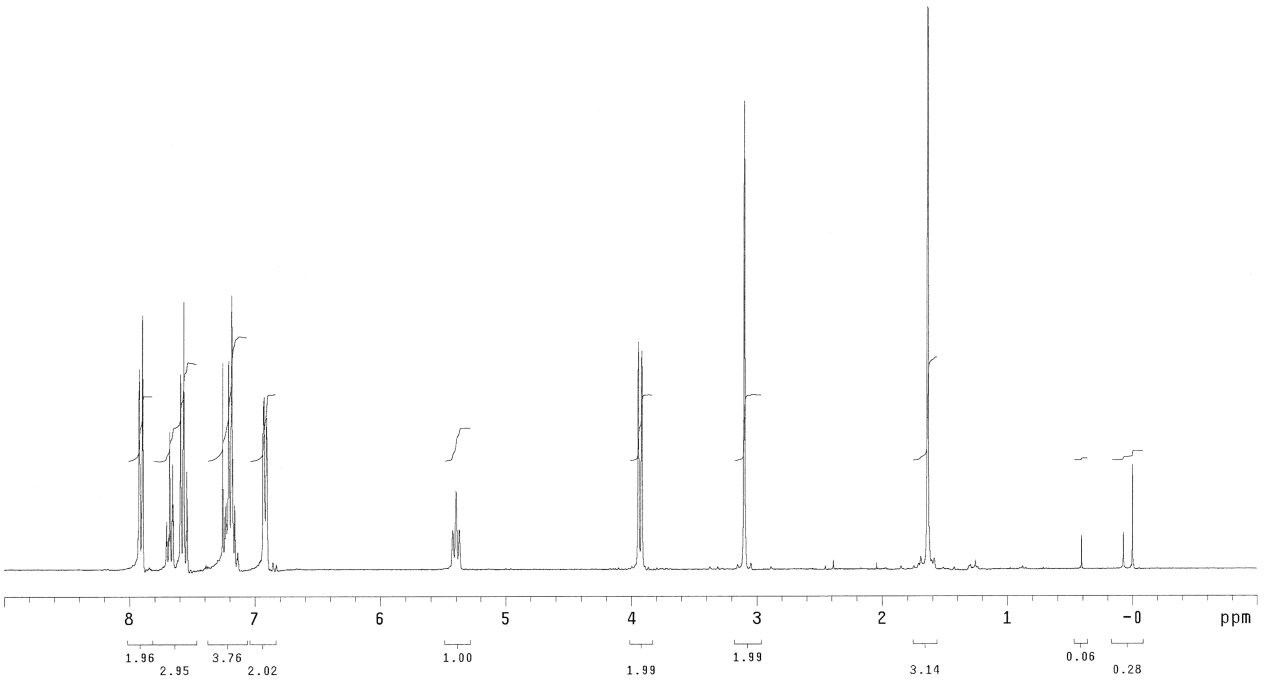
(**26**)

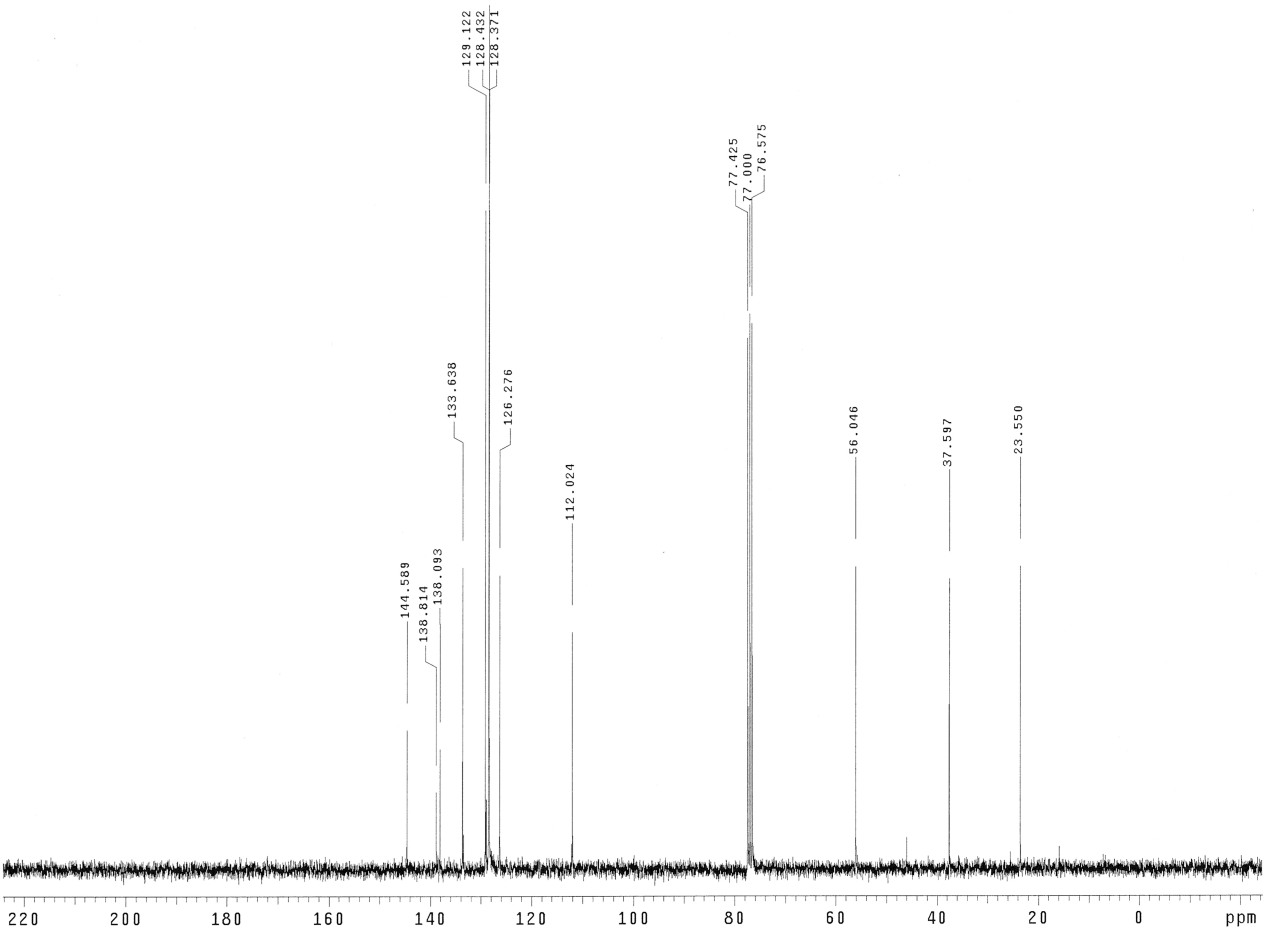

7.845
7.843
7.841
7.817
7.813
7.487
7.465
7.460
7.261
7.257
7.201
7.177
6.932
6.927
6.905
0.000
8
7
6
5
4
3
2
1
-0
ppm
1.84
1.99
1.03
3.04
0.90
1.95
1.00
0.98
0.97
1.04
0.99
1.03
4.14
2.79
1.07
1.74
0.29

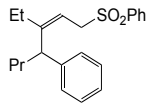

142.661
141.159
138.609
133.600
128.993
128.408
128.379
127.718
126.140
115.841
77.425
77.205
77.000
76.575
55.508
50.430
42.932
30.919
30.736
26.266
26.191
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph

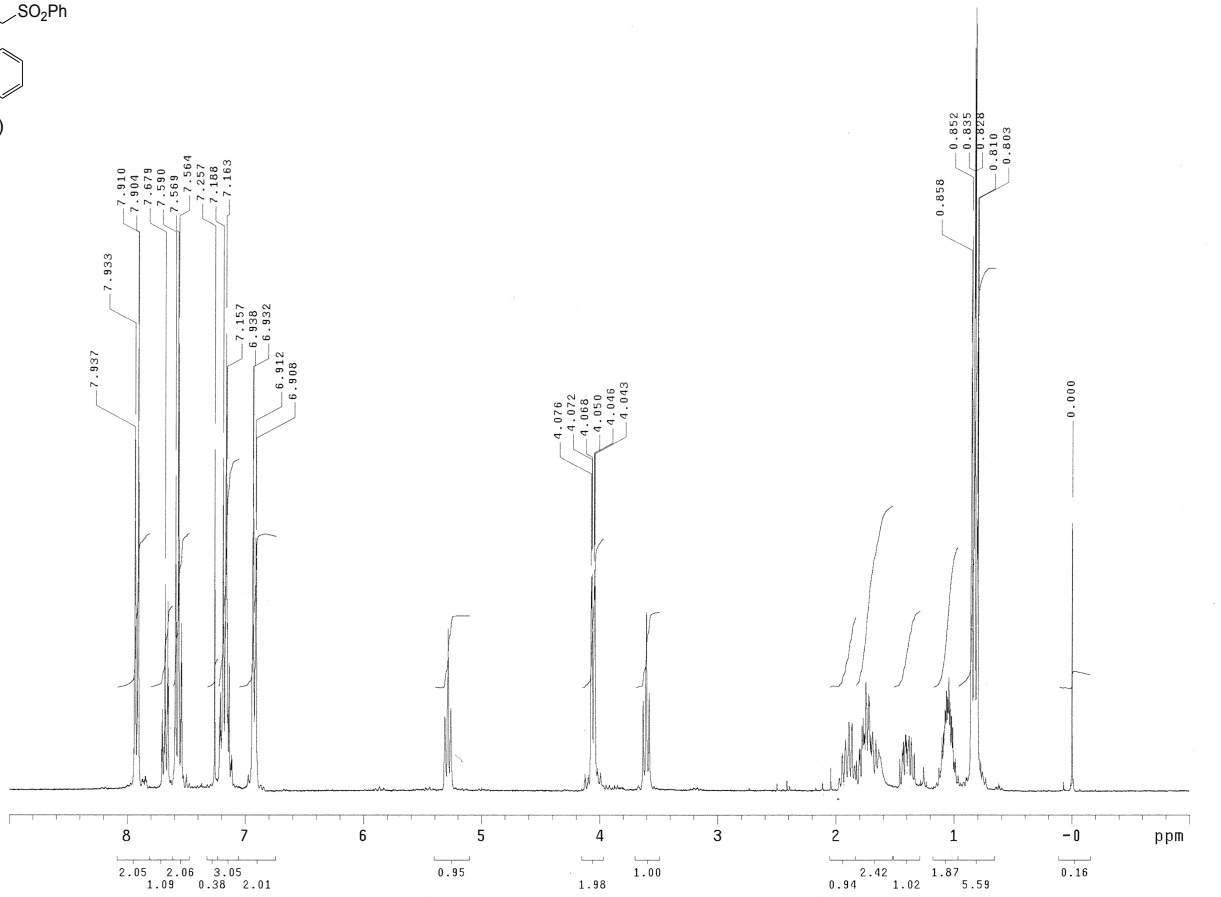
(**27**)

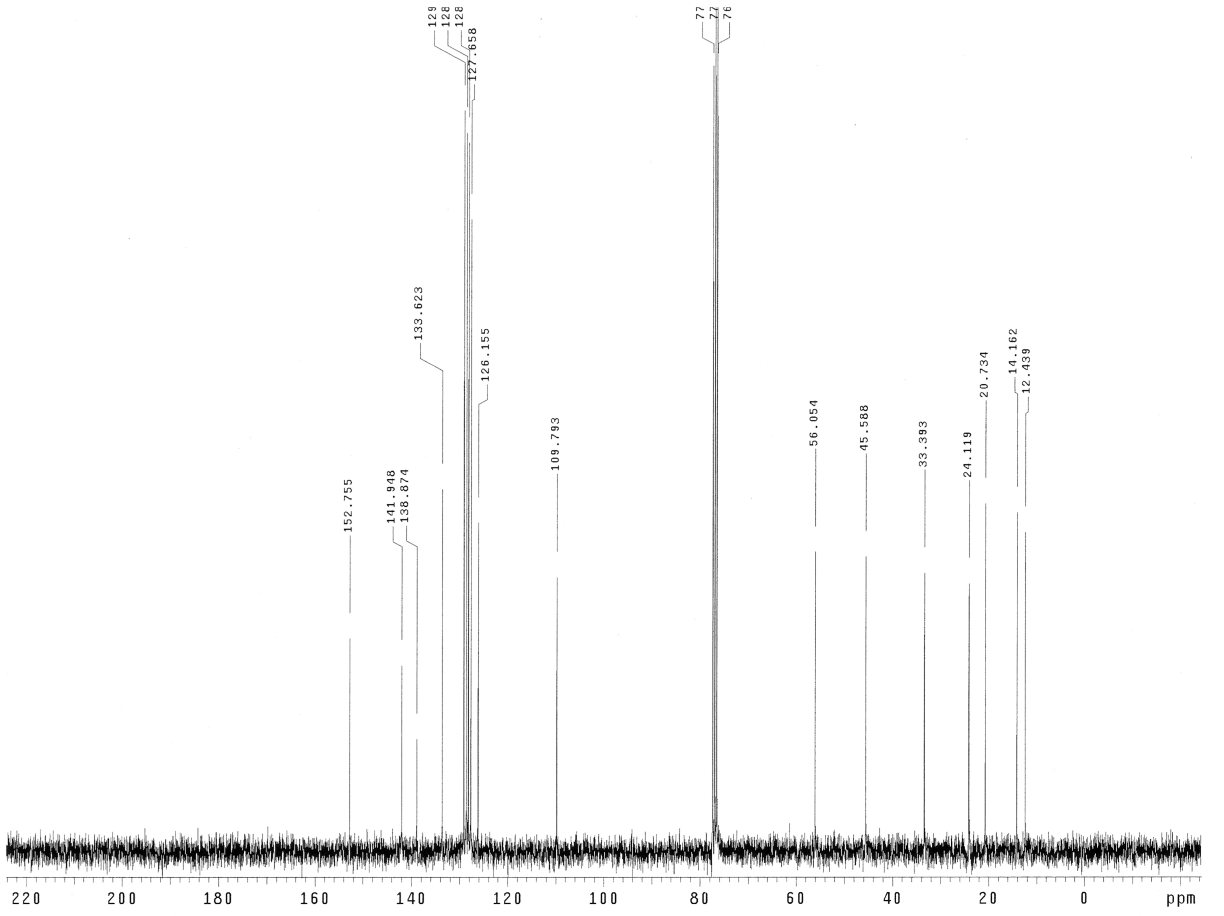

8
7
6
5
4
3
2
1
-0
ppm
1.96
2.95
3.76
2.02
1.00
1.99
1.99
3.14
0.06
0.28

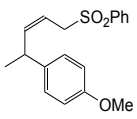

129.122
128.432
128.371
77.425
77.000
76.575
133.638
126.276
112.024
144.589
138.814
138.093
56.046
37.597
23.550
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Et
SO2Ph
Pr

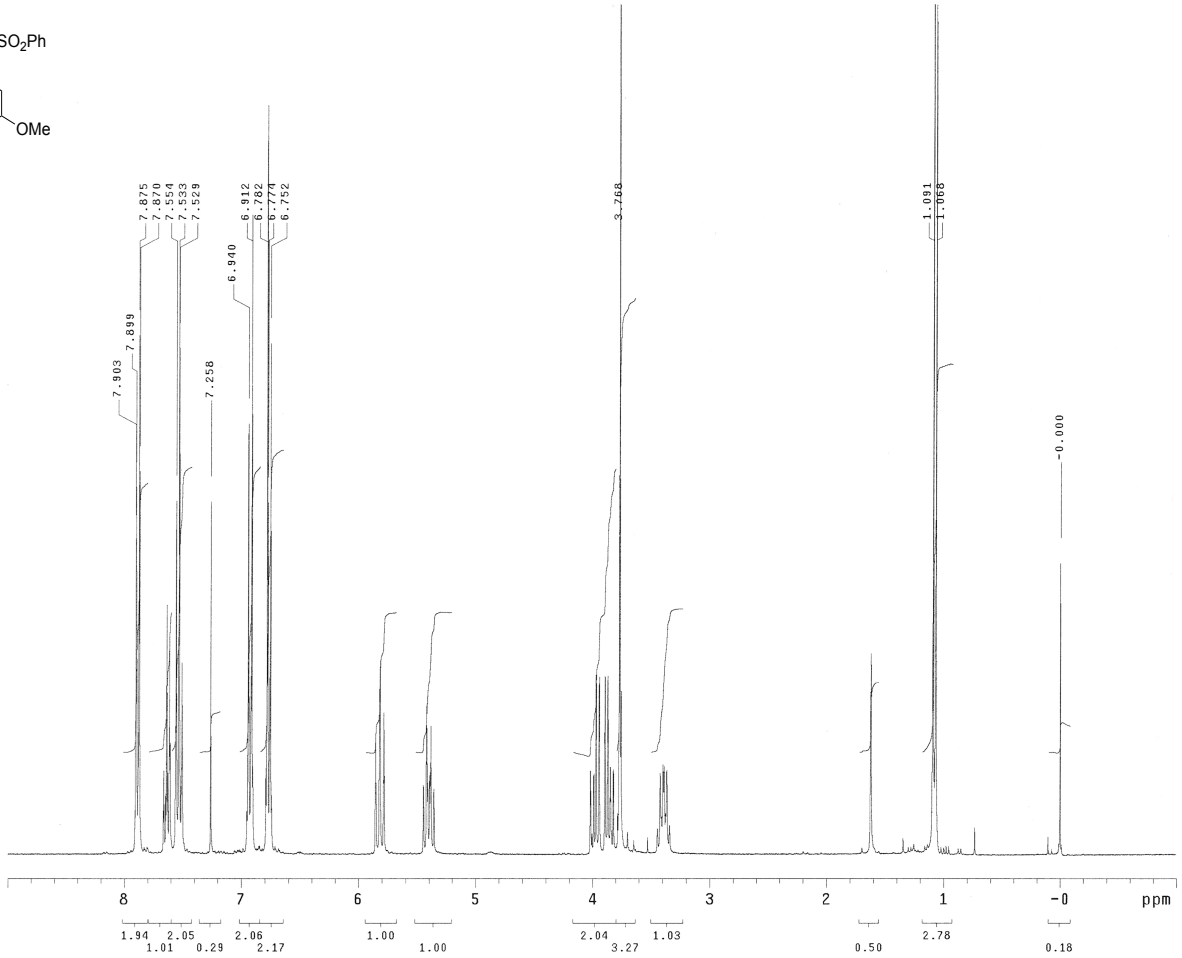
(**28**)

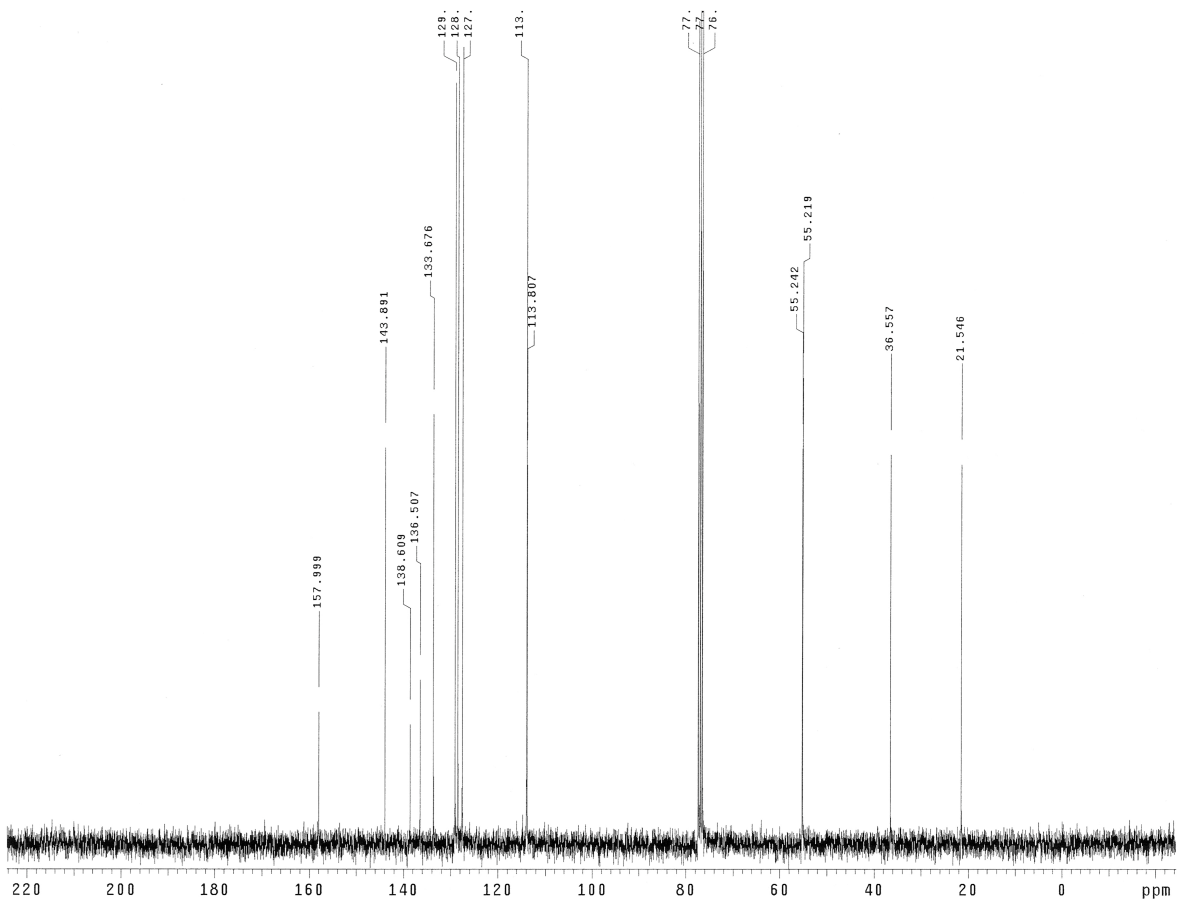

7.937
7.933
7.910
7.904
7.679
7.590
7.569
7.564
7.257
7.188
7.163
7.157
6.938
6.932
6.912
6.908
4.076
4.072
4.068
4.050
4.046
4.043
0.858
0.852
0.835
0.828
0.810
0.803
0.000
8
7
6
5
4
3
2
1
-0
ppm
2.05
2.06
1.09
3.05
0.38
2.01
0.95
1.98
1.00
0.94
2.42
1.02
1.87
5.59
0.16

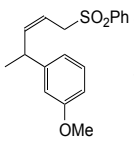

152.755
141.948
138.874
133.623
129.
128.
128.
128.
127.658
126.155
109.793
77.
77.
77.
76.
56.054
45.588
33.393
24.119
20.734
14.162
12.439
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe

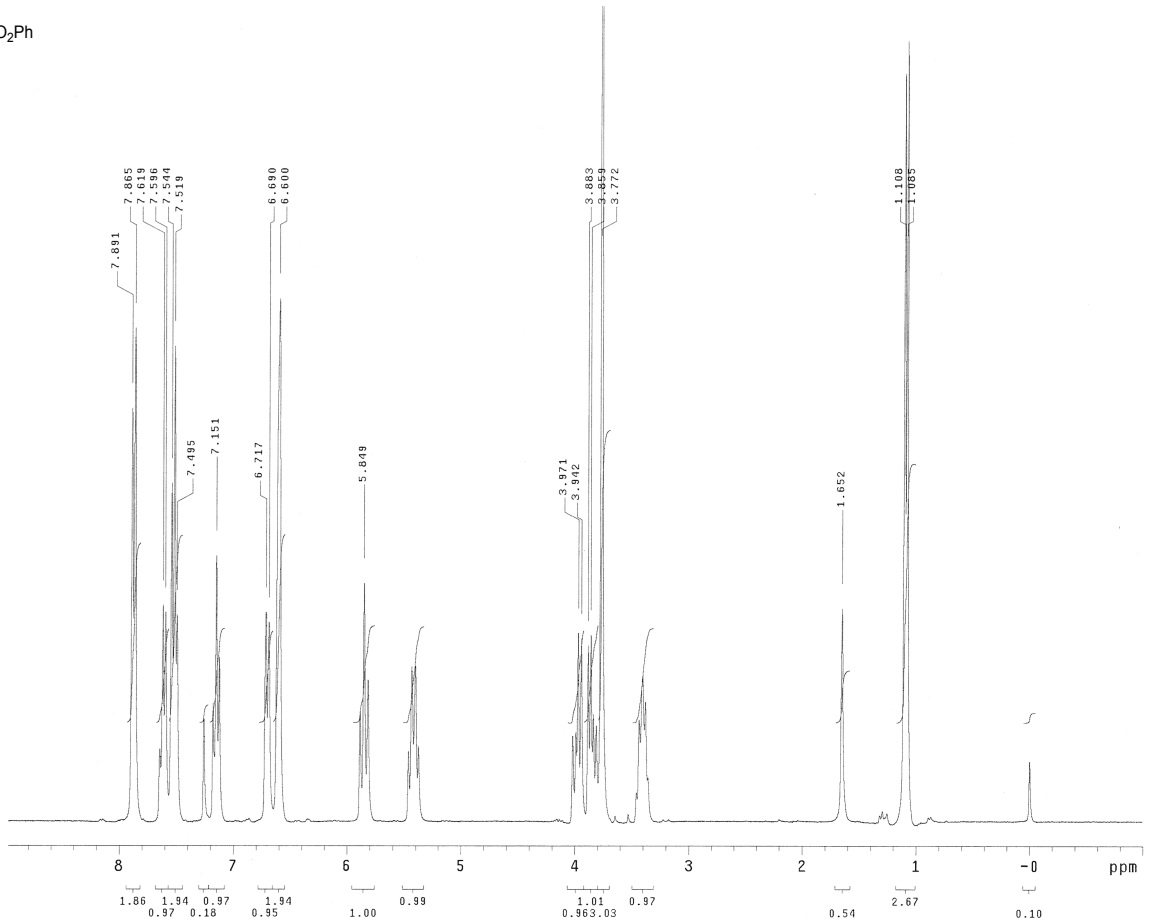
(**29**)

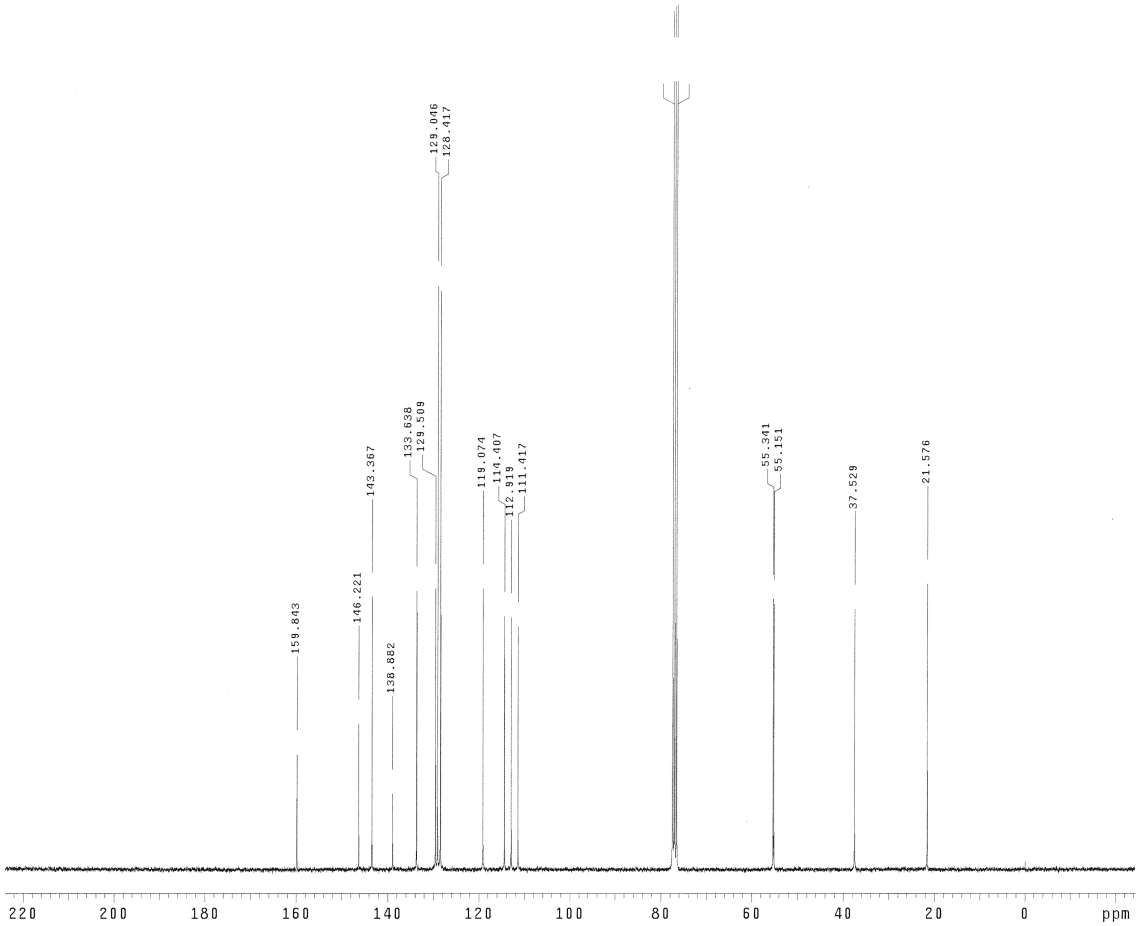

7.903
7.899
7.875
7.870
7.554
7.533
7.529
7.258
6.940
6.912
6.792
6.771
6.752
3.768
1.091
1.068
0.000
8
7
6
5
4
3
2
1
-0
ppm
1.94
2.05
1.01
0.29
2.06
2.17
1.00
1.00
2.04
3.27
1.03
0.50
2.78
0.18

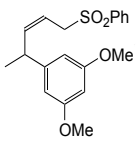

157.999
143.891
138.609
136.507
133.676
129.
128.
127.
113.
113.807
77.
77.
76.
55.242
55.219
36.557
21.546
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe

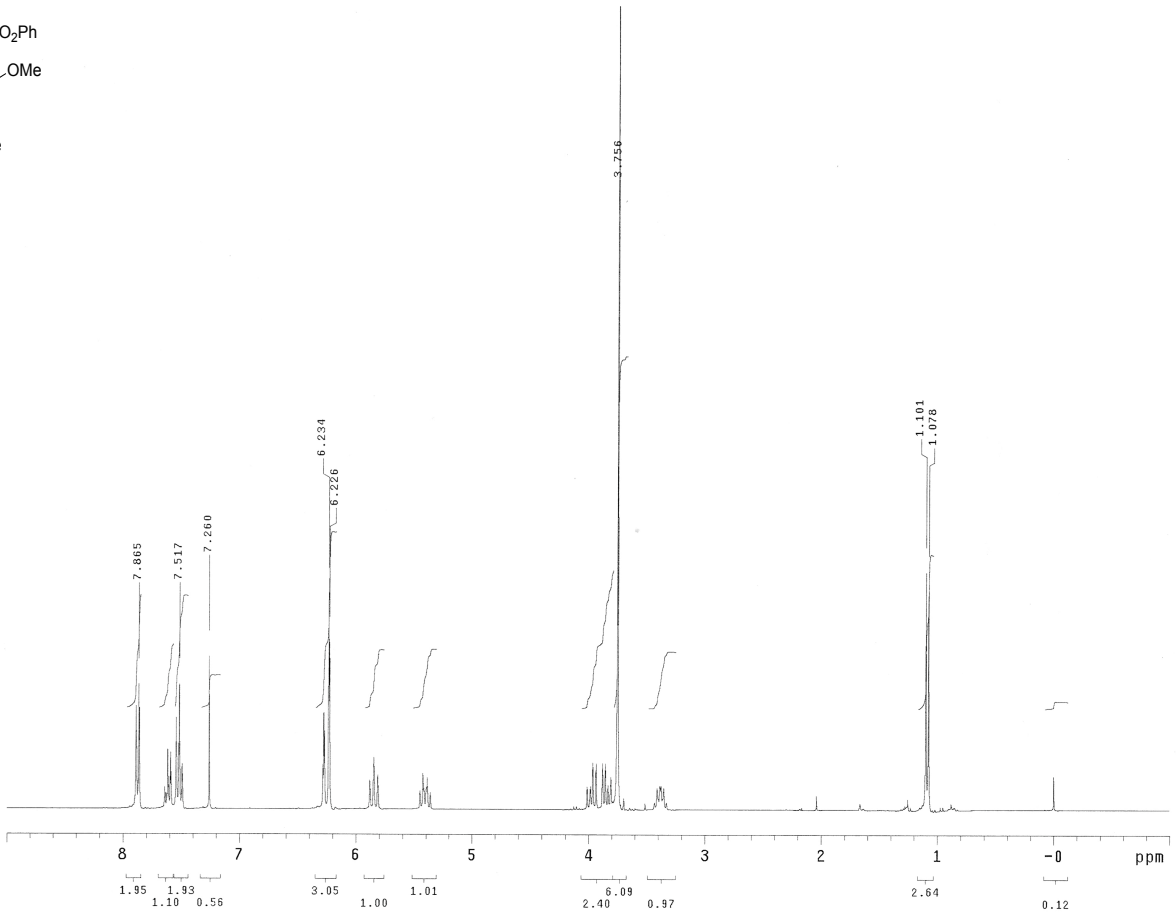
(**30**)

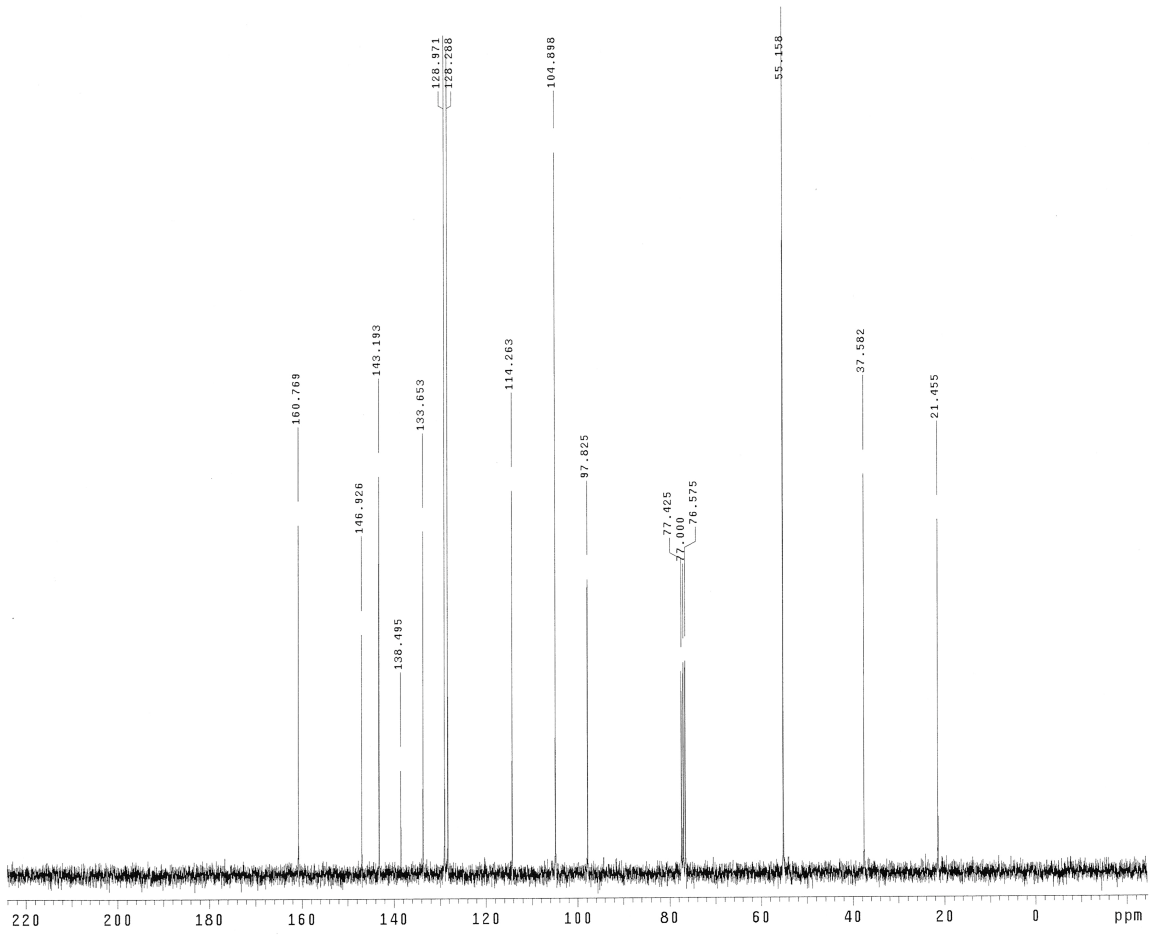

7.891
7.865
7.619
7.596
7.544
7.519
7.495
7.151
6.717
6.690
6.600
5.849
3.971
3.942
3.883
3.859
3.772
1.652
1.108
1.085
8
7
6
5
4
3
2
1
-0
ppm
1.86
1.94
0.97
0.97
0.18
1.94
0.95
1.00
0.99
1.01
0.96
3.03
0.97
0.54
2.67
0.10

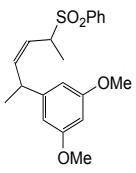

159.843
146.221
143.367
138.882
133.638
129.509
129.046
128.417
119.074
114.407
112.919
111.417
55.341
55.151
37.529
21.576
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe
OMe

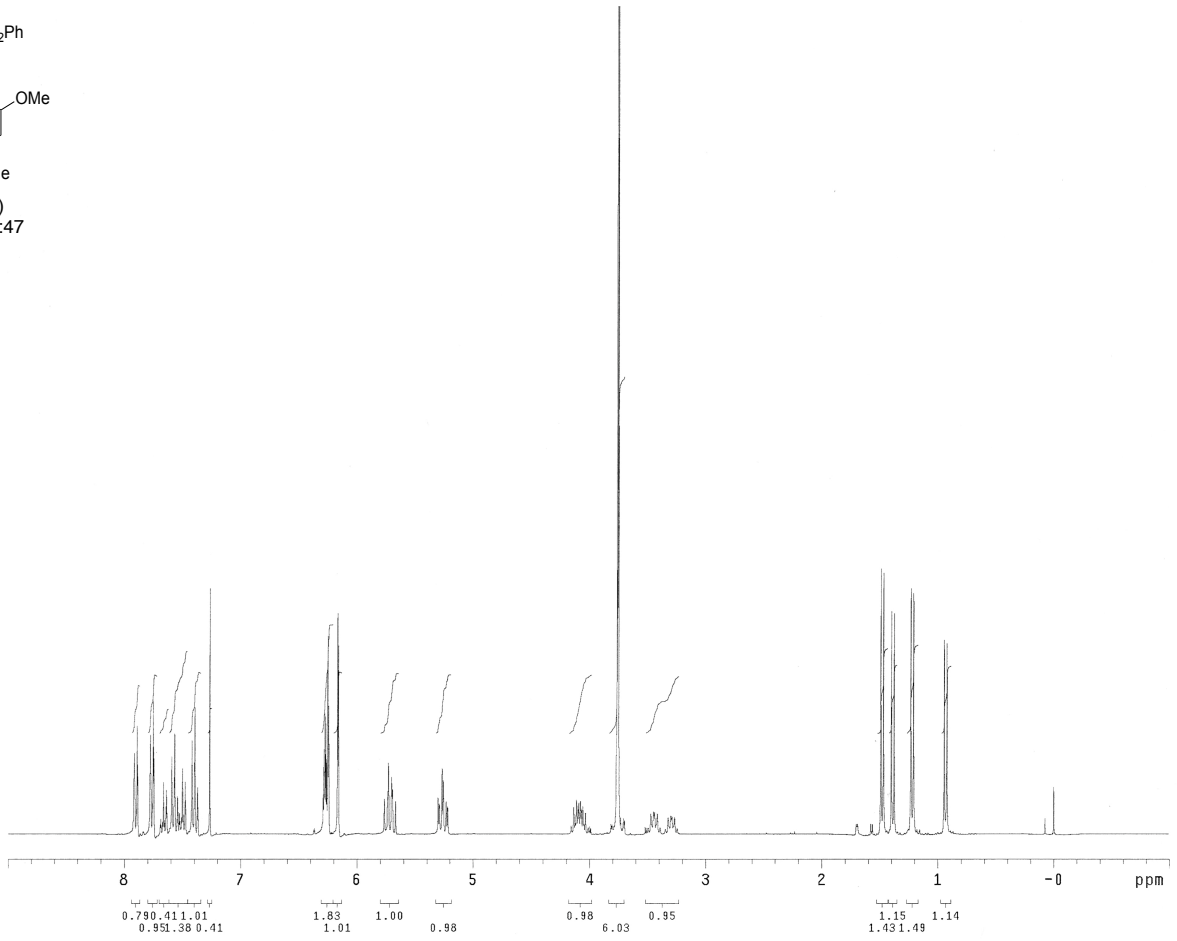
(**31**)

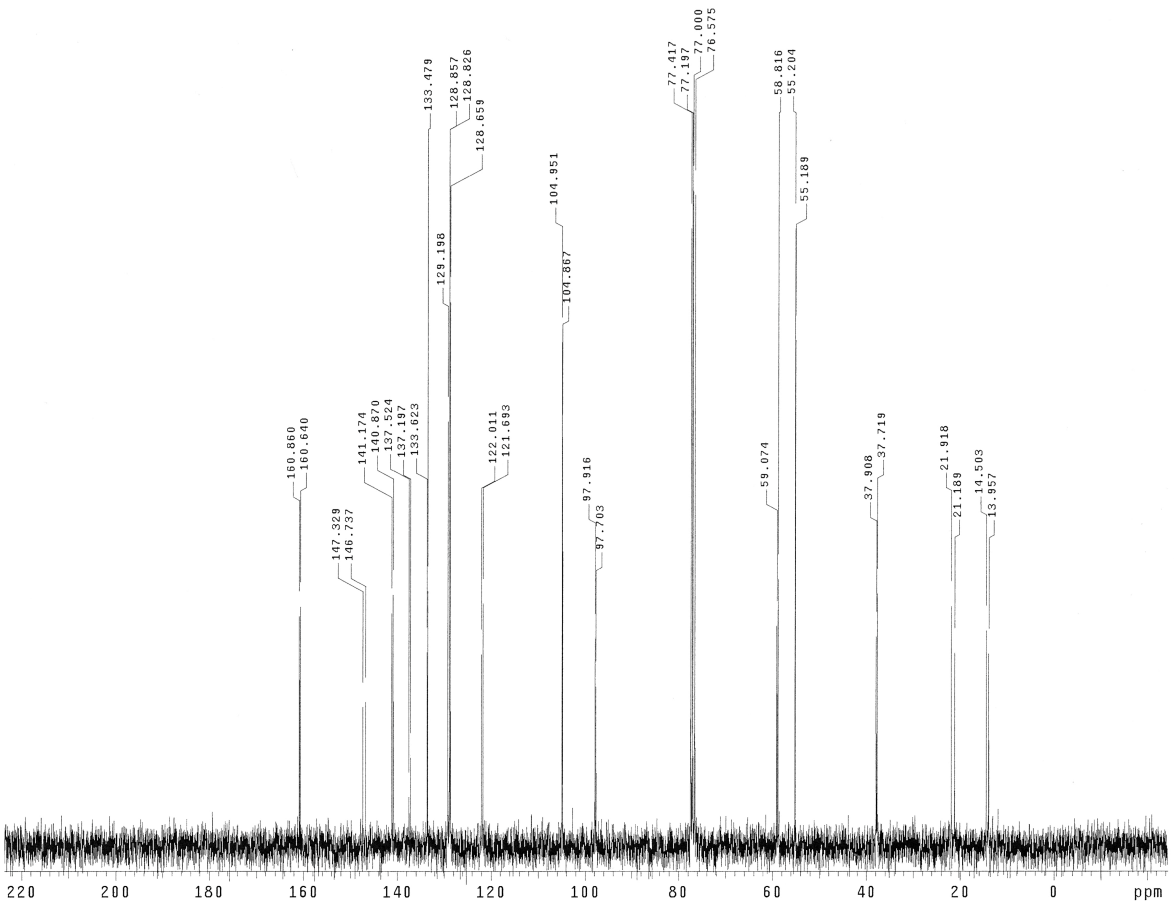

7.865
7.517
7.260
6.234
6.226
3.756
1.101
1.078
8
7
6
5
4
3
2
1
-0
ppm
1.95
1.93
1.10
0.56
3.05
1.00
1.01
6.09
2.40
0.97
2.64
0.12

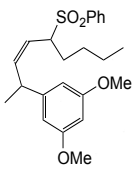

160.769
146.926
143.193
138.495
133.653
128.971
128.288
114.263
104.898
97.825
77.425
77.000
76.575
55.158
37.582
21.455
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe
OMe

(**32**)
ds 53:47

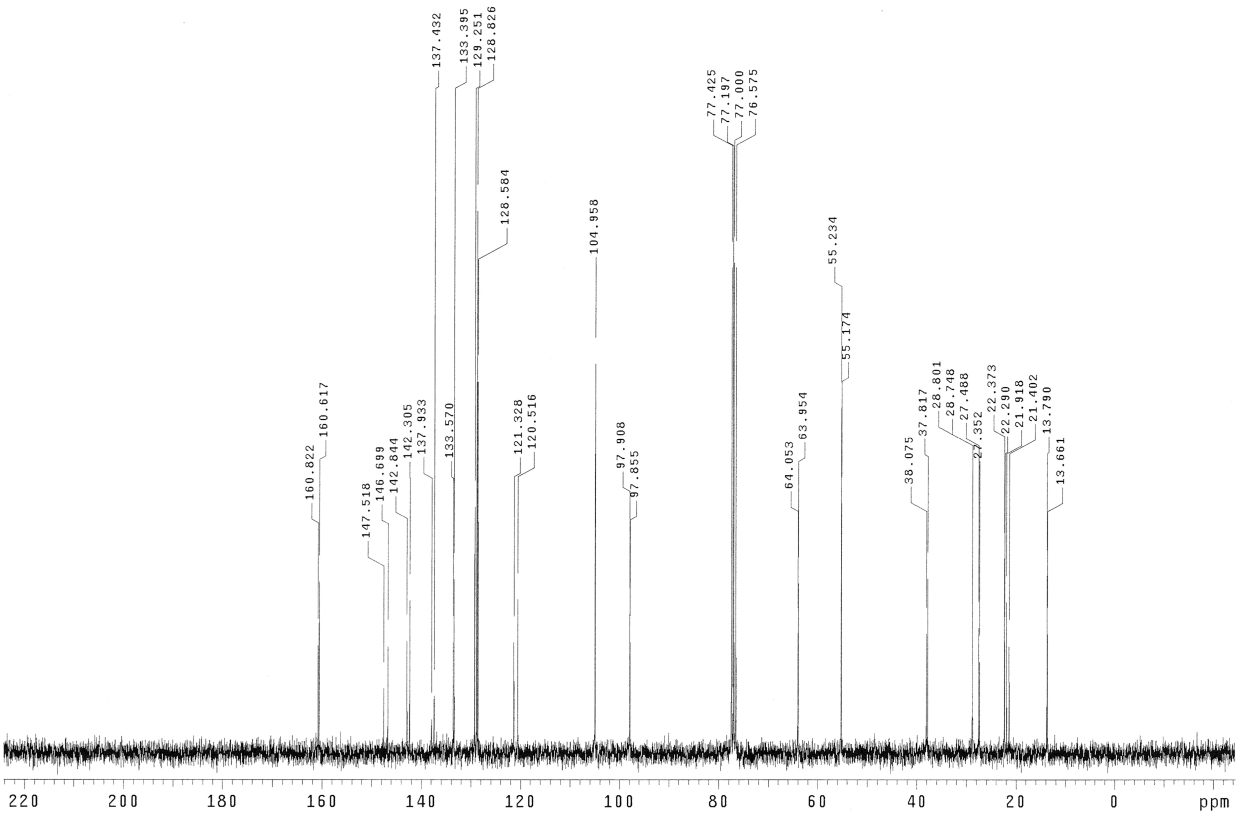

8
7
6
5
4
3
2
1
-0
ppm
0.79 0.41 1.01
0.95 1.38 0.41
1.83
1.01
1.00
0.98
0.98
6.03
0.95
1.15
1.43
1.14
1.49

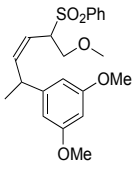

160.860
160.640
147.329
146.737
141.174
140.870
137.524
137.197
133.623
133.479
129.198
128.857
128.826
128.659
122.011
121.693
104.951
104.867
97.916
97.703
77.417
77.197
77.000
76.575
59.074
58.816
55.204
55.189
37.908
37.719
21.918
21.189
14.503
13.957
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe
OMe

