Preparation of Chiral-at-Iron-Substituted Allyl and Vinyl Sulfones. Subsequent Enolate Generation and Stereo- and Regioselective Alkylation

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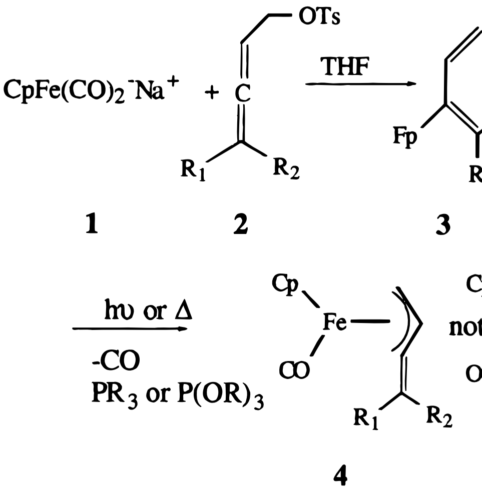
Summary: The (η^5-cyclopentadienyl)Fe(CO)$_2$ (Fp) anion adds to allenic sulfone (CH$_2$=C=CHSO$_2$Ph) to generate predominantly iron-substituted allyl or vinyl sulfones, depending on the reaction conditions chosen. Following a phosphine for CO ligand substitution, these allyl or vinyl sulfones can be deprotonated to yield carbanions, which can be alkylated regio- and stereoselectively. These alkylation reactions are unusual for allyl sulfones in that the ratio of α: γ alkylation changes dramatically as the electrophile structure changes.

For several years, we have been interested in exploring how metal-centered chirality would affect the stereochemical outcome of [4 + 2] cycloaddition reactions.[1] In conjunction with these interests, we want to prepare racemic then ultimately optically active chiral-at-iron 1,3-dienyl complexes (**5**). We have reported that the CpFe(CO)$_2$ anion (Fp anion)[2] (**1**) reacted with allenic electrophiles (**2**) in a S$_N$2′ fashion to generate Fp-substituted 1,3-dienyl complexes (**3**). Thermal and photochemical attempts to do a phosphine or phosphite for CO substitution in solution lead only to the isolation of η^3-butadienyl complexes (**4**) rather than the desired dienyl complex (**5**).



We have begun to pursue a strategy toward chiral-at-iron-substituted dienes (**5** and more highly substituted analogs thereof) that will ultimately rely on a Julia olefination.[3] In this communication, we report the preparation of chiral-at-iron-substituted allyl and vinyl sulfones which will be required to pursue that strategy as well as their subsequent deprotonation followed by stereo- and regioselective alkylation.

Allenyl sulfones (**9**) have found widespread use in organic synthesis as dienophiles and as diene precursors.[4] The central allene carbon in these sulfones is highly electrophilic, and hence, they readily undergo nucleophilic addition reactions. The simplest allenyl phenylsulfone (**9**) is easily prepared from propargyl chloride (**6**; Scheme 1).[5] The Cp(CO)$_2$Fe anion (**1**) was added to **9** to generate the iron-substituted allylic and vinyl sulfones (**10** and **11**) (35−45%).[6] Isolated yields of **10** and **11** are consistently in the 40% range for a variety of reaction scales tried. We always recover a

