Reactions of Transition-Metal Cyclopropyl and η^1-Allyl Complexes with Sulfur Dioxide and Disulfur Monoxide

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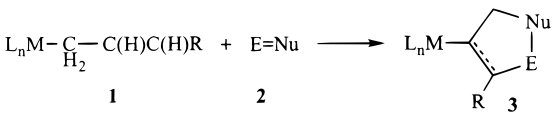
The preparations of several cyclopentadienyl iron dicarbonyl cyclopropyl and η^1-allyl complexes as well as $(Me_2PhP)(CO)_4$ manganese allyl complexes are reported. The iron complexes participated in 3 + 2 cycloaddition reactions with sulfur dioxide (SO_2) and disulfur monoxide (S_2O) to yield regioisomeric transition-metal substituted 1,2-oxathiolane 1-oxides (sulfenate esters) and 1,2-dithiolane 1-oxides (thiosulfinate esters), respectively. The manganese allyl complexes reacted with both SO_2 and S_2O to produce insertion products.

Introduction

Cycloaddition reactions between transition-metal η^1-2-alkynyl (**1**) and η^1-allyl complexes (**1**) and unsaturated electrophilic reagents (**2**) have been studied in detail for many years, and the pioneering work in this area was done by the Rosenblum and Wojcicki groups.[1] These 3 + 2 cycloaddition reactions have been shown to yield transition-metal-substituted five-membered-ring heterocycles and carbacycles (**3**) and offer alternative approaches to these ring systems when the metal is subsequently cleaved from the ring.[1−3]



Several years ago, we reported a variant of this 3 + 2 cycloaddition reaction which yields transition-metal-substituted five-membered-ring thiosulfinate esters.[1a,2] More recently, we have explored an example of this reaction first reported by Wojcicki in 1977,[4] involving the cycloaddition of cyclopentadienyl iron dicarbonyl 2-alkynyl complexes with ketenes as a route to cyclopentenones,[5] and we have reported some new transition-metal-mediated unsaturated cyclic sulfenate ester preparations.[6] In continuation of our efforts in this area, we report here the preparation of cyclopentadienyl iron dicarbonyl cyclopropyl and η^1-allyl complexes and $(Me_2PhP)(CO)_4$ manganese η^1-allyl complexes and their reactions with SO_2 and S_2O. We note that five- and six-membered-ring sulfur-containing heterocycles will presumably begin attracting increased attention as synthetic targets because of a recent report that 1,2-dithiolanes and 1,2-dithianes look particularly promising as inhibitors of HIV type 1 replication.[7] This replication inhibition is apparently a result of their ability to attack the conserved zinc fingers (presumably via the sulfur of the heterocycle) of retroviral nucleocapsid proteins, causing zinc ejection from the protein.

Experimental Section

General. All nuclear magnetic resonances (NMR) were obtained using a Varian VXR-200 FT NMR spectrometer. All absorptions are expressed in parts per million relative to residual undeuterated solvents. All infrared (IR) spectra were obtained using a Perkin-Elmer 1620 FT-IR spectrophotometer. All elemental analyses were performed by Atlantic Microlab Inc. of Norcross, GA. High-resolution mass spectral analyses (HRMS) were performed by the Nebraska Center for Mass Spectrometry. Thin-layer chromatography was carried out on 0.20 mm precoated Polygram aluminum oxide plates or 0.25 mm precoated Polygram SIL G/UV silica plates. Routine column chromatography was effected on alumina absorption (150 mesh, neutral), purchased from Aldrich, or silica gel 60 purchased from VWR Scientific. Tetrahydrofuran was distilled from sodium/benzophenone under nitrogen atmosphere immediately prior to use. Toluene and pentane were distilled from calcium hydride prior to use. All reactions were carried out under an atmosphere of dry nitrogen unless otherwise noted. Cyclopentadienyl iron dicarbonyl dimer, manganese carbonyl dimer, and dimethylphenyl phosphine were pur-

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(1) For recent reviews of transition-metal mediated 3 + 2 cycloadditions see: (a) Welker, M. E. *Chem. Rev.* **1992**, *92*, 97. (b) Chan, D. M. T. In *Comprehensive Organic Syntheses*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 5, p 271. (c) Wojcicki, A. *Coord. Chem. Rev.* **1990**, *105*, 35. (d) Rosenblum, M. *J. Organomet. Chem.*, **1986**, *300*, 191.