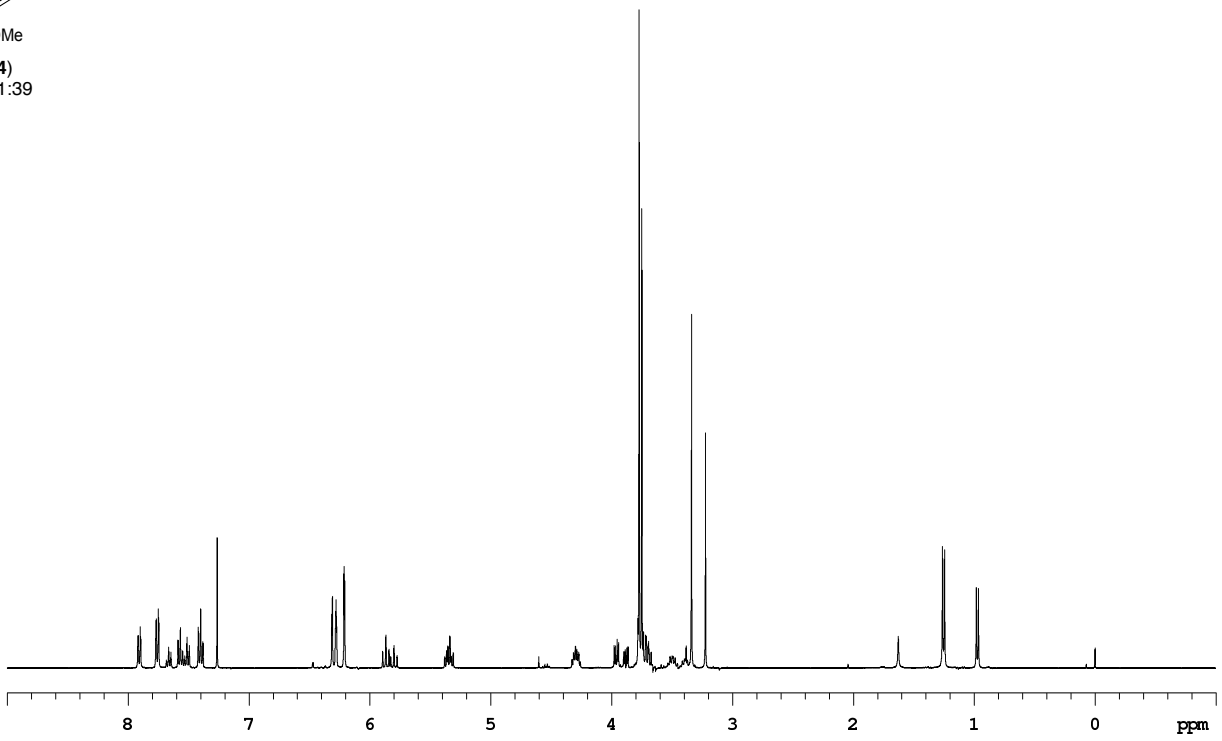
(**33**)
ds 61:39

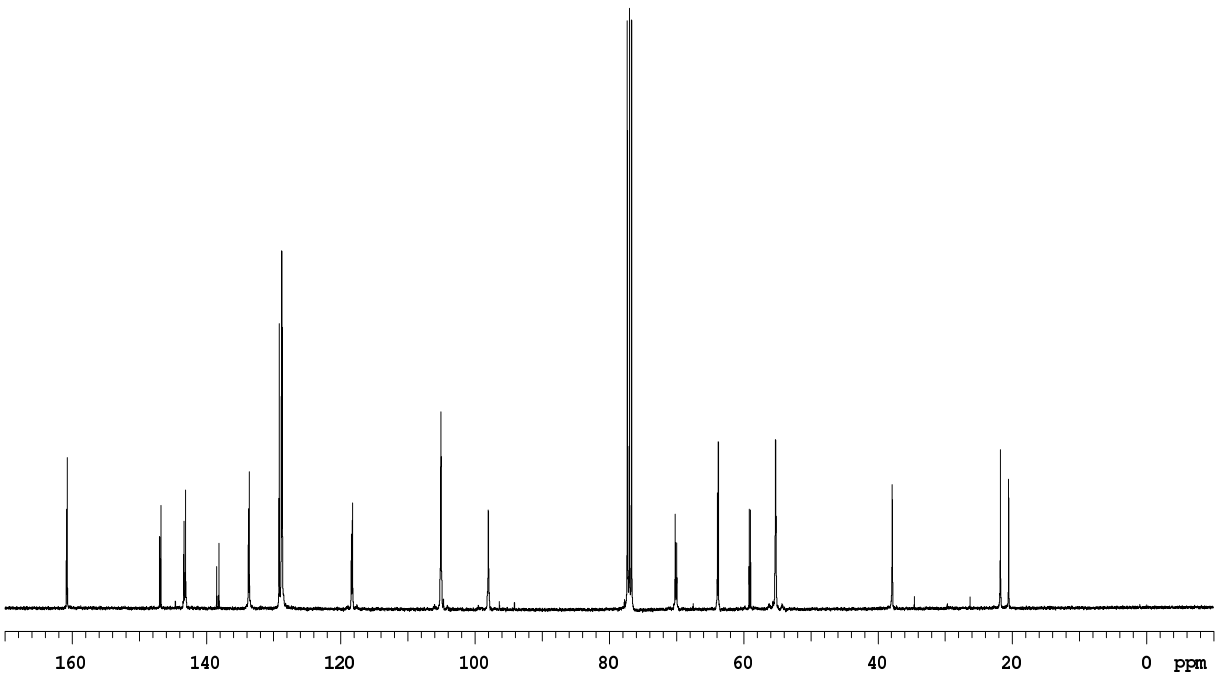
8
7
6
5
4
3
2
1
-0
ppm
0.83 1.24 0.31
1.21 1.79
1.13
1.86
1.00
0.99
6.09
1.08
0.37
0.55
0.98
1.21 3.33 1.05
1.85 3.13
0.13

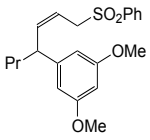

160.822
160.617
147.518
146.698
142.844
142.305
137.933
137.432
133.570
133.395
129.251
128.826
128.584
121.328
120.516
104.958
97.908
97.855
77.425
77.197
77.000
76.575
64.053
63.954
55.234
55.174
38.075
37.817
28.801
28.748
27.488
27.352
22.373
22.290
21.918
21.402
13.790
13.661
220
200
180
160
140
120
100
80
60
40
20
0
ppm



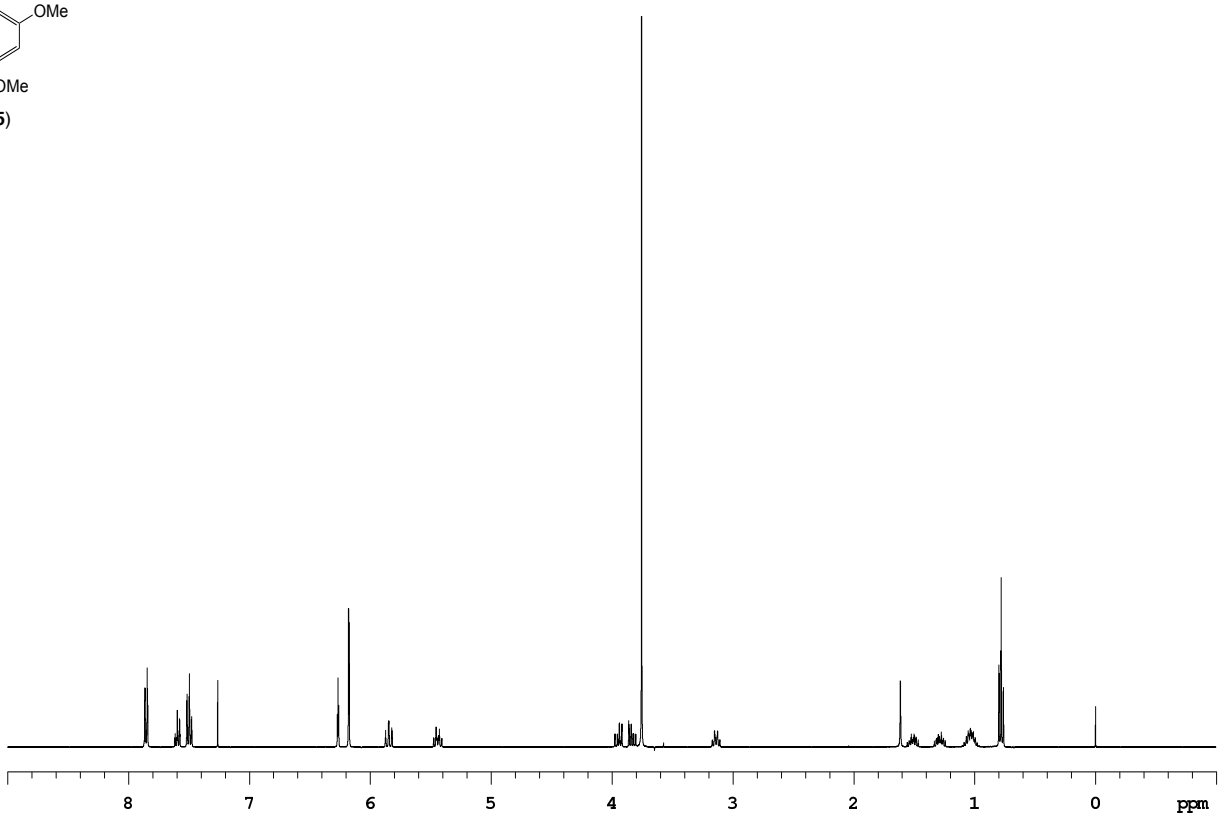
(**34**)
ds 61:39

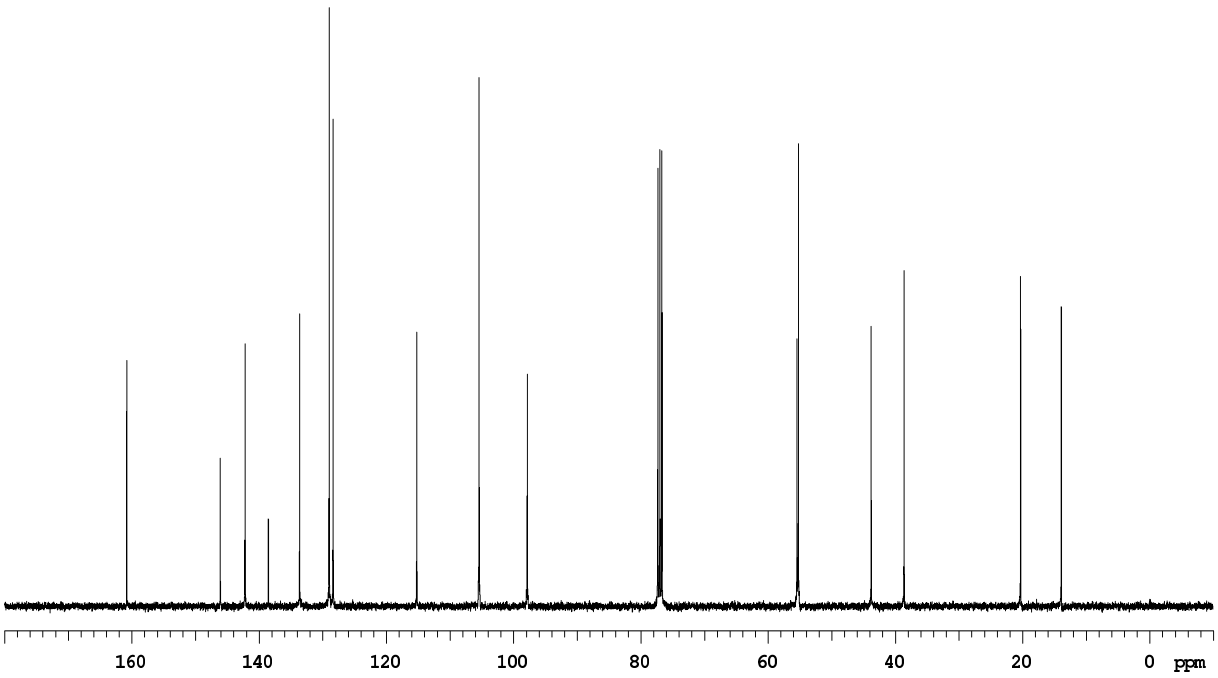


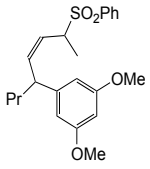




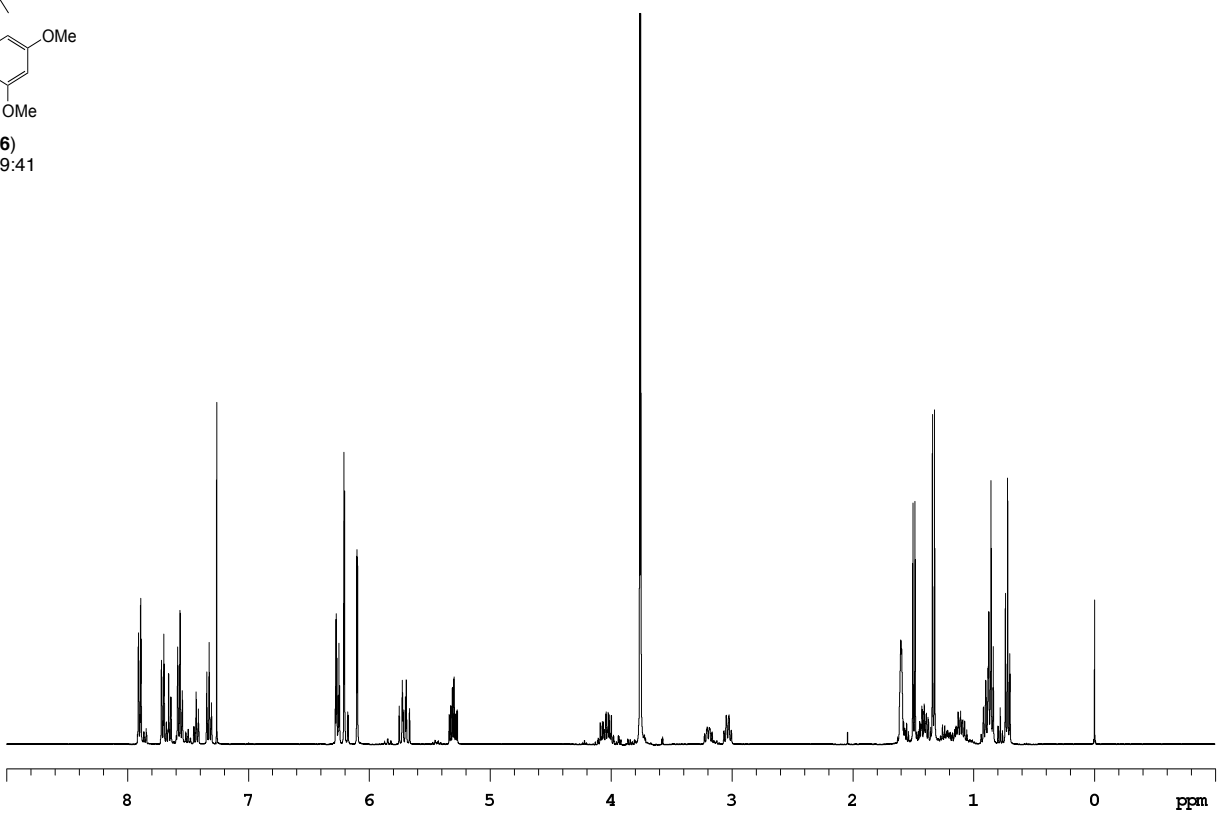
(**35**)

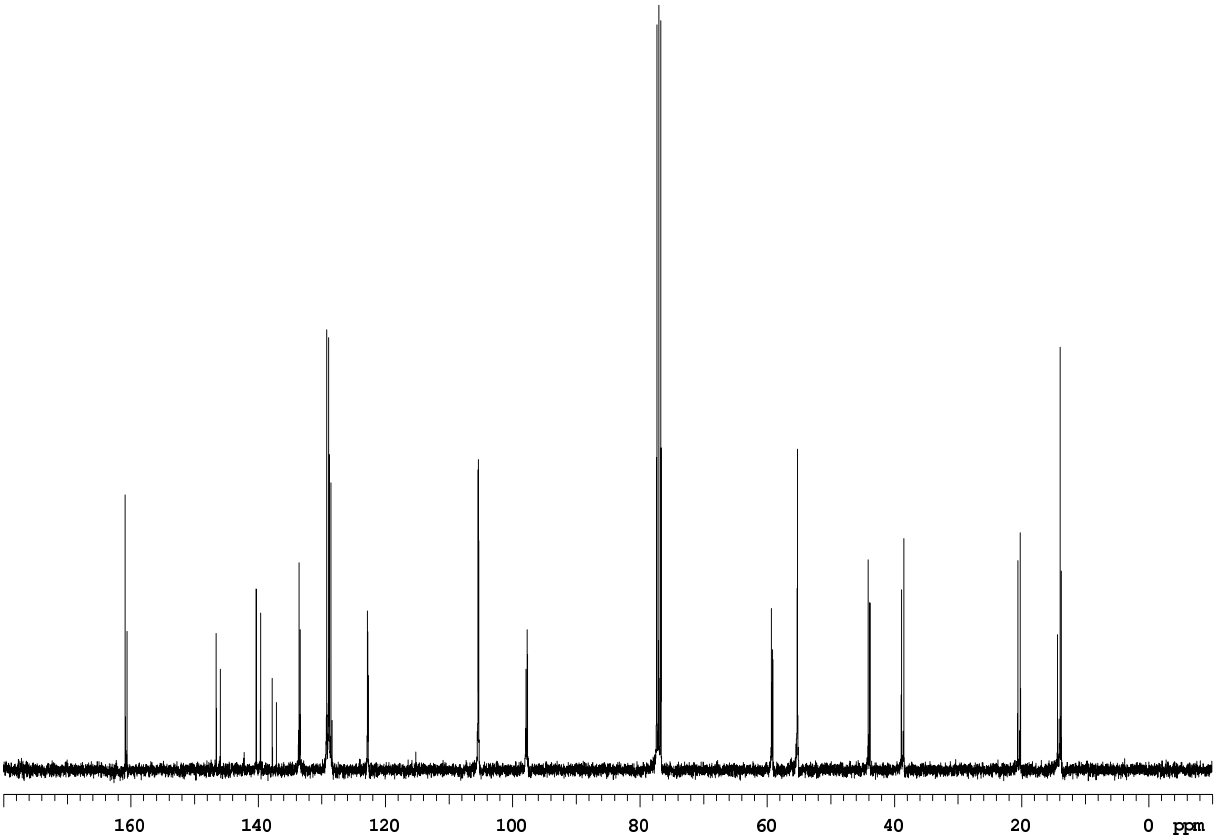


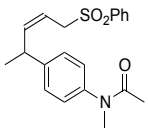




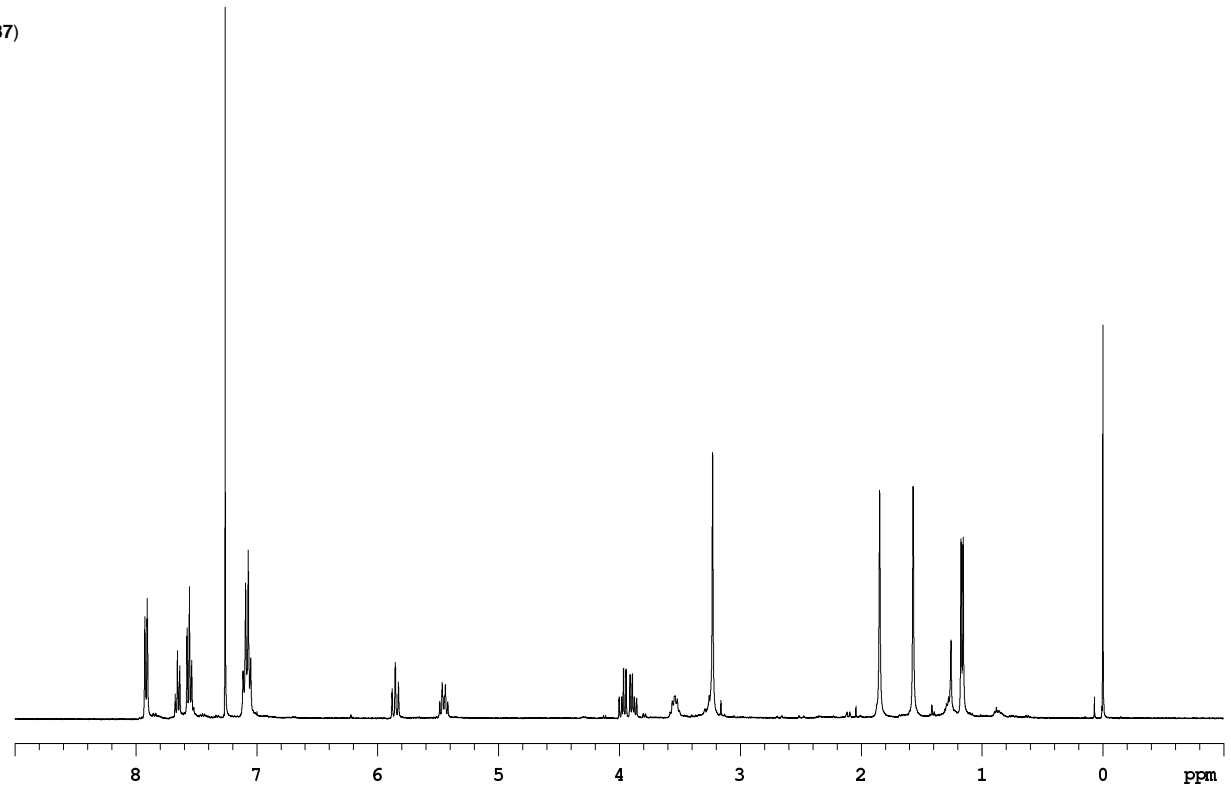
(**36**)
ds 59:41

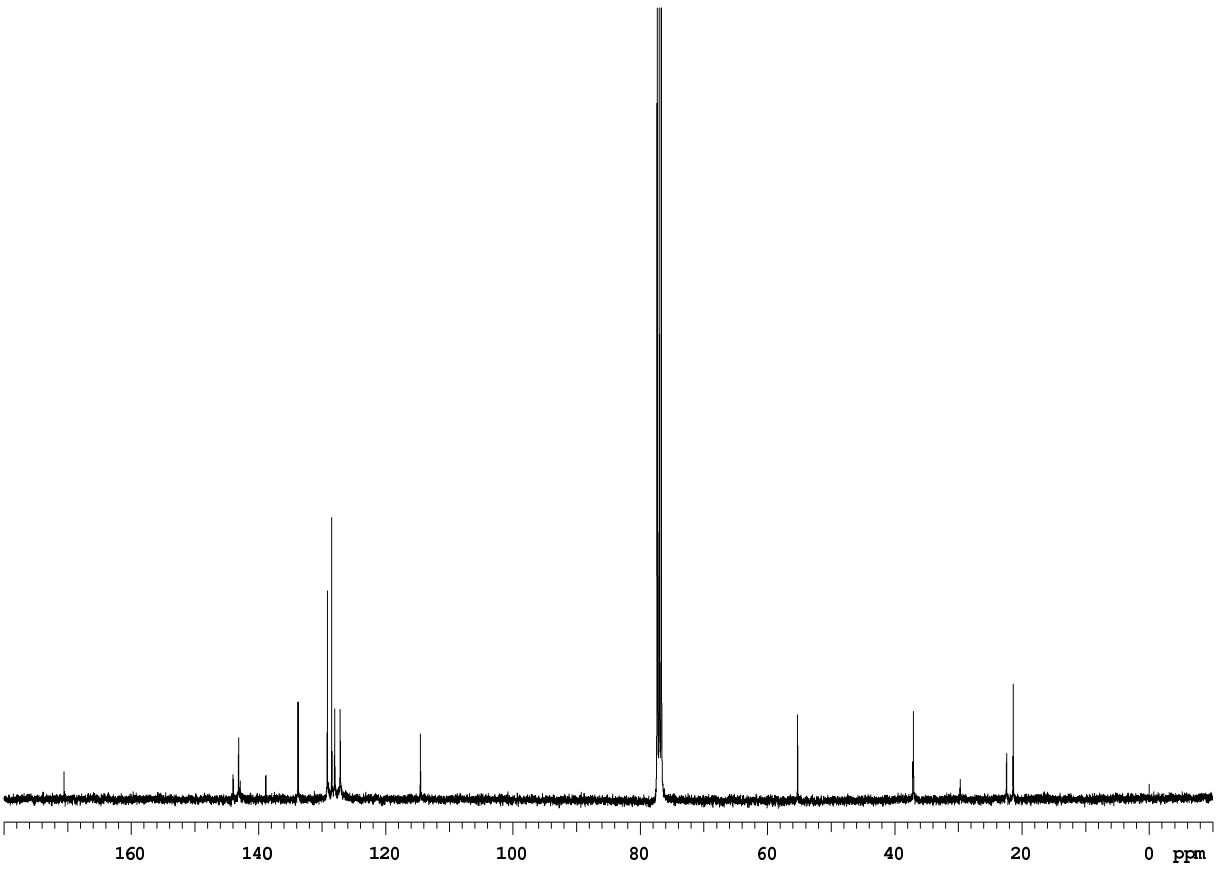


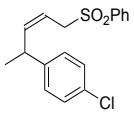




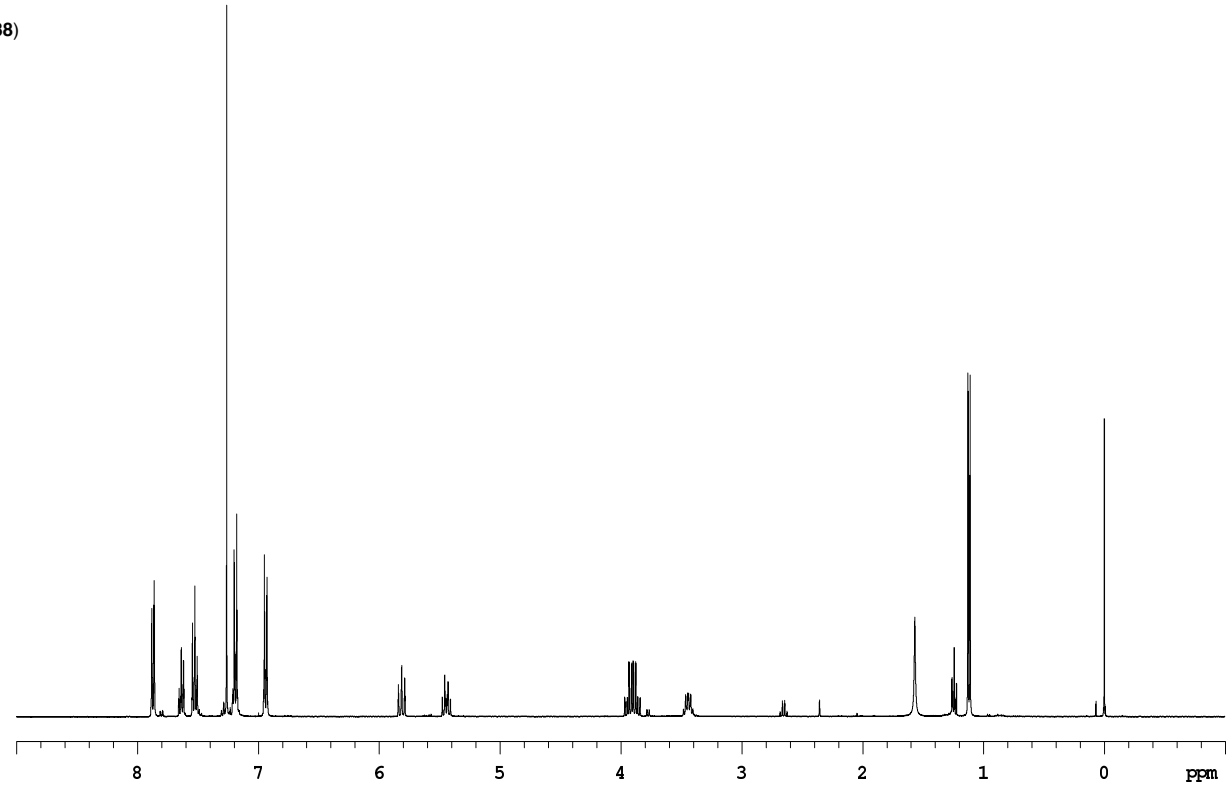
(**37**)

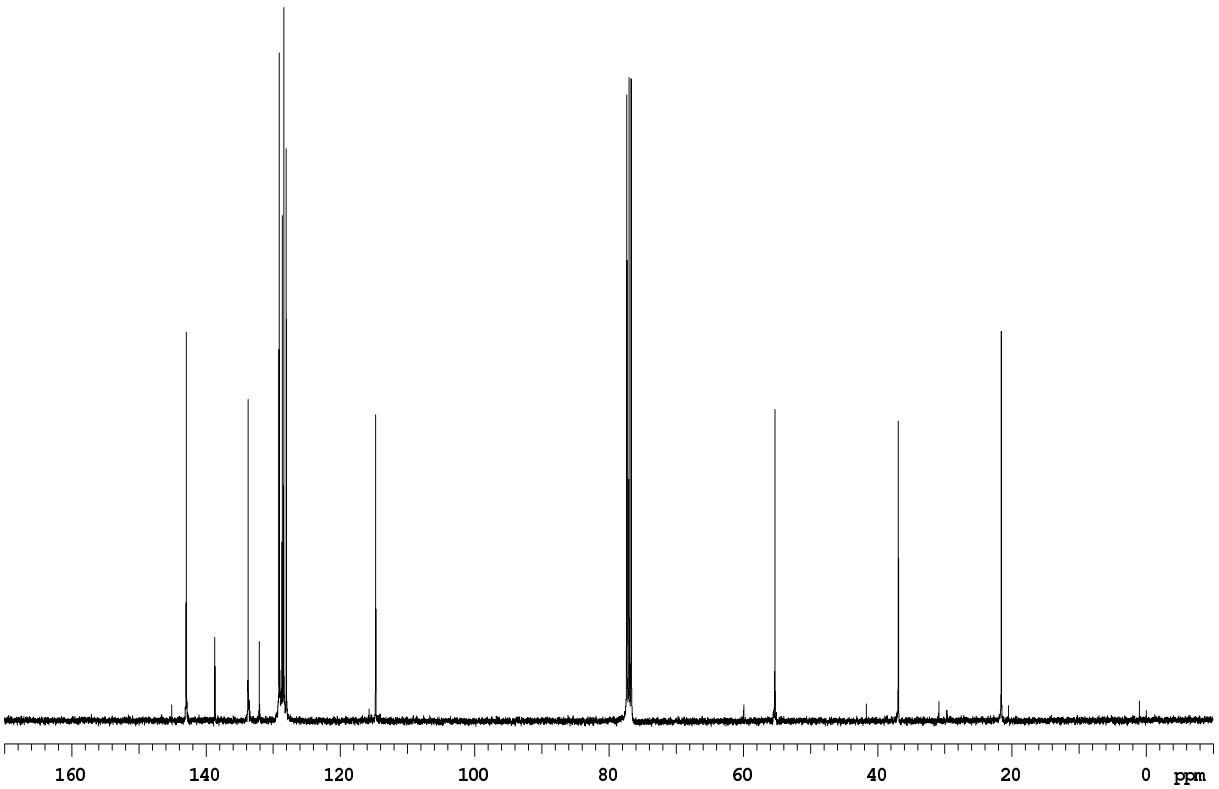


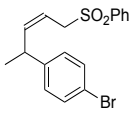




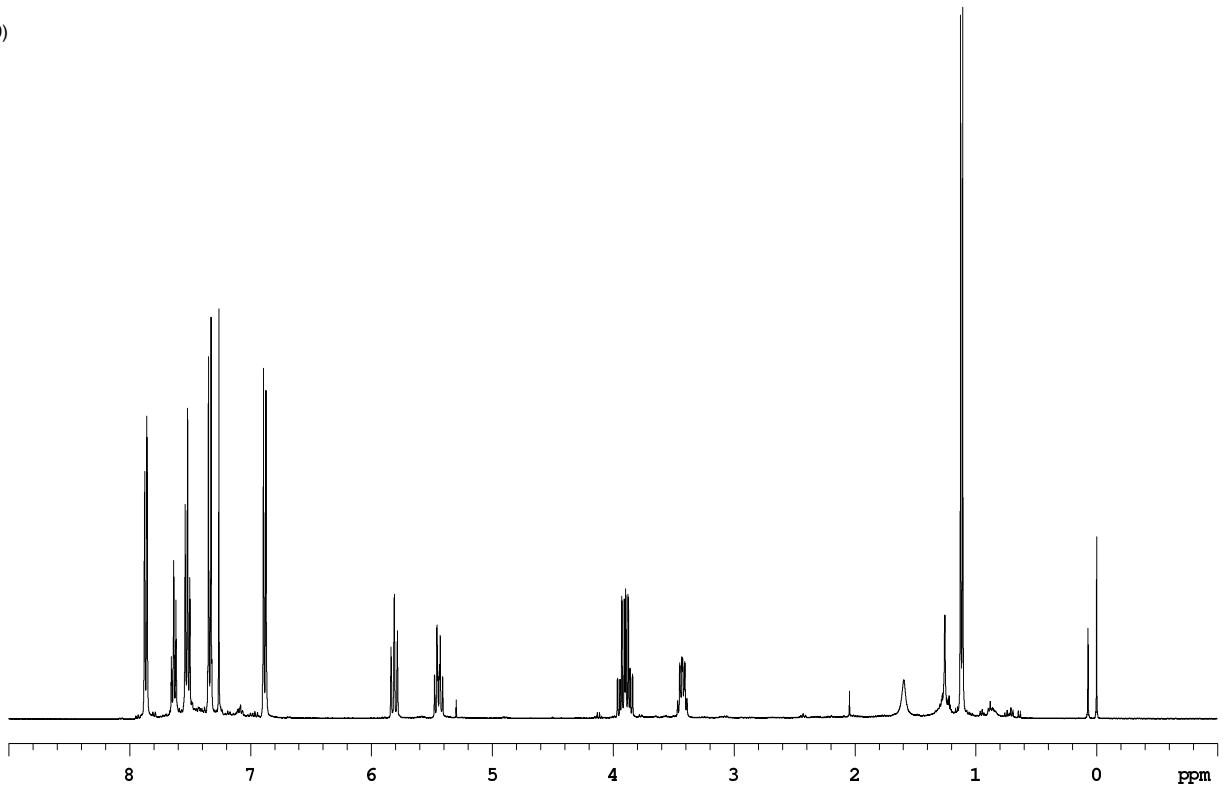
(**38**)

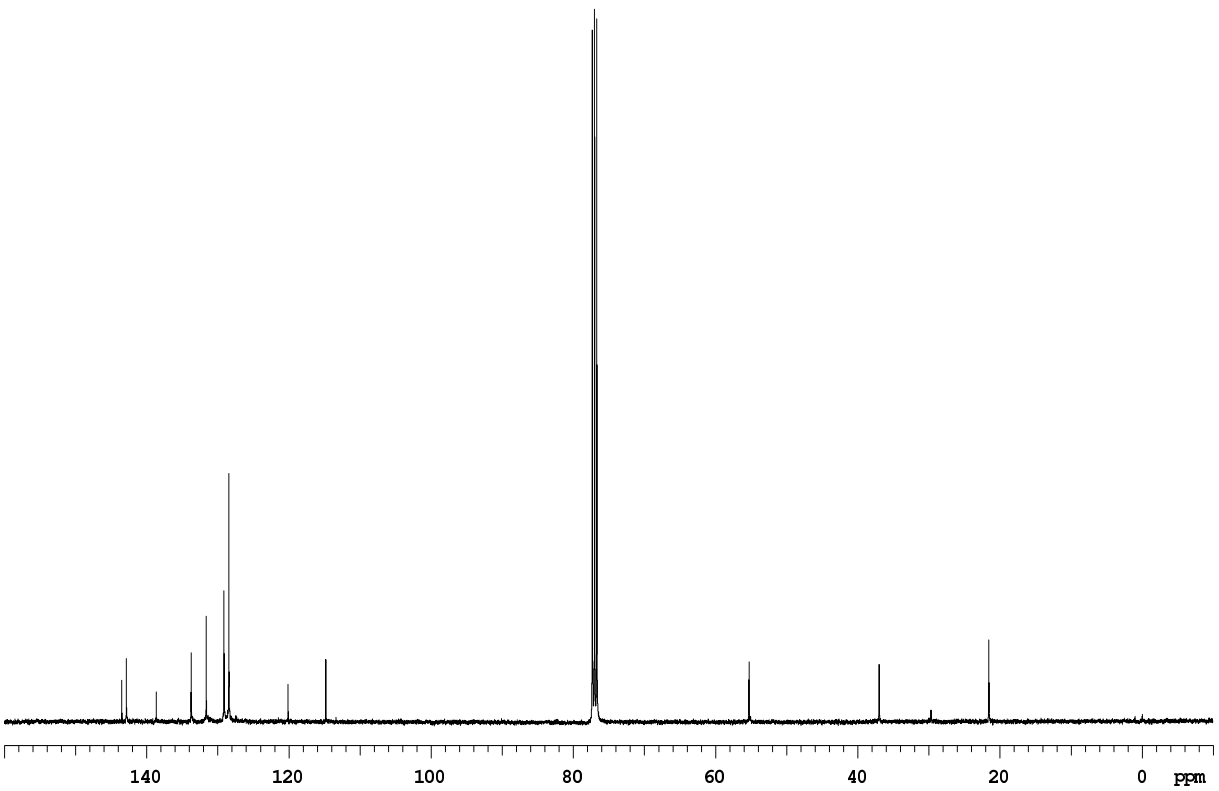


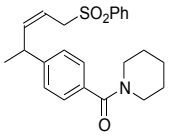




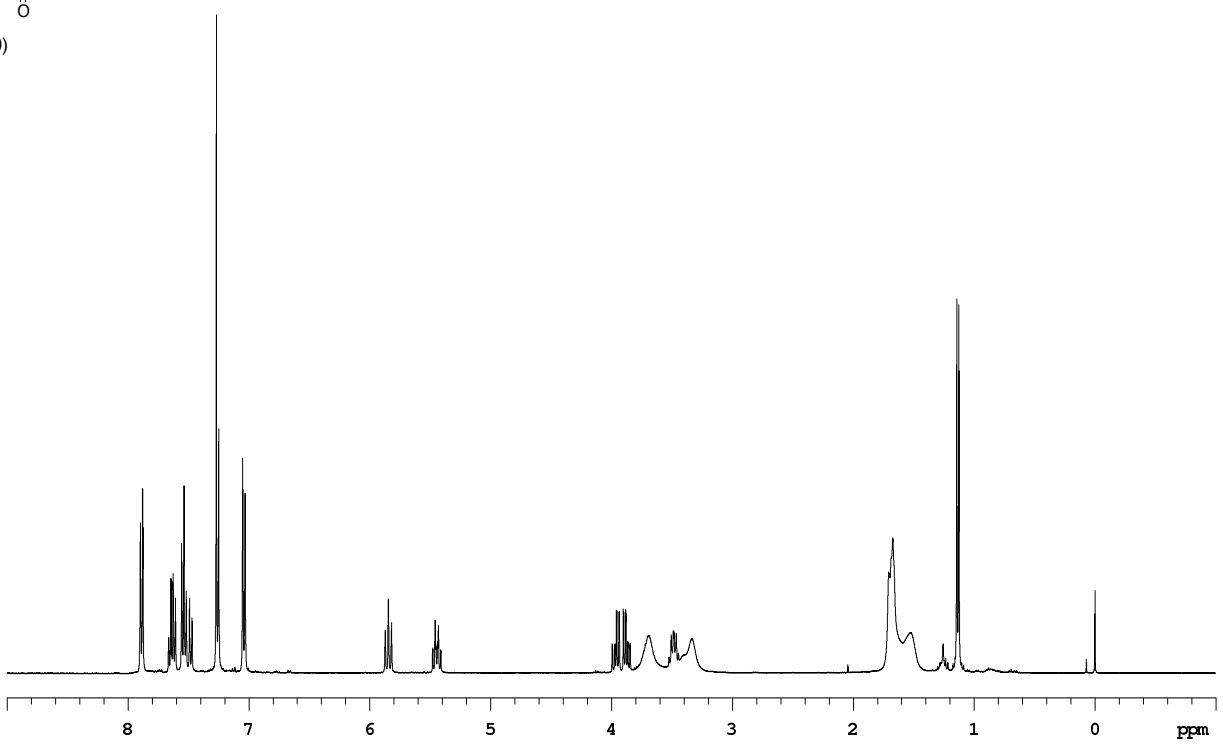
(**39**)

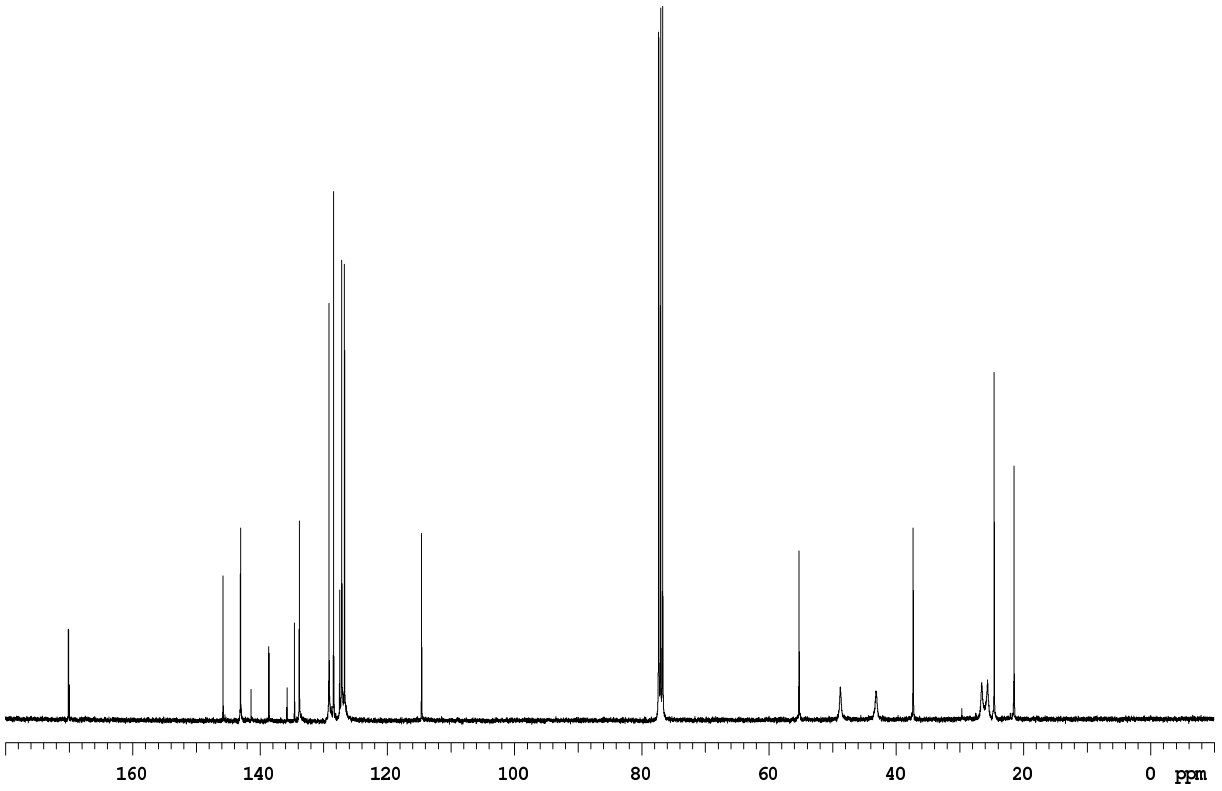


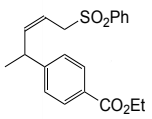




(**40**)

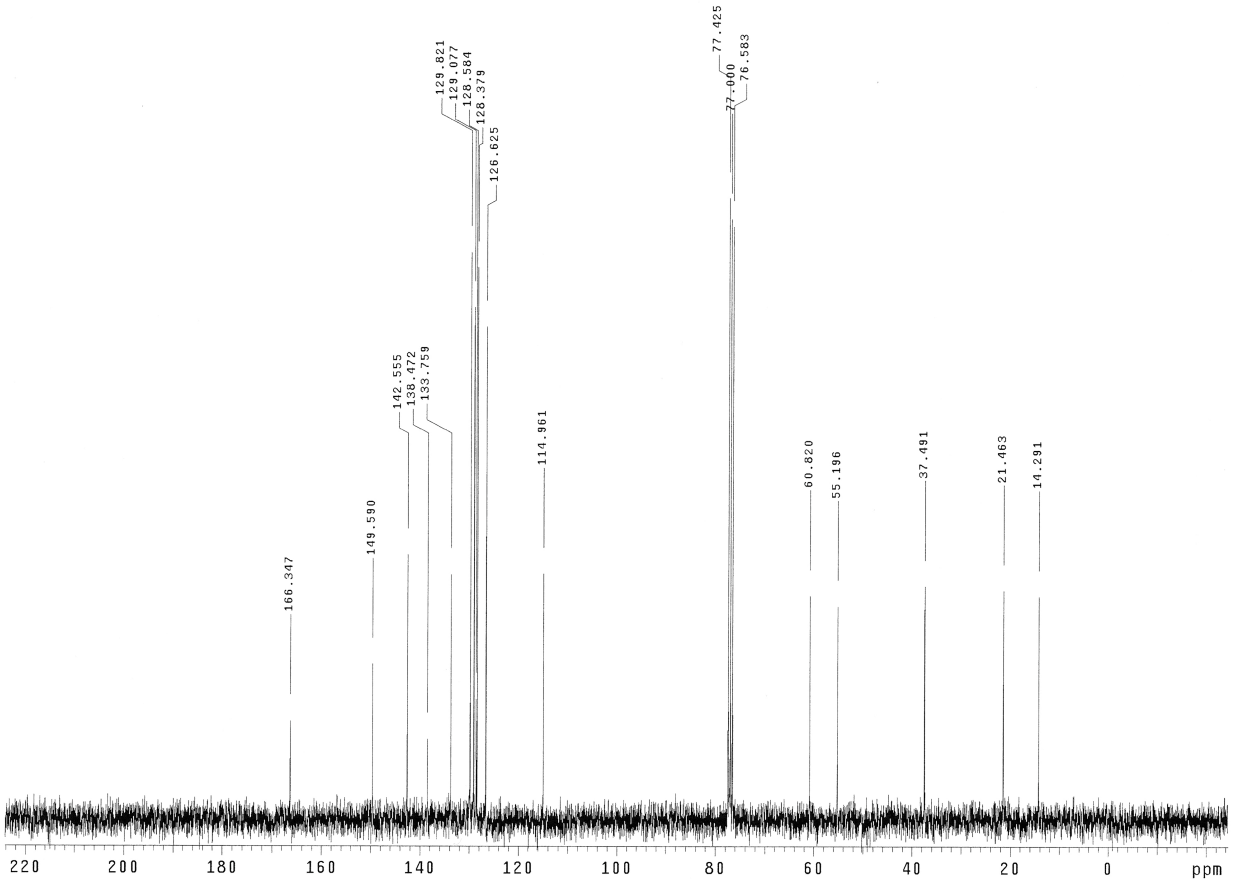


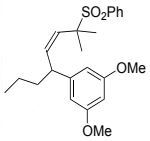



SO2Ph
CO2Et

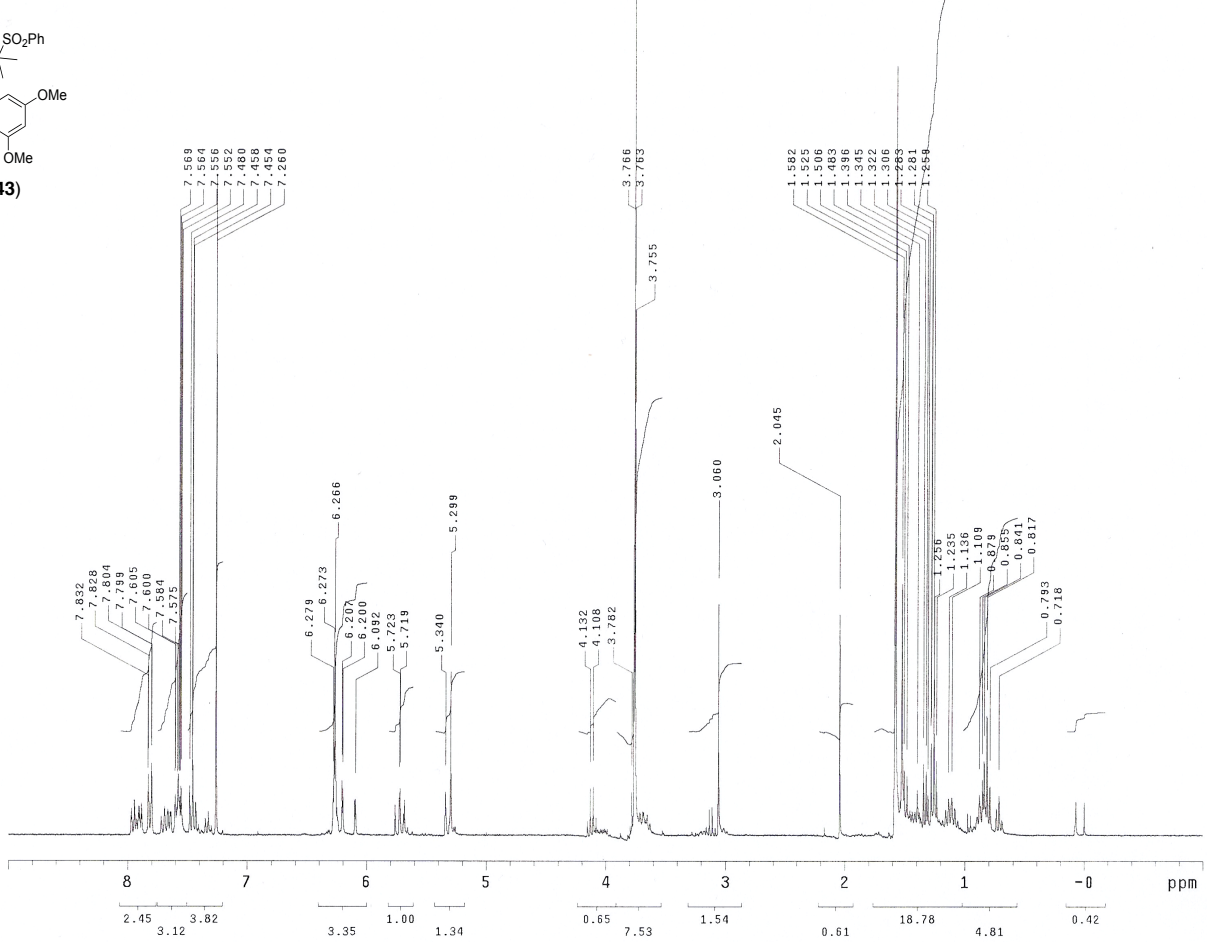
(**41**)