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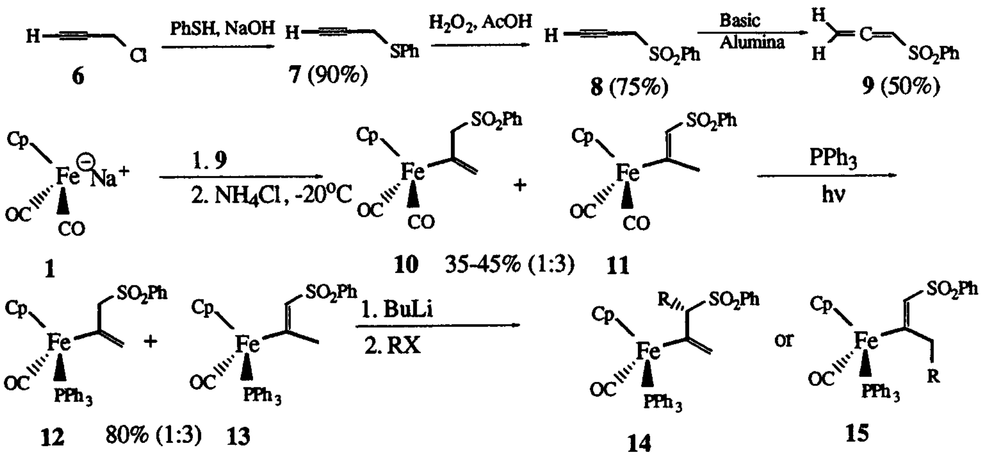
(6) Cyclopentadienyliron dicarbonyl anion (**1**) was prepared from [CpFe(CO)$_2$]$_2$ (0.600 g, 1.69 mmol) in THF (100 mL) using the method of Piper and Wilkinson.[2] Allenic sulfone (**9**) (0.72 g, 4.00 mmol) was dissolved in THF (100 mL) and cooled to −78 °C. Iron anion (**1**) was added to **9** slowly using a double-ended needle, and the mixture was allowed to stir 2 h at −78 °C. The temperature was permitted to rise to −20 °C over several hours and then quenched by the addition of NH$_4$Cl (aq) (25 mL) followed by water (100 mL). The aqueous was extracted with EtOAc (3 × 100 mL), and the combined extracts were dried (MgSO$_4$). The solvent was removed by rotary evaporation, and the product was chromatographed on alumina. Elution with hexane yielded [CpFe(CO)$_2$]$_2$ (by TLC comparison to an authentic sample), and elution with 9:1 hexane:EtOAc yielded **10**:**11** (1:3) (0.47 g, 1.31 mmol, 39%). Complexes **10** and **11** have surprisingly different solubility characteristics, so this mixture of **10**:**11** could be triturated with 1:1 hexane:EtOAc to remove **10** and leave **11** behind as a yellow solid (350 mg). ^{1}H NMR (C$_6$D$_6$): 8.11 (m, 2H), 6.99 (m, 3H), 6.82 (q, J = 1.2 Hz, 1H), 3.79 (s, 5H), 2.66 (d, J = 1.2 Hz, 3H). ^{13}C NMR (C$_6$D$_6$): 214.94, 145.32, 135.08, 131.94, 129.11, 128.94, 127.17, 85.85, 34.01. IR (KBr): 2018, 1964, 1299, 1136, 1082 cm^{-1}. Anal. Calcd for C$_{16}$H$_{14}$FeO$_4$S: C, 53.65; H, 3.94. Found: C, 54.49; H, 4.31. LR FAB MS: 359 (25, M + H$^+$), 330 (15, M$^+$ − CO), 302 (50, M$^+$ − 2CO), 274 (25), 217 (100). HR FAB MS calcd for C$_{16}$H$_{15}$FeO$_4$S (M + H$^+$): 359.0040. Found: 359.0050. Complex **10** was also recovered as a yellow solid (100 mg) from the liquid by adding hexane to induce precipitation. ^{1}H NMR (C$_6$D$_6$): 7.70 (m, 2H), 6.96 (m, 3H), 6.03 (s, 1H), 5.47 (s, 1H), 4.40 (s, 5H), 3.87 (s, 2H). ^{13}C NMR (C$_6$D$_6$): 216.56, 141.84, 139.32, 136.51, 132.82, 129.00, 128.20, 86.39, 74.53. IR (KBr): 2013, 1955, 1304, 1146, 1083 cm^{-1}. Anal. Calcd for C$_{16}$H$_{14}$FeO$_4$S: C, 53.65; H, 3.94. Found: C, 53.56; H, 4.00.