(2) (a) Fulcher, B. C.; Hunter, M. L.; Welker, M. E. *Synth. Commun.* **1993**, *23*, 217. (b) Raseta, M. E.; Mishra, R. K.; Cawood, S. A.; Welker, M. E.; Rheingold, A. L. *Organometallics* **1991**, *10*, 2936. (c) Powell, K. R.; Elias, W. J.; Welker, M. E. *J. Organomet. Chem.* **1991**, *407*, 81. (d) Brown, D. S.; Owens, C. F.; Wilson, B. G.; Welker, M. E.; Rheingold, A. L. *Organometallics* **1991**, *10*, 871. (e) Urove, G. A.; Welker, M. E.; Eaton, B. E. *J. Organomet. Chem.* **1990**, *384*, 105. (f) Raseta, M. E.; Cawood, S. A.; Welker, M. E.; Rheingold, A. L. *J. Am. Chem. Soc.* **1989**, *111*, 8268. (g) Urove, G. A.; Welker, M. E. *Organometallics* **1988**, *7*, 1013.

(3) The Turos and Baker groups have also made significant contributions to this area of chemistry. For lead references see: (a) Jiang, S.; Chen, T.; Turos, E. *Organometallics* **1995**, *14*, 4710. (b) Abram, T. S.; Baker, R.; Exon, C. M.; Rao, V. B.; Turner, R. W. *J. Chem. Soc., Chem. Commun.* **1984**, 987.

(4) Chen, L. S.; Lichtenberg, D. W.; Robinson, P. W.; Yamamoto, Y.; Wojcicki, A. *Inorg. Chim Acta* **1977**, *25*, 165.

(5) Stokes, H. L.; Ni, L. M.; Belot, J. A.; Welker, M. E. *J. Organomet. Chem.* **1995**, *487*, 95.

(6) Hurley, A. L.; Welker, M. E.; Day, C. S. *Organometallics* **1998**, *17*, 2832.

(7) (a) Huang, M.; Maynard, A.; Turpin, J. A.; Graham, L.; Janini, G. M.; Covell, D. G.; Rice, W. G. *J. Med. Chem.* **1998**, *41*, 1371. (b) Rice, W. G.; Baker, D. C.; Schaeffer, C. A.; Graham, L.; Bu, M.; Terpening, S.; Clanton, D.; Schultz, R.; Bader, J. P.; Buckheit, R. W.; Field, L.; Singh, P. K.; Turpin, J. A. *Antimicrob. Agents and Chemother.* **1997**, *41*, 419. For a review see: Rice, W. G.; Turpin, J. A. *Rev. Med. Virology* **1996**, *6*, 187.

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chased from Strem Chemicals and used as received. Crotyl chloride was purchased from Fluka and used as received. Cyclopropyl bromide was purchased from Acros and used as received. Magnesium bromide, *trans*-2-phenyl-1-cyclopropane carbonyl chloride, methallyl chloride, and triethyl aluminum were purchased from Aldrich and used as received. 4,5-Diphenyl-3,6-dihydro-1,2-dithiin 1-oxide (**17**) was synthesized according to a literature procedure.[2a] $CpFe(CO)_2CH_2CH{=}CH_2$ (**16**),[8] $CpFe(CO)_2CH_2CH{=}CHCH_3$ (**22**),[9] and $(Me_2PhP)Mn(CO)_4CH_2CH{=}CH_2$ (**27a**)[10] were synthesized according to literature procedures via addition of a THF solution of the respective anion to a THF solution of the appropriate chloride.