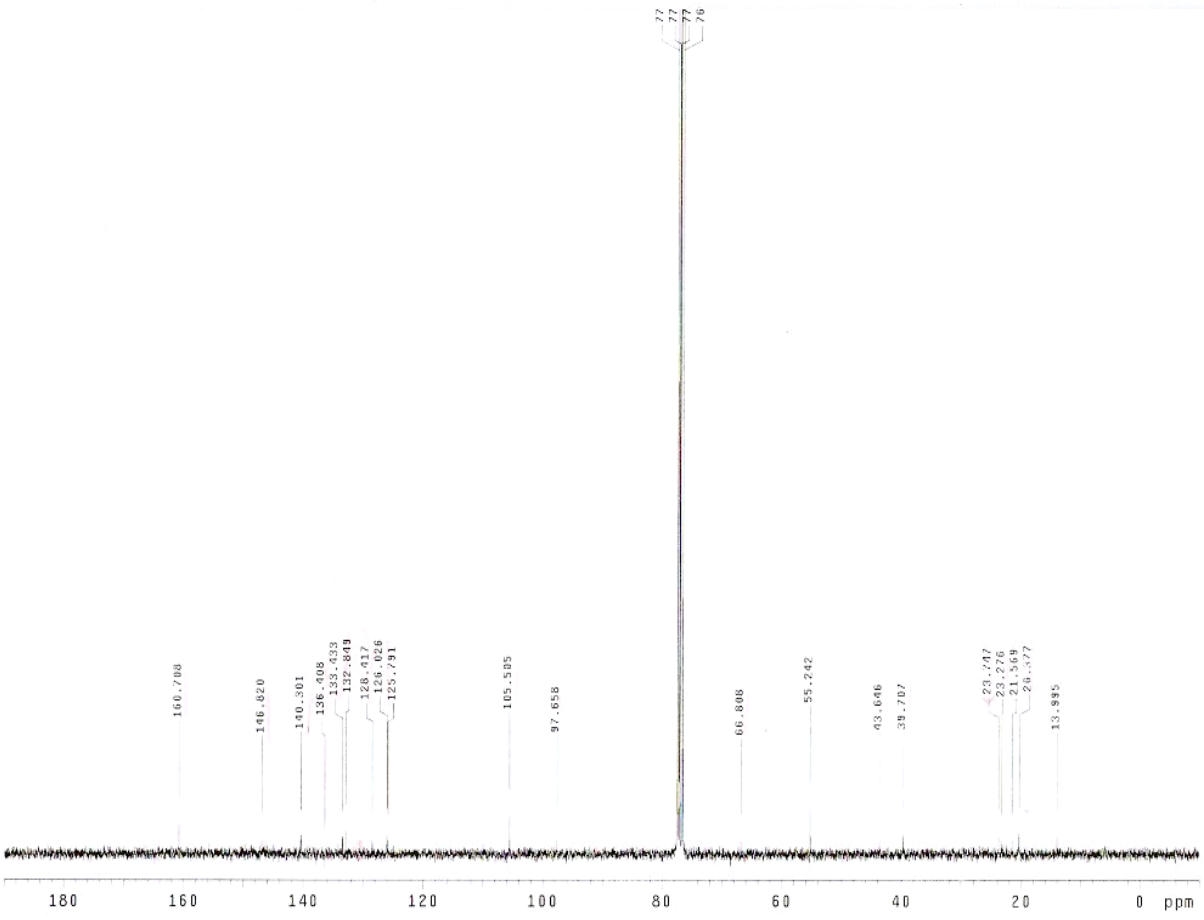
8
7
6
5
4
3
2
1
-0
ppm
3.90
2.97
0.26
1.97
1.00
1.00
2.07
1.97
0.97
0.22
2.91
2.74
0.09

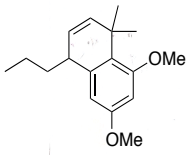

166.347
149.590
142.555
138.472
133.759
129.821
129.077
128.584
128.379
126.625
114.961
77.425
77.000
76.583
60.820
55.196
37.491
21.463
14.291
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe
OMe

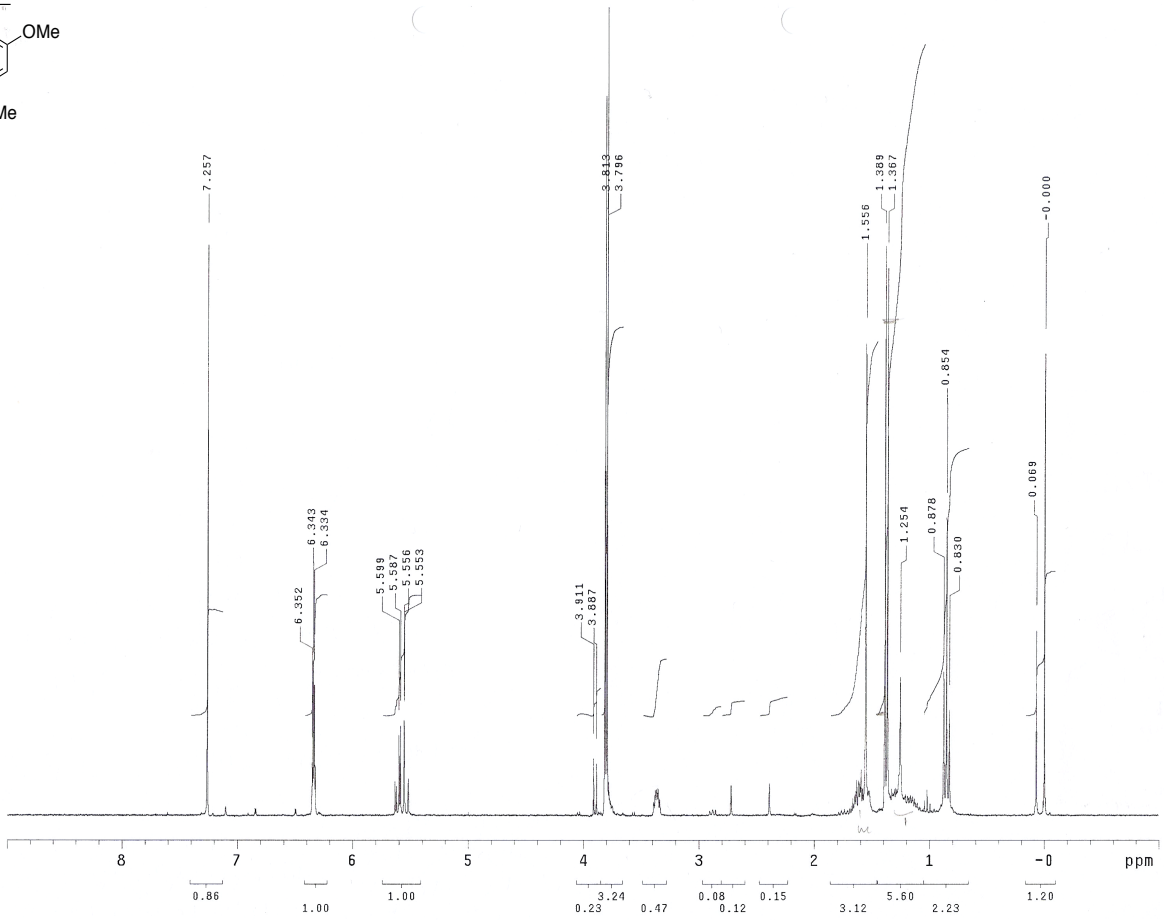
(**43**)

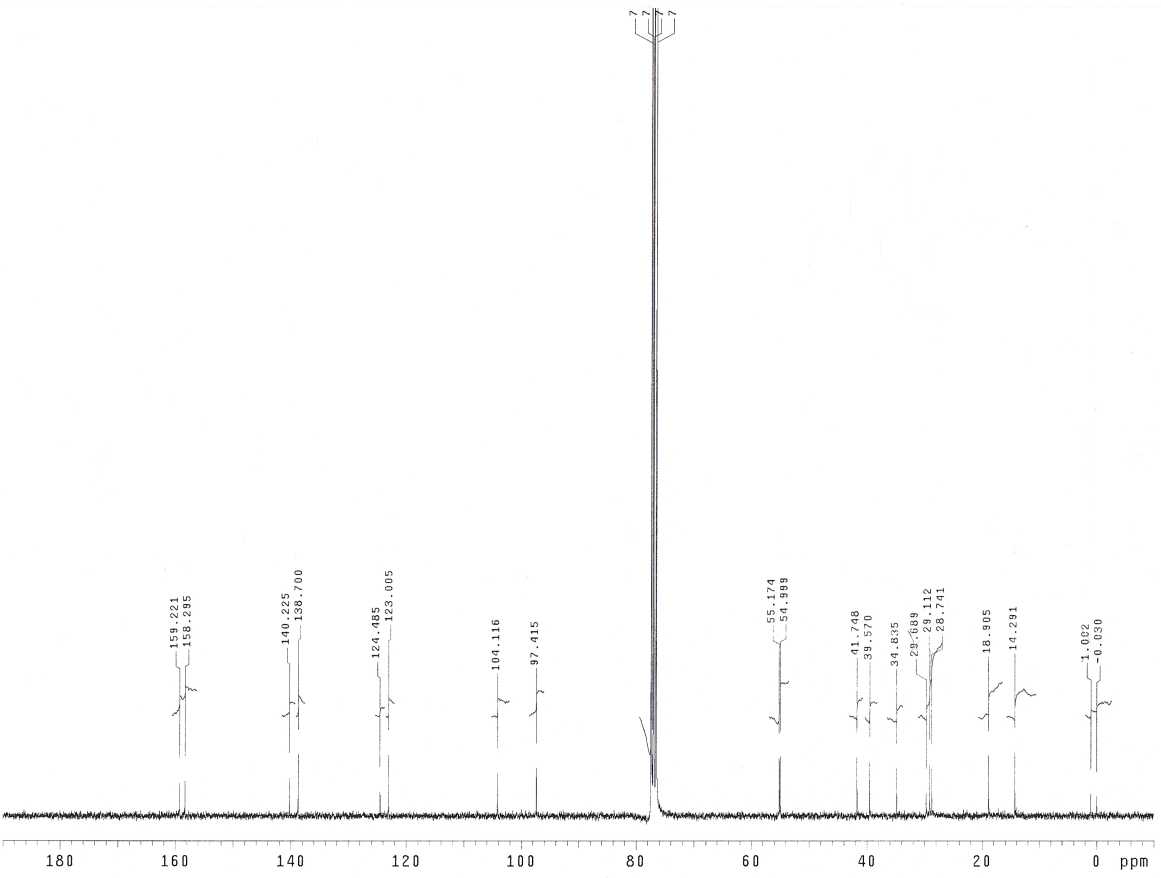

7.832
7.828
7.804
7.799
7.605
7.600
7.584
7.575
7.569
7.564
7.556
7.552
7.480
7.458
7.454
7.260
6.279
6.273
6.266
6.207
6.200
6.092
5.723
5.719
5.340
5.299
4.132
4.108
3.782
3.766
3.763
3.755
3.060
2.045
1.582
1.525
1.506
1.483
1.396
1.345
1.322
1.306
1.283
1.281
1.259
1.256
1.235
1.135
1.110
0.879
0.855
0.841
0.817
0.793
0.718
8
7
6
5
4
3
2
1
-0
ppm
2.45
3.82
3.12
3.35
1.00
1.34
0.65
7.53
1.54
0.61
18.78
4.81
0.42

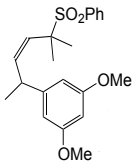

77
77
77
76
160.708
146.820
140.301
136.408
133.433
132.849
128.417
126.026
125.791
105.585
97.658
66.808
55.242
43.646
39.707
23.747
23.276
21.569
20.377
13.995
180
160
140
120
100
80
60
40
20
0
ppm


OMe
OMe

(**44**)

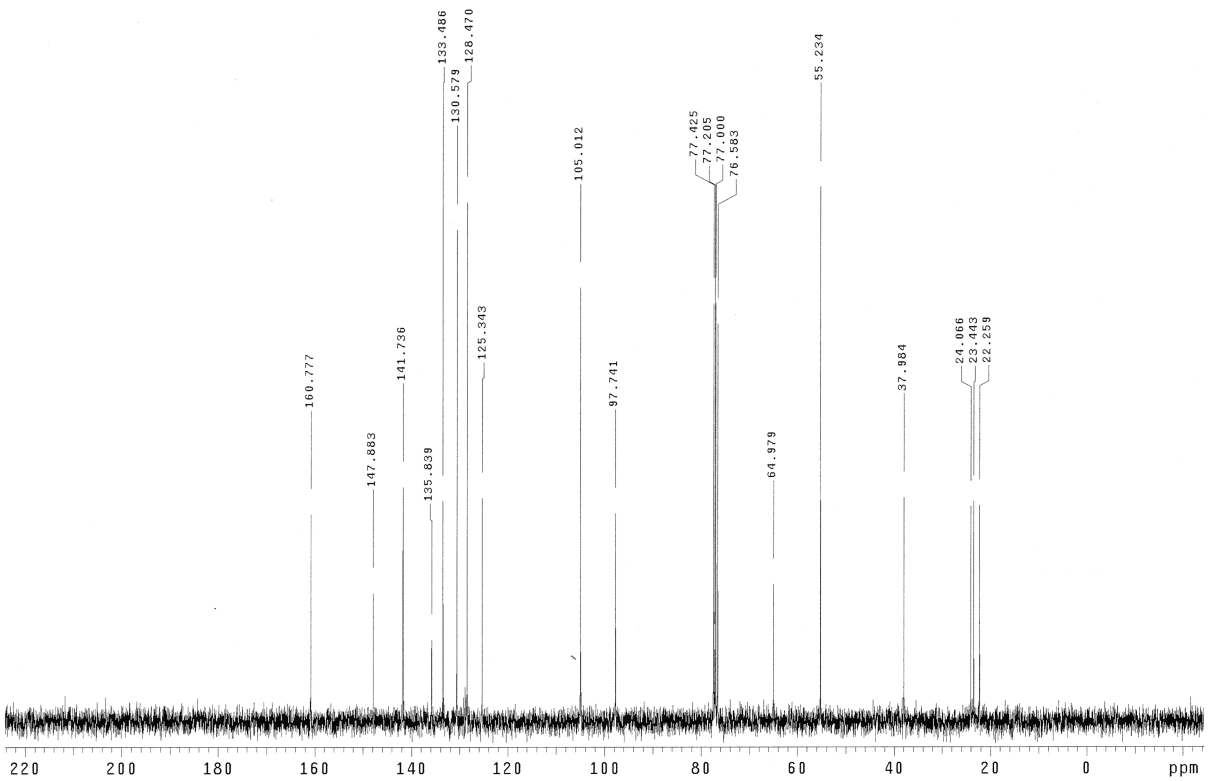

7.257
6.352
6.343
6.334
5.598
5.587
5.556
5.553
3.911
3.887
3.813
3.796
1.556
1.389
1.367
1.254
0.878
0.854
0.830
0.069
-0.000
8
7
6
5
4
3
2
1
-0
ppm
0.86
1.00
1.00
3.24
0.23
0.47
0.08
0.12
0.15
3.12
5.60
2.23
1.20

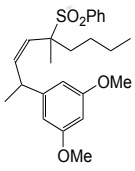

159.221
158.295
140.225
138.700
124.485
123.005
104.116
97.415
77.423
77.000
76.577
55.174
54.939
41.748
39.570
34.835
29.689
29.112
28.741
18.905
14.291
1.002
-0.030
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe
OMe

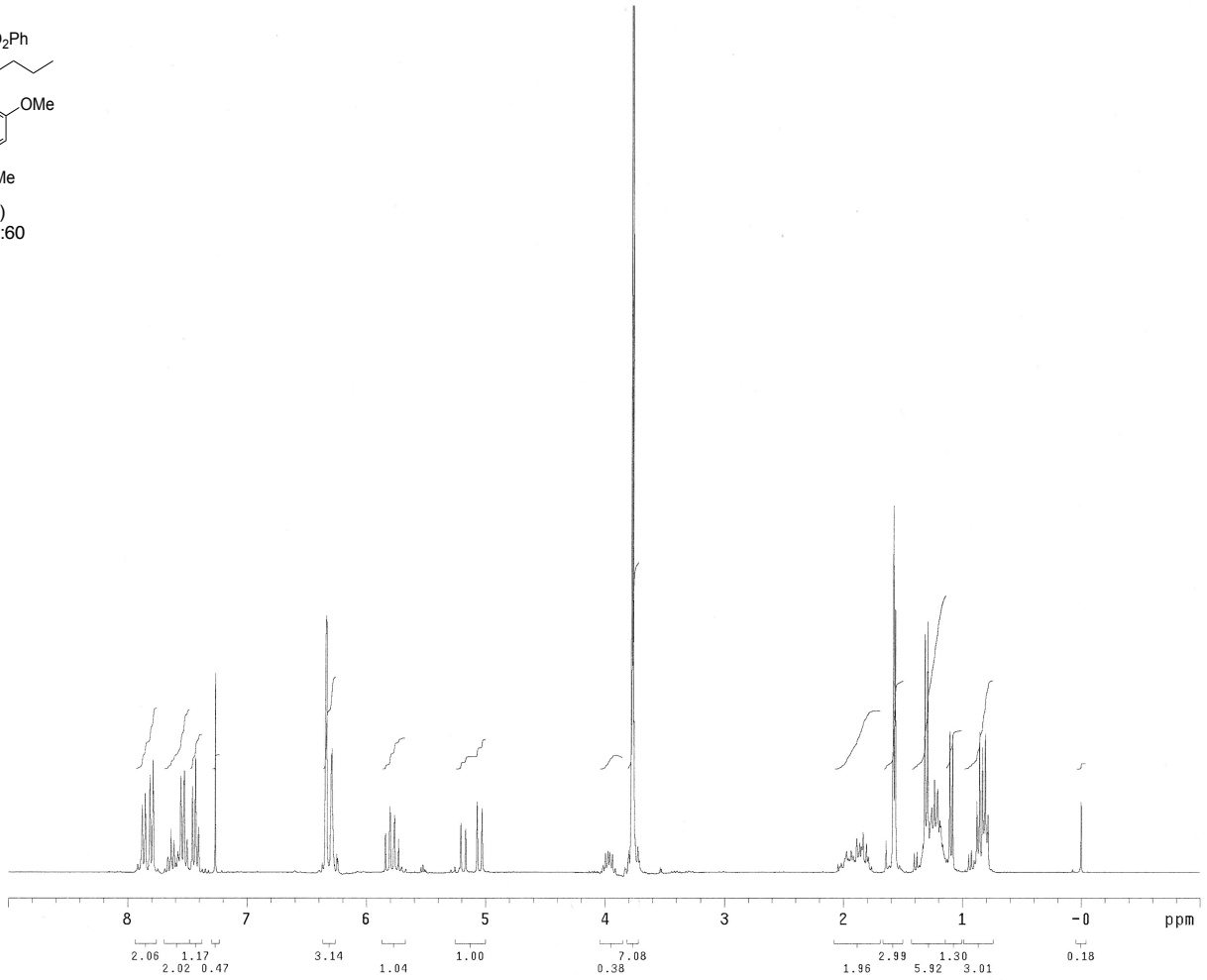
(**45**)

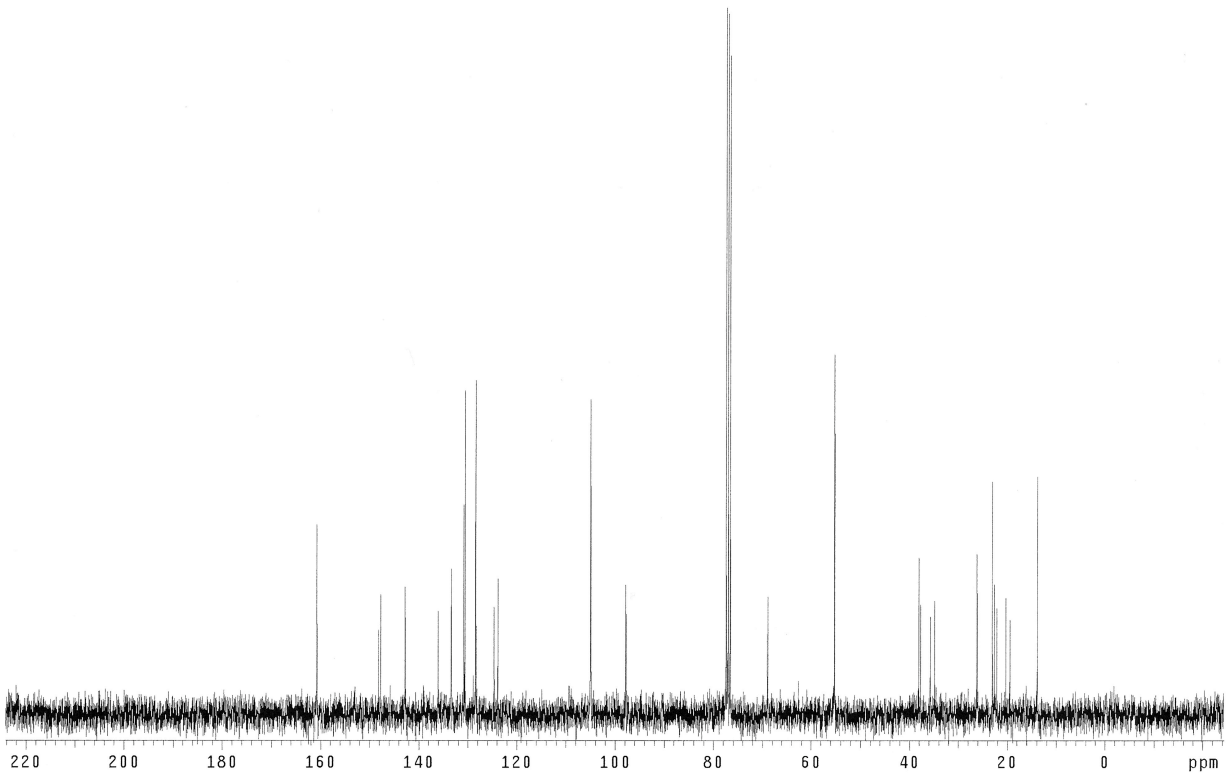
7.261
6.362
6.370
3.772
1.580
1.567
1.234
1.212
8
7
6
5
4
3
2
1
-0
ppm
1.77
1.83
0.96
0.79
1.78
0.98
1.00
0.95
0.88
6.02
5.06
2.50
0.14

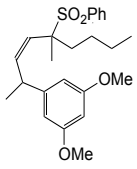

160.777
147.883
141.736
135.839
133.486
130.579
128.470
125.343
105.012
97.741
77.425
77.205
77.000
76.583
64.979
55.234
37.984
24.066
23.443
22.259
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe
OMe

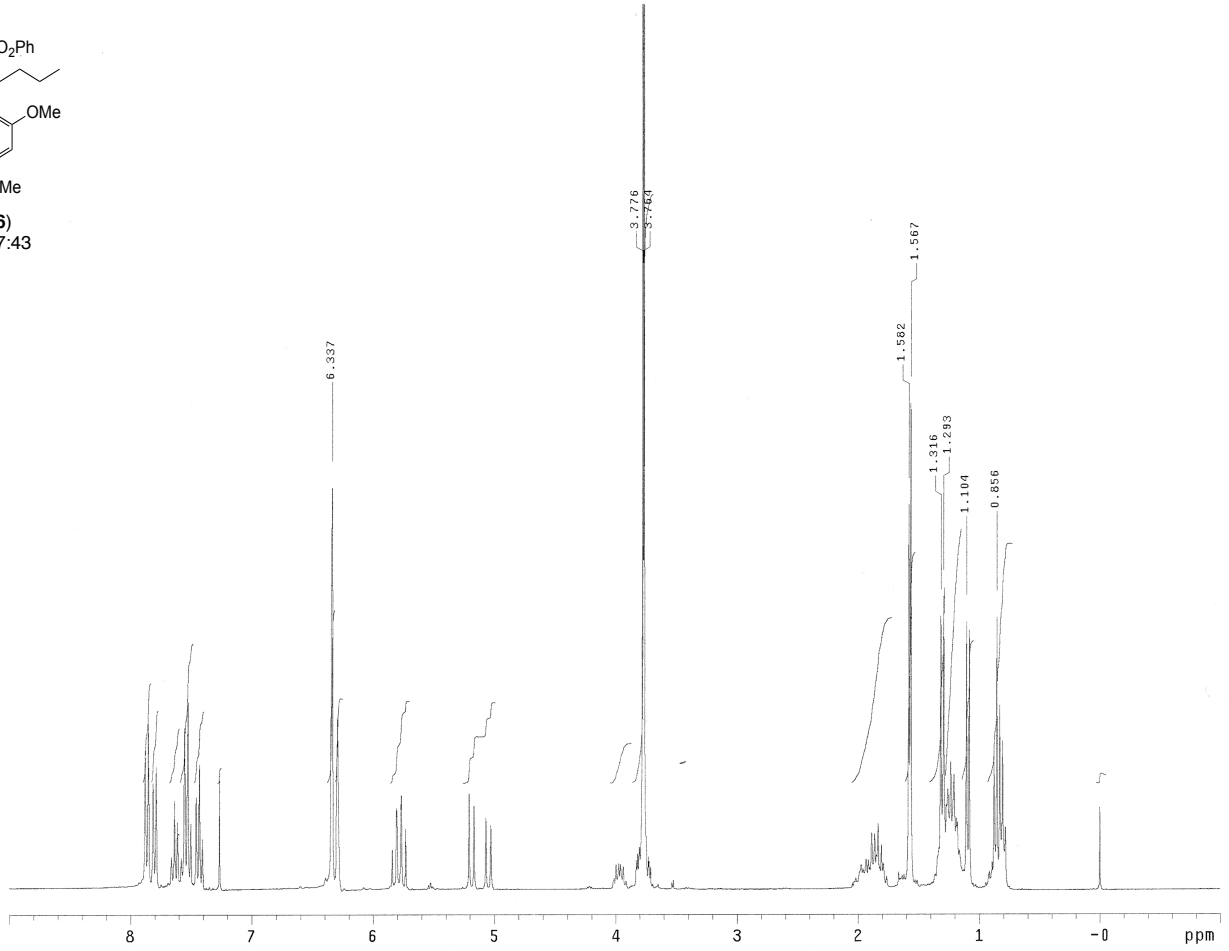
(**46**)
ds 40:60

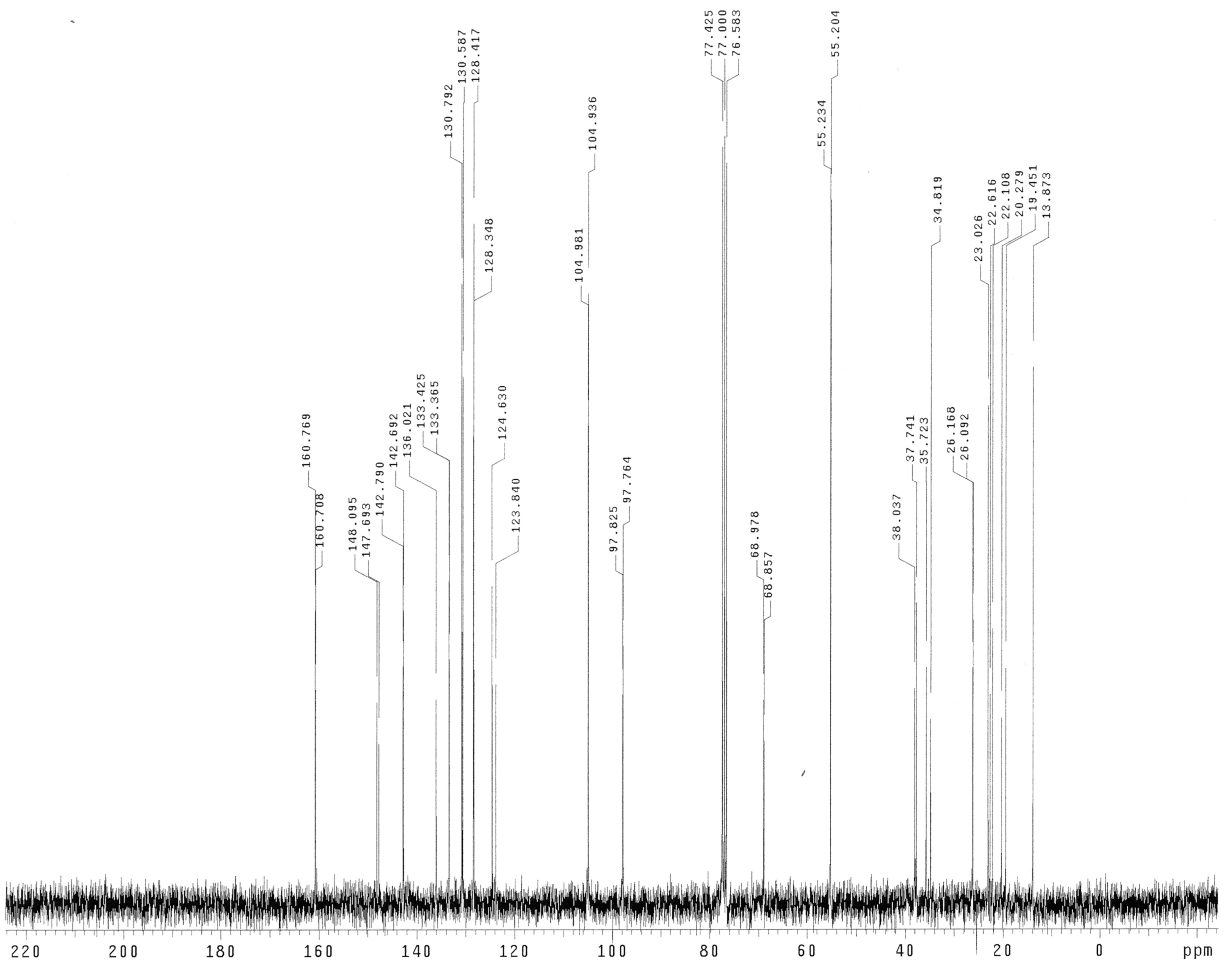

8
7
6
5
4
3
2
1
-0
ppm
2.06
1.17
2.02
0.47
3.14
1.04
1.00
7.08
0.38
2.99
1.96
1.30
5.92
3.01
0.18

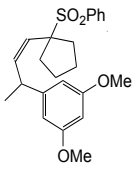

220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe
OMe

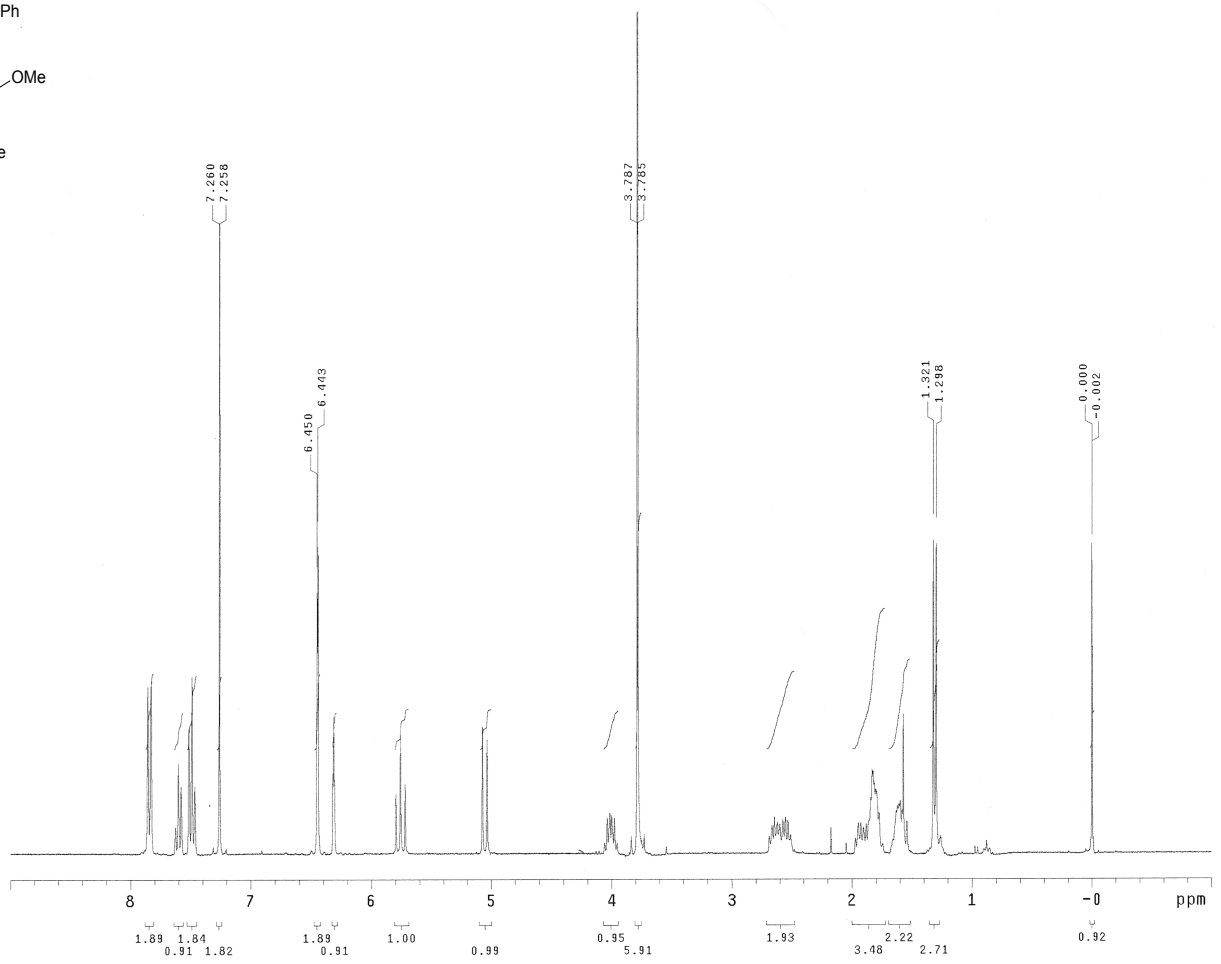
(**46**)
ds 57:43

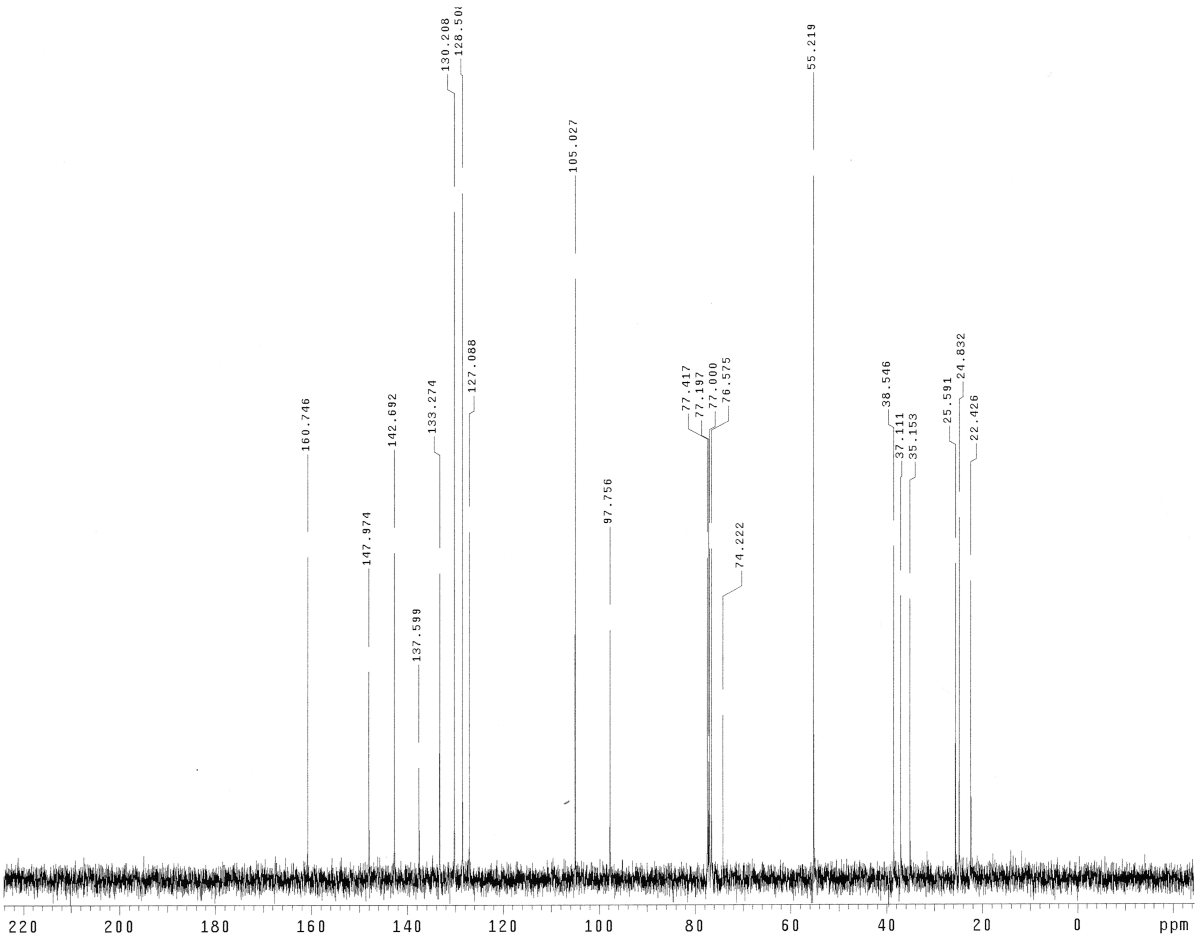

6.337
3.776
3.764
1.567
1.582
1.316
1.293
1.104
0.856
8
7
6
5
4
3
2
1
-0
ppm

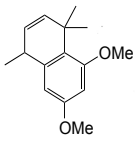

160.769
160.708
148.095
147.693
142.790
142.692
136.021
133.425
133.365
130.792
130.587
128.417
128.348
124.630
123.840
104.981
104.936
97.825
97.764
77.425
77.000
76.583
68.978
68.857
55.234
55.204
38.037
37.741
35.723
34.819
26.168
26.092
23.026
22.616
22.108
20.279
19.451
13.873
220
200
180
160
140
120
100
80
60
40
20
0
ppm


SO2Ph
OMe
OMe

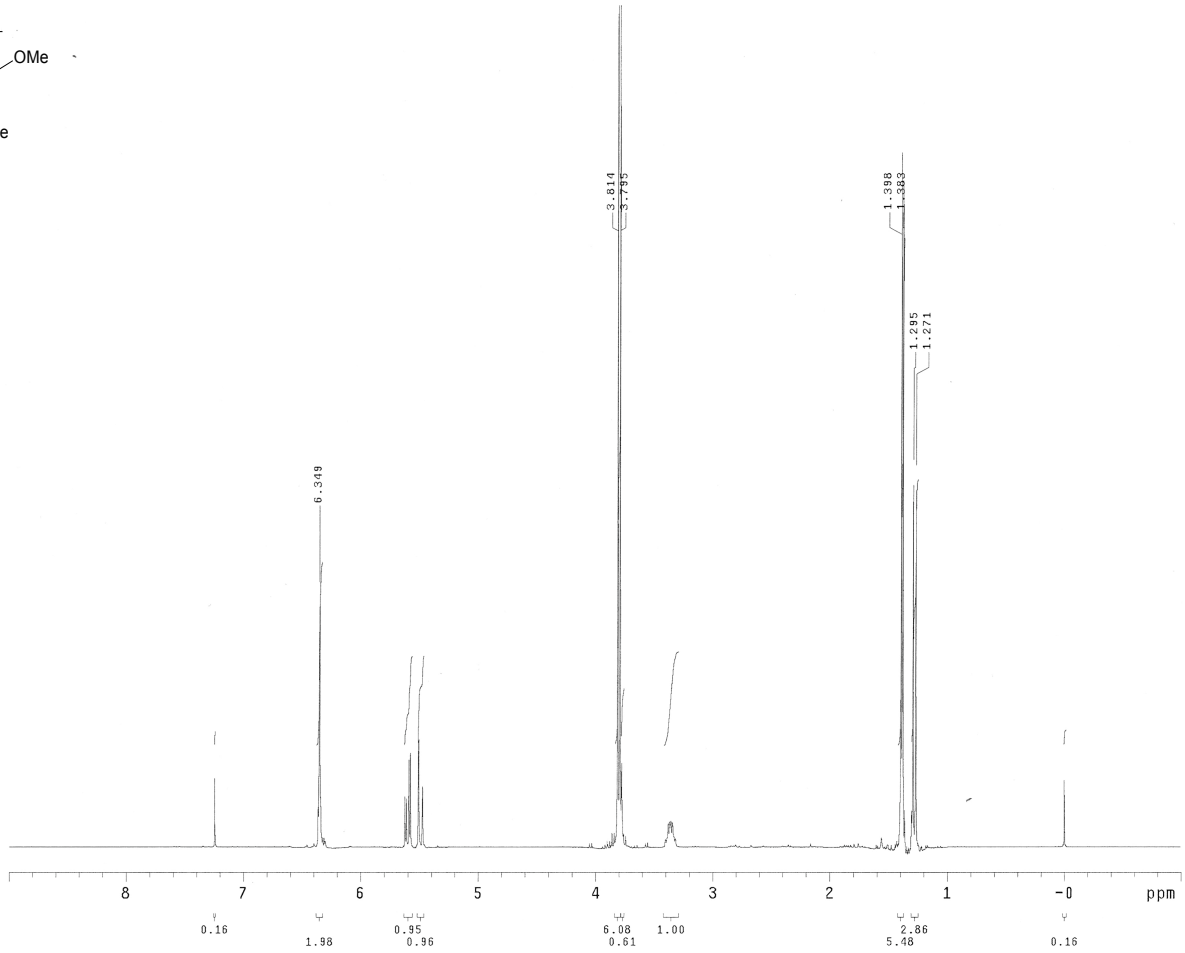
(**47**)

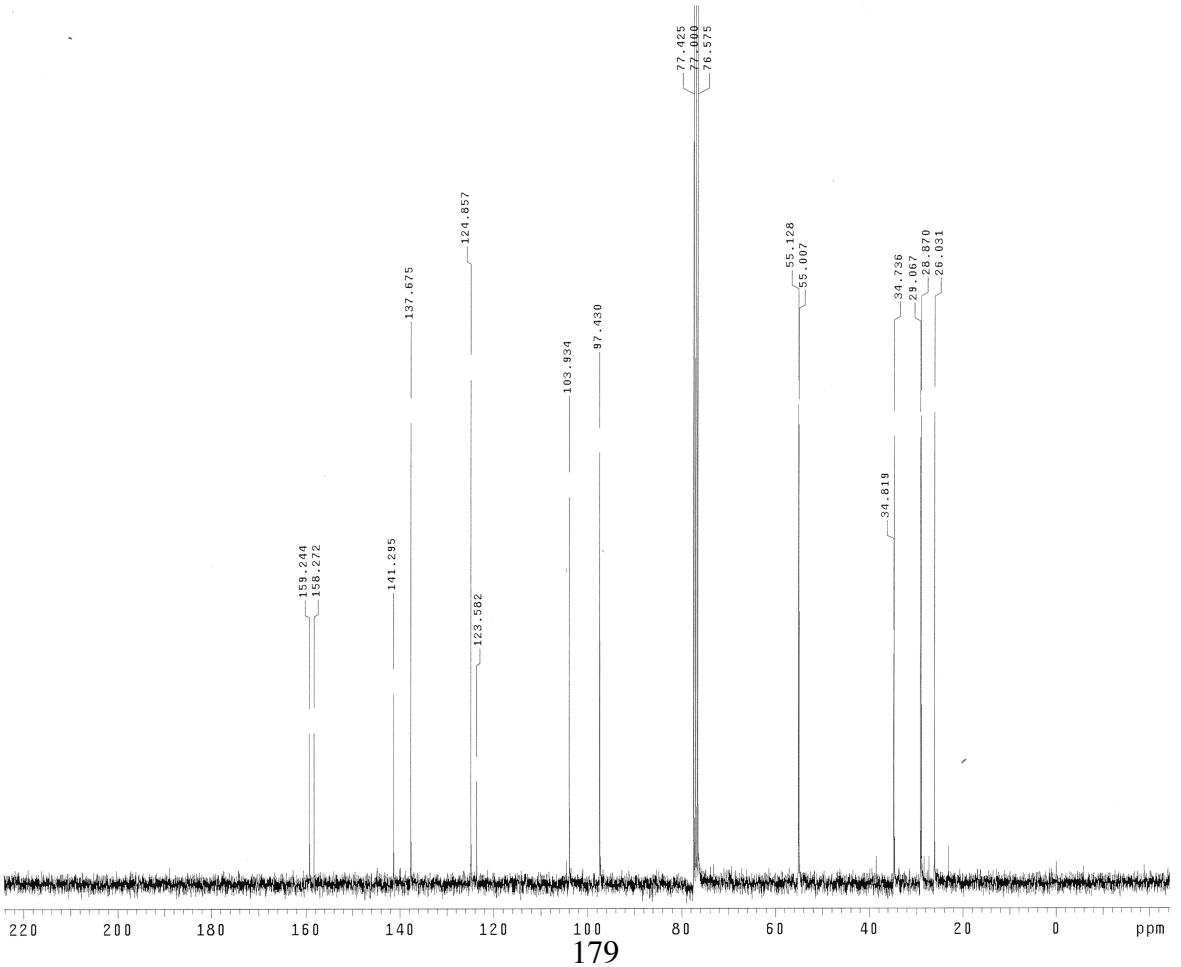

7.260
7.258
6.450
6.443
3.787
3.785
1.321
1.298
0.000
-0.002
8
7
6
5
4
3
2
1
-0
ppm
1.89
1.84
0.91
1.82
1.89
0.91
1.00
0.99
0.95
5.91
1.93
2.22
3.48
2.71
0.92

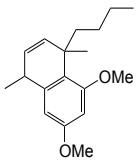

160.746
147.974
142.692
137.599
133.274
130.208
128.508
127.088
105.027
97.756
77.417
77.197
77.000
76.575
74.222
55.219
38.546
37.111
35.153
25.591
24.832
22.426
220
200
180
160
140
120
100
80
60
40
20
0
ppm


OMe
OMe

(**48**)

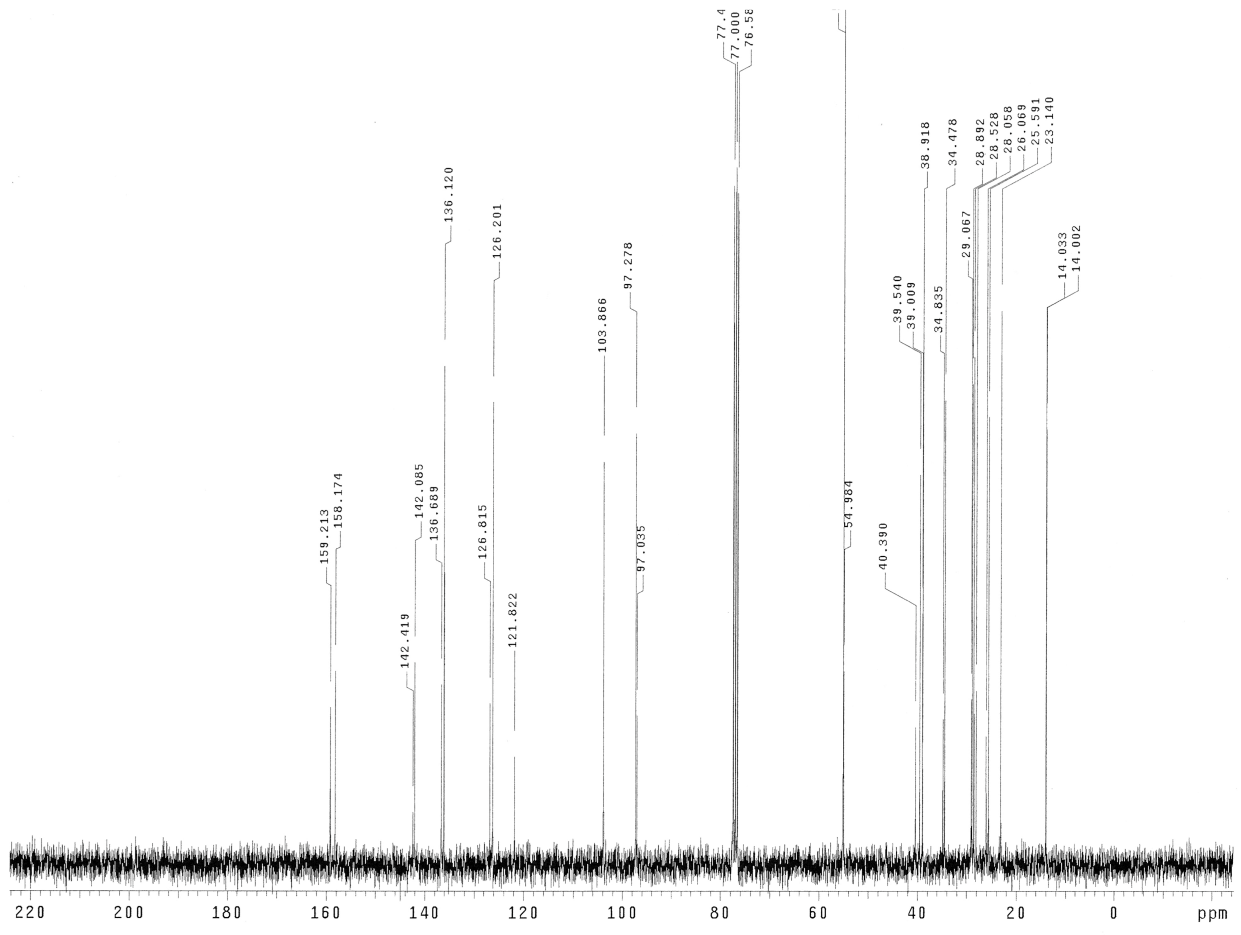

6.349
3.814
3.795
1.398
1.383
1.295
1.271
8
7
6
5
4
3
2
1
-0
ppm
0.16
1.98
0.95
0.96
6.08
0.61
1.00
2.86
5.48
0.16


77.425
77.000
76.575
159.244
158.272
141.295
137.675
124.857
123.582
103.934
97.430
55.128
55.007
34.819
34.736
29.067
28.870
26.031
220
200
180
160
140
120
100
80
60
40
20
0
ppm