S0276-7333(97)00448-2 CCC: $14.00

Scheme 1



R = Me	dr 12.5:1	**14a**:**15a**	20:1 (90%)
R = Et	dr >20:1	**14b**:**15b**	8:1 (73%)
R = n-Pr		**14c**:**15c**	1:1.5 (75%)
R = Allyl		**14d**:**15d**	1:5 (70%)
R = Benzyl		**14e**:**15e**	<1:20 (85%)

significant amount of $[CpFe(CO)_2]_2$ dimer from these reactions, so we suspect **9** reacts with **1** in redox and/or acid−base chemistry to an appreciable extent. Isolated yields of **10** and **11** based on recovered iron dimer $[CpFe(CO)_2]_2$ are in the 60−80% range. Iron-substituted allyl sulfone (**10**) can be easily separated from the vinyl sulfone (**11**) by hexane:ethyl acetate (1:1) trituration if desired. The ratio of **11**:**10** increased as the temperature at which the reaction is quenched with water increases (1:1.5 at −40 °C, 3:1 at −20 °C). The kinetic product (**10**) also rearranged to **11** upon standing at 25 °C in $CDCl_3$. The *E* stereochemistry of vinyl sulfone (**11**) was proven by X-ray crystallography.[7]

Phosphine substitution on **10** to give **12** (80%), on **11** to give **13** (80%), or on the **10**/**11** mixture to produce **12** and **13** (80%) was easily achieved in toluene at 0 °C using a 150 W flood lamp.[8] The structure of the iron-substituted allyl sulfone (**12**) has now also been confirmed by X-ray crystallography (Figure 1).[9] In the solid state, this complex (**12**) adopts a conformation where the alkenyl CH_2 (C(7), Figure 1) and the carbon monoxide ligand are *anti*, analogous to the conformations adopted by chiral-at-iron acyl complexes where the acyl group oxygen and carbon monoxide ligands are *anti*.[10]

We have recently determined that the **12**/**13** mixture (86%), pure **12** (90%), or pure **13** (86%) can be deprotonated with BuLi followed by treatment with MeI to produce a product (**14a**) where alkylation has occurred α to the sulfone with high diastereoselectivity (12.5:1).[11] Since **12** adopts a solid state conformation like the analogous acyl complexes[10] and they alkylate *anti* to the PPh_3 ligand, we would anticipate that **12** would react to produce the diastereomer shown (**14a**). This observed diastereoselectivity is apparently a kinetic ratio since the anion of **12** was generated and quenched with MeI at −78 °C, and we find that this diastereoselectivity does

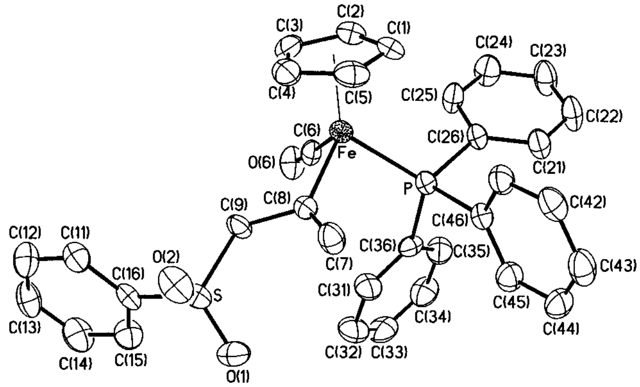


Figure 1. ORTEP diagram with labeling scheme for $C_{33}H_{29}FeO_3PS$ (**12**). Selected bond distances (Å) and angles (deg): Fe−C(6) 1.725(5), Fe−C(8) 1.995(4), Fe−P 2.2065(14), C(7)−C(8) 1.328(5), C(8)−C(9) 1.523(5); C(6)−Fe−C(8) 96.0(2), C(8)−Fe−P 92.52(12), C(6)−Fe−P 89.20(14), C(7)−C(8)−C(9) 119.8(4), C(7)−C(8)−Fe 126.0(3).

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(7) Complete details of the X-ray crystallographic characterization of **11** are provided in the Supporting Information. Crystallographic data for **11**: monoclinic, $P2_1$, $Z = 2$, $a = 9.831(3)$ Å, $b = 8.009(2)$ Å, $c = 11.212(2)$ Å, $\beta = 115.03(2)°$, $V = 799.9(4)$ Å^3, $D_{calc} = 1.487$ g/cm^3; Mo Kα radiation ($\lambda = 0.710\ 73$ Å); 1745 independent reflections with $2.00 < \theta < 25.01$ collected, $R = 0.0500$, $R_w = 0.1313$, GOF = 1.327.

