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Title(English)	Iron-catalyzed Selective Addition of Aryl Grignard Reagents to α，β，γ，δ-Unsaturated Sulfones, Phosphine Oxides, and Phosphonates and Its Synthetic Application
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論 文 要 旨

THESIS SUMMARY

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要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

This thesis, entitled "Iron-catalyzed Selective Addition of Aryl Grignard Reagents to α,β,γ,δ-Unsaturated Sulfones, Phosphine Oxides, and Phosphonates and Its Synthetic Application", describes the development of a new iron-catalyzed regio- and stereoselective addition of aryl Grignard reagents to a few electron-deficient dienes and its synthetic application.

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 synthetic 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 sulfonyl compounds were treated with aryl Grignard reagents in the presence of $FeCl_2$ to afford virtually single δ-aryl-*cis*-β,γ-unsaturated sulfones after hydrolysis. Deuteration and the treatment with alkyl halides gave the deuterated and alkylated products with the exclusive *cis*-olefinic stereochemistry. For example, (1*E*,3*E*)-1,3-pentadienyl phenyl sulfone, phenyl Grignard reagent (PhMgBr), and $FeCl_2$ (10 mol%) afforded magnesiated intermediate resulting from the phenyl delivery via the *s*-*cis*-diene-iron complex, which upon hydrolysis, deuteration, or alkylation with MeI gave (*Z*)-4-phenyl-2-pentenyl phenyl sulfone, (*Z*)-1-deuterio-4-phenyl-2-pentenyl phenyl sulfone, or (*Z*)-5-phenyl-3-hexen-2-yl phenyl sulfone in good yields. The δ-aryl-*cis*-β,γ-unsaturated sulfones obtained here were bis-alkylated to give α,α-dialkylated allyl sulfones, which were then subjected to the intramolecular Friedel-Crafts reaction to give bicyclic compounds. For example, lithiation and methylation of (*Z*)-5-(3,5-dimethoxyphenyl)-3-octen-2-yl phenyl sulfone afforded (*Z*)-5-(3,5-dimethoxyphenyl)-2-methyl-3-octen-2-yl phenyl sulfone, which was treated with $AlCl_3$ to give 6,8-dimethoxy-1,1-dimethyl-4-propyl-1,4-dihydronaphthalene in good yields. In this overall sequence, the sulfonyl group plays a triple role: (i) to effect the selective δ-conjugate addition, (ii) to enable alkylation at allylic position, and (iii) to work as a leaving group in the Friedel-Crafts reaction.

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 were treated with aryl Grignard reagents in the presence of $FeCl_2$ to afford virtually single δ-aryl-*cis*-β,γ-unsaturated phosphine oxides after hydrolysis. Alternatively, deuteration and the treatment with alkyl halides gave the deuterated and alkylated products with the exclusive *cis*-olefinic stereochemistry. For example, [(1*E*,3*E*)-1,3-heptadienyl]diphenylphosphine oxide, PhMgBr, and $FeCl_2$ (10 mol%) afforded magnesiated intermediate, which upon hydrolysis, deuteration, or alkylation with MeI gave [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide, [(*Z*)-1-deuterio-4-phenyl-2-heptenyl]diphenylphosphine oxide, or

[(*Z*)-5-phenyl-3-octen-2-yl]diphenylphosphine oxide in good yields. The δ-aryl-*cis*-β,γ-unsaturated phosphine oxides obtained herein could be used as precursors for the Wittig reaction, giving stereo-defined arylated dienes with high stereoselectivity. For example, [(*Z*)-4-phenyl-2-heptenyl]diphenylphosphine oxide was treated with *n*-BuLi and benzaldehyde to afford a 96:4 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene. Thus, while the original *cis*-olefin of the phosphine oxide isomerized a little, the newly generated olefin was exclusively *trans*. Alternatively, the same reaction with octanal afforded an 86:14 mixture of (5*Z*,7*E*)- and (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene. Thus, in the Wittig reaction with an *aliphatic* aldehyde, the original *cis*-olefin of the phosphine oxide was completely retained, but the newly formed olefin was a mixture of *trans* and *cis* double bonds.

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 were treated with aryl Grignard reagents in the presence of $FeCl_2$ to afford virtually single δ-aryl-*cis*-β,γ-unsaturated phosphonates after hydrolysis. Alternatively, deuteration and the treatment with alkyl halides gave the deuterated and alkylated products with the exclusive *cis*-olefinic stereochemistry. For example, diethyl (1*E*,3*E*)-1,3-heptadienylphosphonate, PhMgBr, and $FeCl_2$ (10 mol%) afforded magnesiated intermediate, which upon hydrolysis, deuteration, or alkylation with MeI gave diethyl (*Z*)-4-phenyl-2-heptenylphosphonate, diethyl (*Z*)-1-deuterio-4-phenyl-2-heptenylphosphonate, or diethyl (*Z*)-5-phenyl-3-octen-2-ylphosphonate in good yields. The δ-aryl-*cis*-β,γ-unsaturated phosphonates obtained herein could be used as precursors for the Wittig reaction, giving stereo-defined arylated dienes with high stereoselectivity. For example, diethyl (*Z*)-4-phenyl-2-heptenylphosphonate was treated with NaHMDS (HMDS=hexamethyldisilazide, $(Me_3Si)_2N^-$) and benzaldehyde to afford a 93:7 mixture of (1*E*,3*Z*)- and (1*E*,3*E*)-1,5-diphenyl-1,3-octadiene. Thus, while the original *cis*-olefin of the phosphonate isomerized a little, the newly generated olefin was exclusively *trans*. Alternatively, the same reaction with octanal afforded an 83:17 mixture of (5*Z*,7*E*)- and (5*Z*,7*Z*)-4-phenyl-5,7-pentadecadiene. Thus, in the Wittig reaction with an *aliphatic* aldehyde, the original *cis*-olefin of the phosphonate was completely retained, but the newly formed olefin was a mixture of *trans* and *cis* double bonds.

It should be noted that 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, as the ligand modification on the P atom is much easier for phosphonates than phosphine oxides, the former facilitates the extension of this reaction to the asymmetric conjugate addition as well as *cis*-selective Wittig reaction.

Chapter 5 "Summary": The results reported in the preceding Chapters 2-4 are summarized and some perspective is described.