OMe
OMe

(**49**)

3.794
3.788
1.359
1.299
1.275
0.785
6.340
8
7
6
5
4
3
2
1
-0
ppm
0.14
1.92
0.98
1.00
5.82
0.96
0.22
0.72
0.08
3.08
2.72
3.80
3.54
0.08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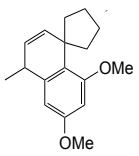
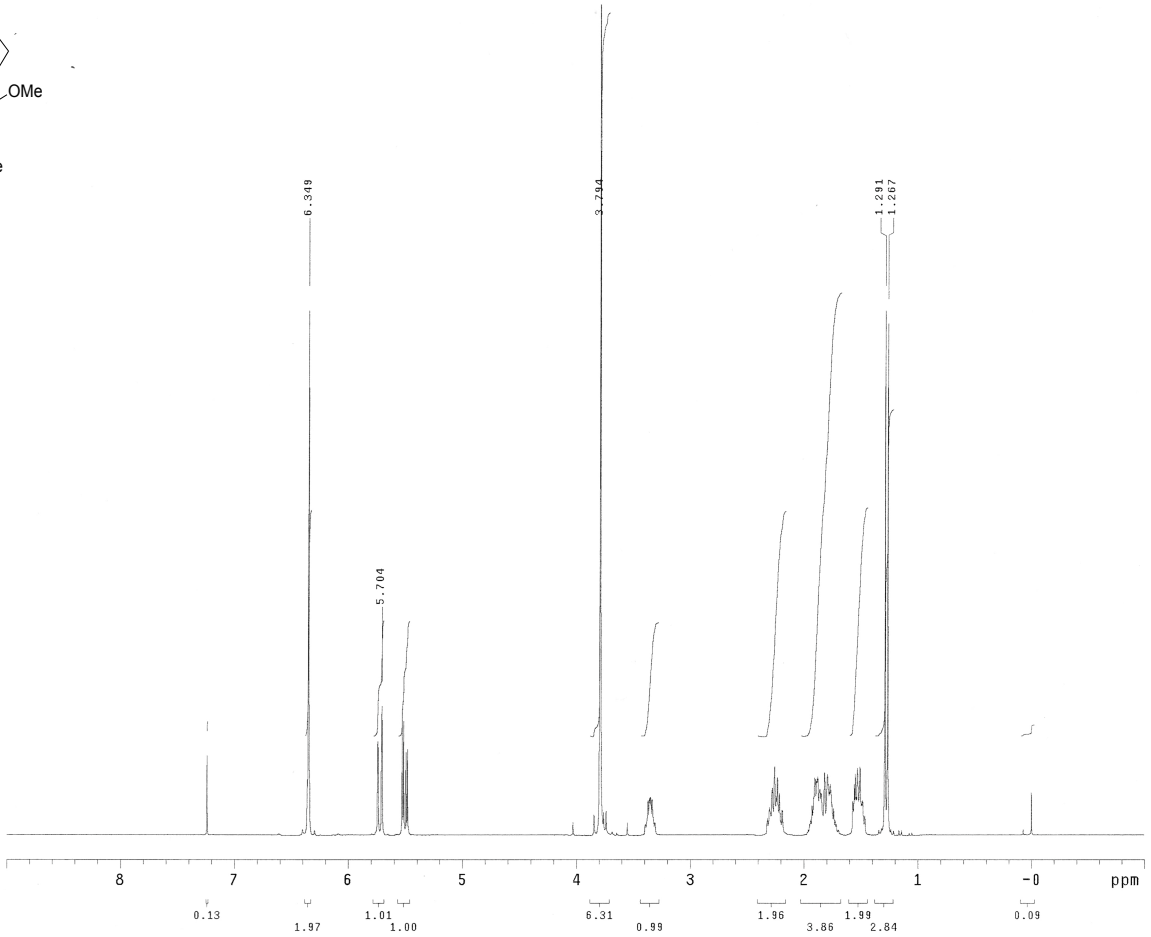

OMe
OMe

(**50**)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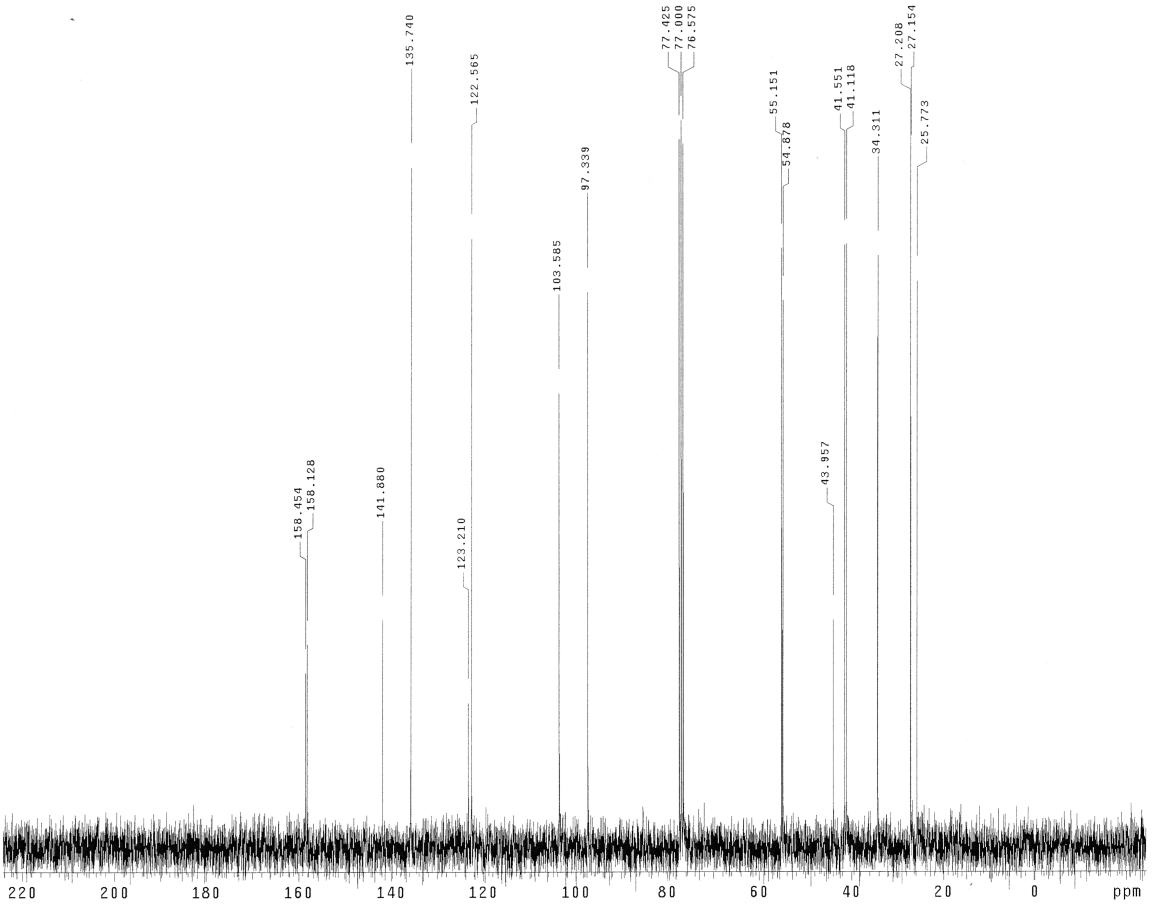
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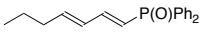
Chapter 3. Supporting Information

Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Phosphine Oxides and Its Synthetic Application


P(O)Ph2

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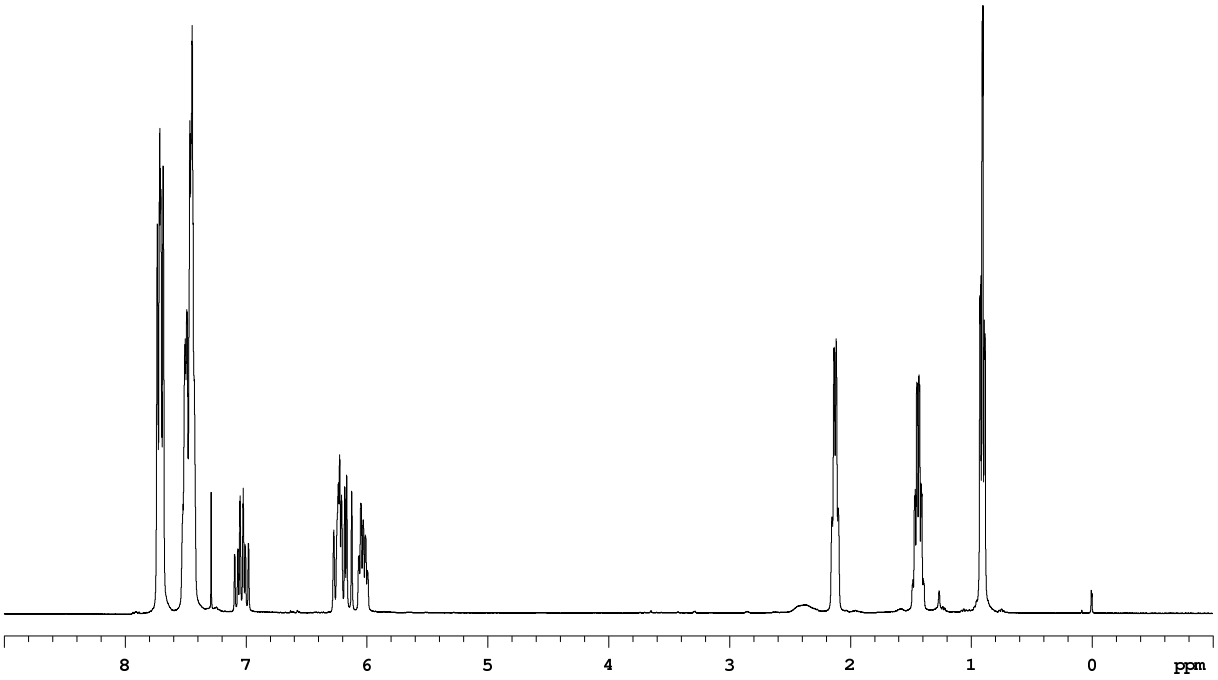
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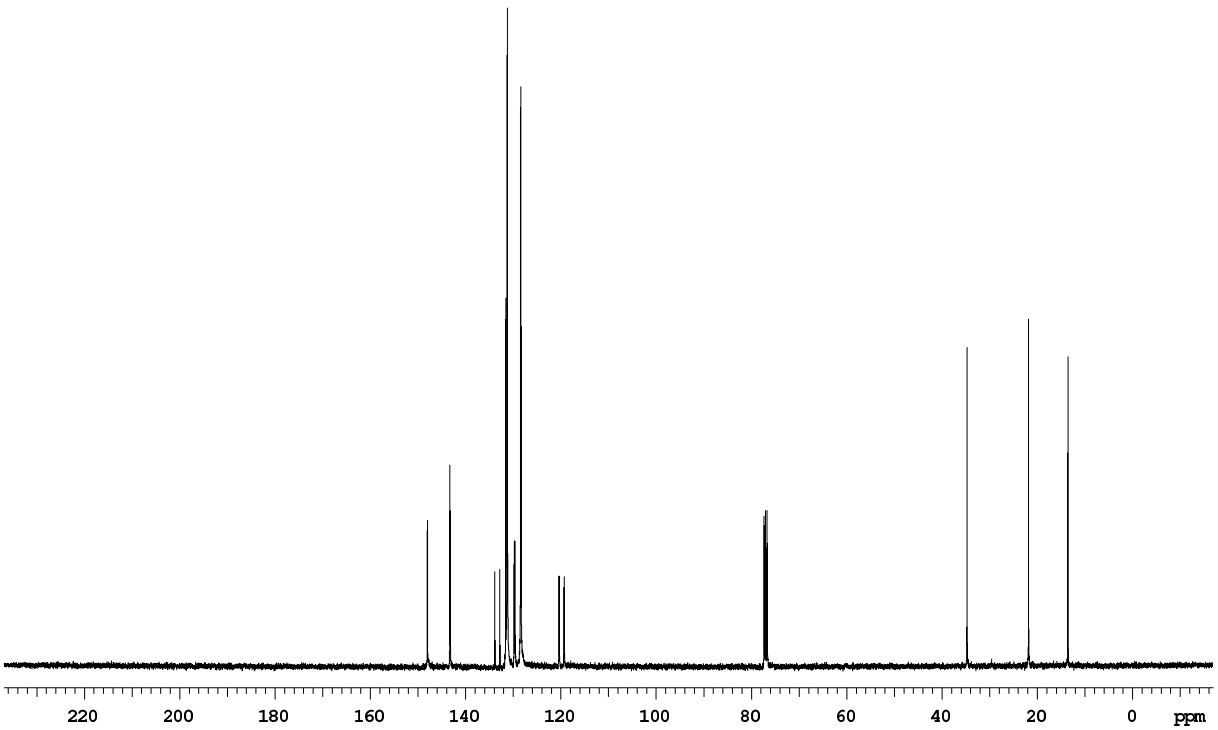
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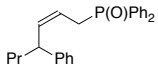
P(O)Ph2
Pr
Ph

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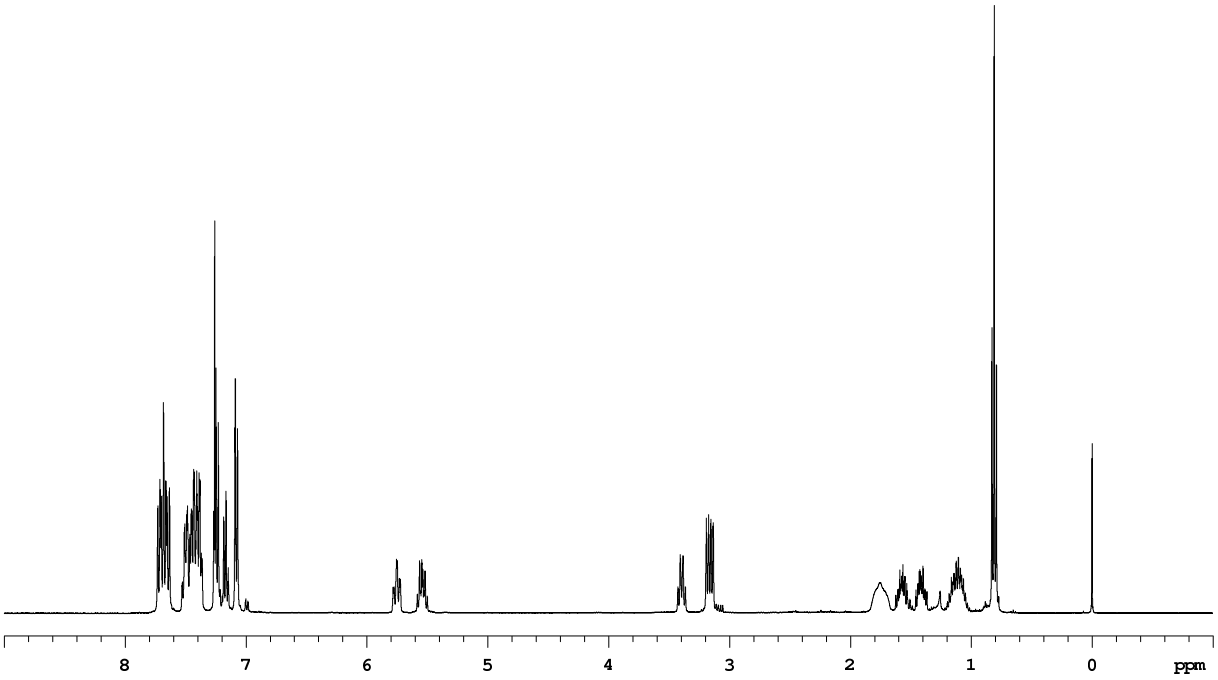
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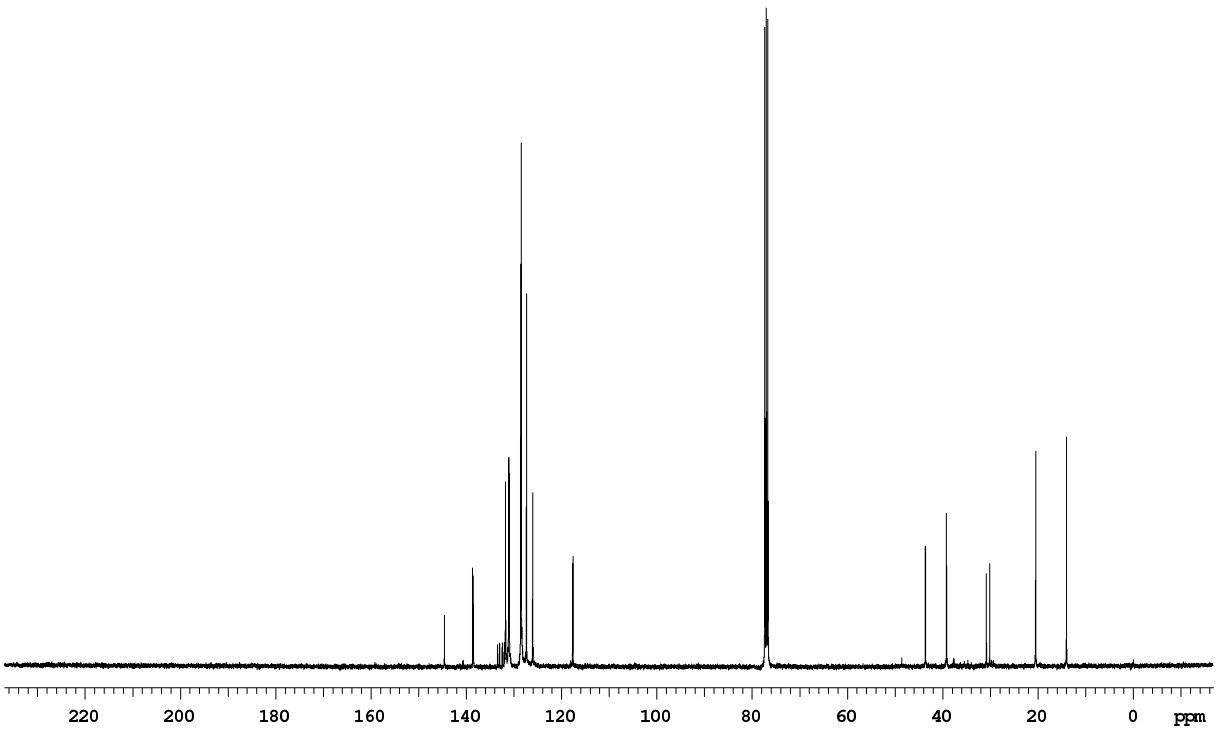
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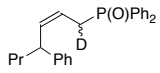

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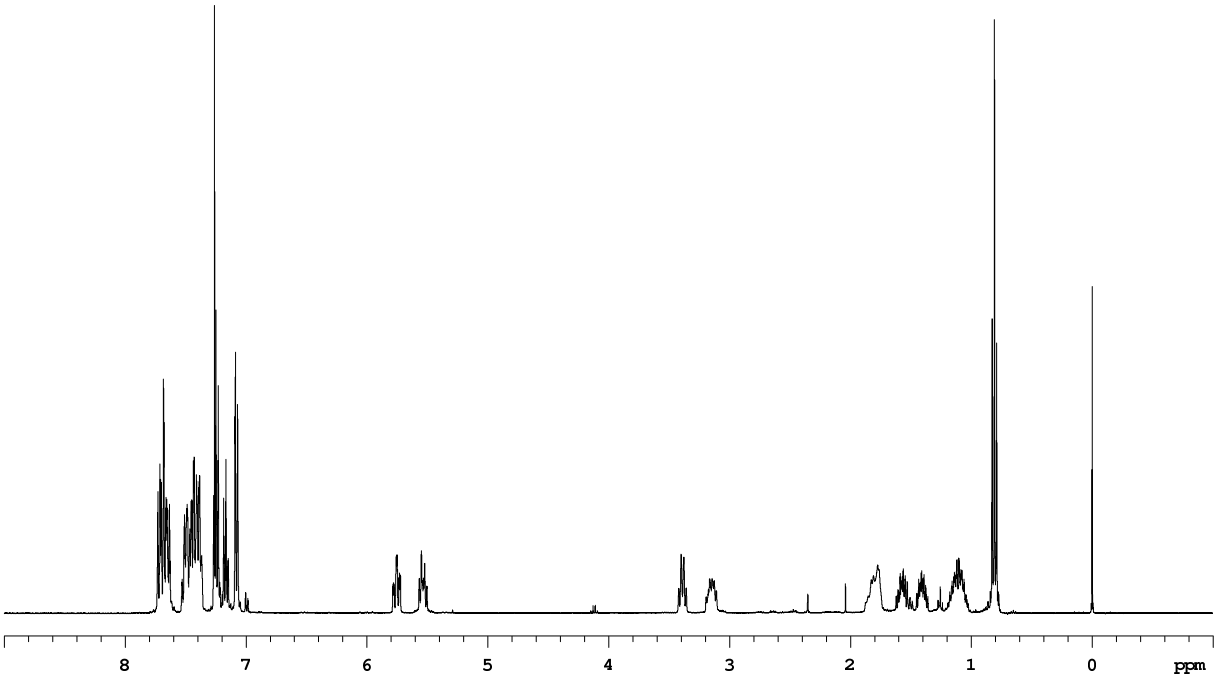
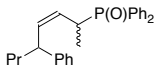
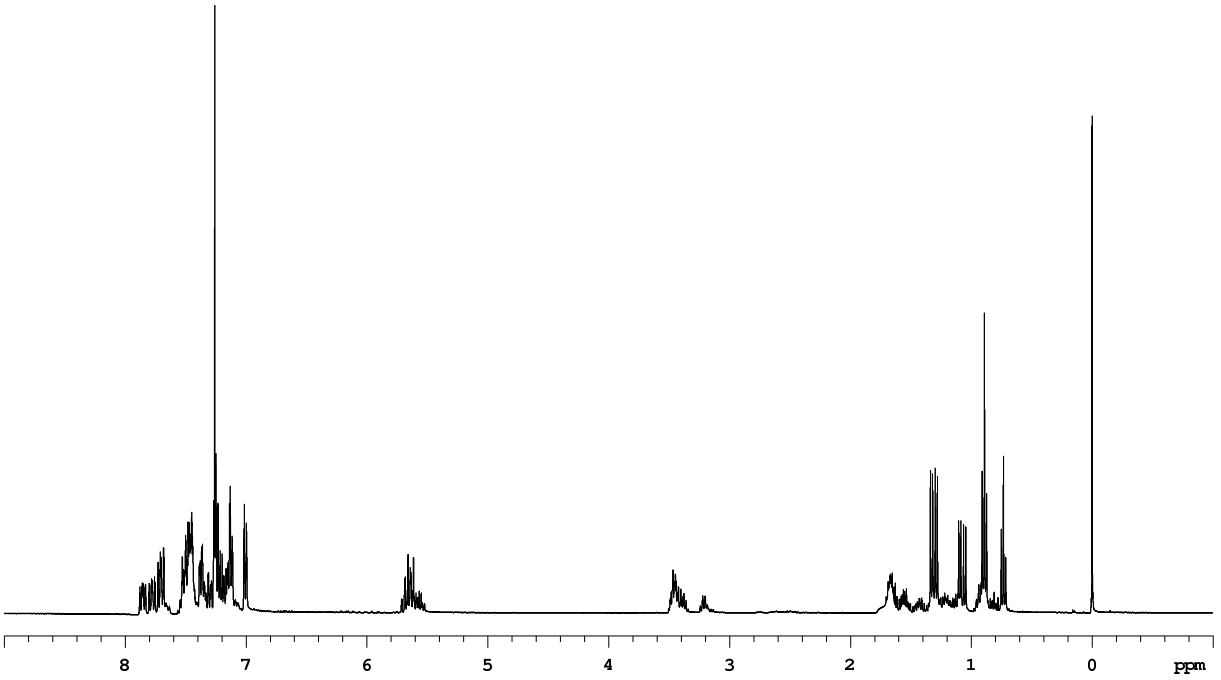



P(O)Ph2
Pr
Ph

(**8**)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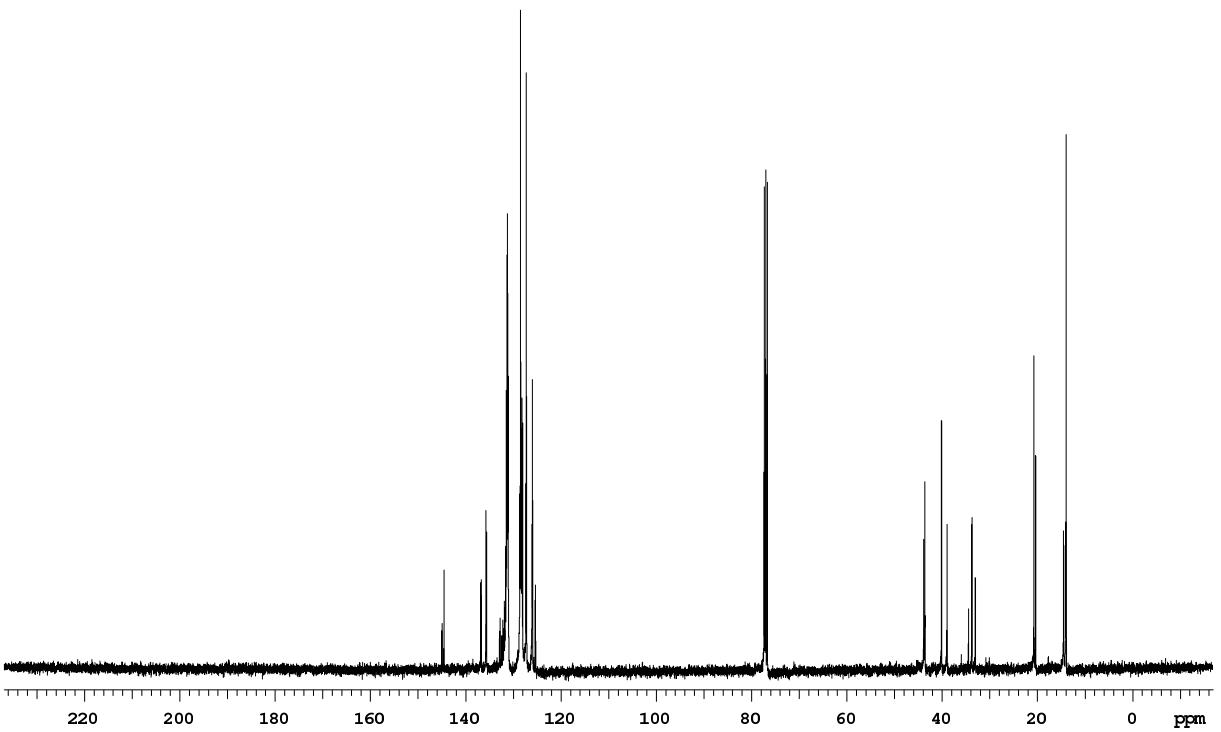
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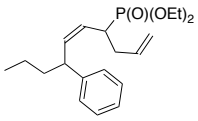
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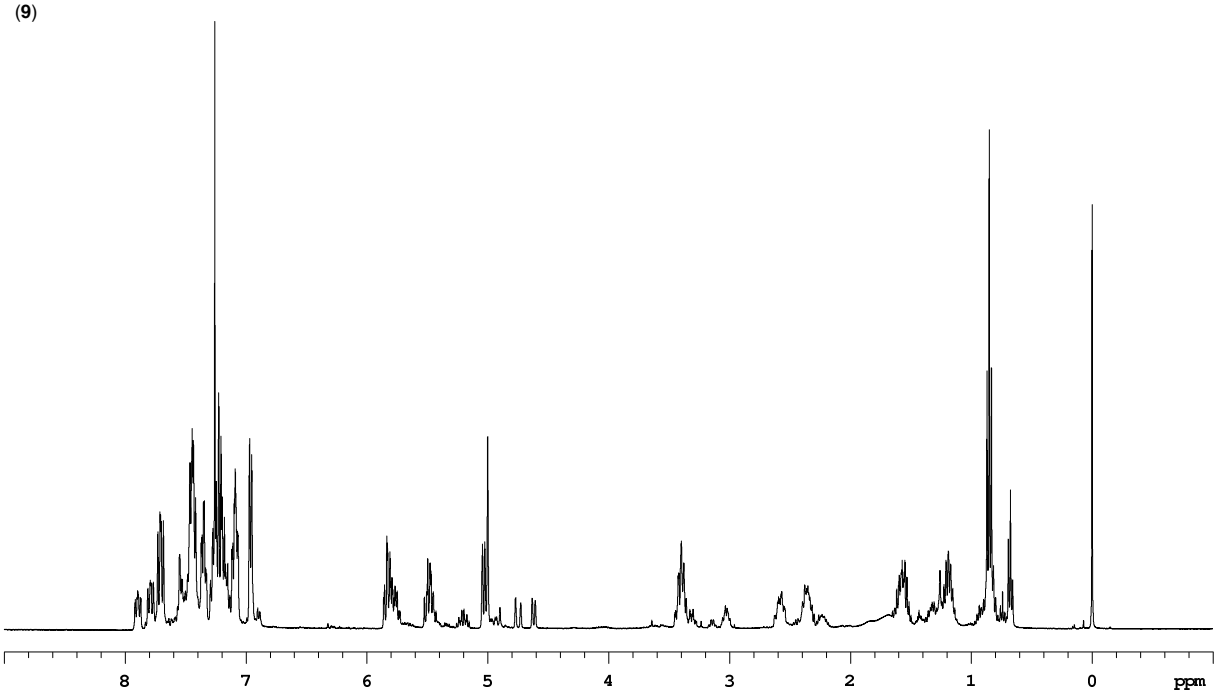
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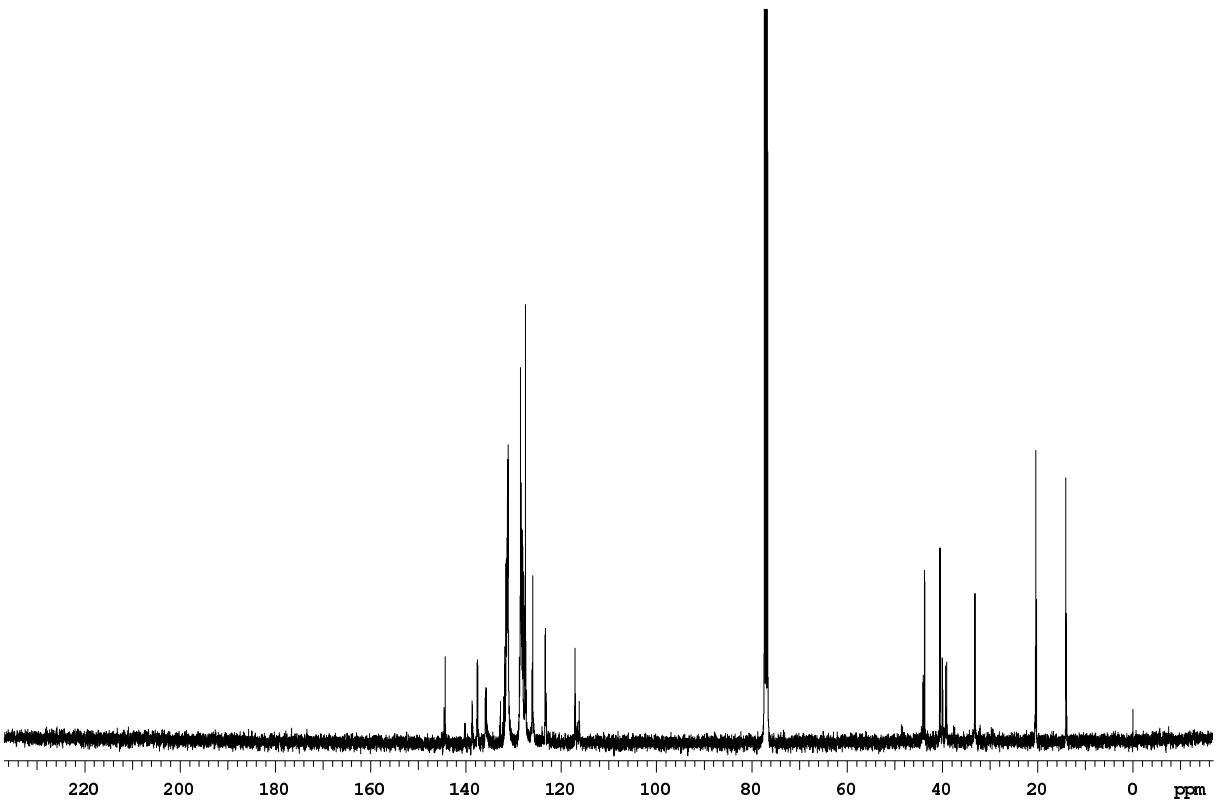
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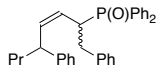
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Pr
Ph
Ph

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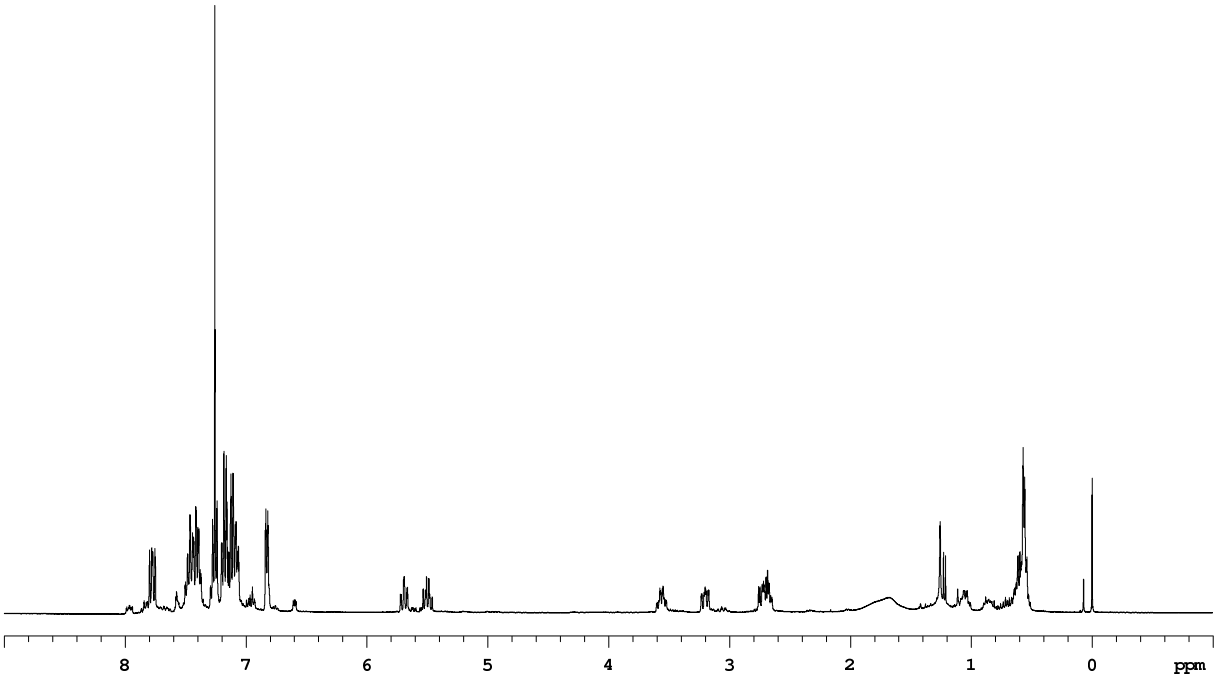
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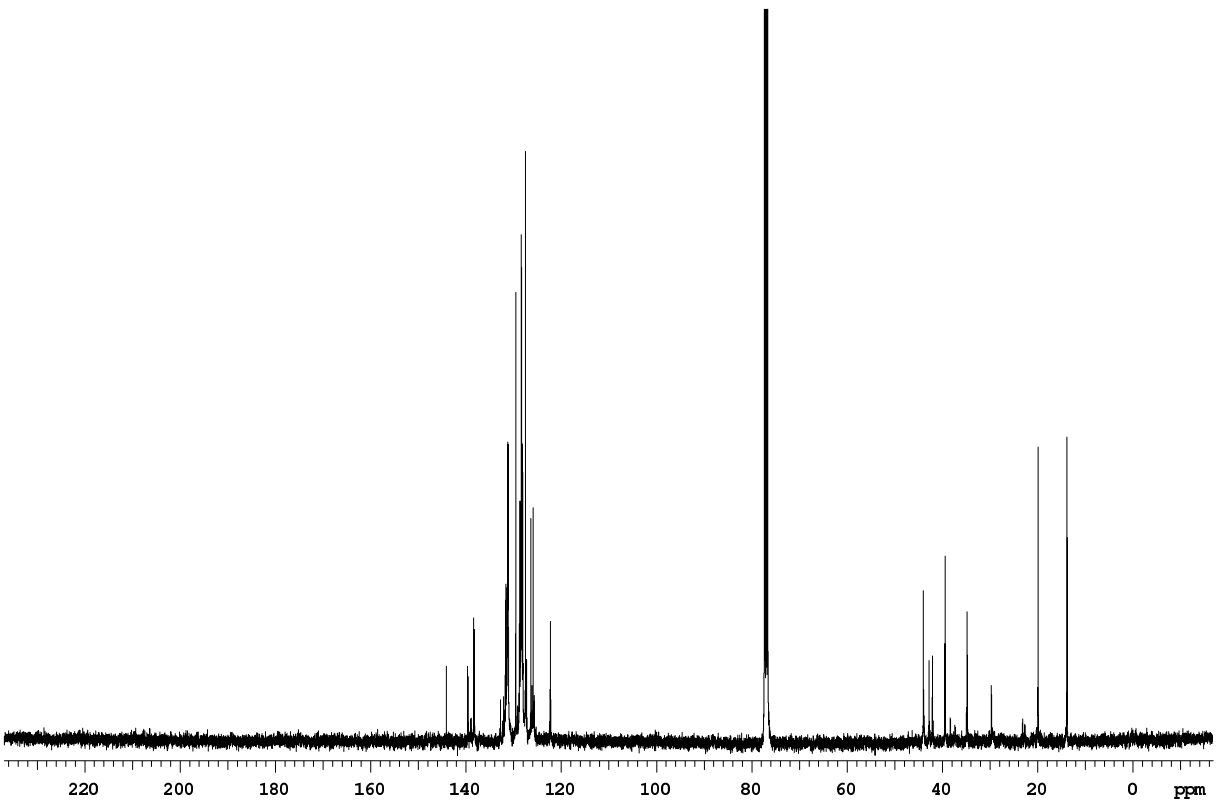
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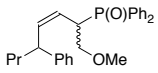
P(O)Ph2
Pr
Ph
OMe

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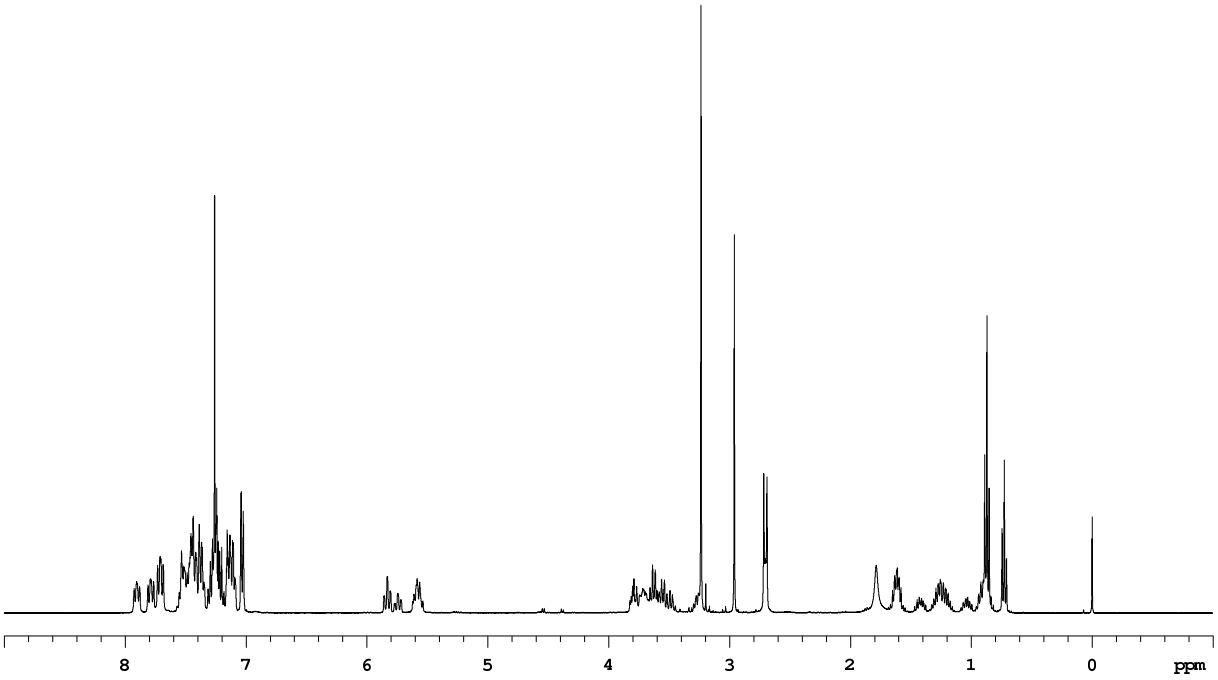
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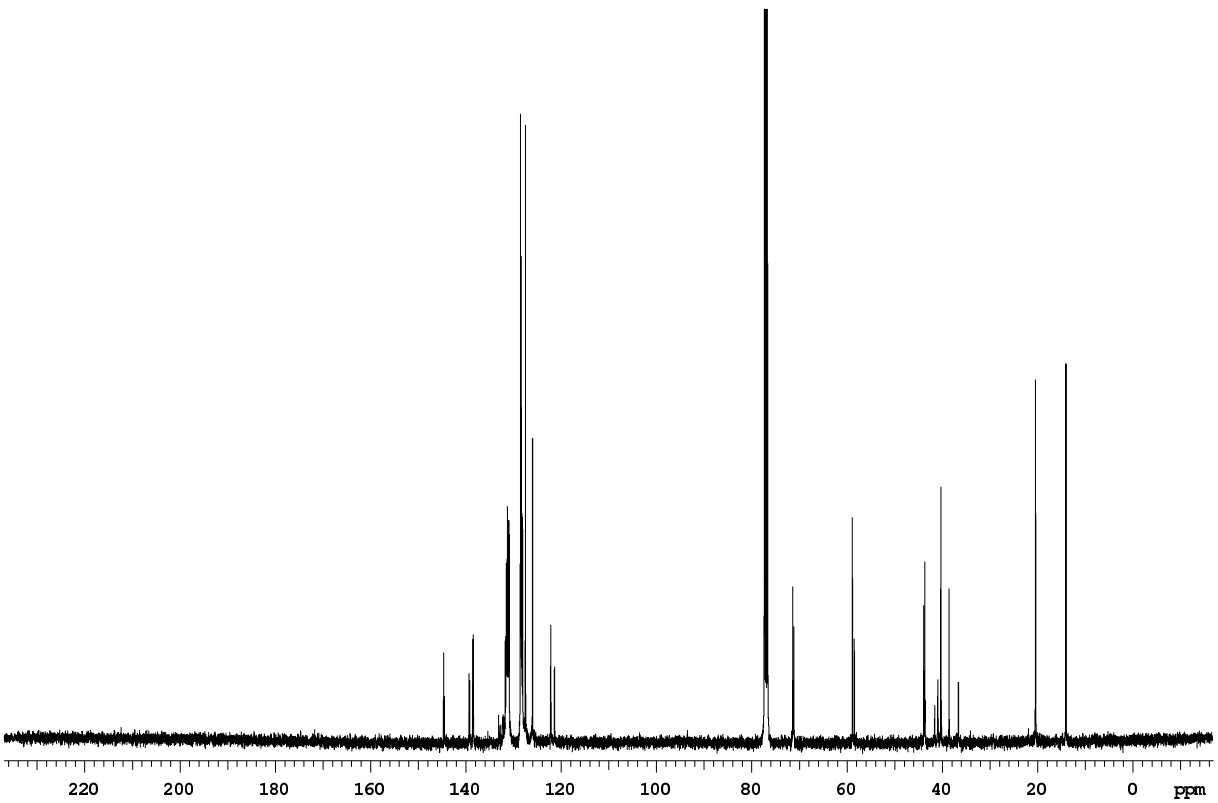
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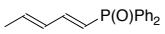
P(O)Ph2

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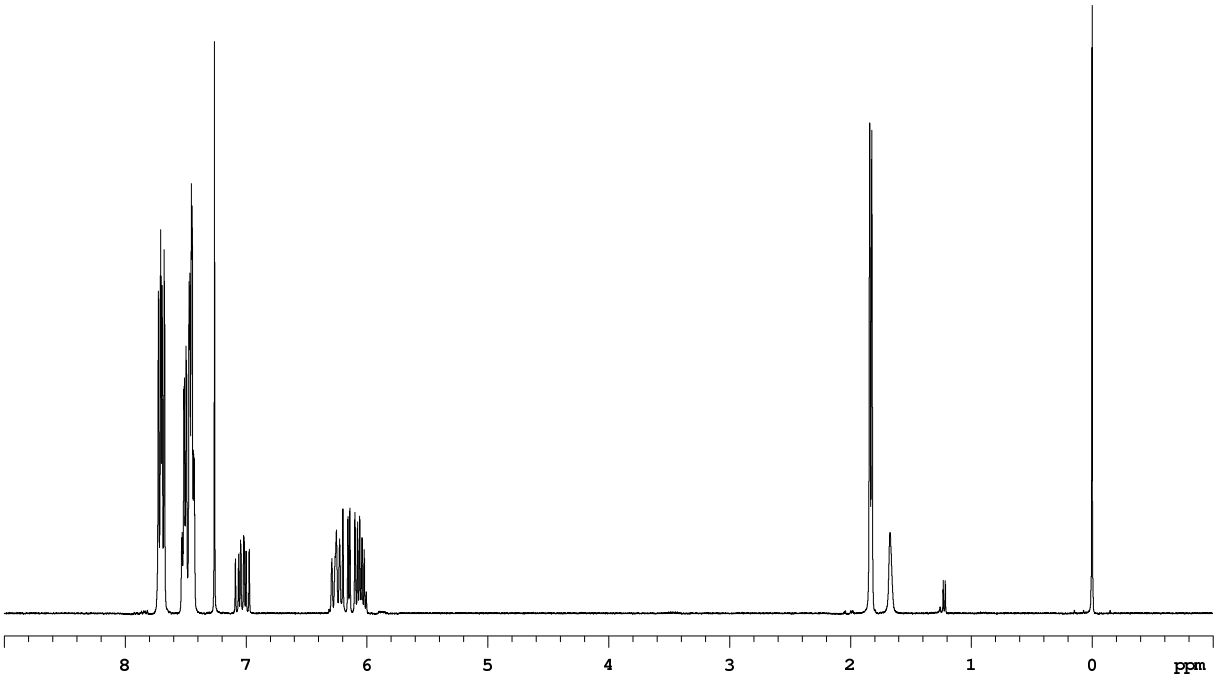
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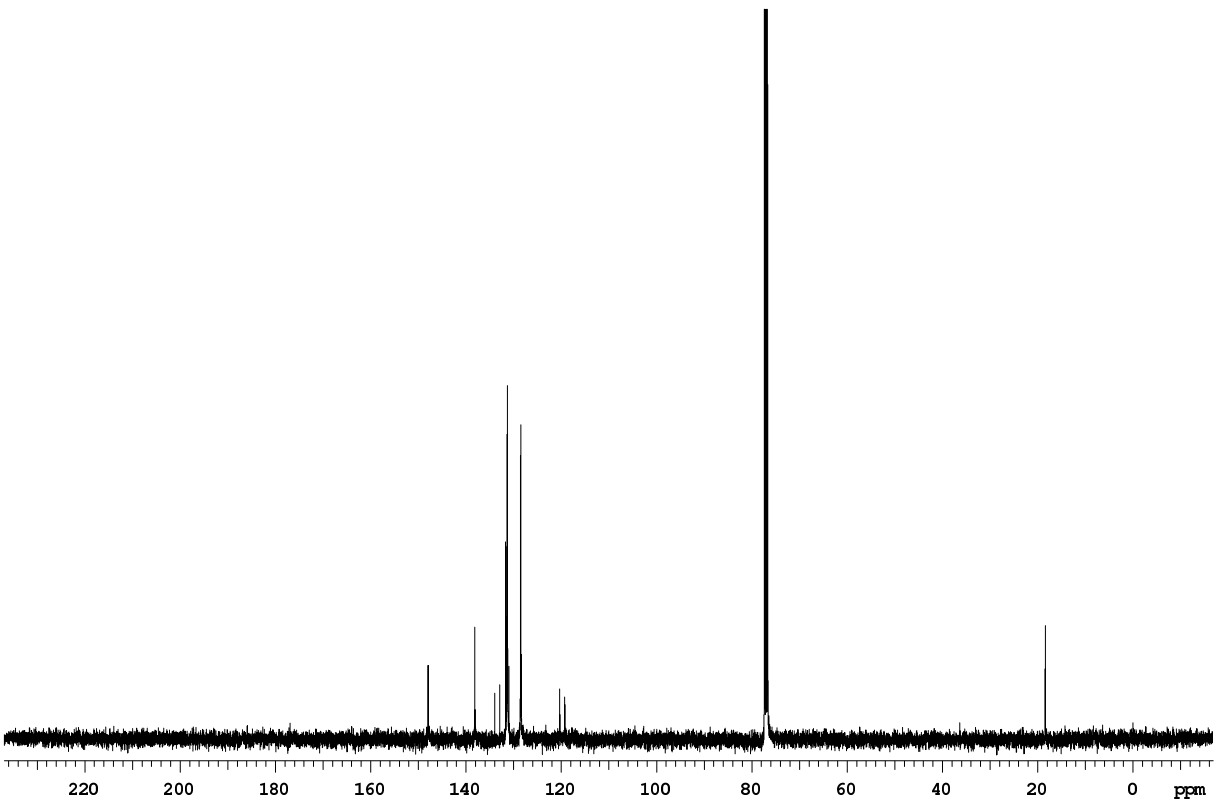
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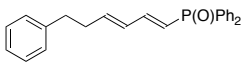
P(O)Ph2