(8) Stokes, H. L.; Ni, L. M.; Belot, J. A.; Welker, M. E. *J. Organomet. Chem.* **1995**, *487*, 95 and references therein. Iron complex (**11**) (0.300 g, 0.84 mmol) and PPh_3 (0.264 g, 1.01 mmol) were dissolved in deoxygenated toluene (20mL) and photolyzed at 0 °C under N_2 for 24 h using a 150 W flood lamp. During this photolysis, the solution color changes from yellow to red-orange. The solvent was removed by rotary evaporation. The crude product was triturated with 9:1 hexane:EtOAc to remove excess PPh_3 and provided **13** as a red-orange solid (398 mg, 0.67 mmol, 80%). ^{1}H NMR (C_6D_6): 7.92 (m, 2H), 7.25−6.99 (m, 18H), 6.50 (s, 1H), 4.03 (d, $J = 1.2$ Hz, 5H), 2.88 (t, $J = 1.4$ Hz, 3H). ^{13}C NMR ($CDCl_3$): 220.3 (d, $J = 33$ Hz), 144.3, 135.0 (d, $J = 42$ Hz), 132.9, 131.5, 130.7, 130.6, 130.1, 128.5, 128.2, 126.9, 85.8, 34.5. IR (KBr): 1925, 1431, 1296, 1255, 1132, 1079 cm^{-1}. LR FAB MS: 593 (17, M + H$^+$), 564 (40, M$^+$ − CO). HR FAB MS calcd for $C_{33}H_{30}FeO_3PS$ (M + H$^+$): 593.1003. Found: 593.1016.

(9) Complete details of the X-ray crystallographic characterization of **12** are provided in the Supporting Information. Crystallographic data for **12**: monoclinic, $P2_1/c$, $Z = 4$, $a = 11.120(4)$ Å, $b = 16.613(4)$ Å, $c = 15.994(3)$ Å, $\beta = 107.00(3)°$, $V = 2825.6(11)$ Å^3, $D_{calc} = 1.393$ g/cm^3; Mo Kα radiation ($\lambda = 0.710\ 73$ Å); 3683 independent reflections with $2.27 < \theta < 22.49$ collected, $R = 0.0418$, $R_w = 0.0805$, GOF = 0.864. Some sulfoxide-containing chiral-at-iron acyls have been reported previously, but to our knowledge these chiral at iron alkenyl sulfones are unknown, see: (a) Davies, S. G.; Gravatt, G. L. *J. Chem. Soc., Chem. Commun.* **1988**, 780. (b) Baker, R. W.; Davies, S. G. *Tetrahedron: Asymmetry* **1993**, *4*, 1479. Chiral-at-iron sulfonyl complexes (analogous to the acyls) have also been reported, see: Flood, T. C.; DiSanti, F. J.; Miles, D. L. *Inorg. Chem.* **1976**, *15*, 1910.

(10) For a review of conformational analysis of the $CpFe(CO)(PPh_3)$ auxiliary, see: Blackburn, B. K.; Davies, S. G.; Whittaker, M. In *Stereochemistry of Organometallic Inorganic Compounds 3*; Bernal, I., Ed.; Elsevier, Amsterdam, 1989; pp 141−223.

deteriorate some when **14a** is subsequently treated with 1N NaOH in C_6D_6 at 25 °C (5:1 after 6 h). Interestingly, the enolate of **12**/**13** also alkylated diastereoselectively with EtI, but the regioselectivity begins to deteriorate. The regiochemistry of the alkylation continues to change when PrI is used and switches to a preference for γ alkylation by the time unsaturated alkyl halides are used as the alkylating agents. Allyl bromide reacted to produce a preponderance of the γ-alkylated product (**15d**), and benzyl bromide alkylated to produce only the γ product (**15e**), as observed by ^{1}H NMR. This change in electrophile alkylation site with change in electrophile structure is very unusual for allylic sulfone anions which alkylate almost exclusively α rather than γ to the sulfone regardless of substrate used.[12] This change in regiochemistry of alkylation is presumably predominantly a steric effect and is due to the presence of both the bulky CpFe(CO)PPh_3 fragment and the SO_2Ph group. However, part of the change in regiochemistry of alkylation may arise from the fact that the softer allylic and benzylic electrophiles have an electronic preference for alkylation at the softer nucleophilc γ carbon[13] or possibly the switch to bromides as alkylating agents for **d** and **e** had an effect on the rates of alkylation at the α and γ sites.