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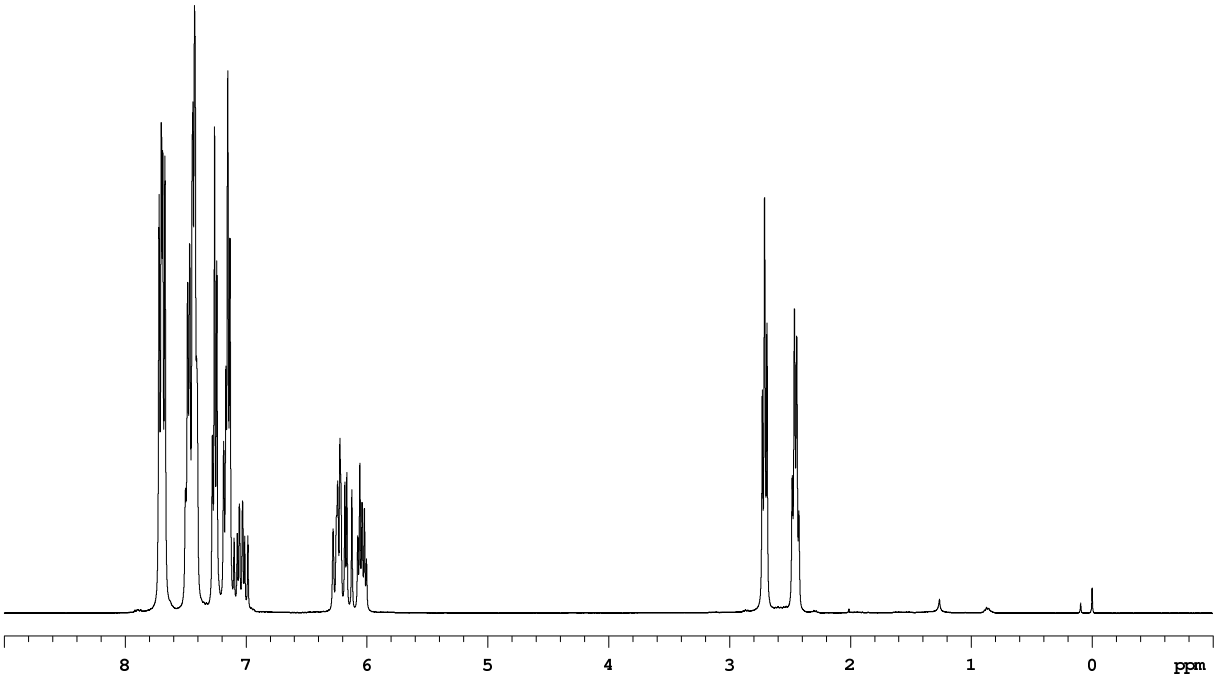
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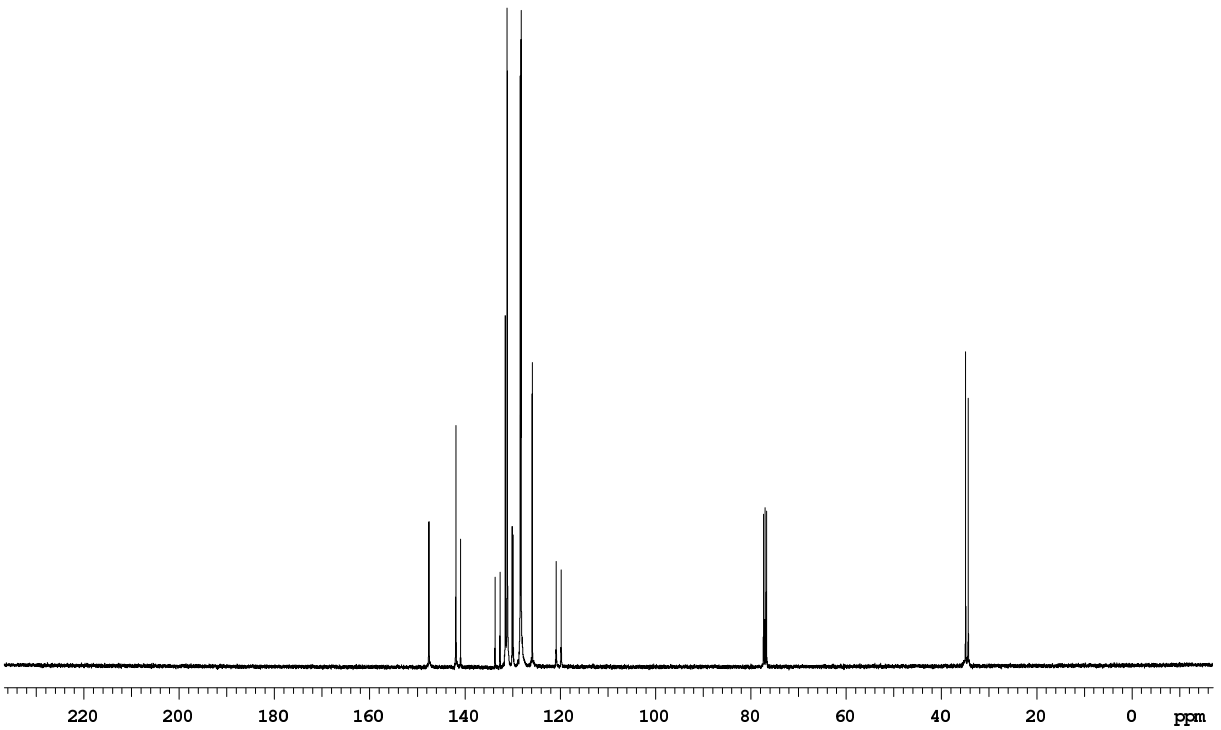
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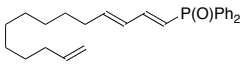
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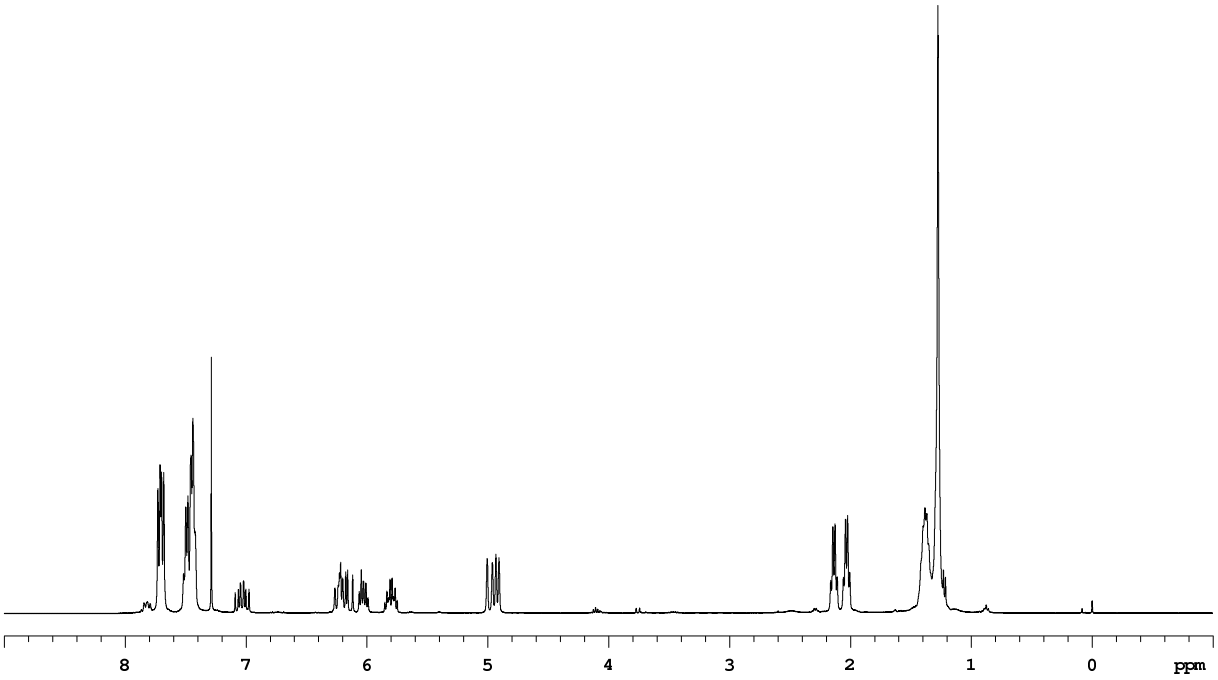
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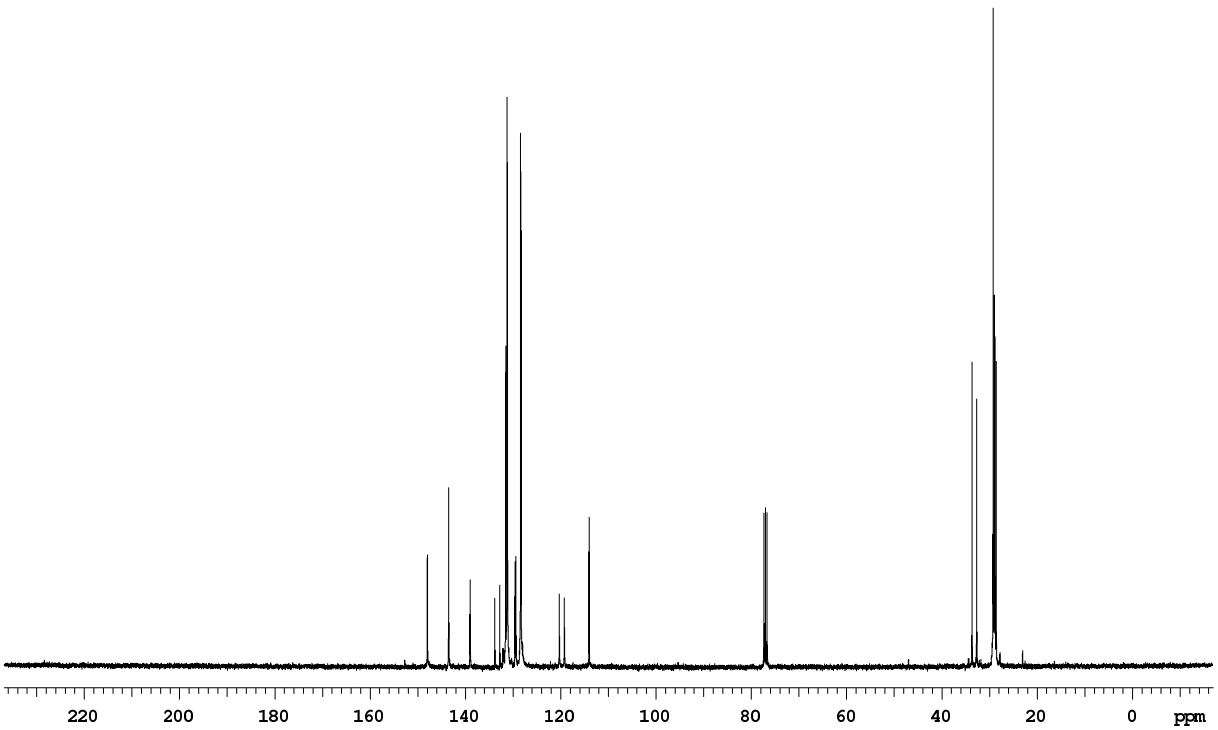
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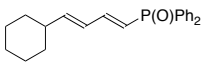
P(O)Ph2

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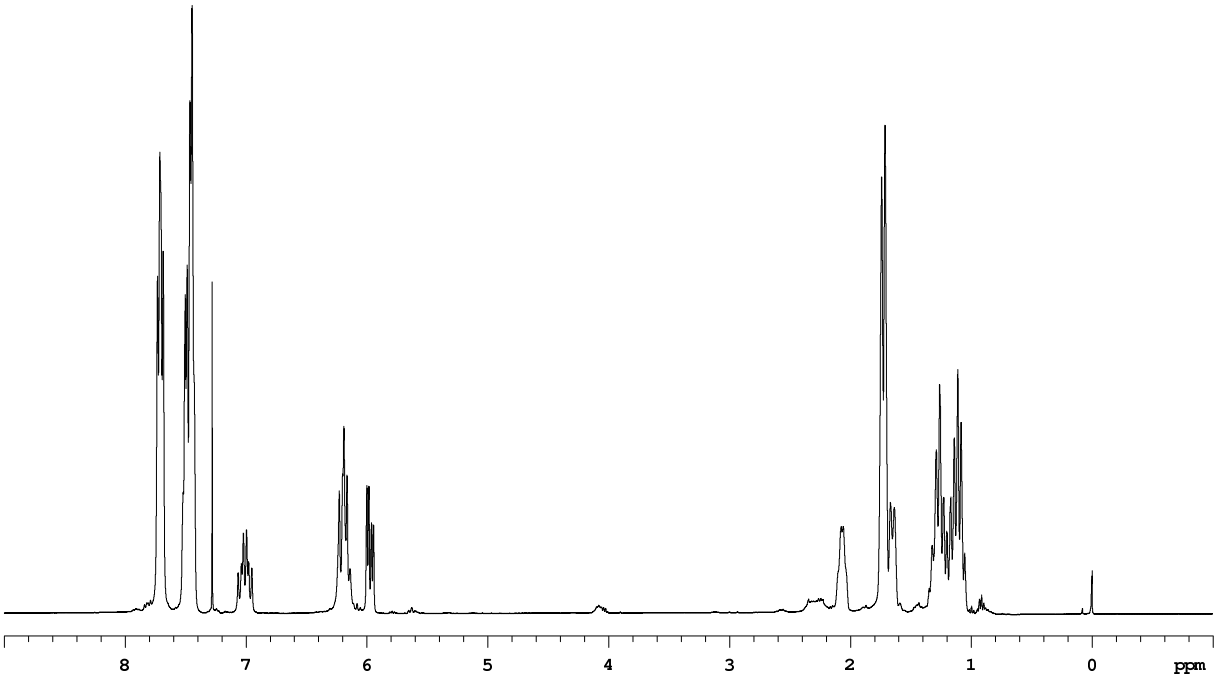
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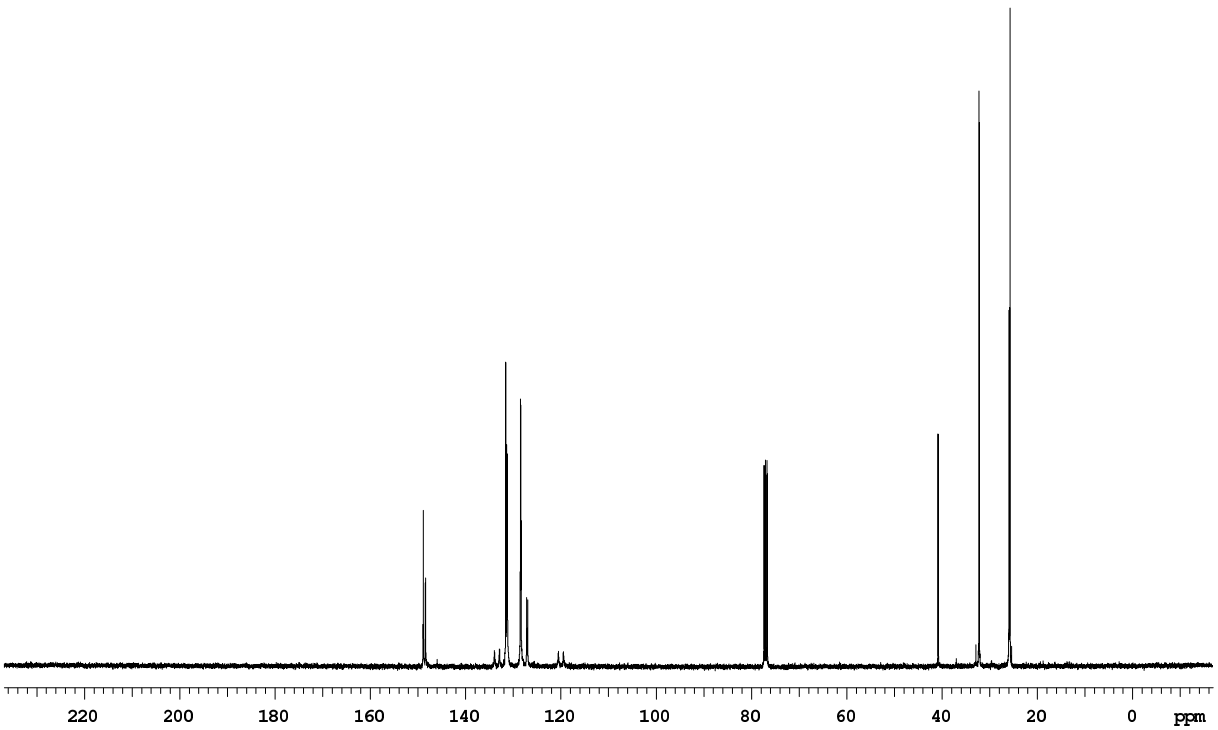
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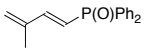
P(O)Ph2

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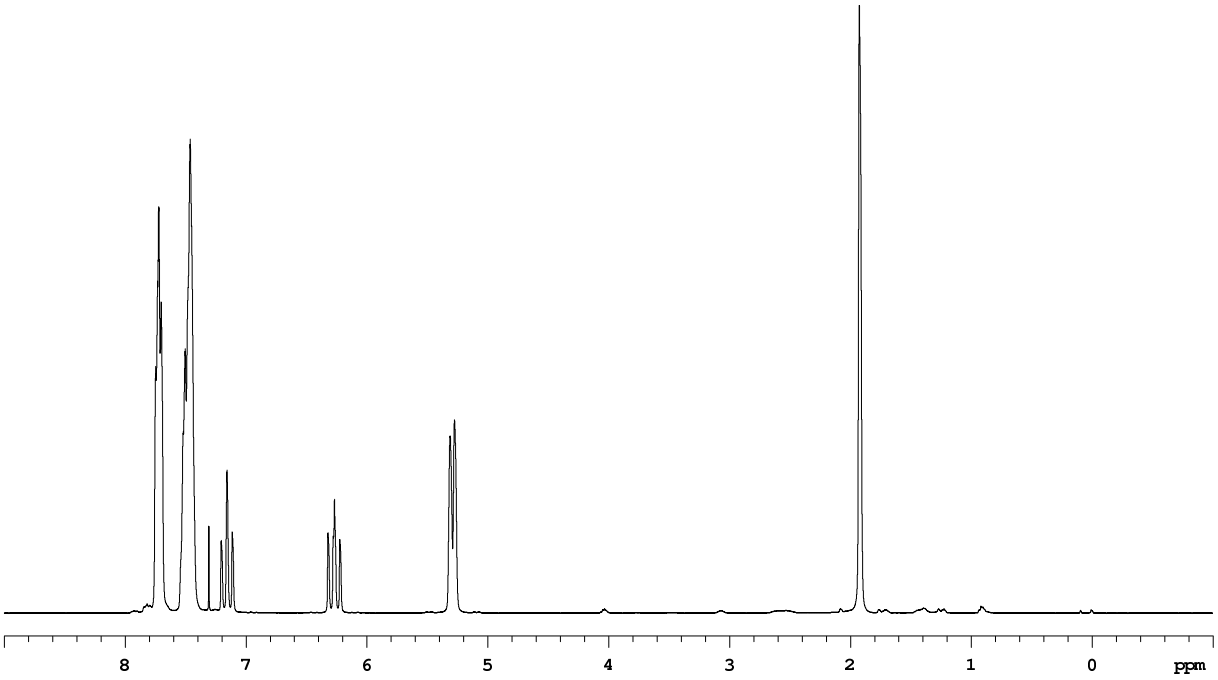
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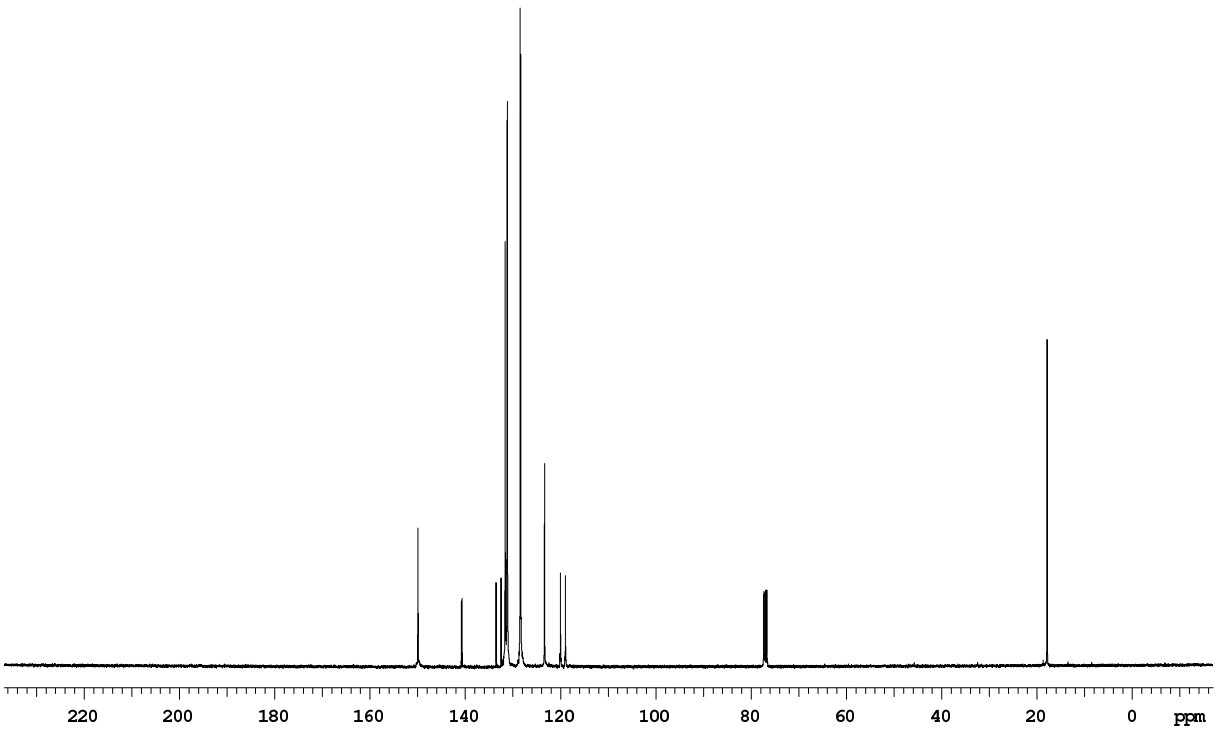
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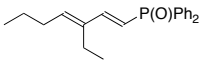
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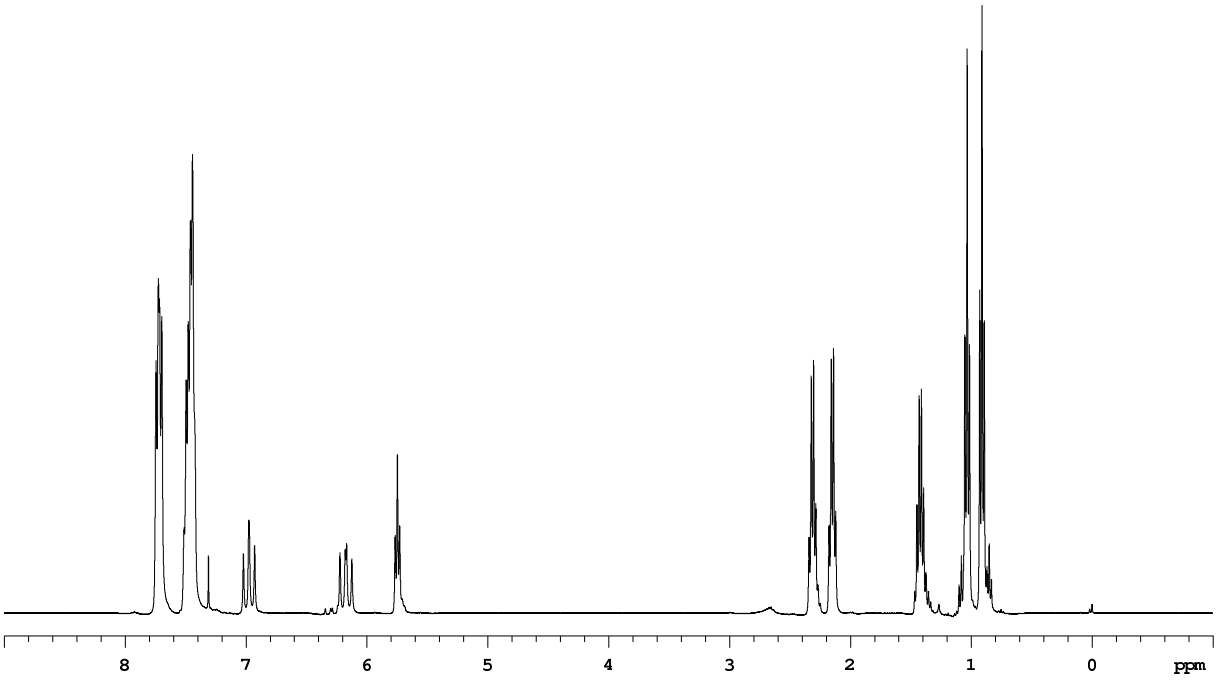
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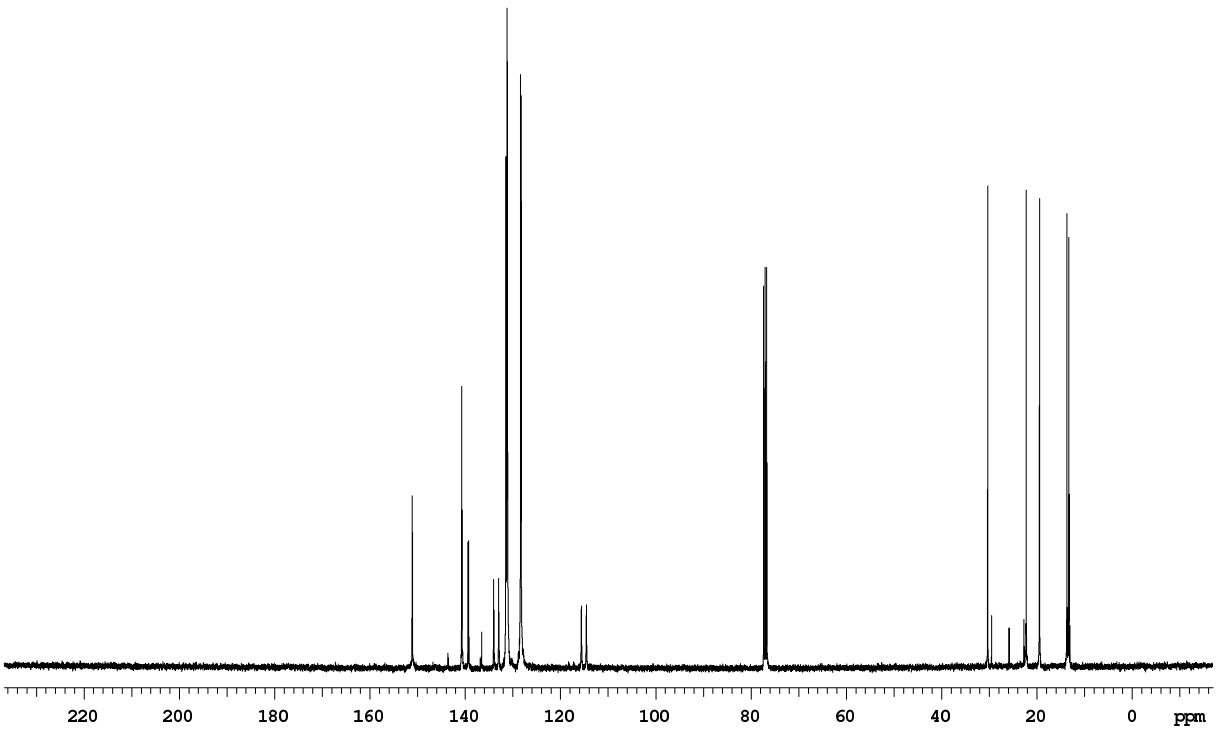
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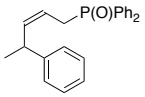
P(O)Ph2

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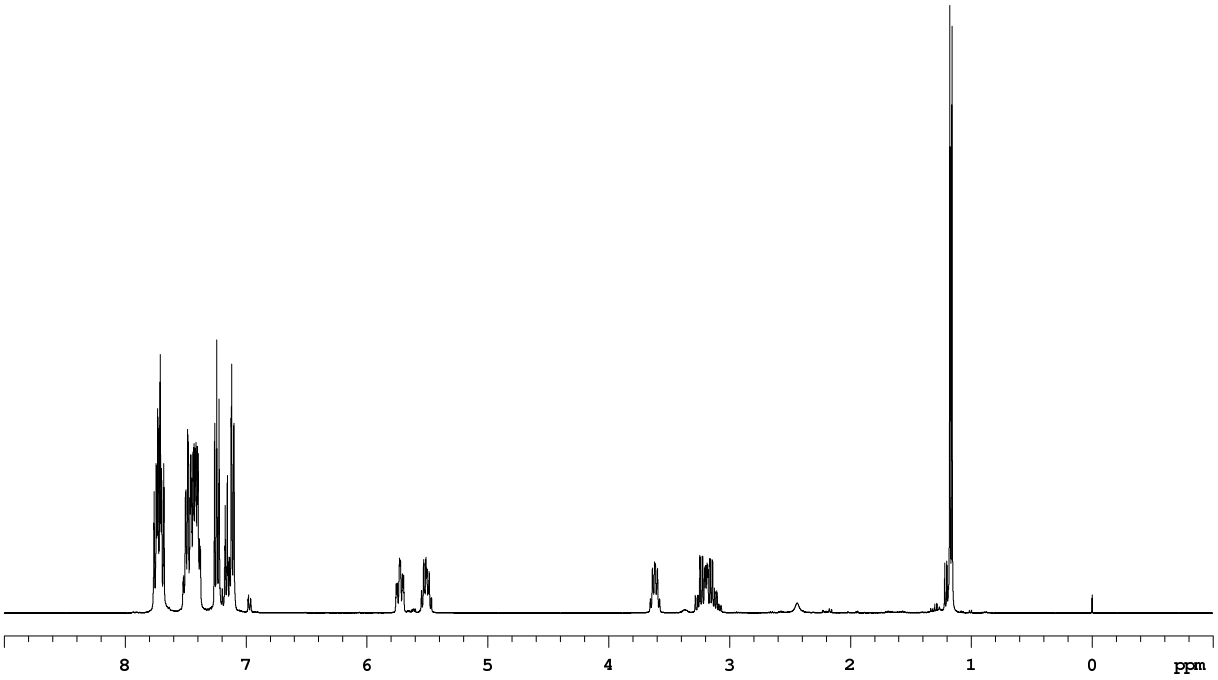
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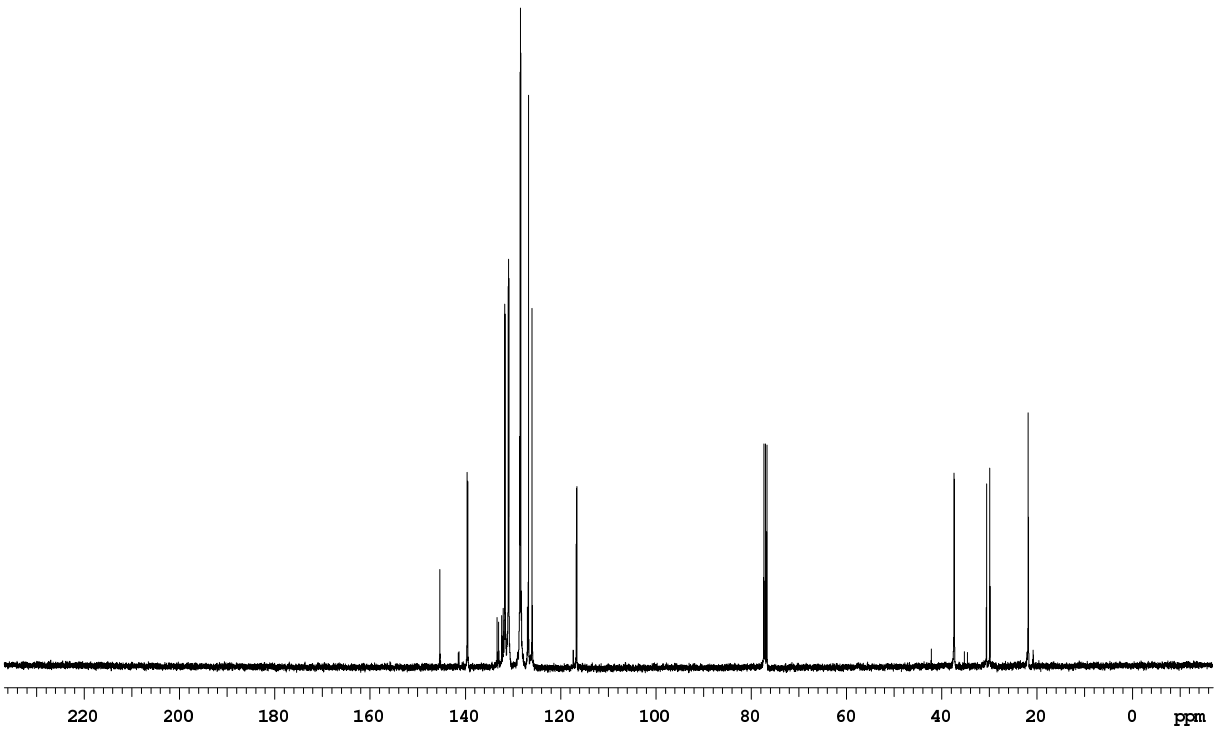
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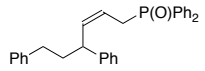
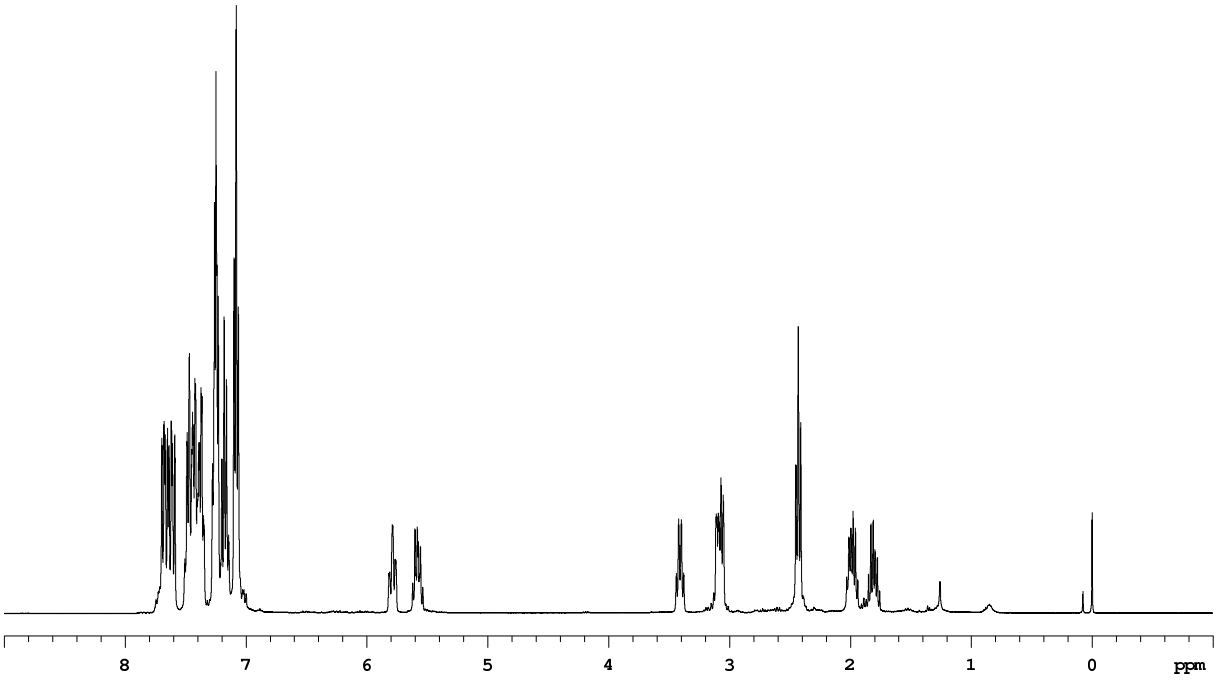

P(O)Ph2
Ph
Ph

(**19**)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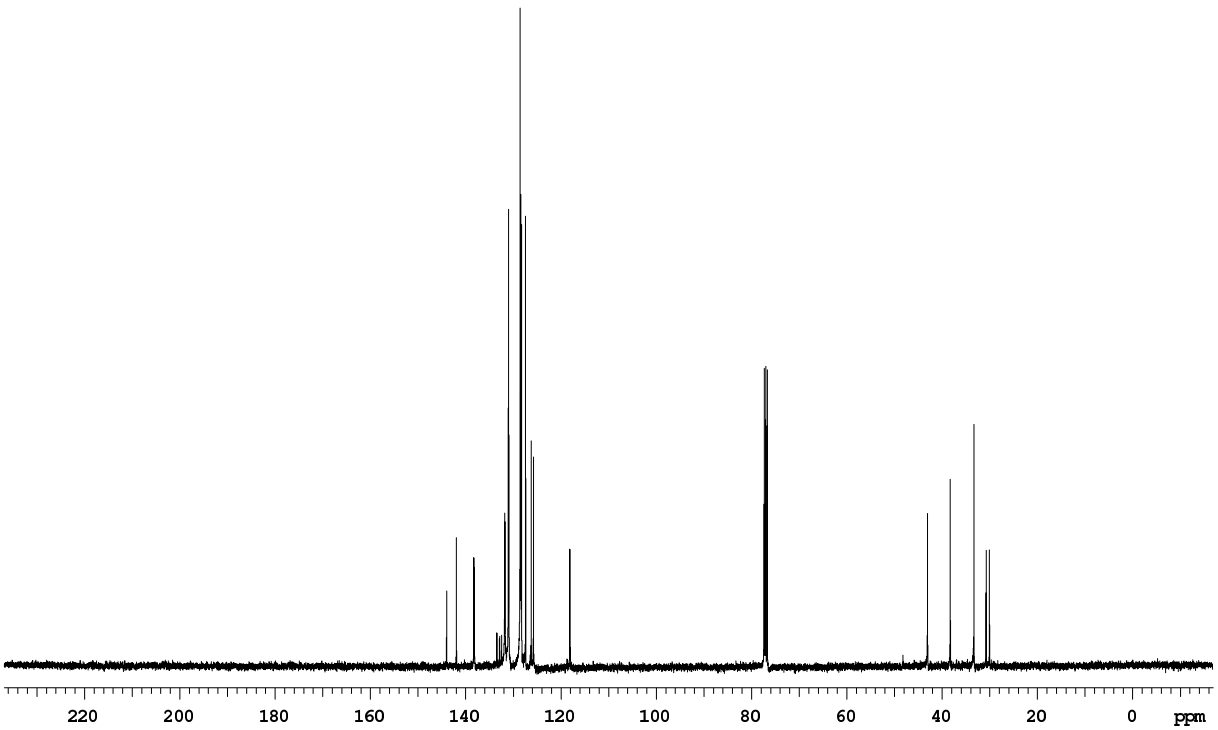
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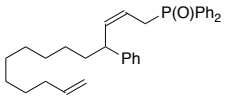
P(O)Ph2
Ph

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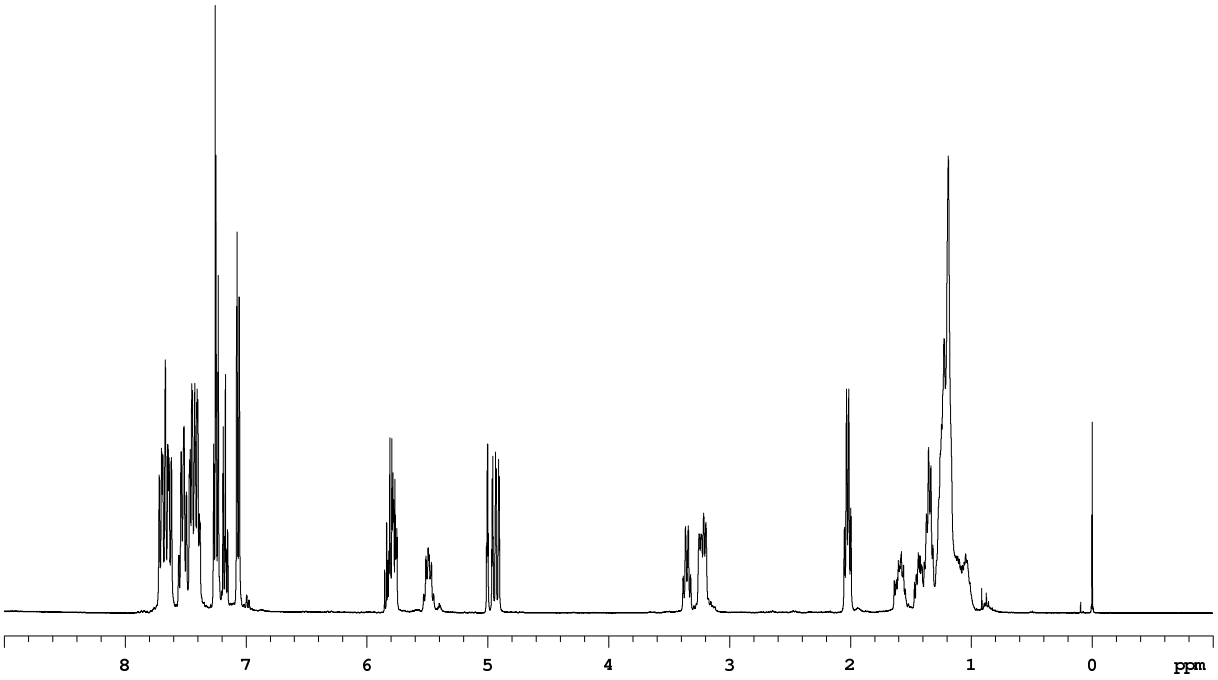
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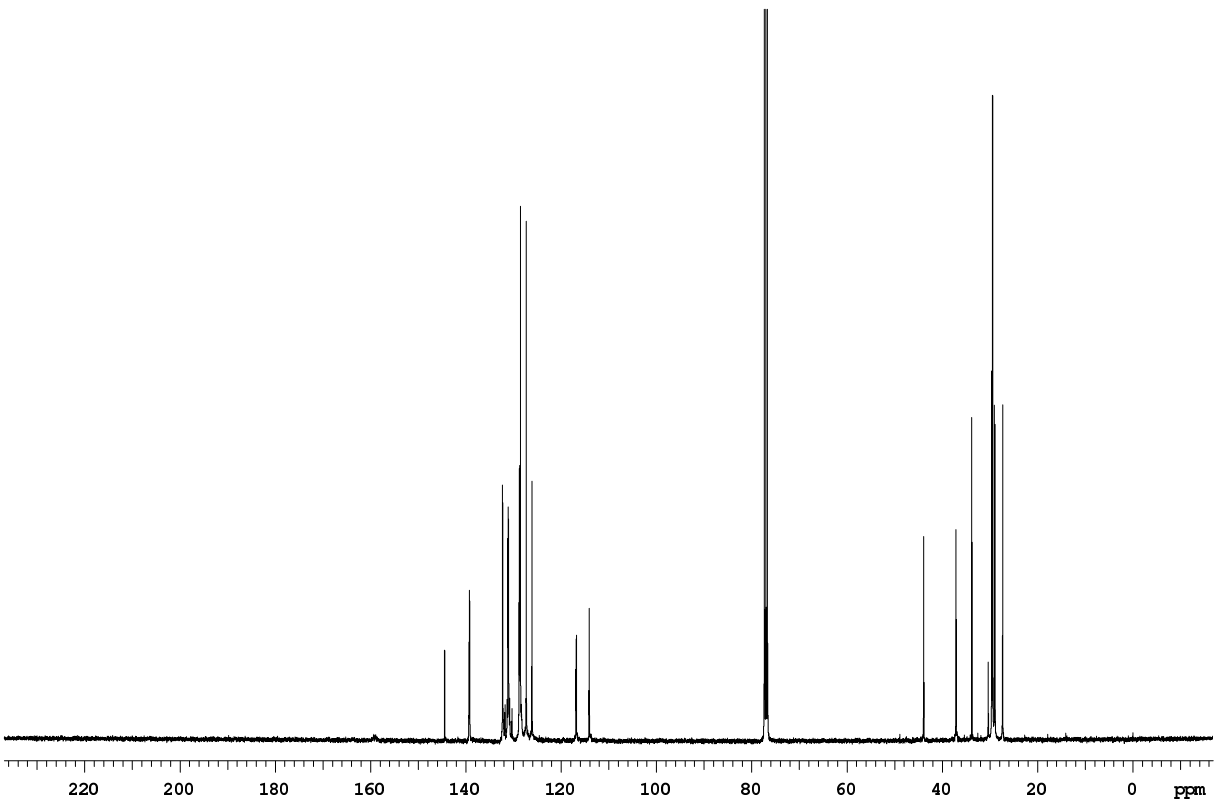
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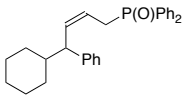
P(O)Ph2
Ph