In summary, we have demonstrated that $CpFe(CO)_2$ anions can add to allenic sulfones to generate predominantly iron-susbsituted allyl or vinyl sulfones, depending on the reaction conditions chosen. These allyl or vinyl sulfones can be deprotonated to yield carbanions, which can be alkylated regio- and stereoselectively. The regiochemistry of these alkylations is unusual in that γ alkylation increases as the size of the alkylating electrophile increases. Successful generation and alkylation of sulfone-stabilized allylic carbanions in the presence of transition-metal complexes should now allow organometallic chemists to explore Julia olefinations as a new method for synthesizing transition-metal dienyl complexes. We will report our efforts along those lines in due course.

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Supporting Information Available: Tables giving details of the X-ray structure determinations, atomic coordinates and isotropic thermal parameters, bond lengths and bond angles, and anisotropic displacement parameters for **11** and **12**, an ORTEP diagram of **11**, and experimental details of the preparation and characterization of **10**−**15** (19 pages). Ordering information is given on any current masthead page.

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(11) Generation and alkylation of the enolate of CpFe(CO)-(PPh_3)$COCH_2SCH_3$ has also been reported, see: Wisniewski, K.; Pakulski, Z.; Zamojski, A.; Sheldrick, W. S. *J. Organomet. Chem.* **1996**, *523*, 1. A representative example of our alkylation procedure follows. Iron allyl sulfone (**12**) (0.050 g, 0.084 mmol) was dissolved in THF (5 mL) and cooled to −78 °C. BuLi (40 μL of a 1.7 M solution in hexanes, 0.105 mmol) was added dropwise, and the orange solution changed to a deep amber color. The anion was allowed to stir 15 min at −78 °C, then CH_3I (0.023 g, 0.17 mmol) was added. The solution was allowed to stir for 2 h at −78 °C then warmed to 25 °C, and during this time, the deep amber anion color changed back to the original orange color. Saturated NaCl (5 mL) was added, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The organic extracts were dried (Na_2SO_4), and the solvent was removed by rotary evaporation. The product was recrystallized from hexane/EtOAc to yield **14a** as a red solid (0.045 g, 0.074 mmol, 88%). ^{1}H NMR (C_6D_6): 8.12 (m, 2H), 7.55 (m, 6H), 7.02 (m, 12H), 6.58 (s, 1H), 5.62 (s, 1H), 4.55 (s, 5H), 4.36 (q, $J = 7.0$ Hz, 1H), 1.18 (d, $J = 7.0$ Hz, 3H). IR (KBr): 1909, 1433, 1298, 1142 cm^{-1}. LR FAB MS: 607 (7, $M + H^+$), 578 (22, $M^+ - CO$), 459 (23), 411 (36), 383 (100). HR FAB MS calcd for $C_{34}H_{32}FeO_3PS$ ($M + H^+$): 607.1135. Found: 607.1128.

(12) (a) Reference 4, pp 111−118. (b) Savoia, D.; Trombini, C.; Umani-Ronchi, A. *J. Chem. Soc., Perkin Trans. 1* **1977**, 123. (c) Jonczyk, A.; Radwan-Pytlewski, T. *J. Org. Chem.* **1983**, *48*, 910. (d) Hayakawa, K.; Nishiyama, H.; Kanematsu, K. *J. Org. Chem.* **1985**, *50*, 512. (e) Trost, B. M.; Schmuff, N. R. *J. Am. Chem. Soc.* **1985**, *107*, 396.

(13) Pearson, R. G.; Songstad, J. *J. Am. Chem. Soc.* **1967**, *89*, 1827.