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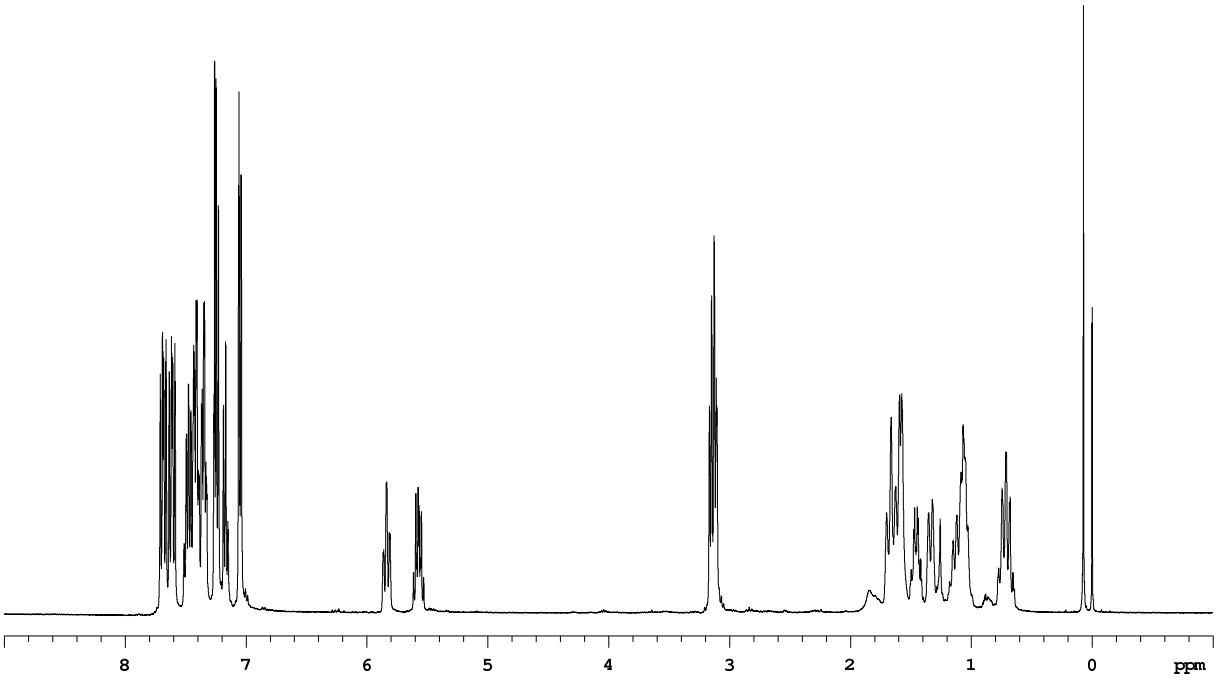
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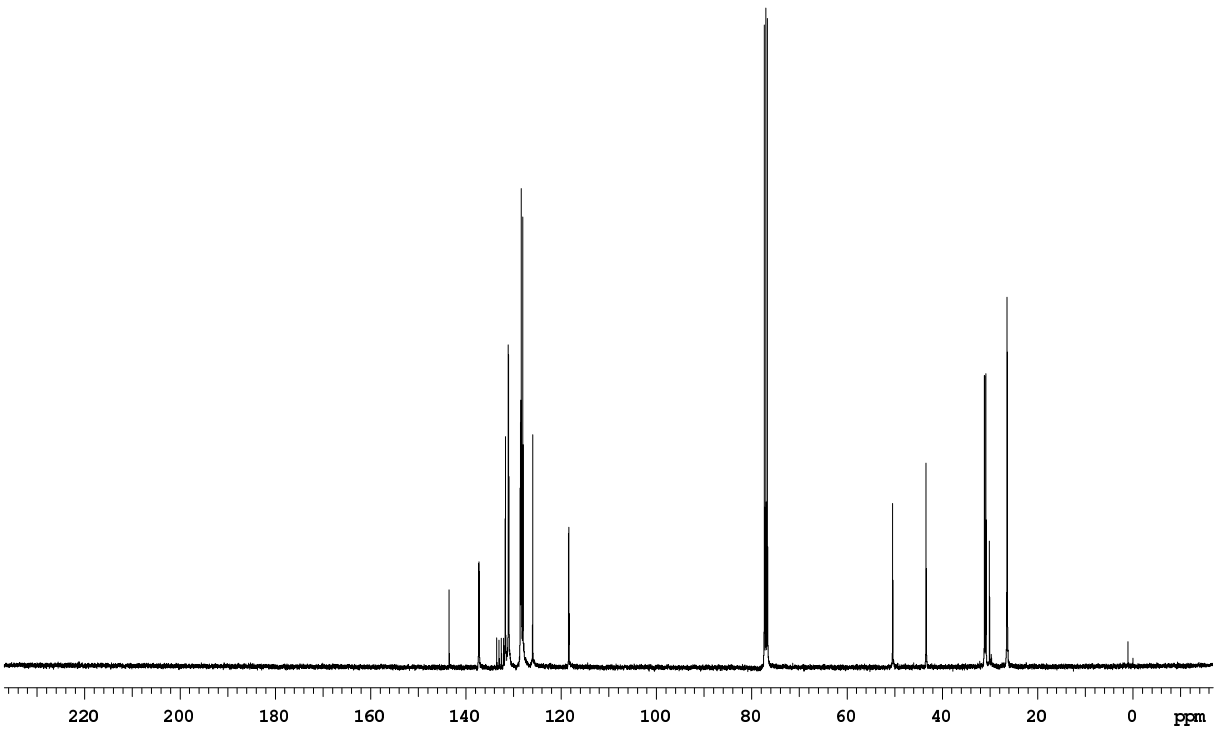
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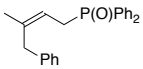
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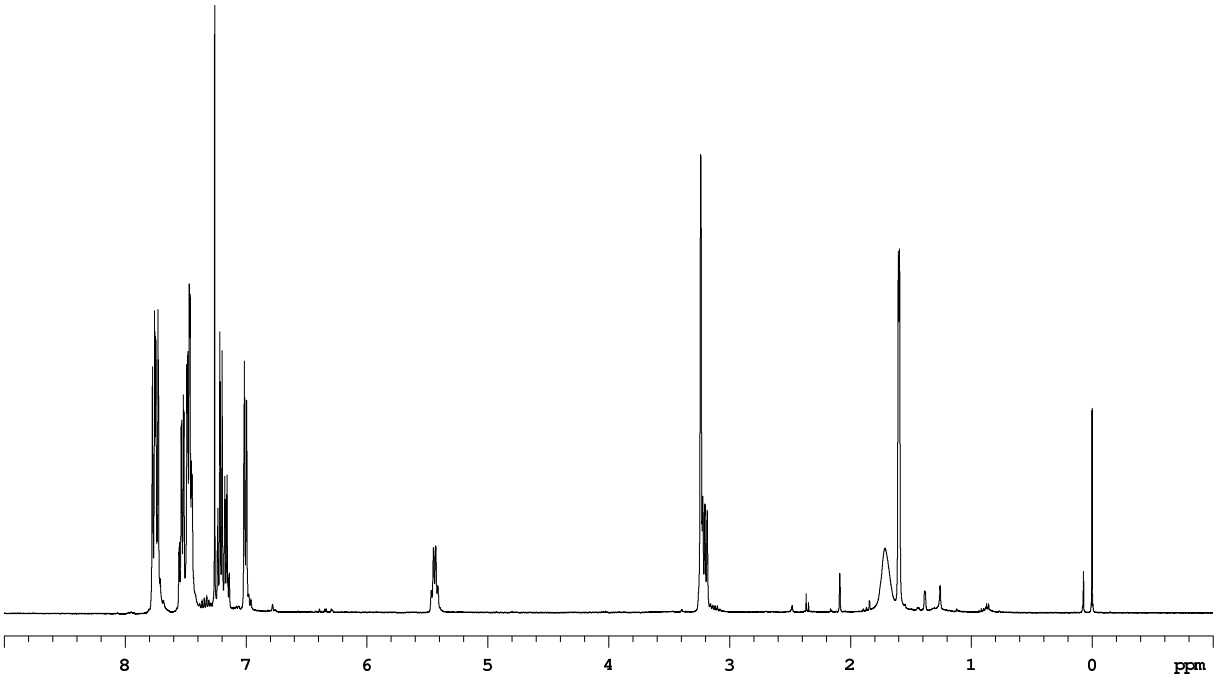
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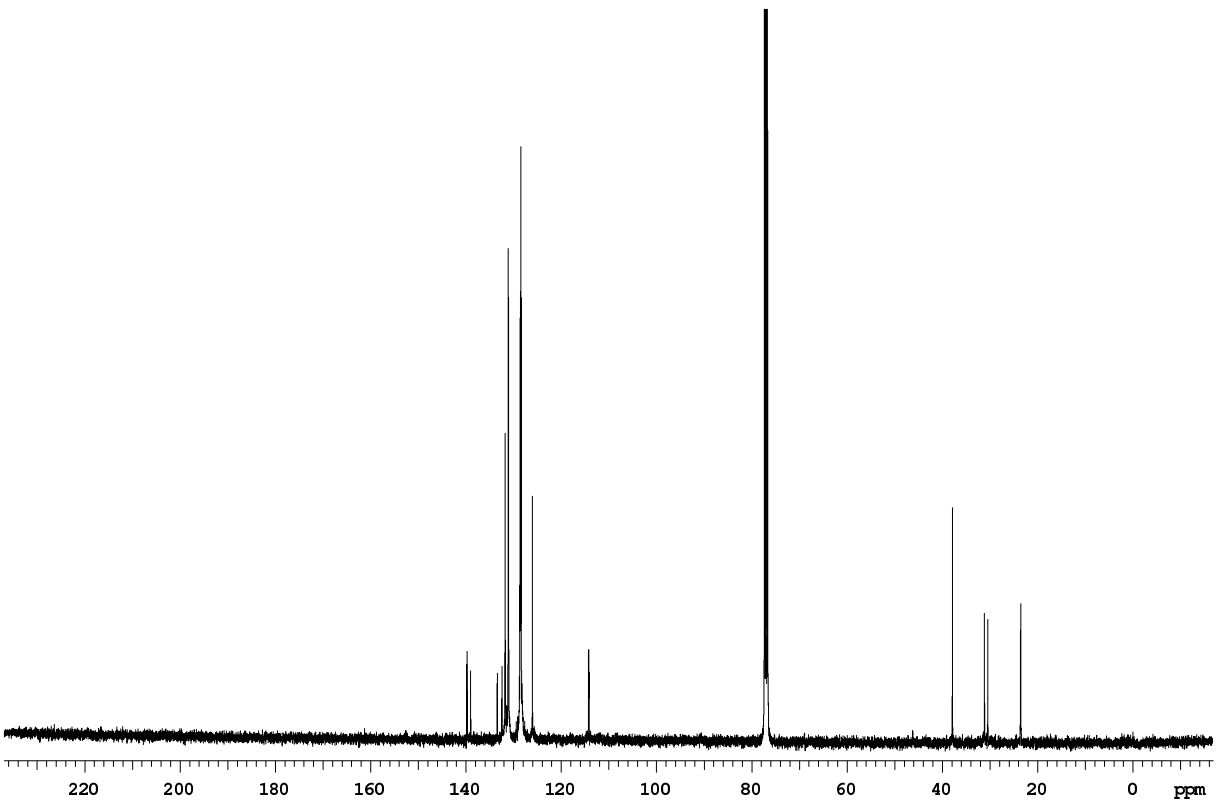
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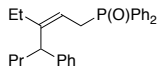
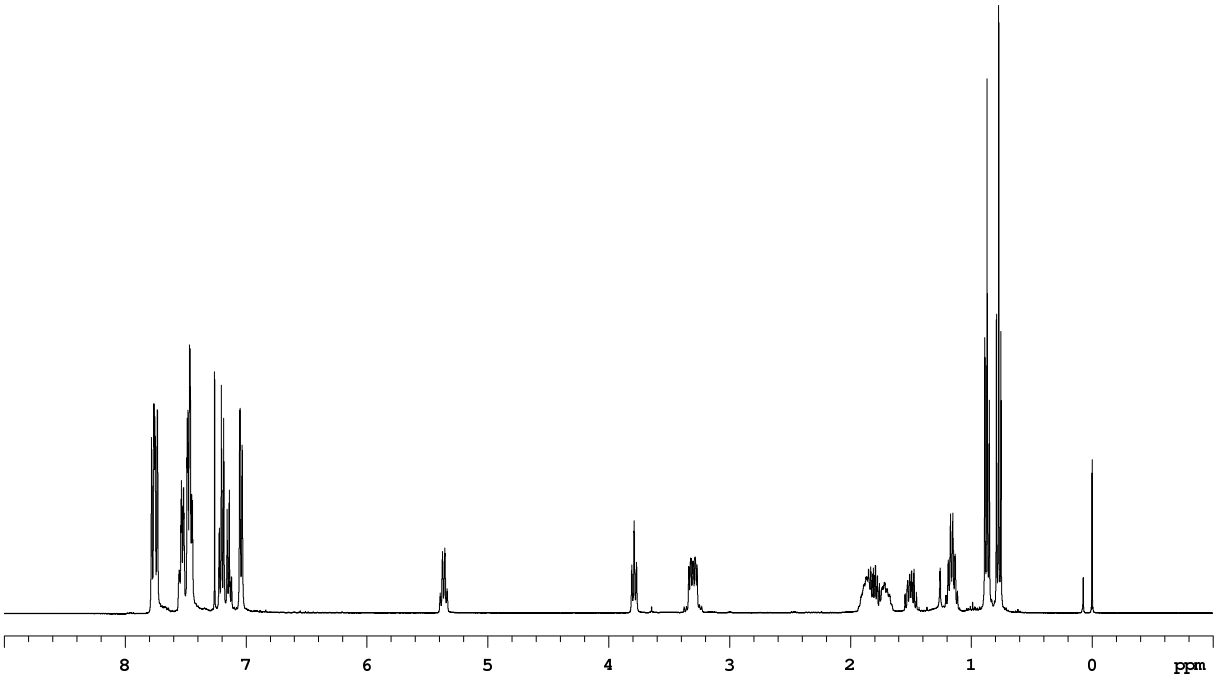

Et
P(O)Ph2
Pr
Ph

(**23**)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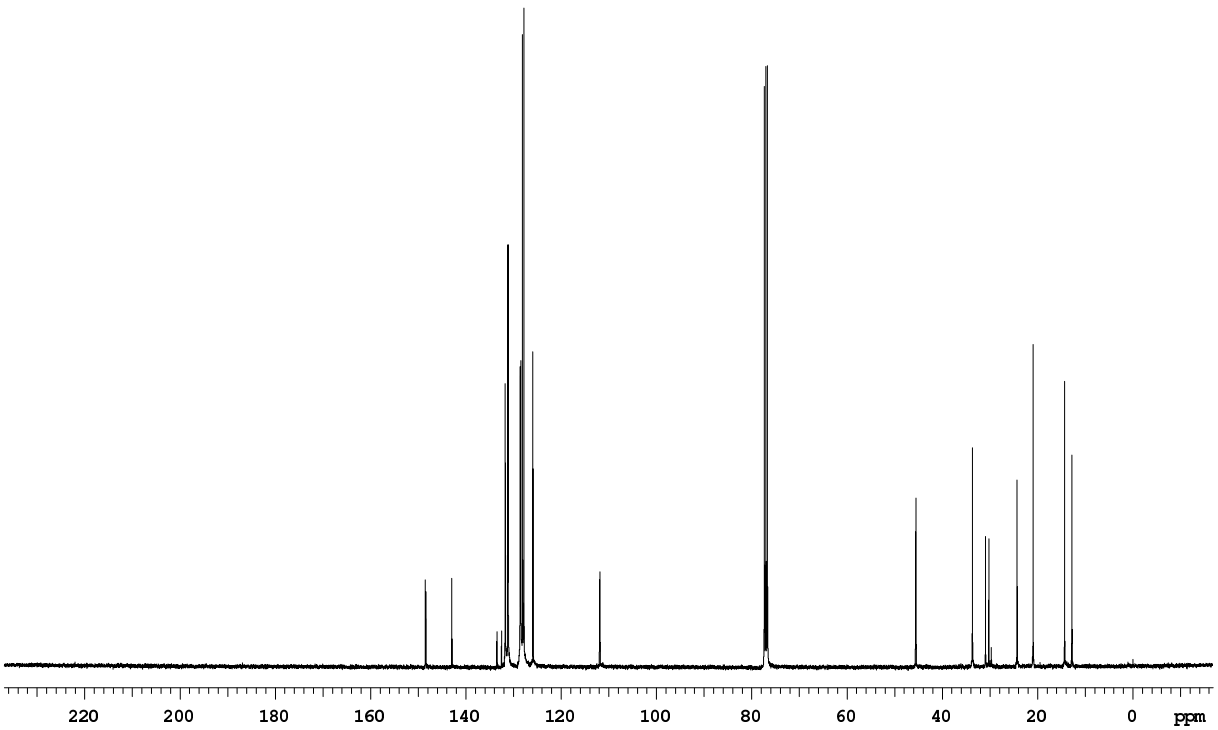
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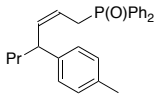
P(O)Ph2
Pr

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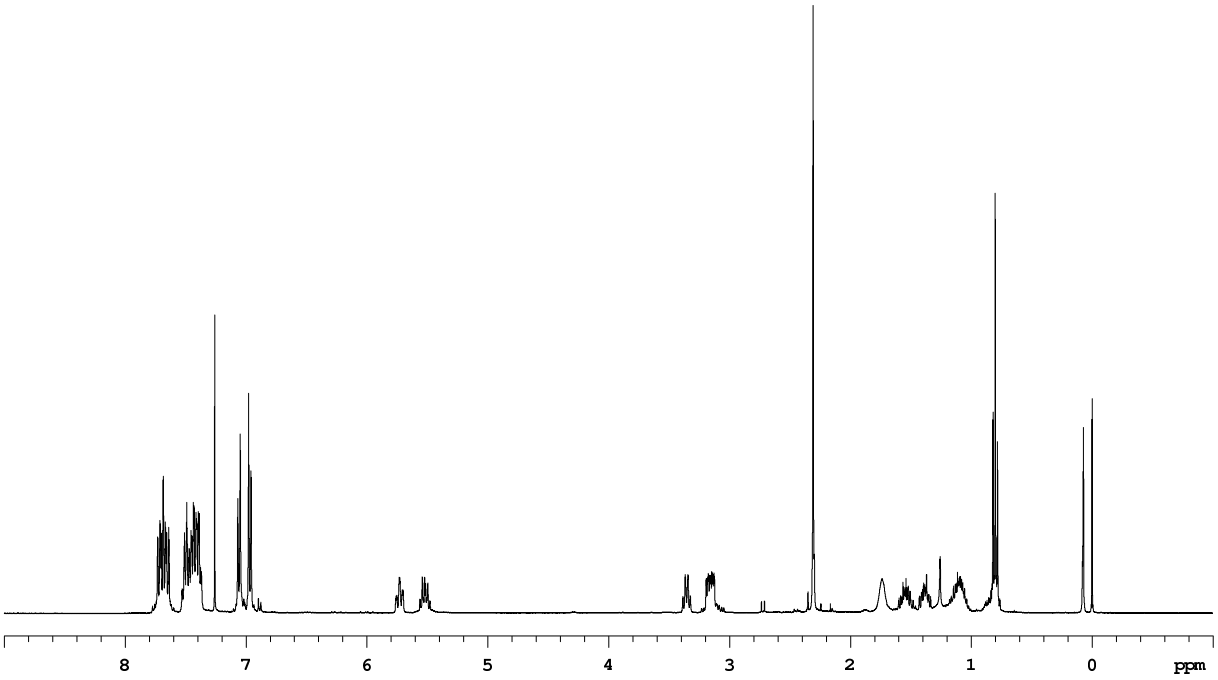
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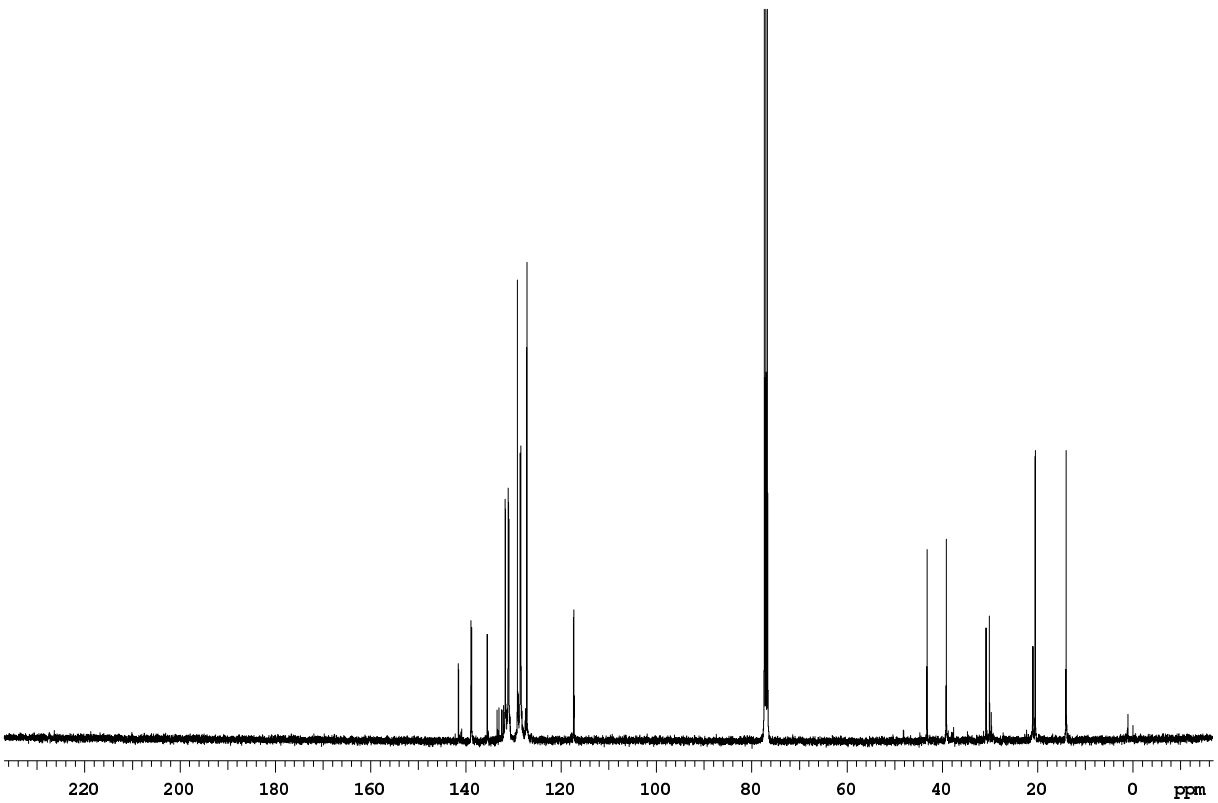
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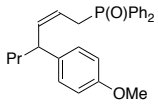
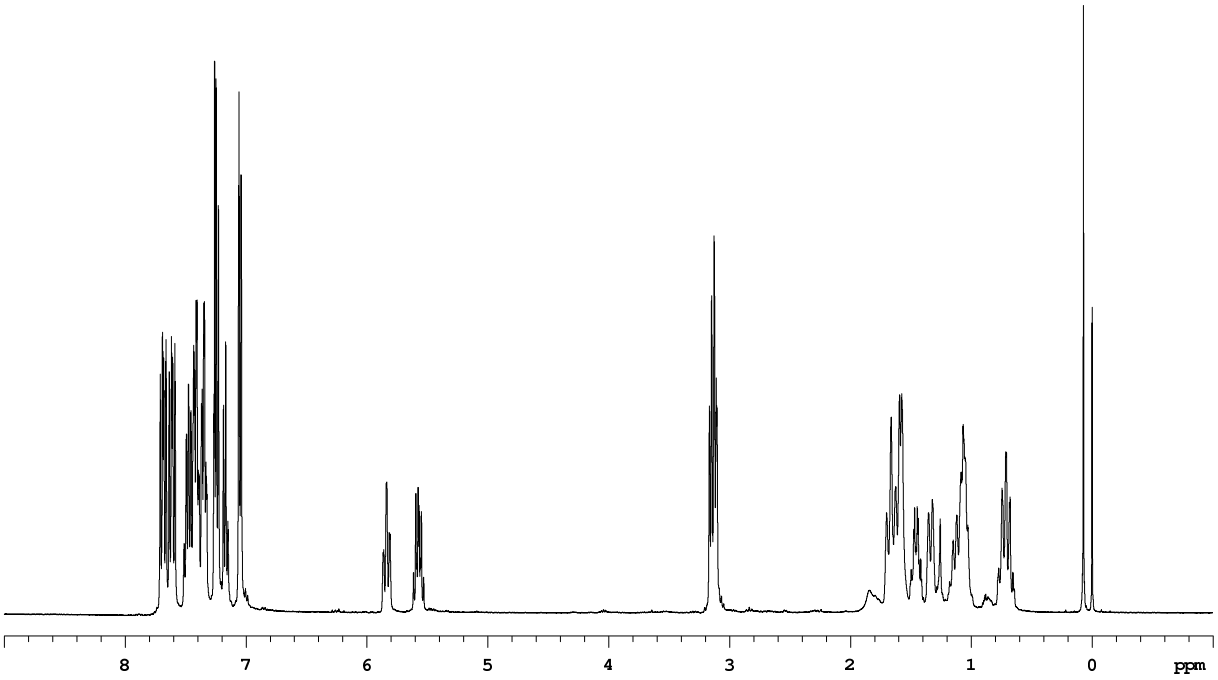

P(O)Ph2
Pr
OMe

(**25**)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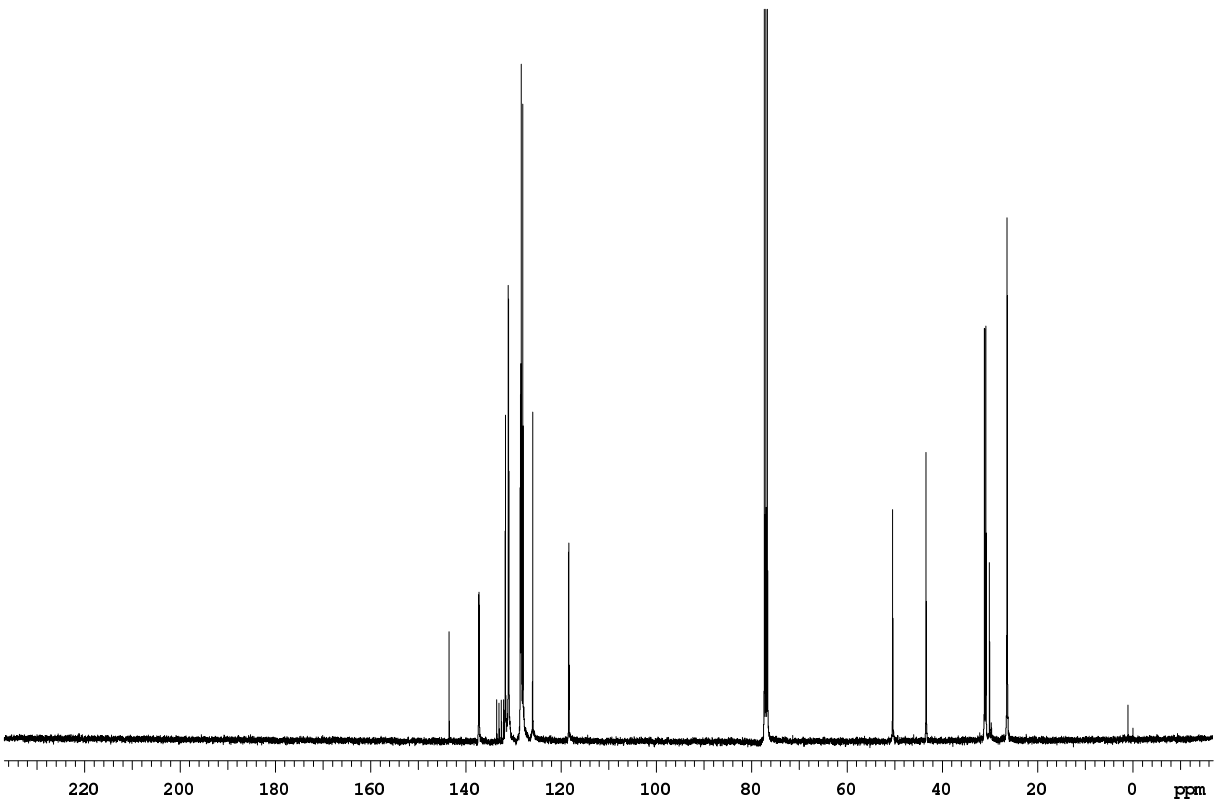
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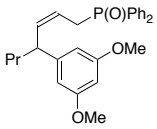
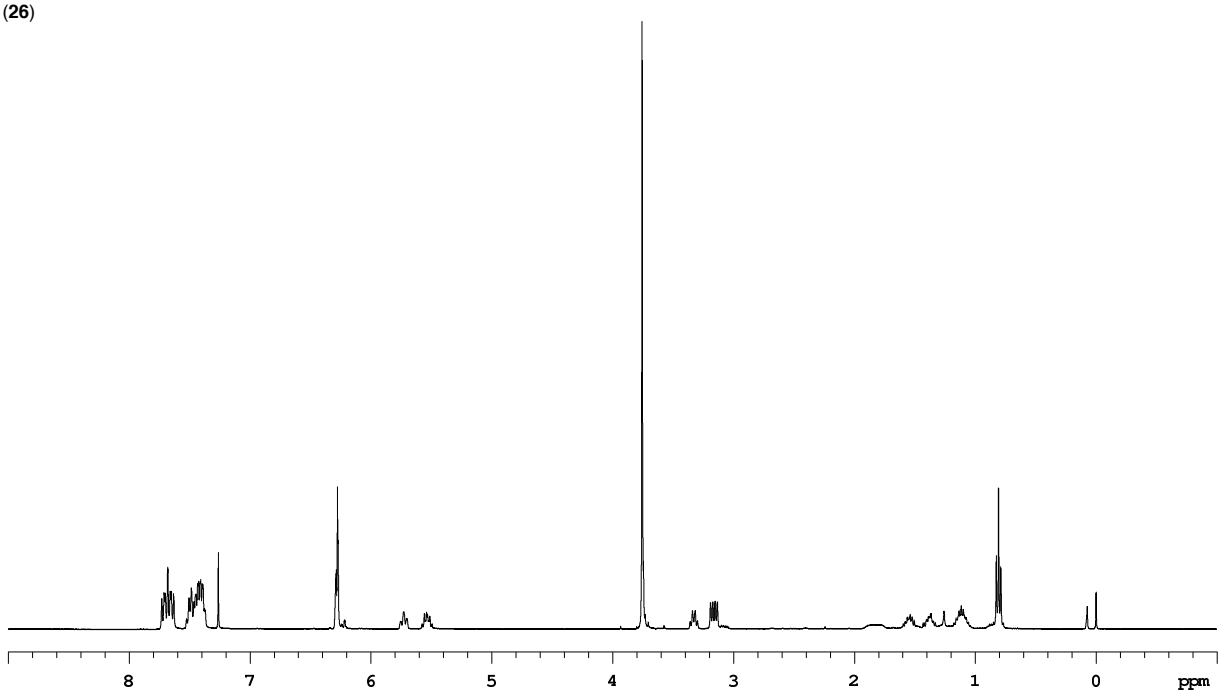

P(O)Ph2
Pr
OMe
OMe

(**26**)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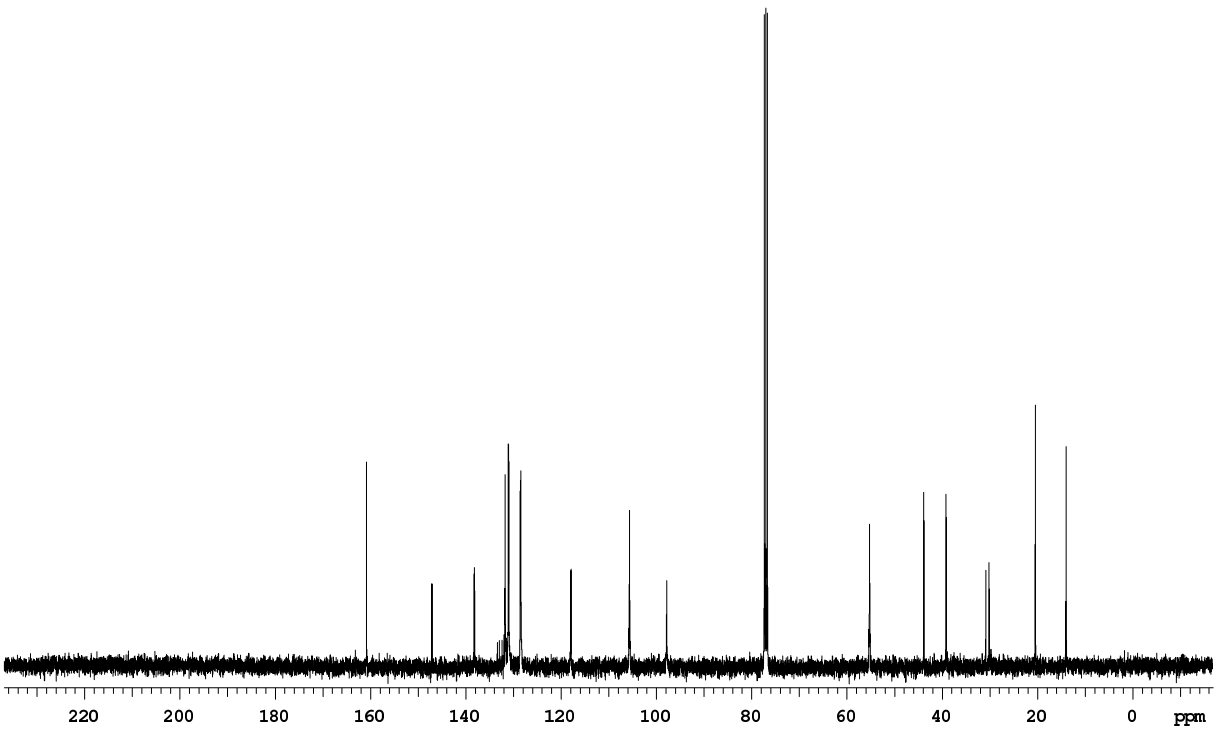
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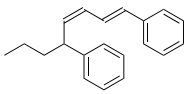

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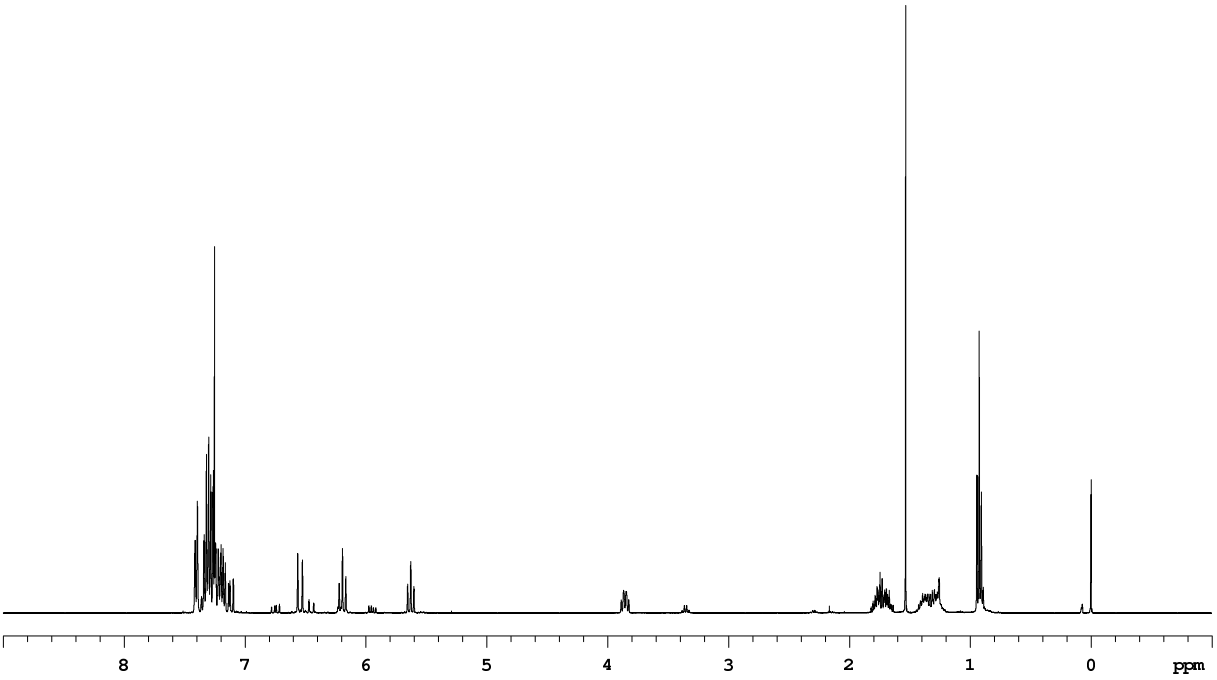

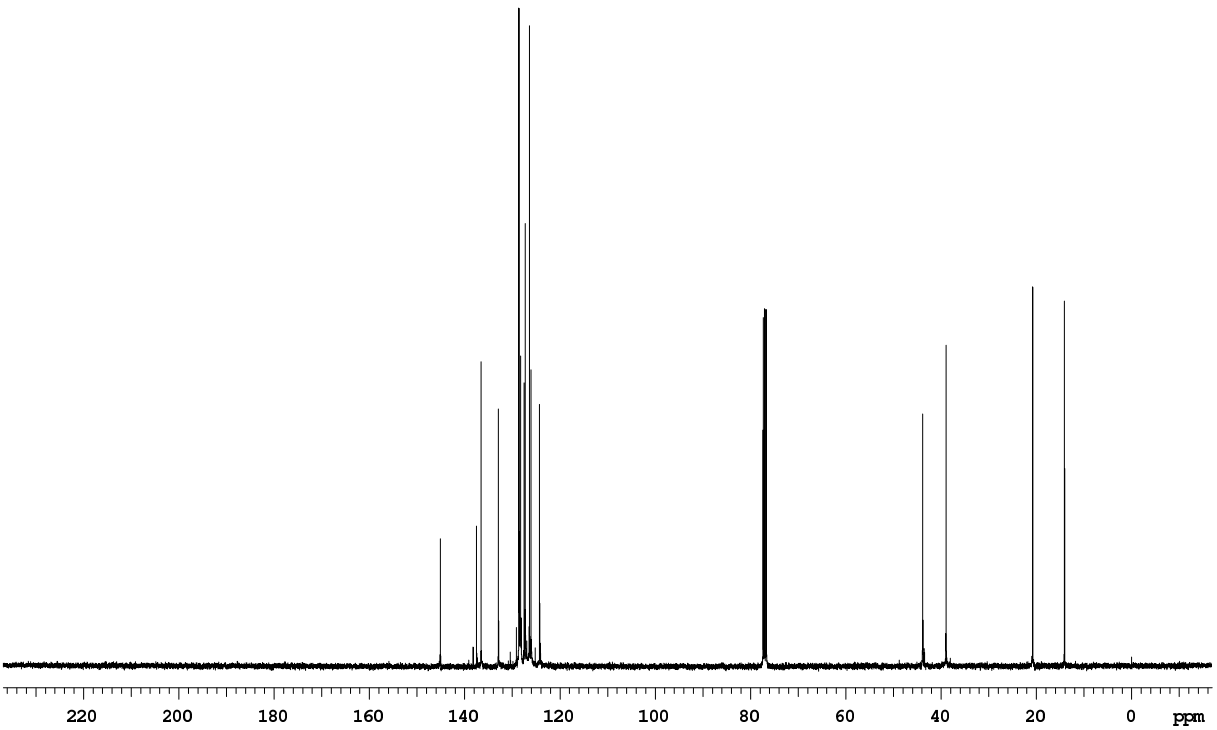

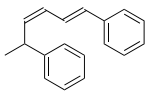

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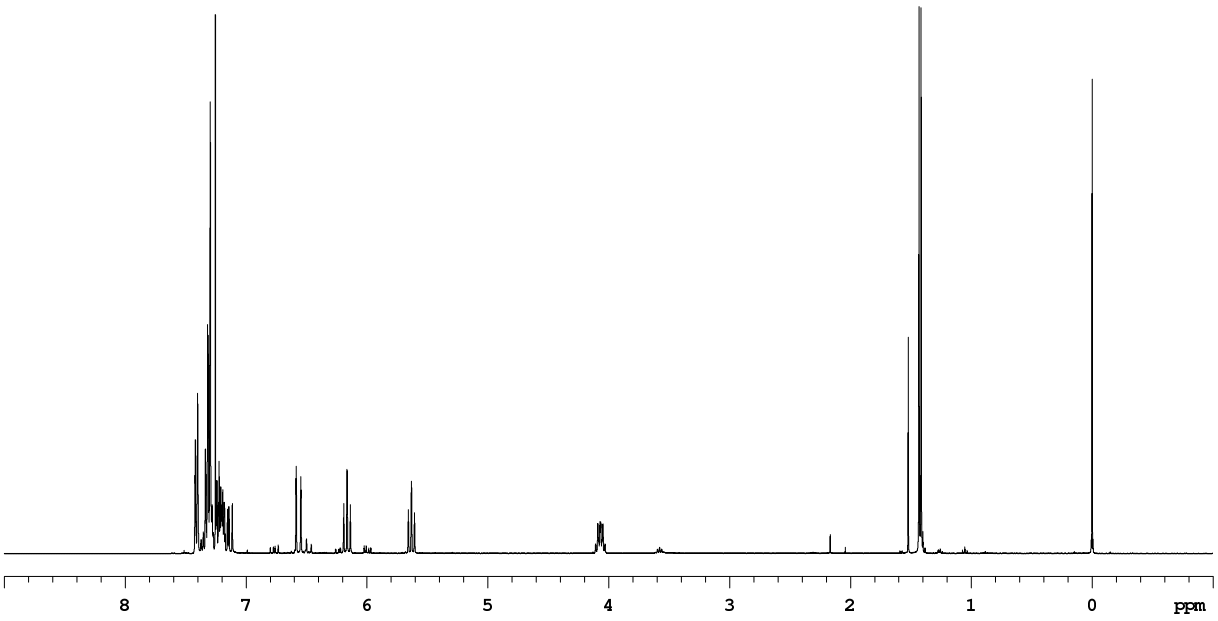

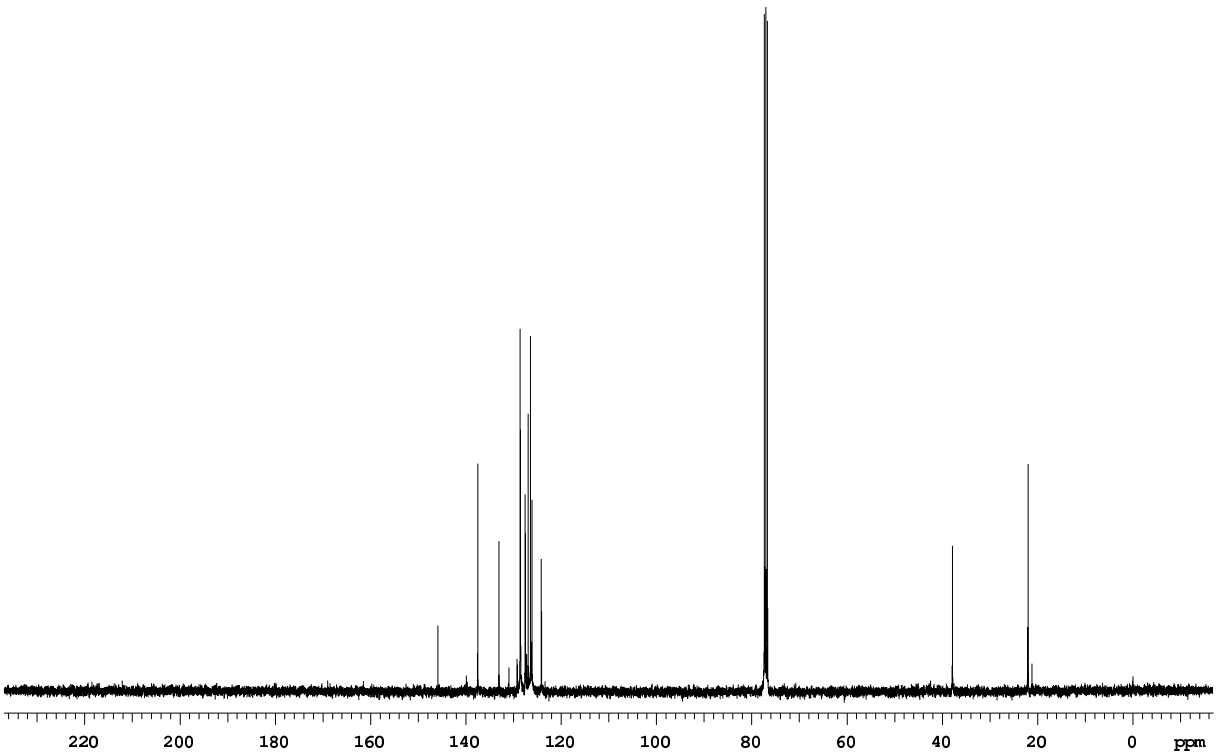

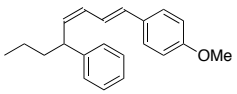

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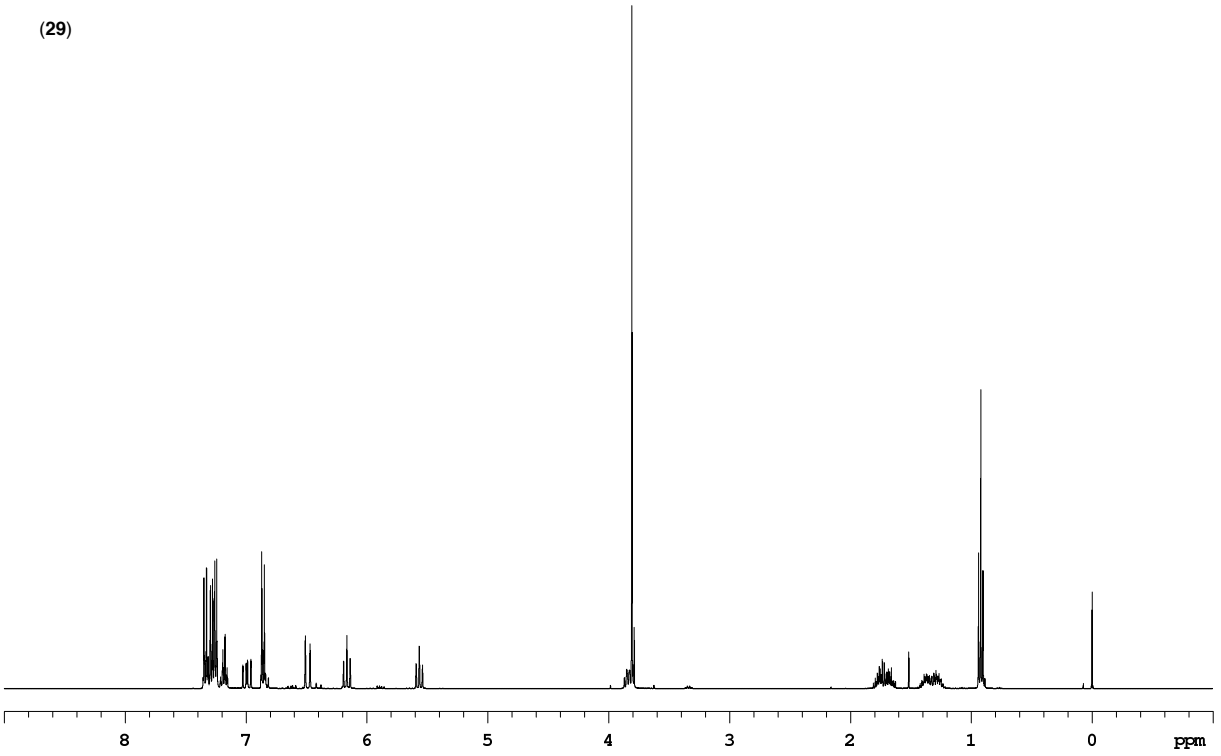

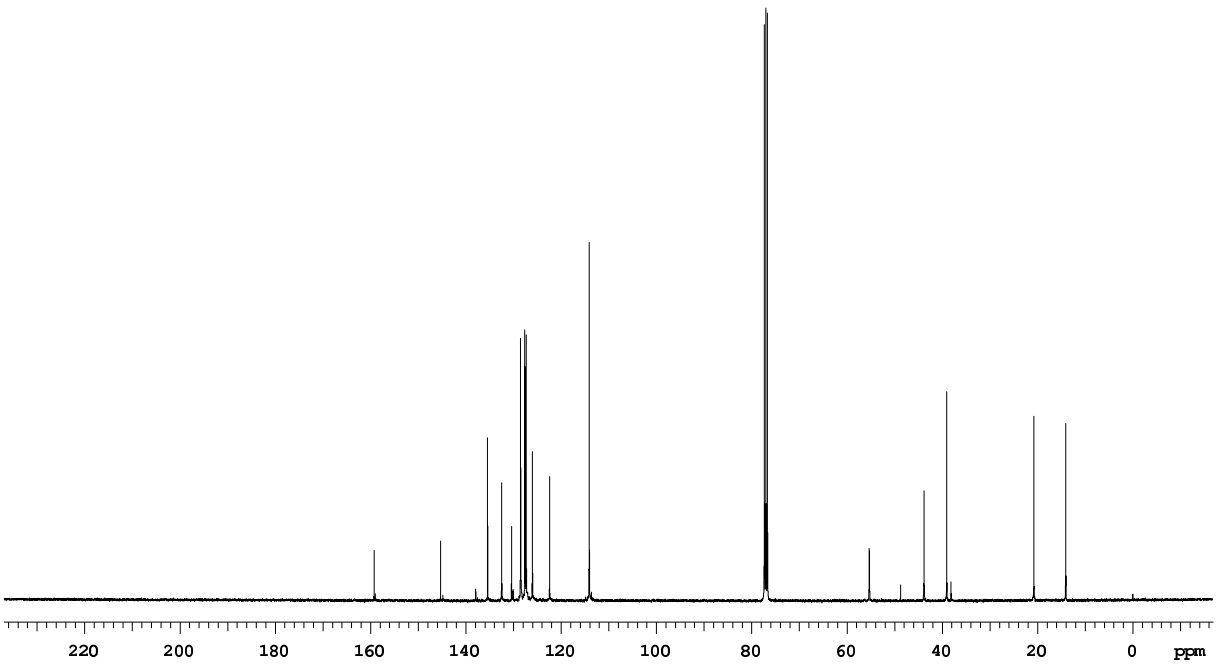

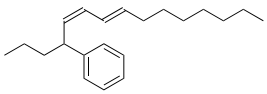

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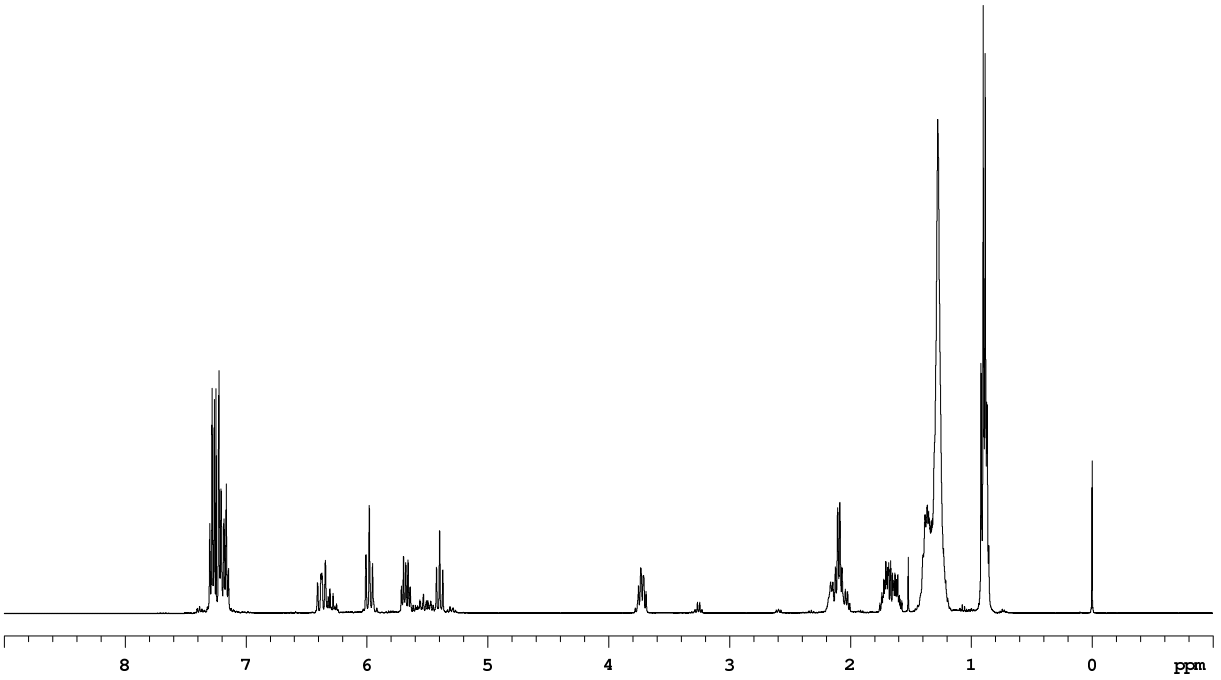
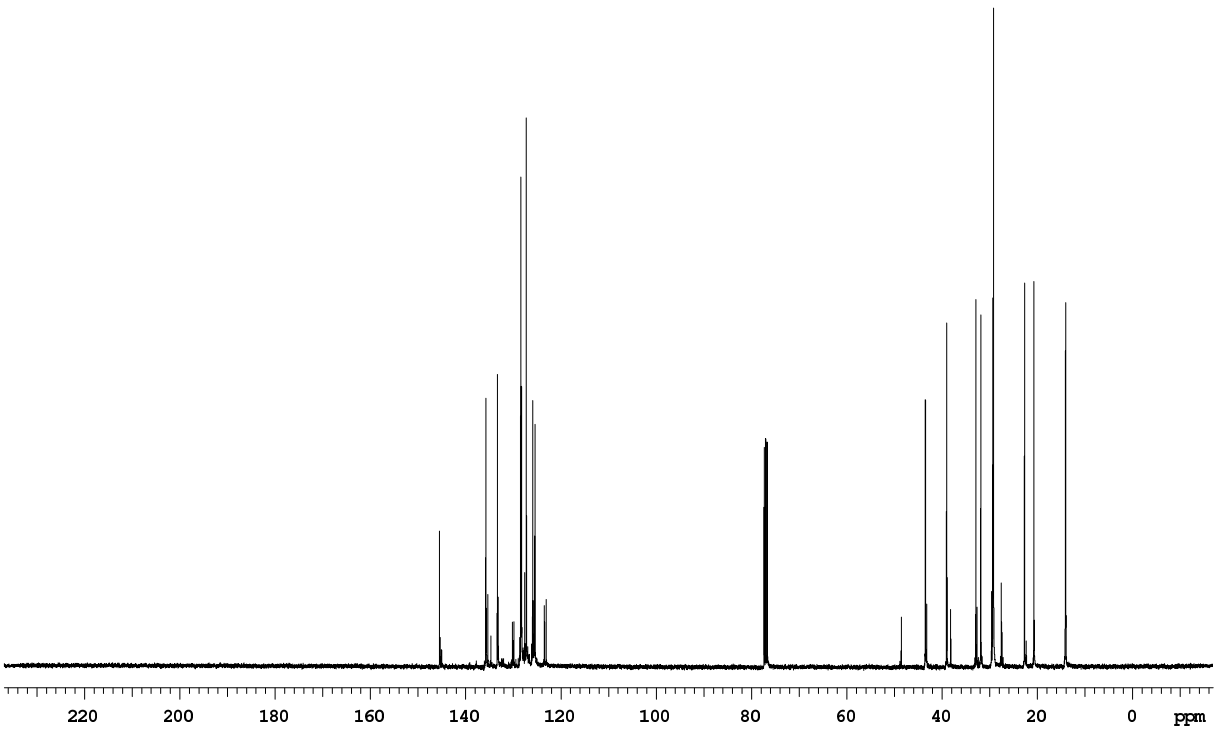
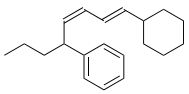
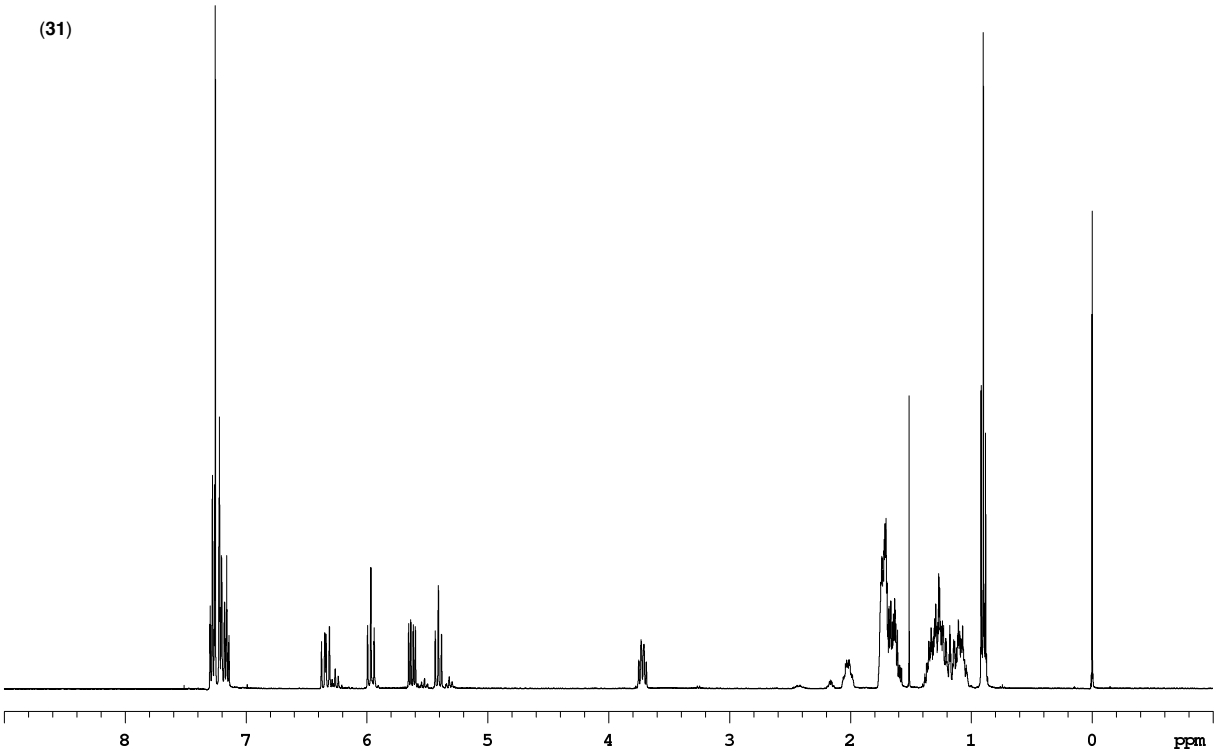
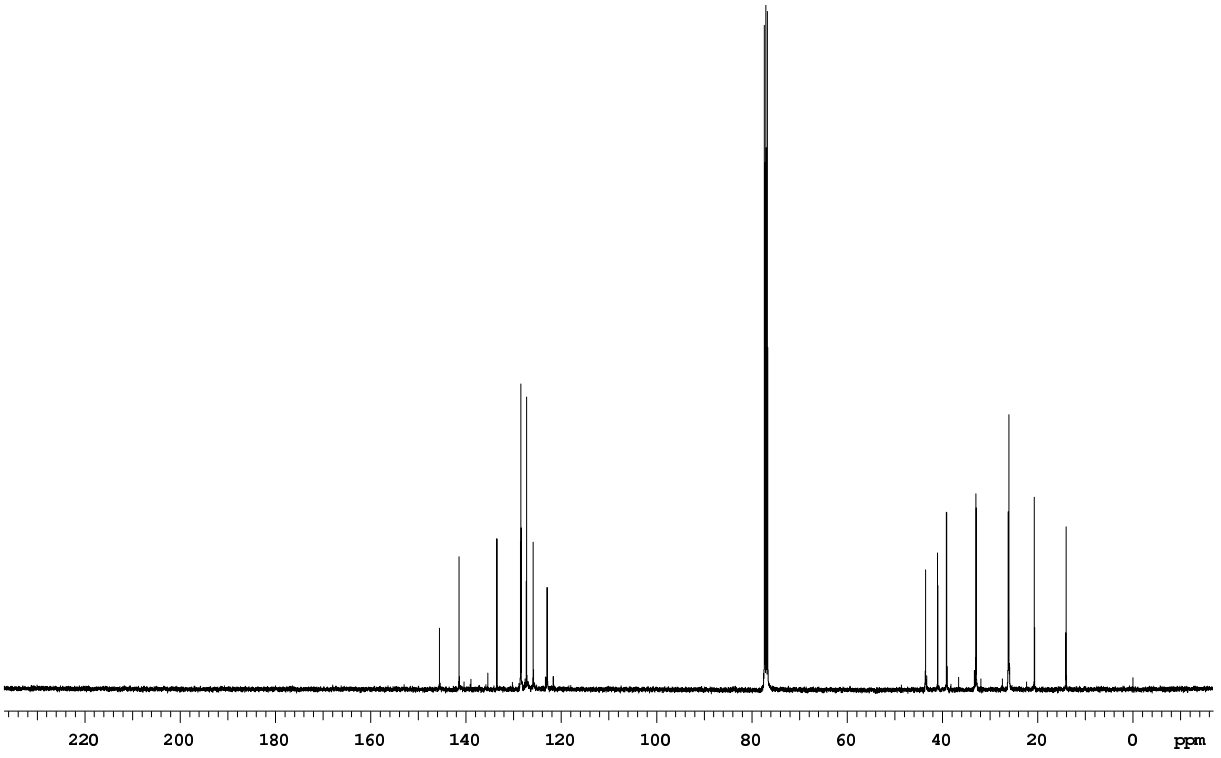


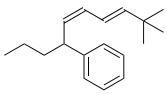




(**31**)







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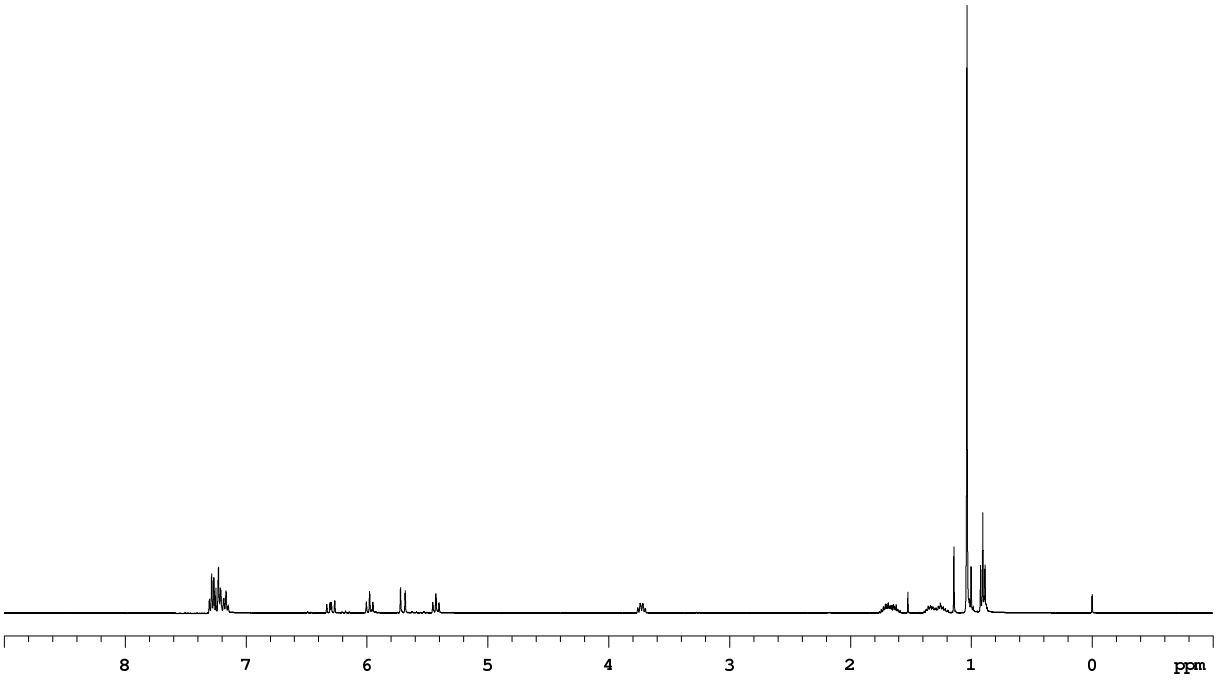
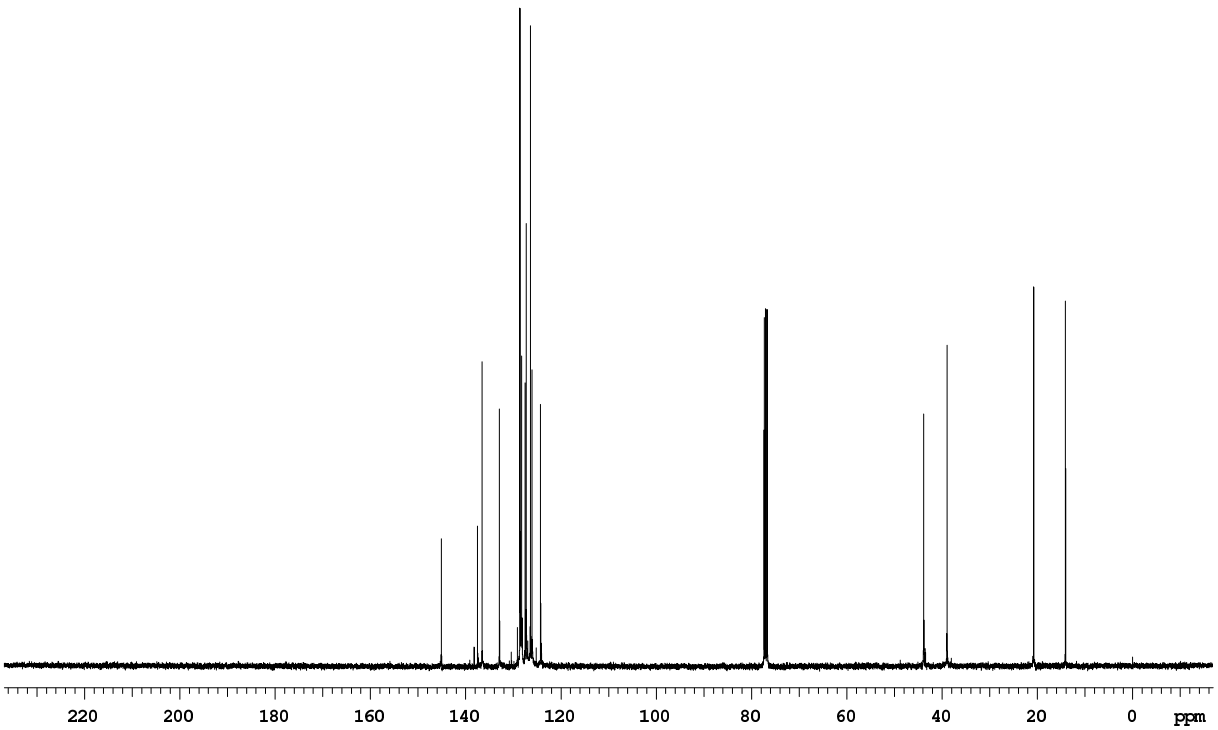
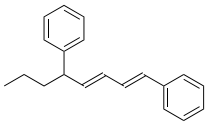
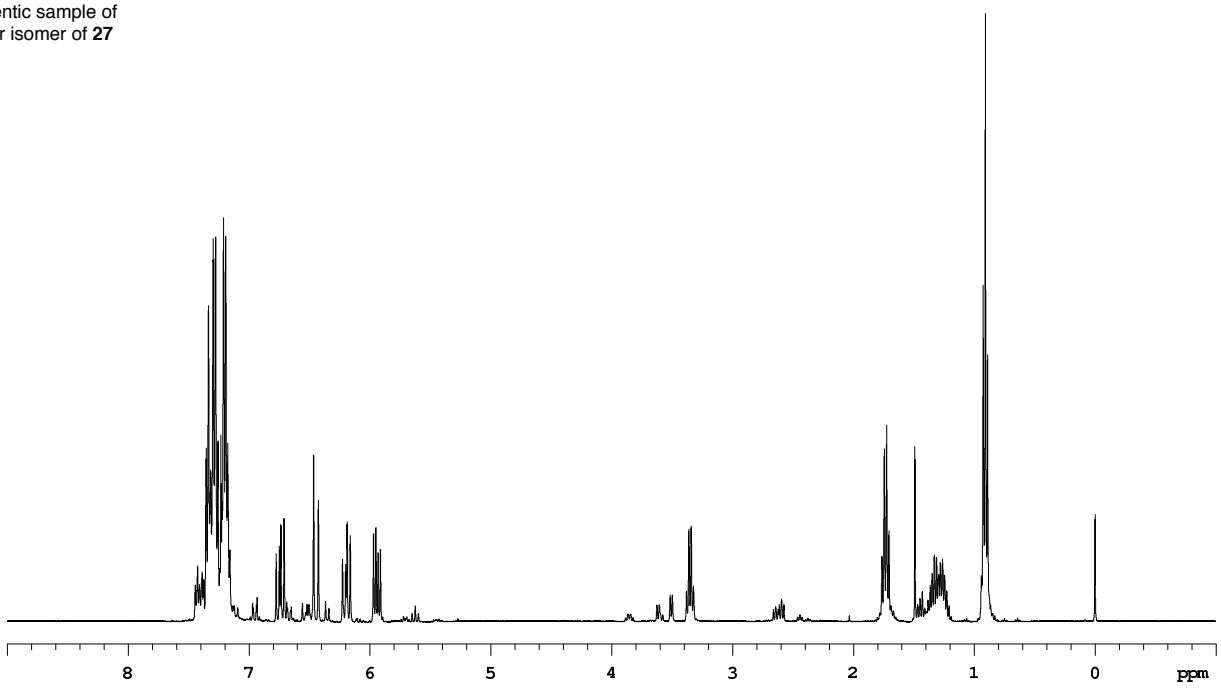
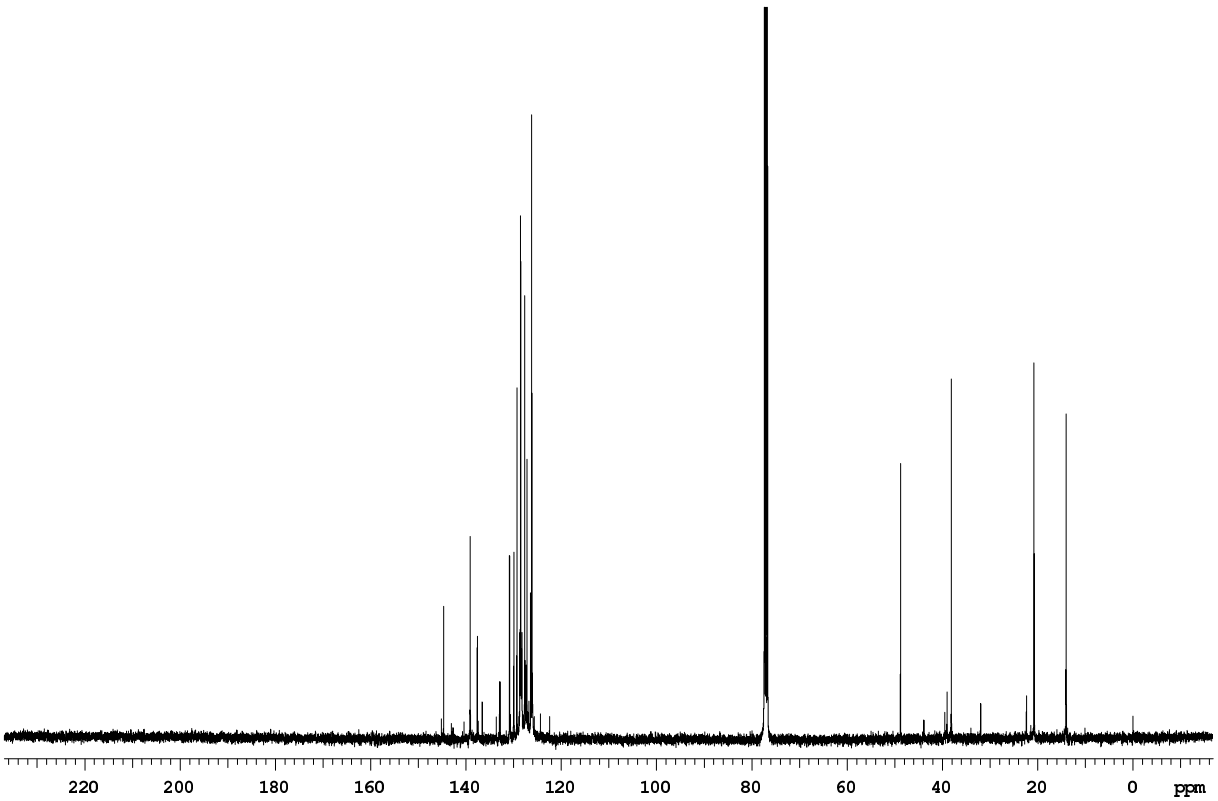


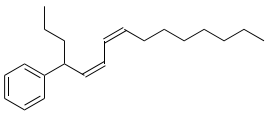




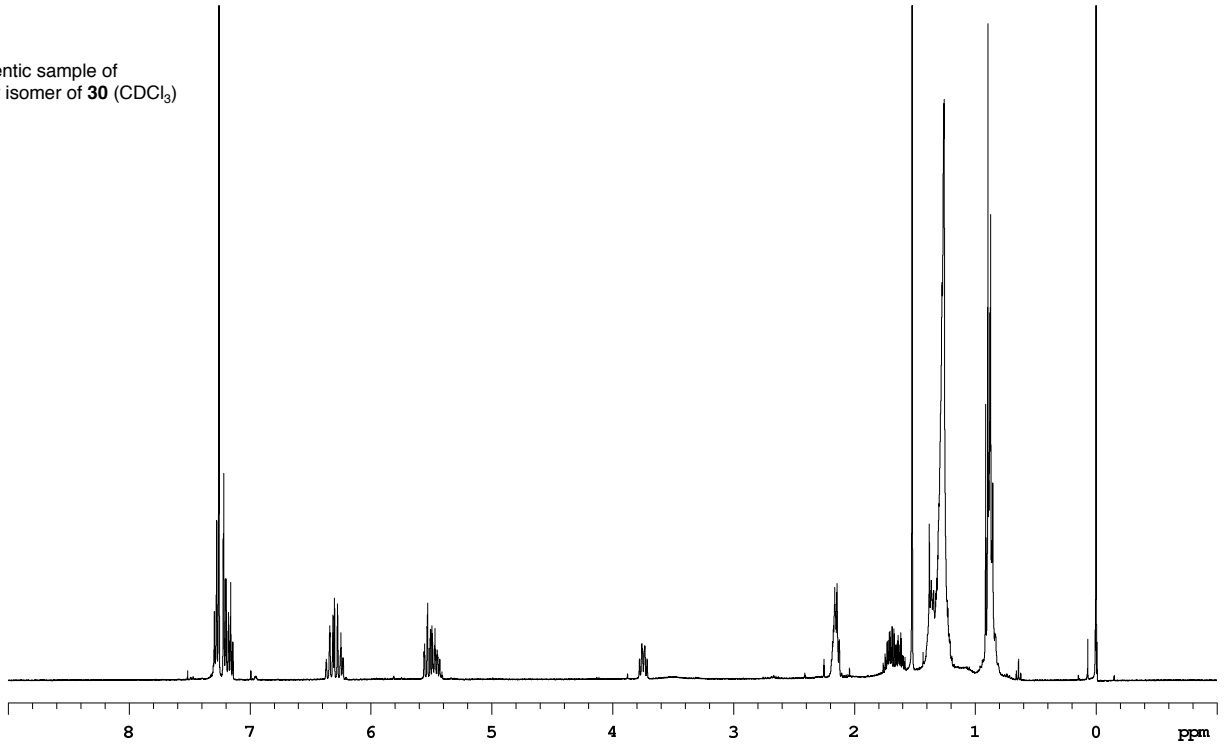
Authentic sample of
minor isomer of **27**

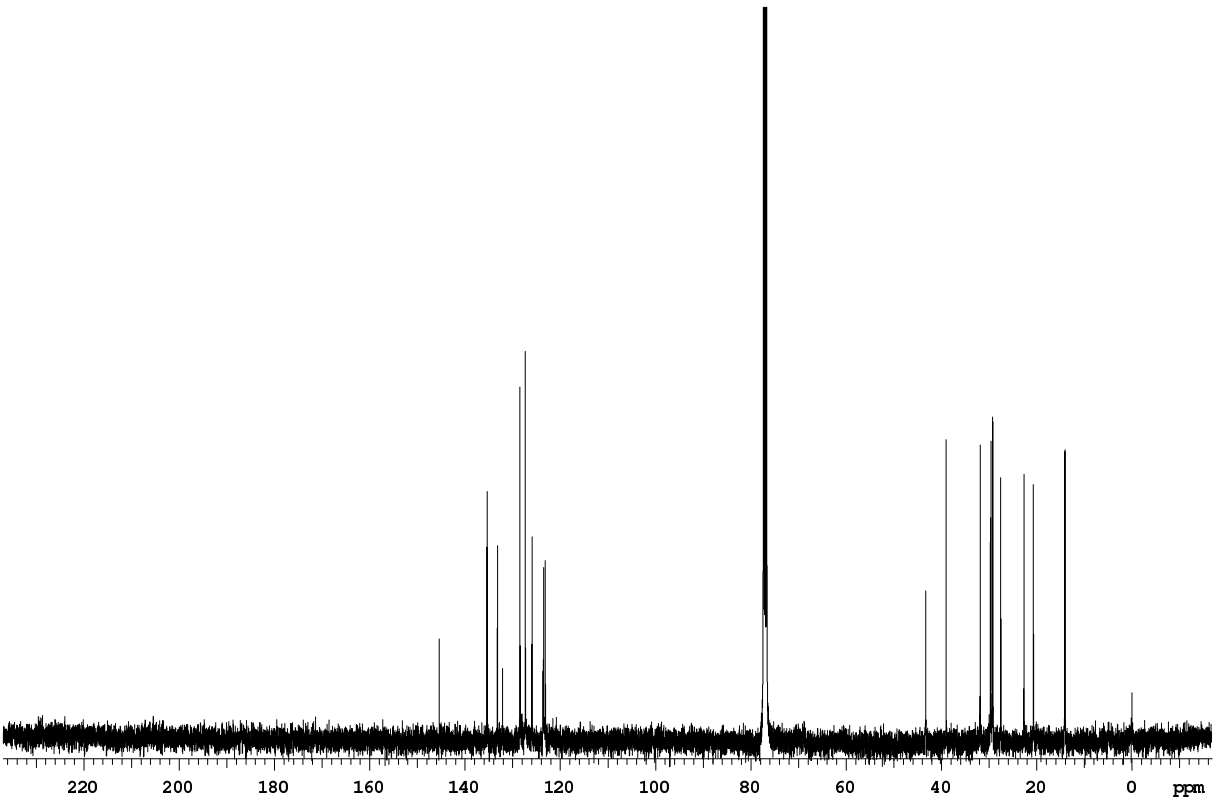


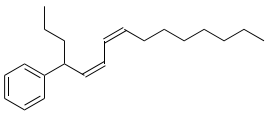




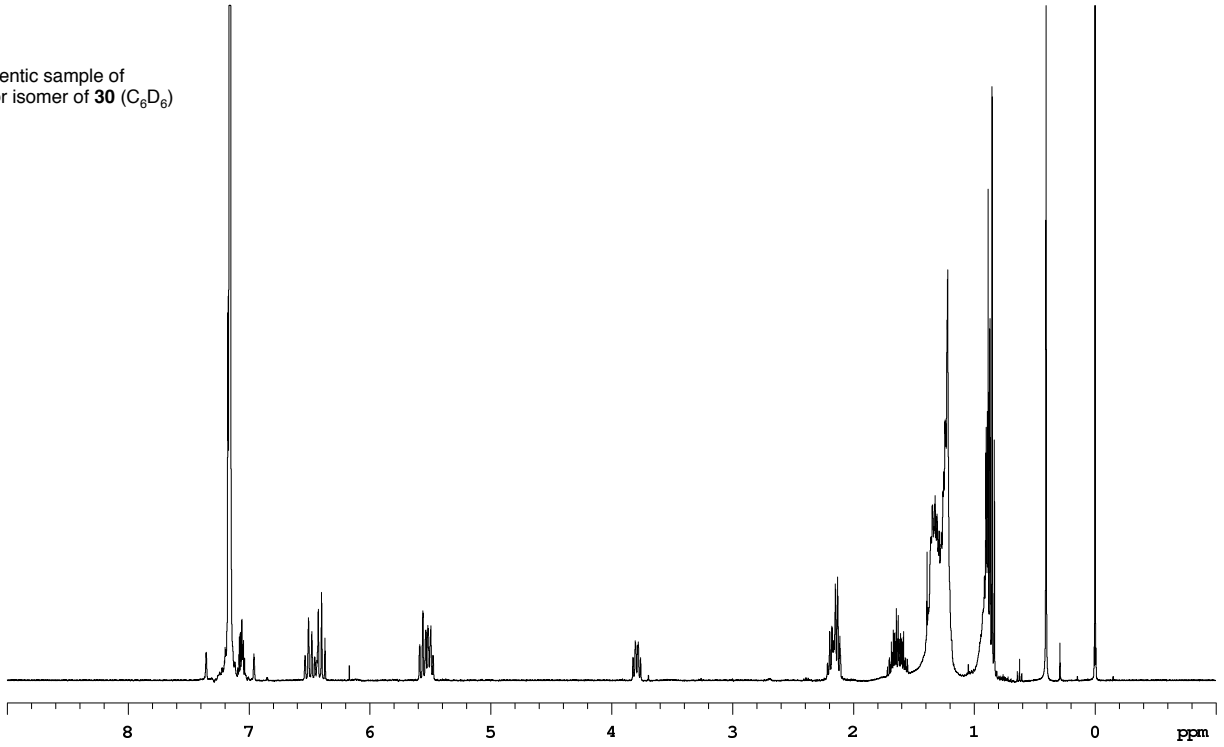
Authentic sample of
minor isomer of **30** ($CDCl_3$)





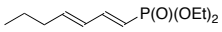


Authentic sample of
minor isomer of **30** (C_6D_6)

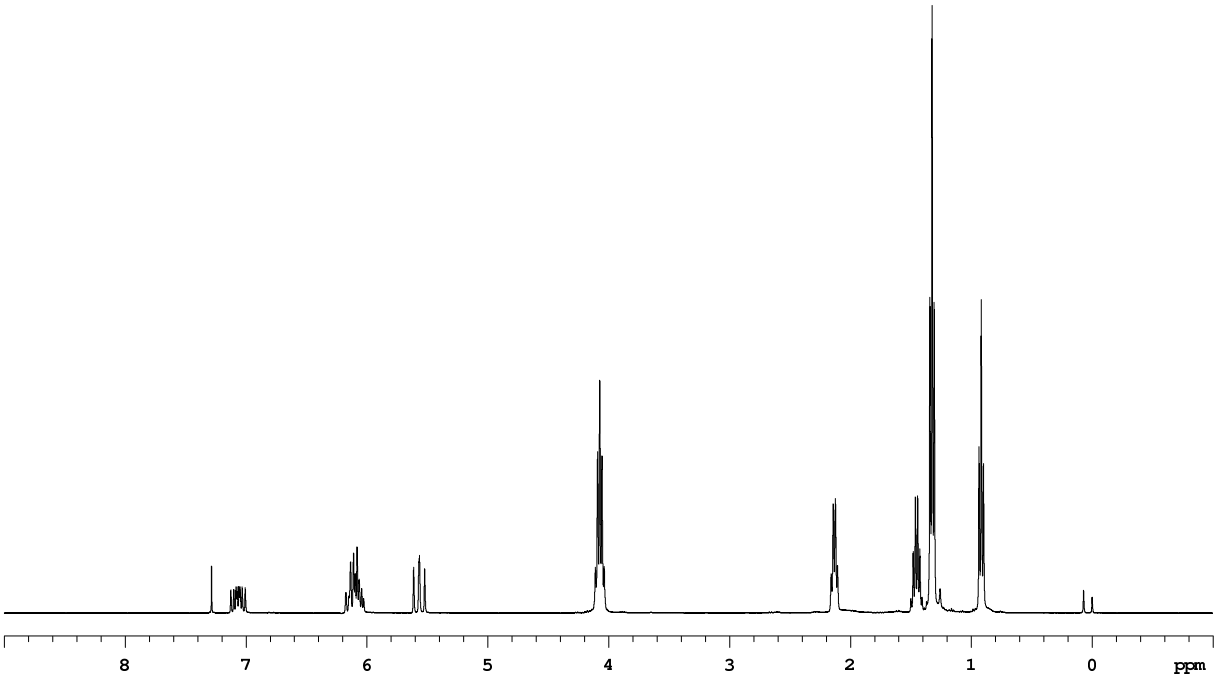


Chapter 4. Supporting Information

Iron-catalyzed Selective δ-Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Phosphonates and Its Synthetic Application


P(O)(OEt)2

(**9**)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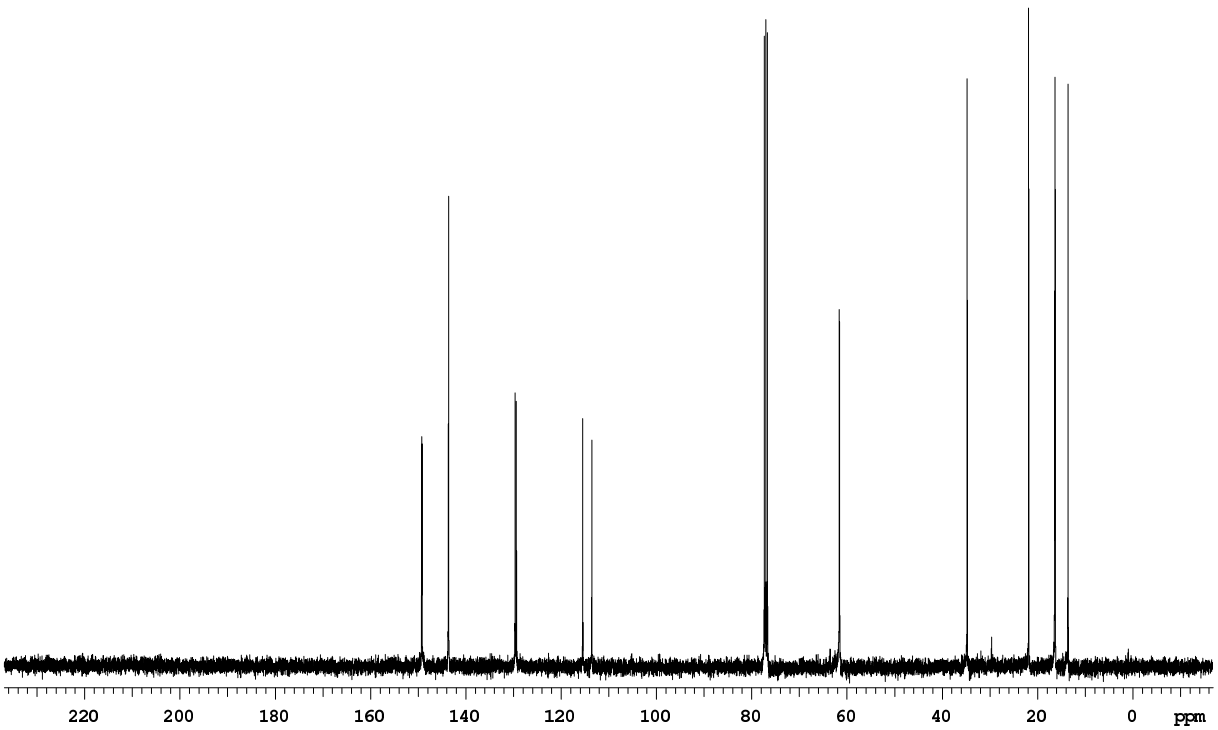
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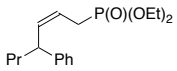
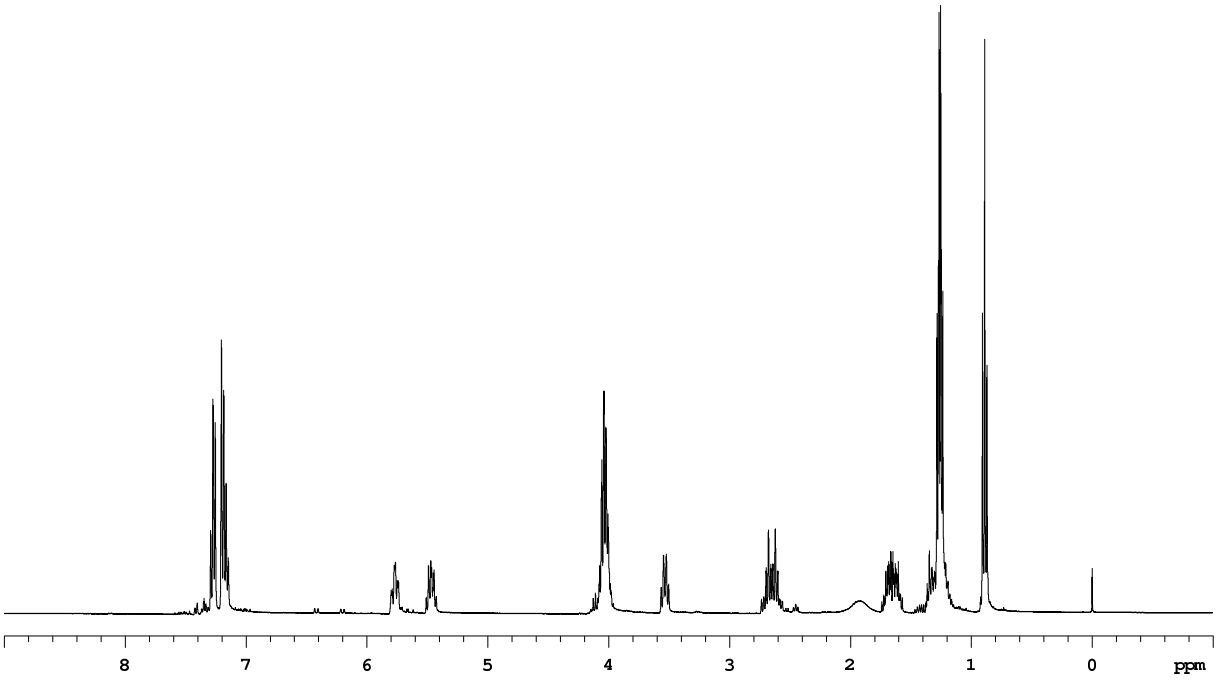

P(O)(OEt)2
Pr
Ph

(**11**)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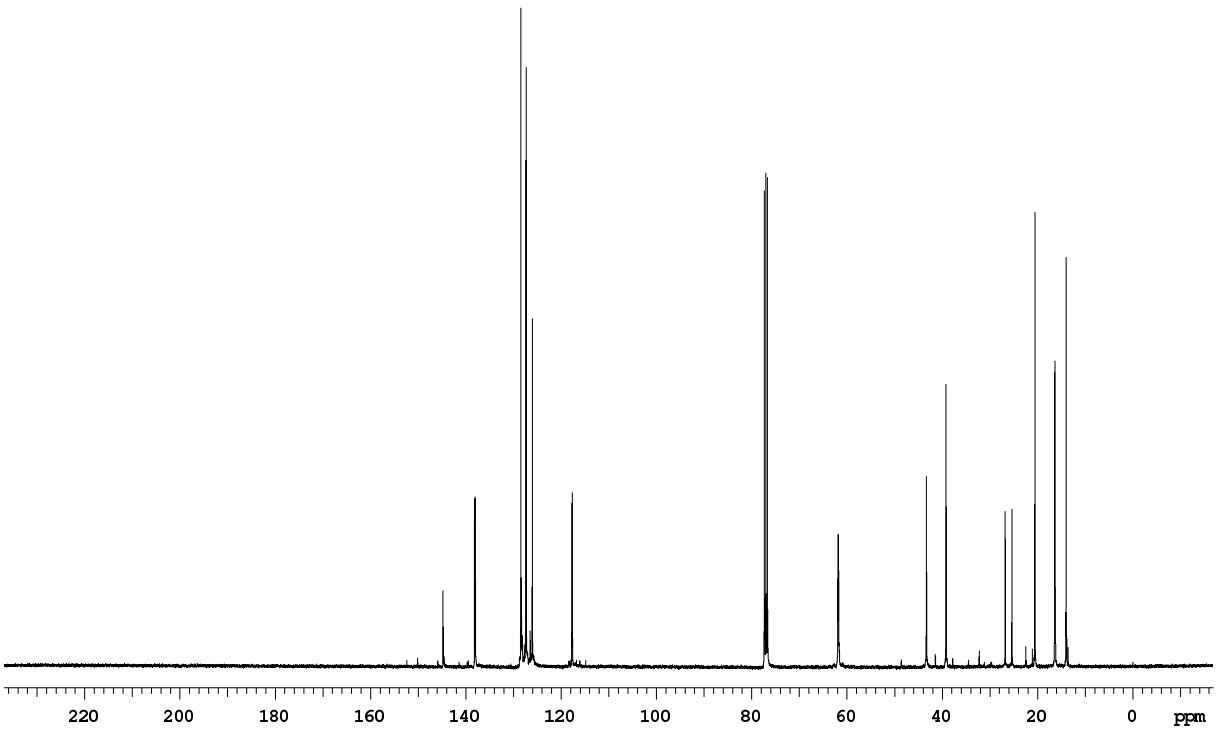
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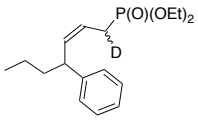
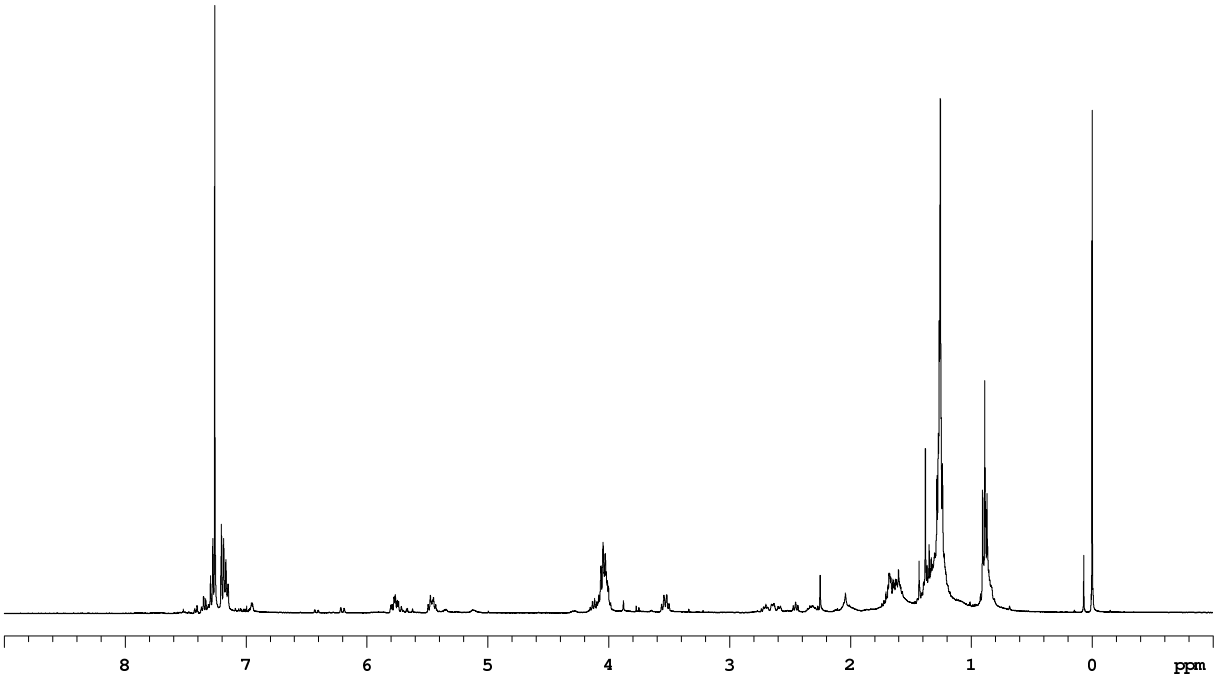
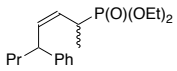


(**11-*d*$_1$**)

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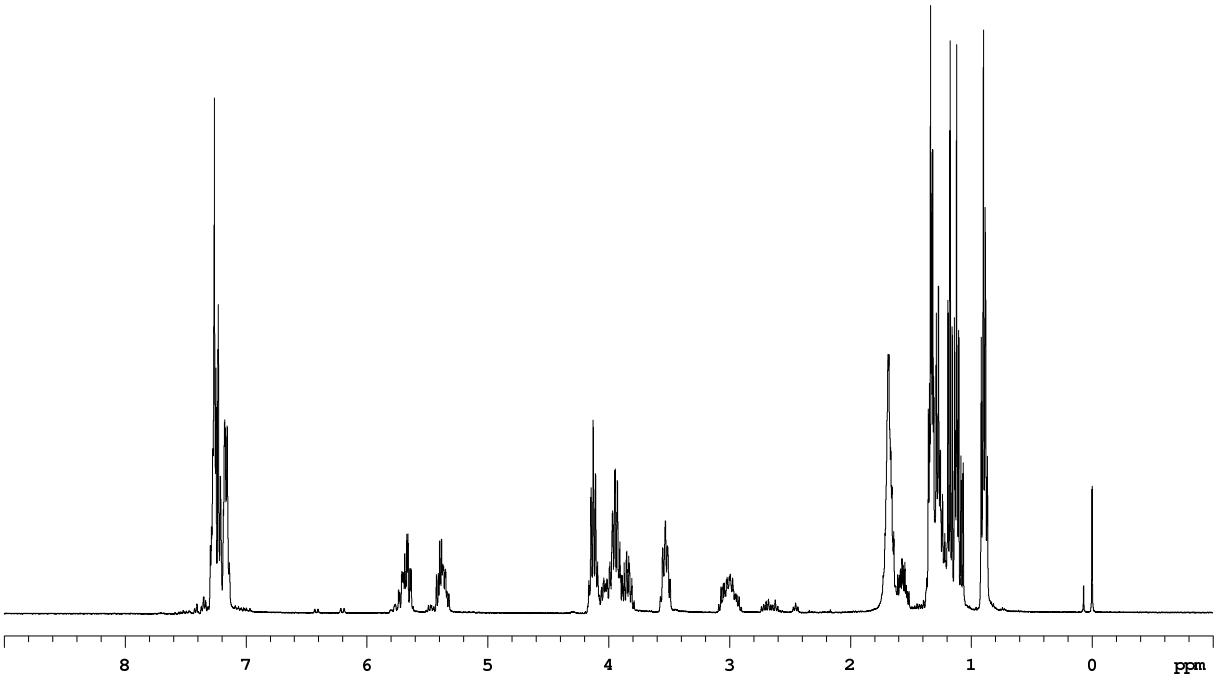
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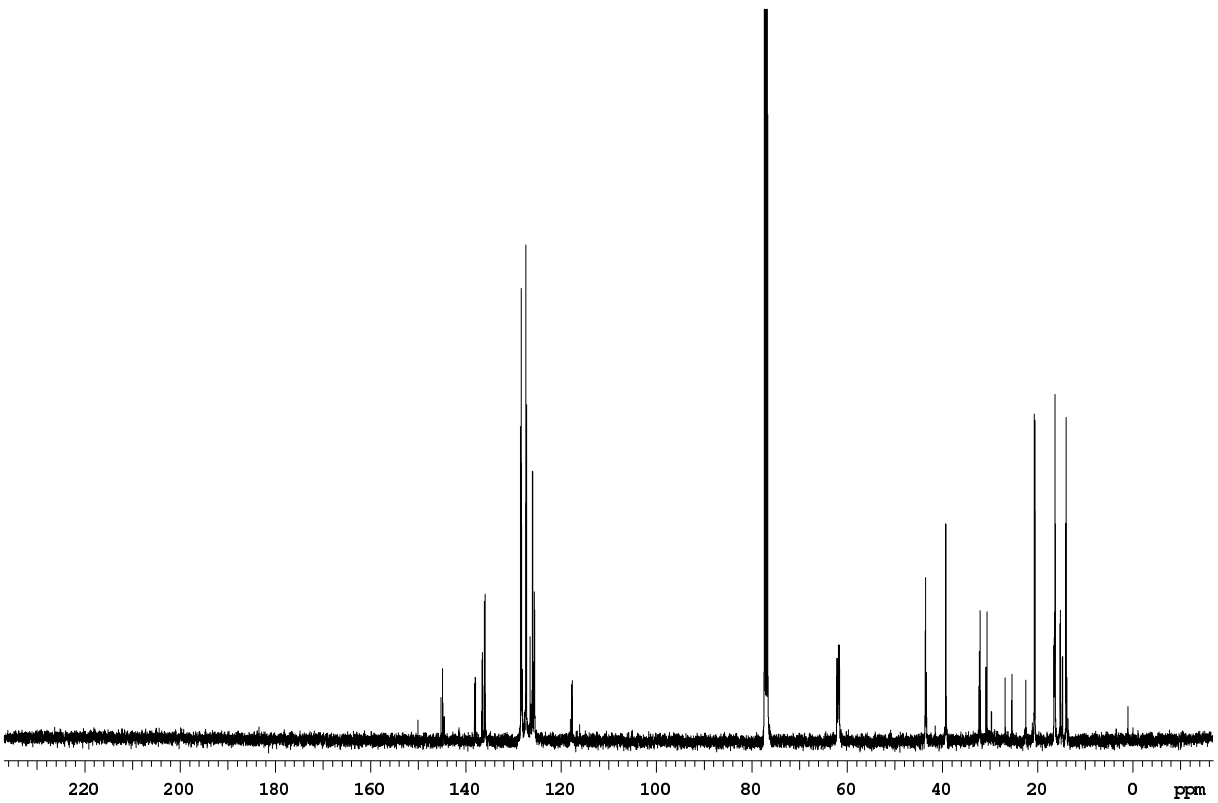
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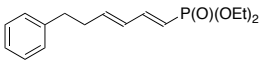
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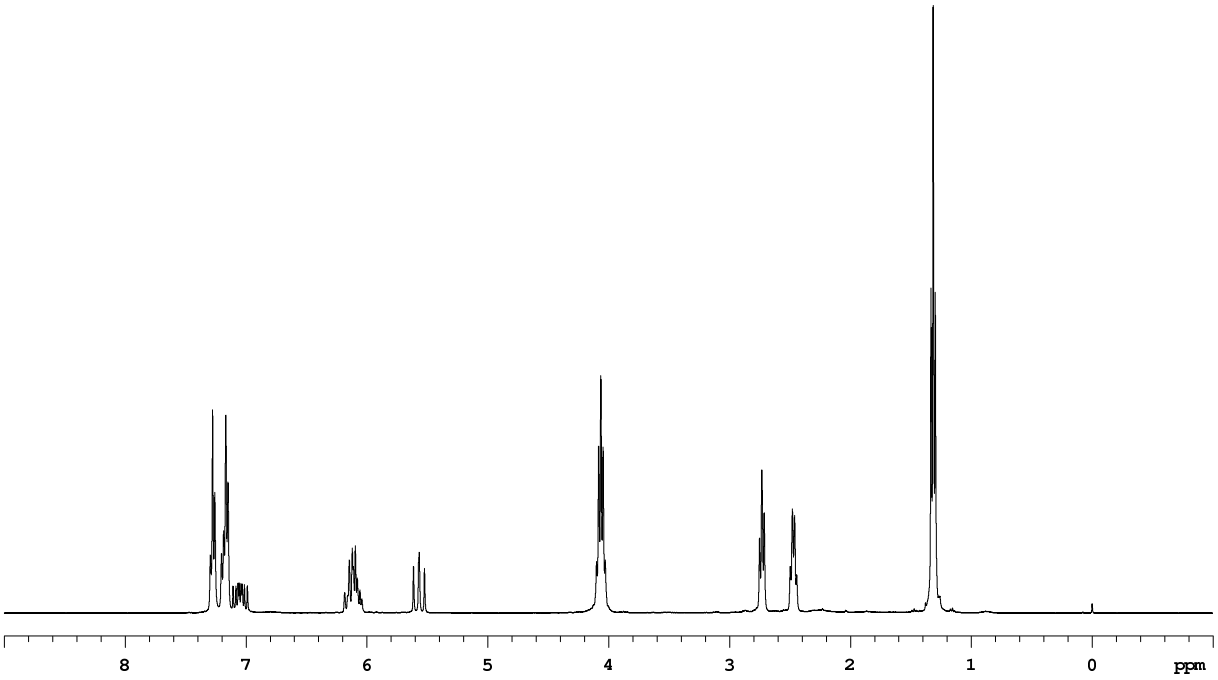
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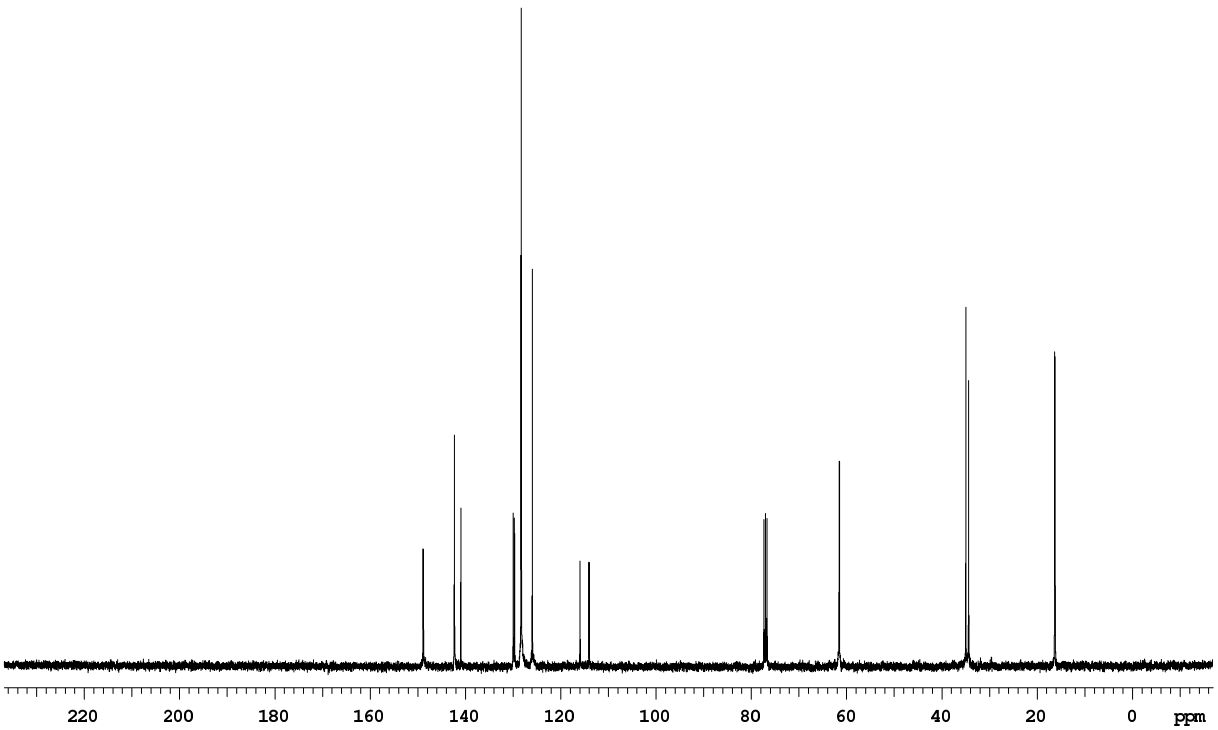
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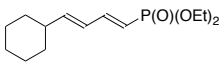
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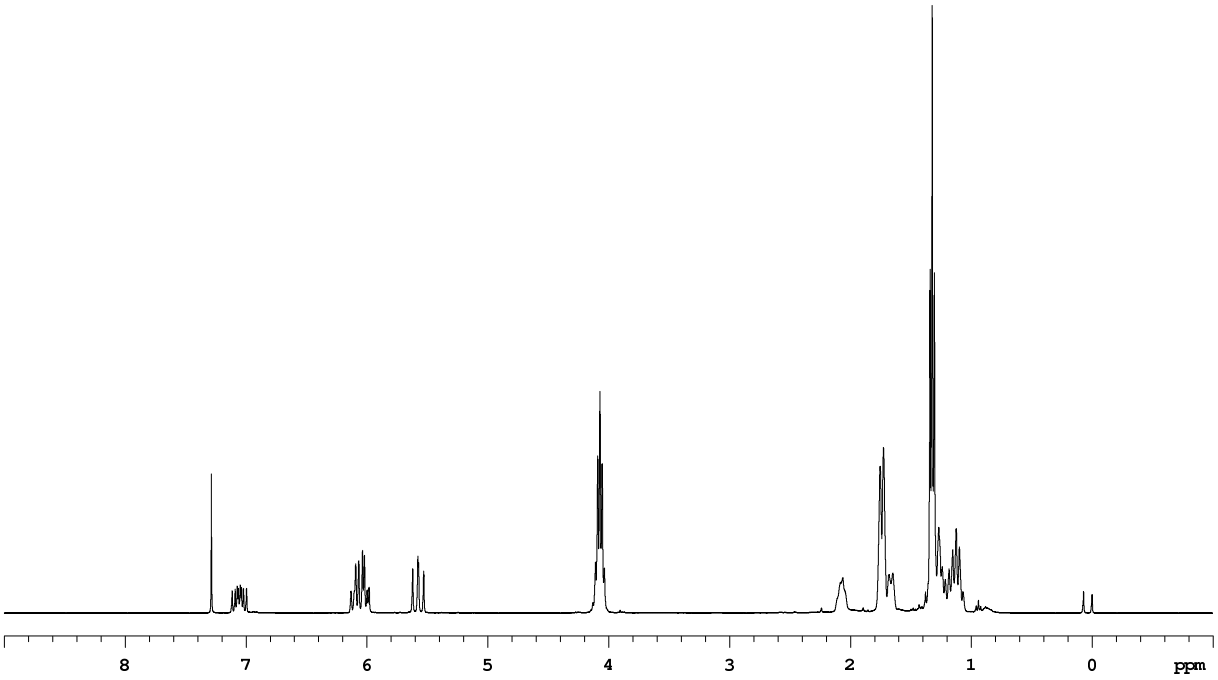
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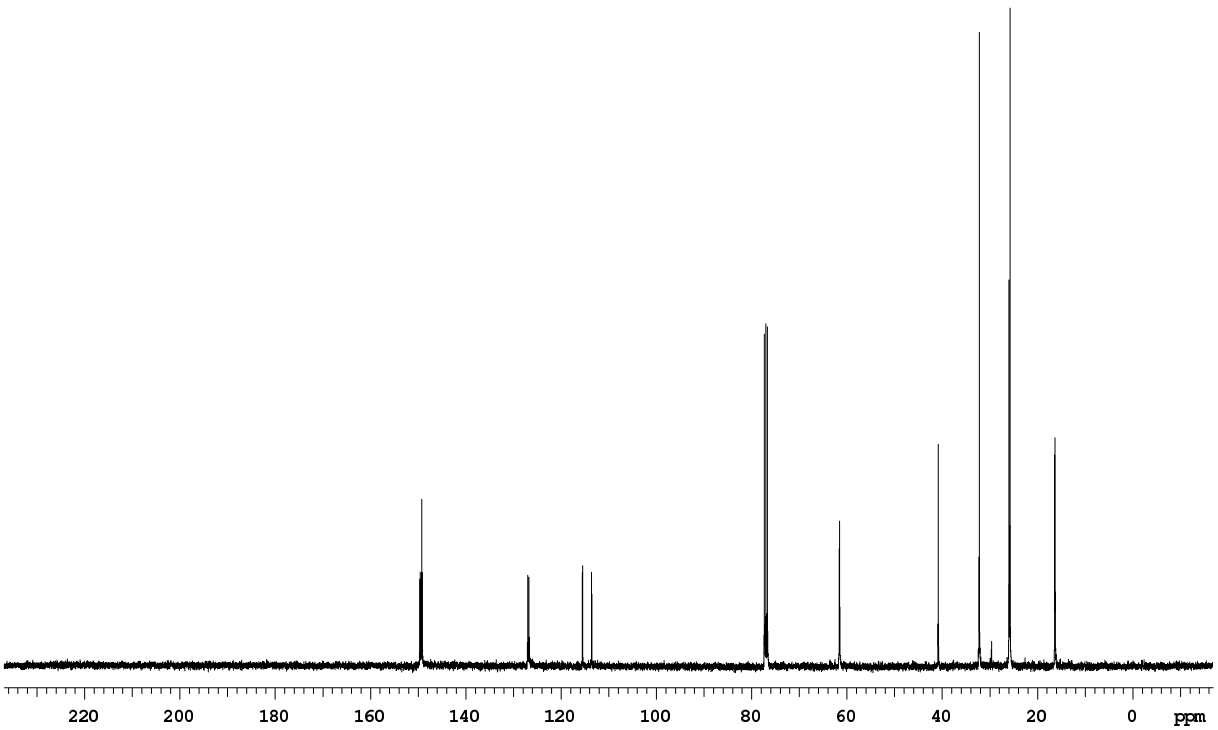
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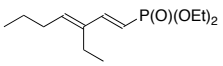
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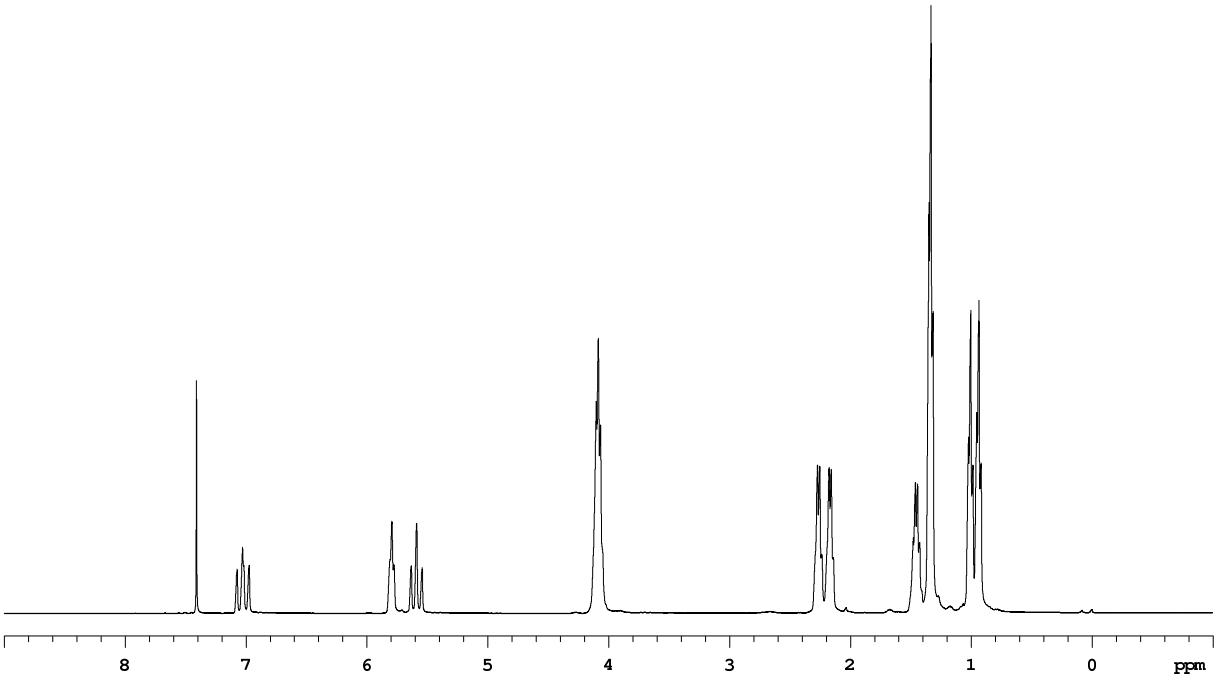
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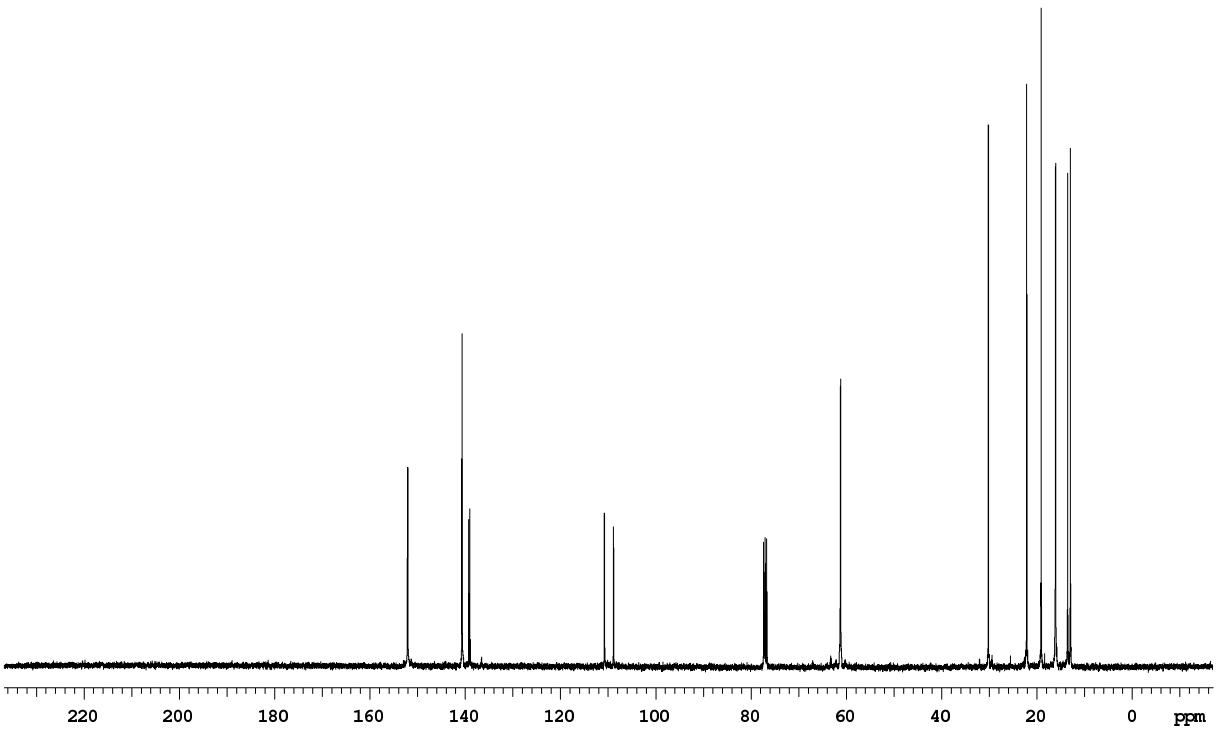
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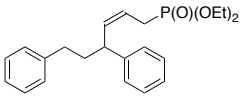
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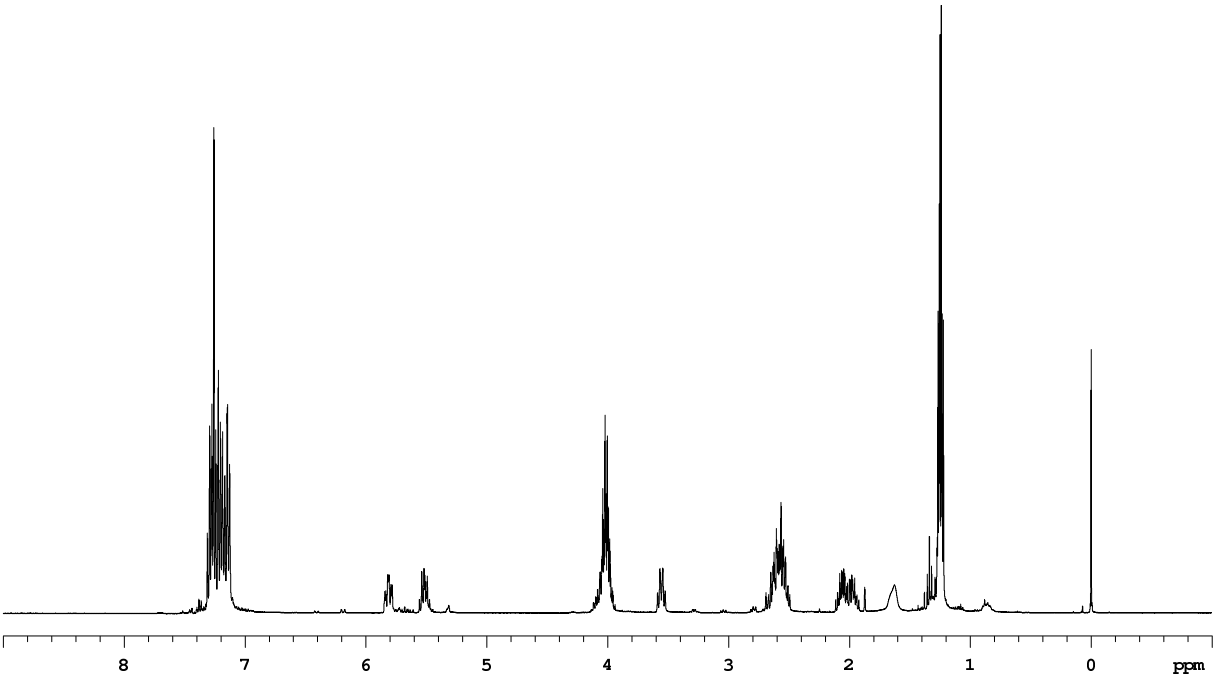
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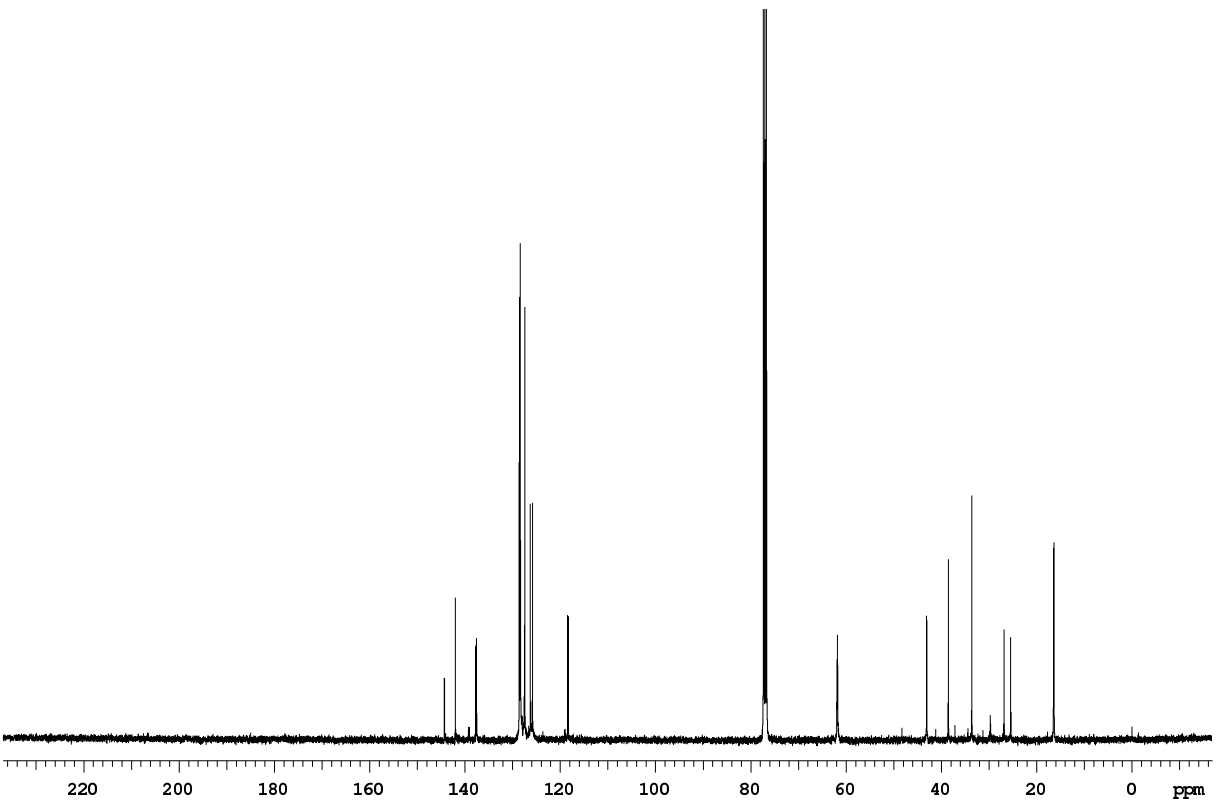
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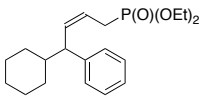
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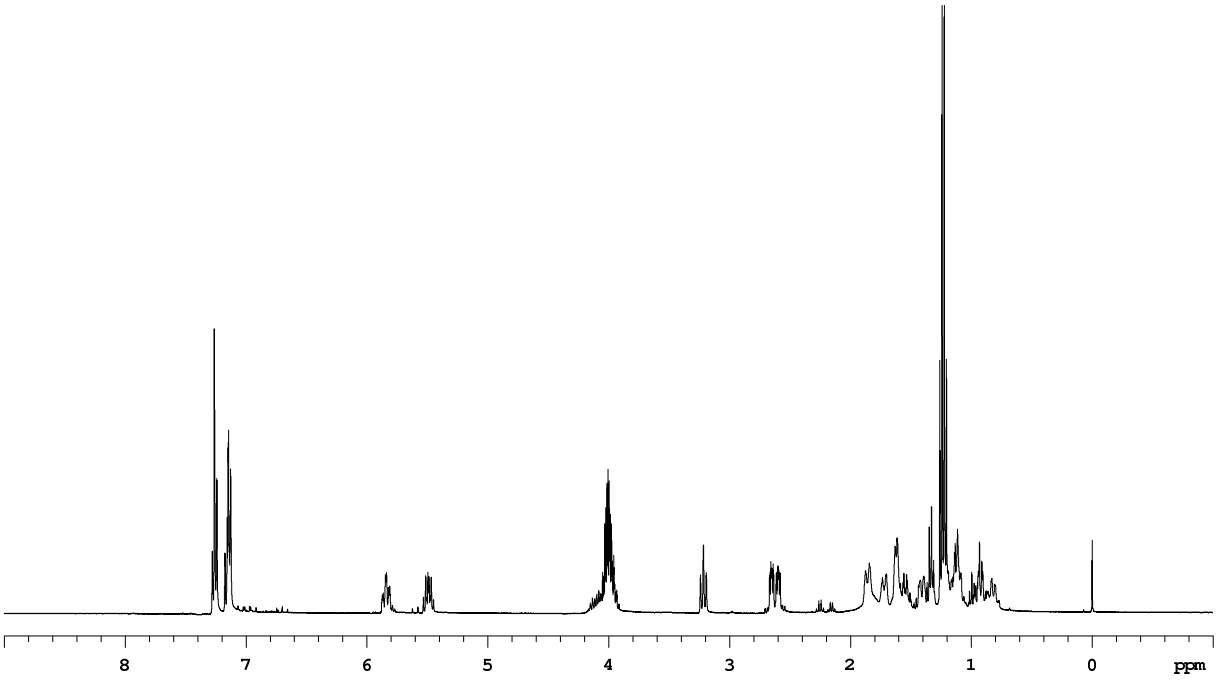
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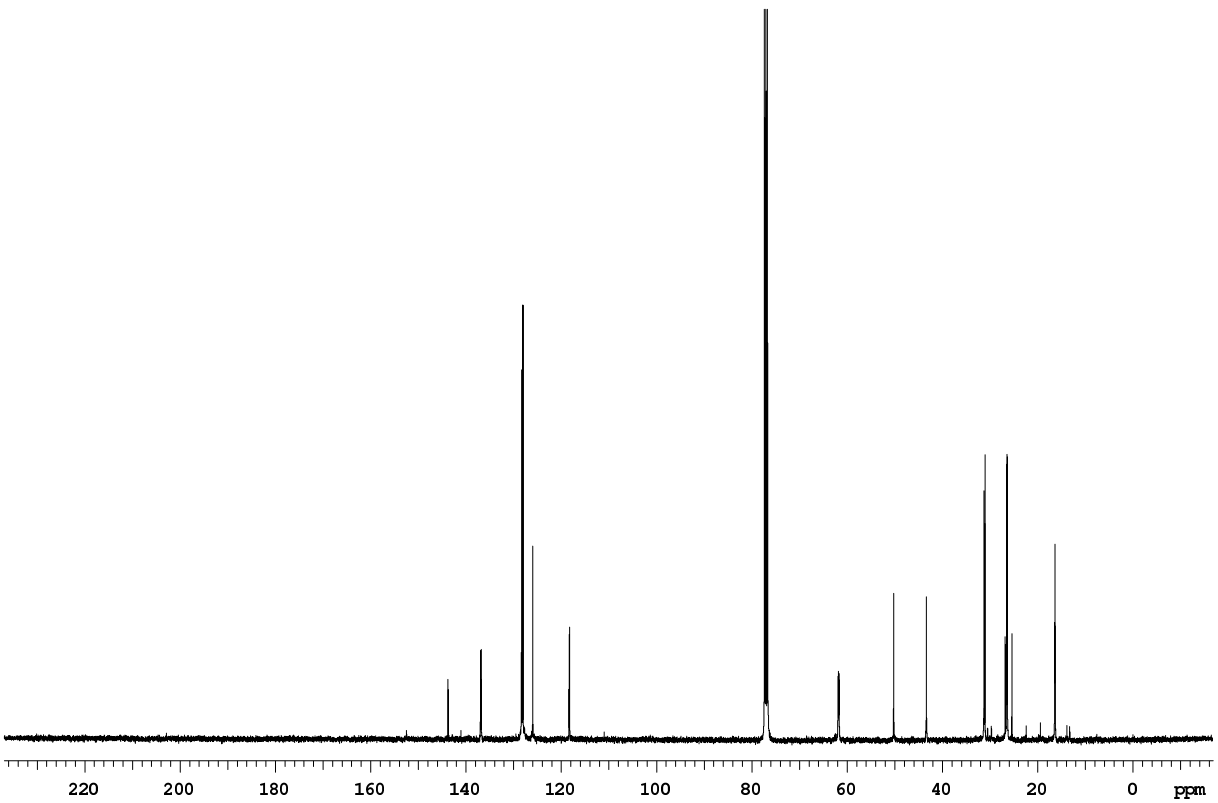
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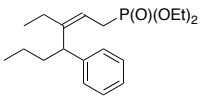
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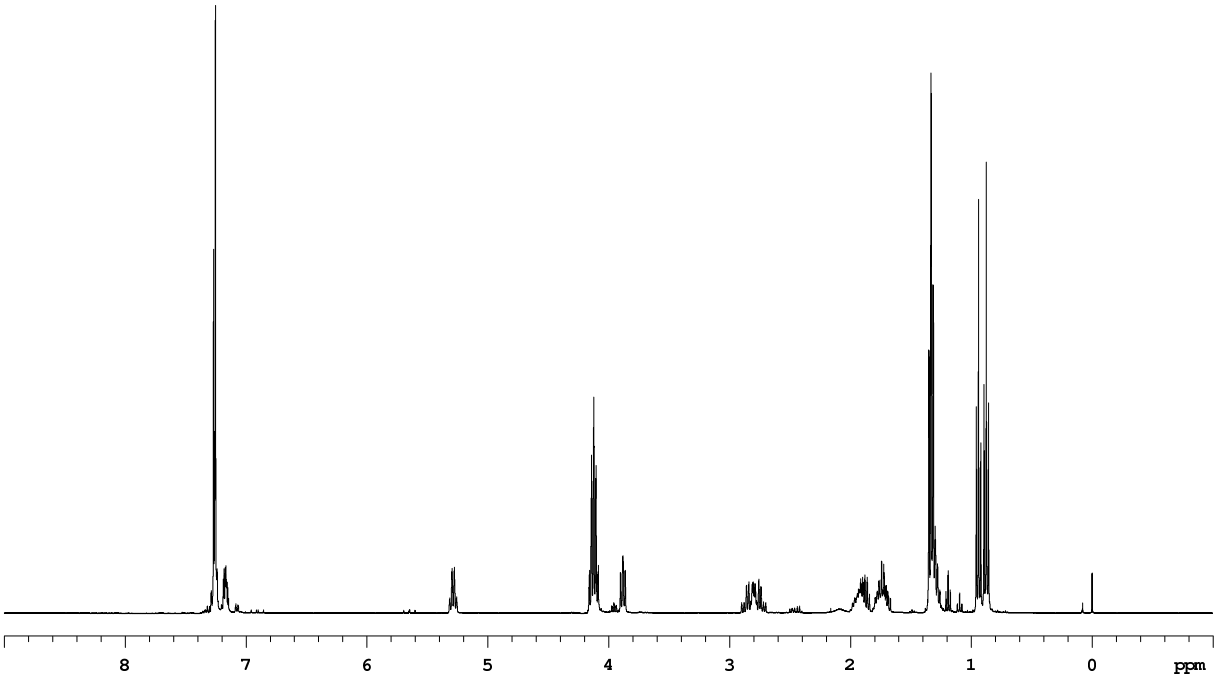
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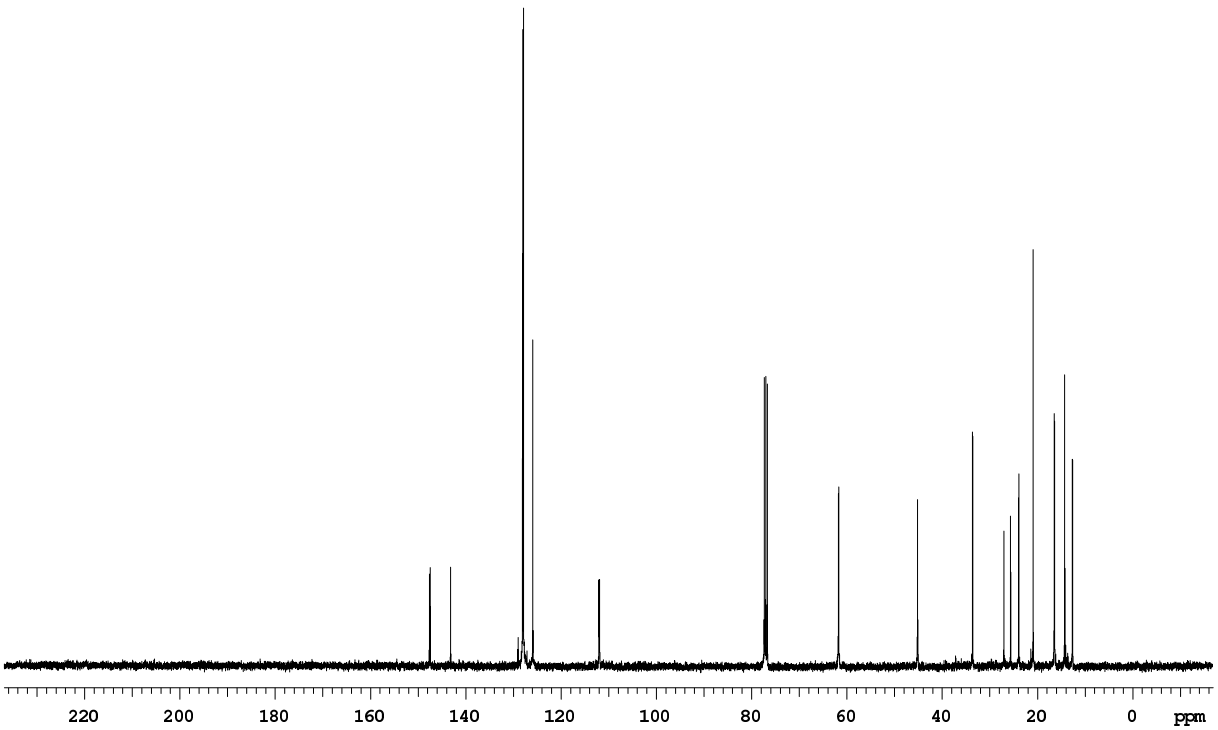
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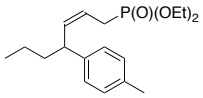
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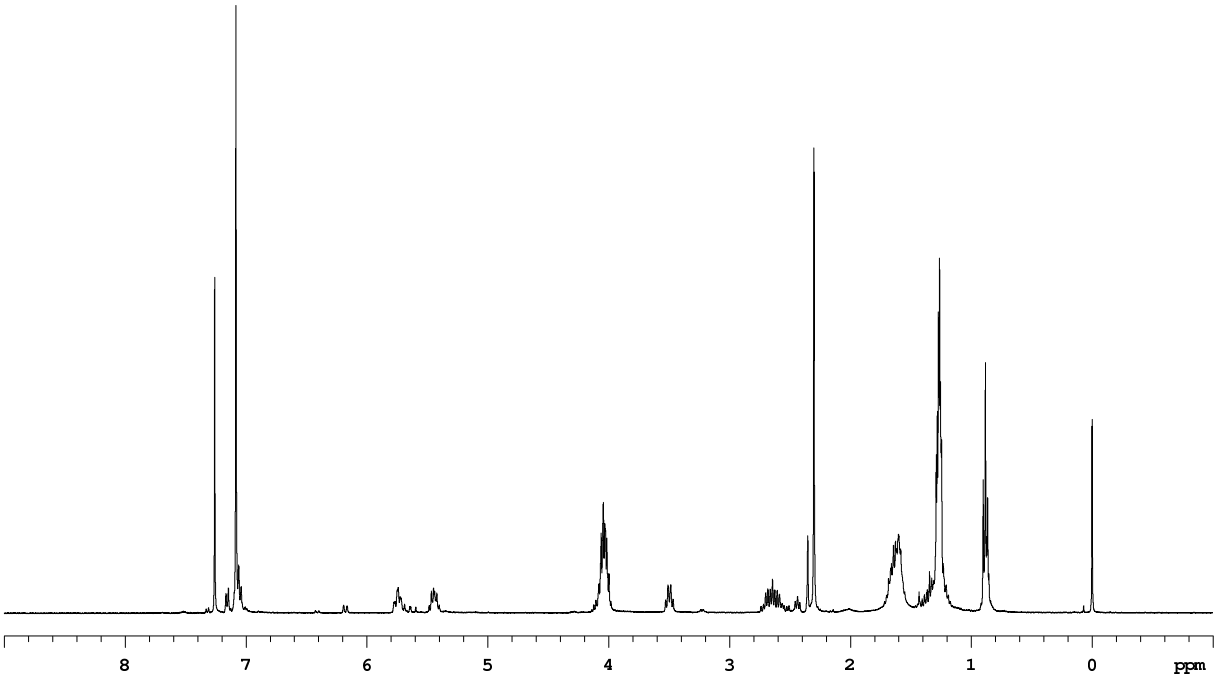
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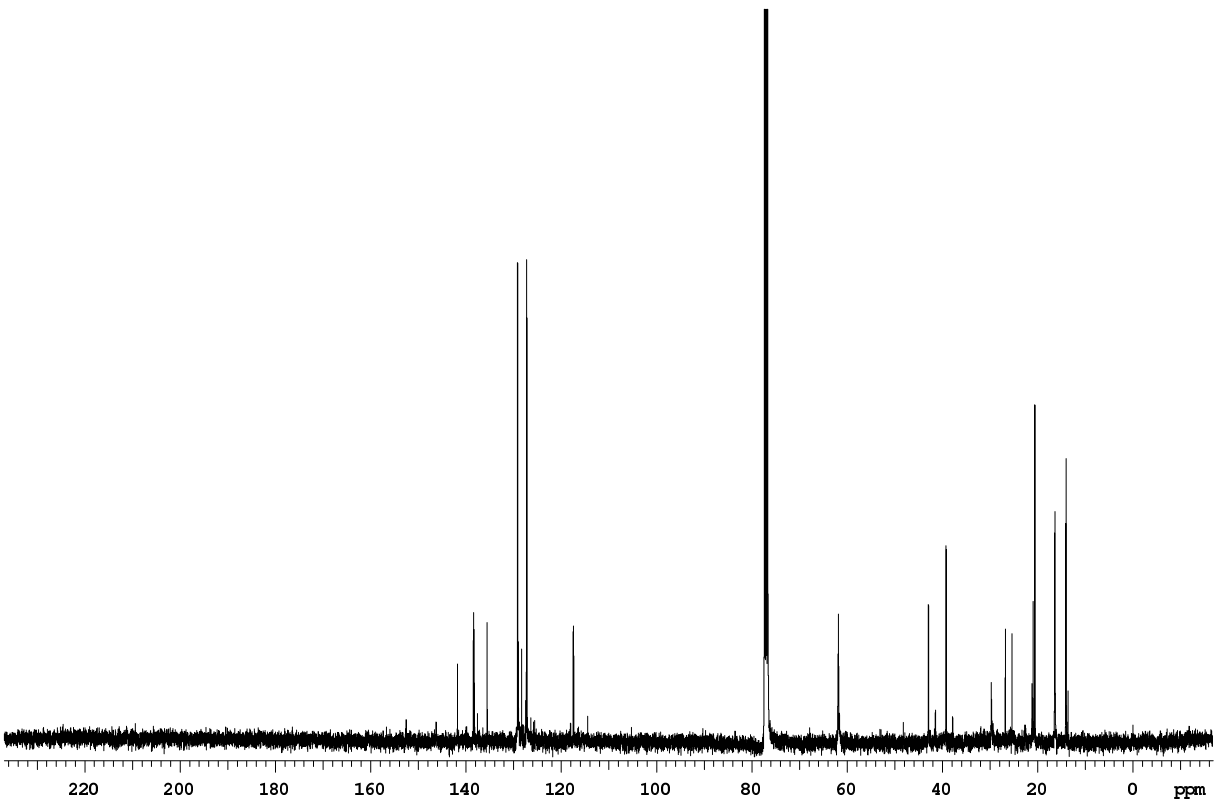
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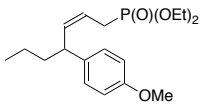
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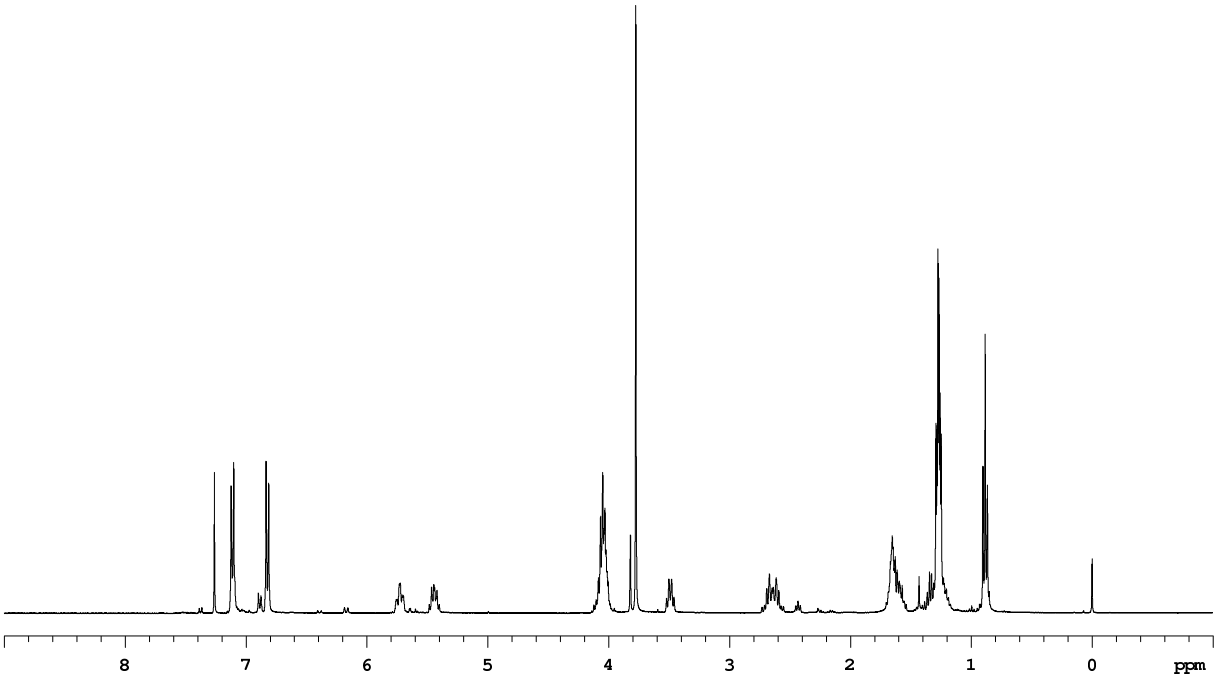
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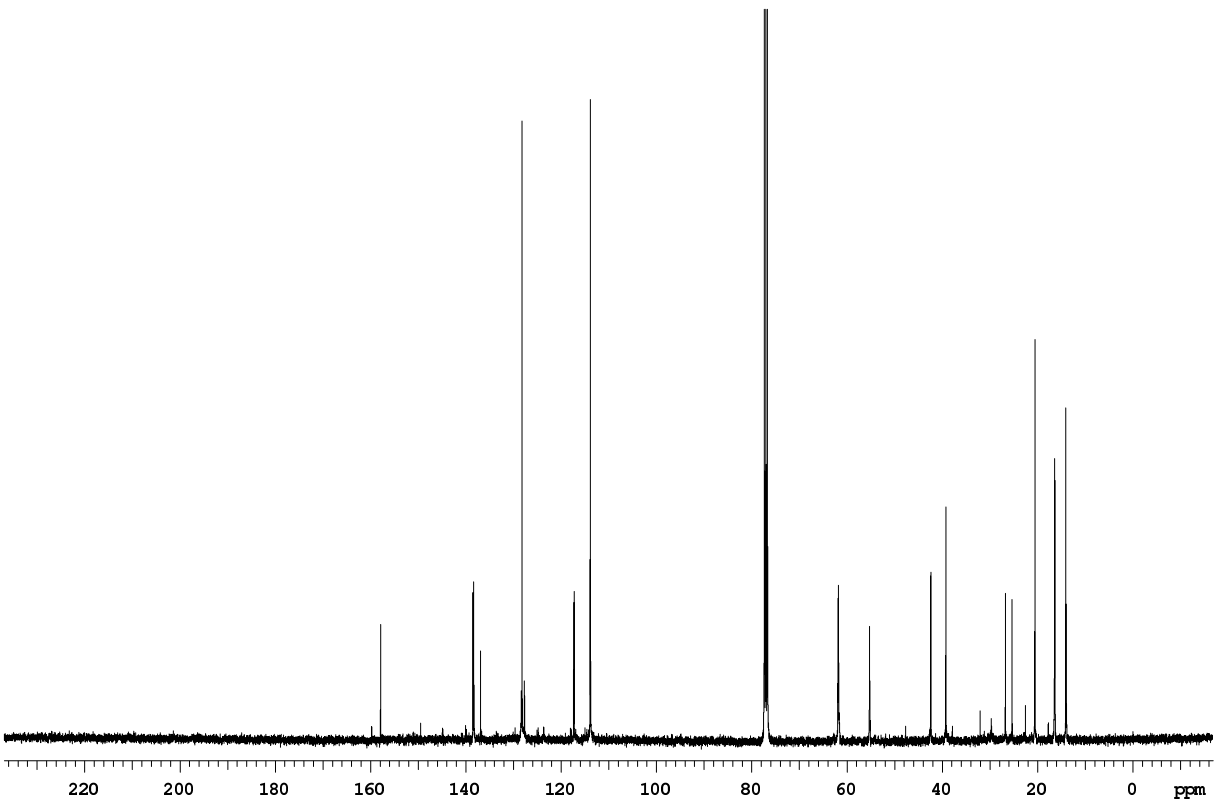
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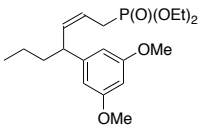
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OMe
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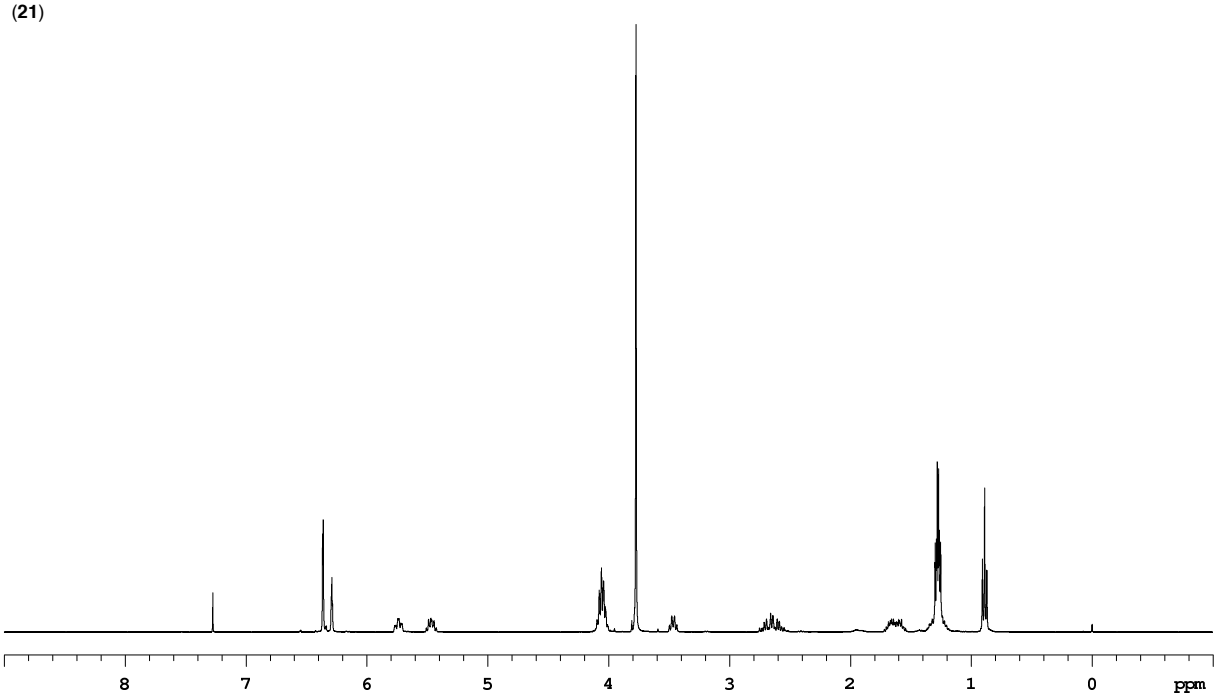
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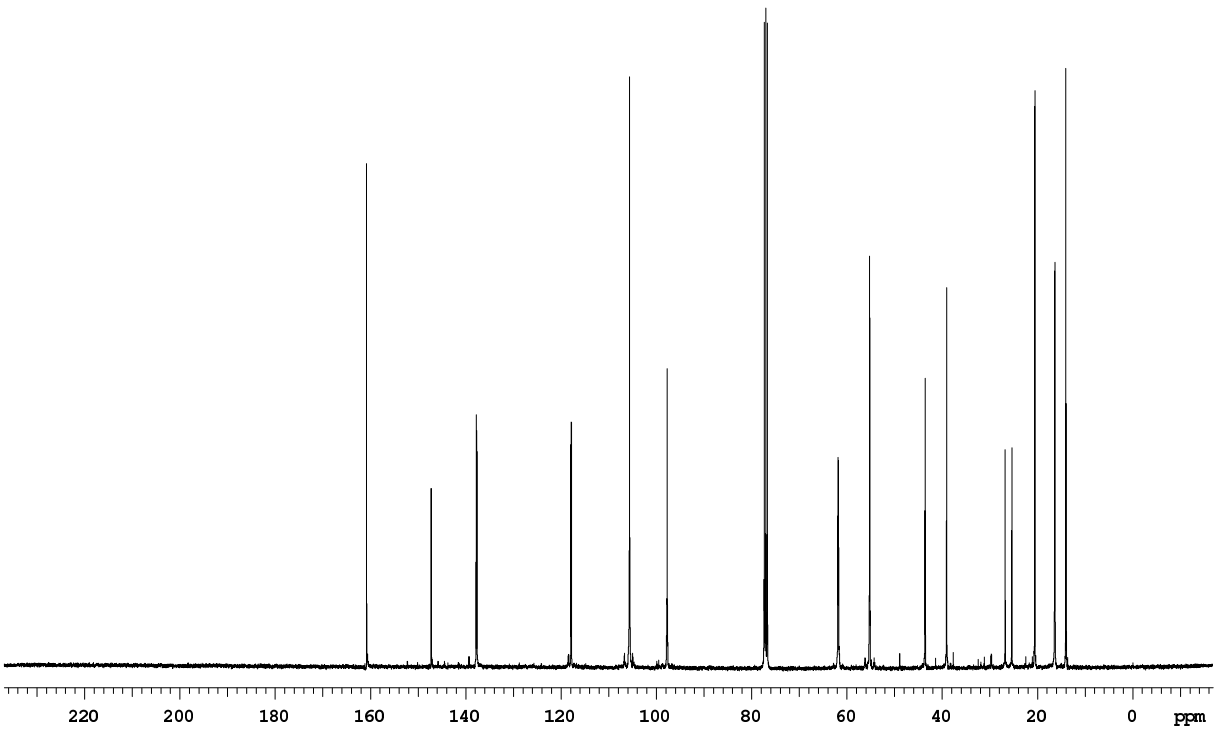
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