Cyclopentadienyl(cyclopropyl)dicarbonyl Iron (9). This compound has been previously reported with limited spectroscopic data.[11] We have found the following prep to be superior to both of the previously reported preparations of **9**.[11] Cyclopentadienyl(cyclopropylcarbonyl)dicarbonyl iron (**13**, R = H) (0.5 g, 2.03 mmol) was synthesized according to literature procedures.[12] This complex was photolyzed at −78 °C using a 450 W low-pressure Hg Hanovia lamp in a Pyrex immersion well for 1 h in toluene (200 mL). The reaction was monitored by thin-layer chromatography (TLC) to ensure complete decarbonylation. The solvent was removed by rotary evaporation. The product, a dark red-brown oil (**9**) (0.38 g, 1.70 mmol, 86%), was used without further purification. IR (NaCl): 2005, 1945 cm^{-1}. ^1H NMR (C_6D_6): 3.99 (s, 5H), 0.77 (m, 2H), 0.50 (m, 1H), 0.25 (m, 2H). ^{13}C NMR (C_6D_6): 217.27, 85.71, 8.81, −9.68. HRMS (*m*/*z*): calcd for M^+ ($C_{10}H_{10}FeO_2$), 218.0030; found 218.0031. Anal. Calcd for $C_{10}H_{10}FeO_2$: C, 55.09; H, 4.62. Found: C, 54.87; H, 4.69.

Cyclopentadienyl(2-phenyl-1-cyclopropylcarbonyl)dicarbonyl Iron (13, R = Ph). The iron dicarbonyl anion $[CpFe(CO)_2{}^-Na^+]$ was generated by stirring a THF solution of $[CpFe(CO)_2]_2$ (0.5 g, 1.4 mmol) over a 1% sodium amalgam for 5 h. The anion was then added using a double-ended needle to a THF solution of *trans*-2-phenyl-1-cyclopropanecarbonyl chloride (2.0 equiv) cooled to −78 °C. This mixture was stirred at −78 °C for 2 h and then allowed to warm to 25 °C overnight. The solvent was removed by rotary evaporation, and the remaining residue was dissolved in pentane and filtered through Celite. The pentane was removed by rotary evaporation to yield a red-brown oil (**13**, R = Ph) (0.89 g, 2.76 mmol, 98%). IR (NaCl): 2017, 1951, 1624 cm^{-1}. ^1H NMR (C_6D_6): 7.09−6.89 (m, 5H), 4.13 (s, 5H), 2.78−2.60 (m, 2H), 1.83−1.74 (m, 1H), 1.04−0.95 (m, 1H). ^{13}C NMR (C_6D_6): 249.45, 215.02, 141.47, 128.71, 128.32, 126.35, 86.15, 51.15, 28.61, 18.97. APT (C_6D_6): 141.47 (C), 128.71 (CH), 128.32 (CH), 126.35 (CH), 86.15 (CH), 51.15 (CH), 28.61 (CH), 18.97 (CH_2). Anal. Calcd for $C_{17}H_{14}FeO_3$: C, 63.35; H, 4.38. Found: C, 63.83; H, 4.63.

Cyclopentadienyl(3-(1,2-oxathiol-3-ane-1-oxide))dicarbonyl Iron (11, 12). The η^1-cyclopropyl iron complex **9** (0.393 g, 1.8 mmol) was dissolved in toluene, purged with nitrogen, and cooled to −78 °C. Sulfur dioxide (10 mL) was condensed at −78 °C into the iron complex solution. It was allowed to stir at −78 °C for 2 h and then warmed to 25 °C overnight. The solvent was removed by rotary evaporation and high vacuum. The crude product was purified by column chromatography on alumina. Pentane removed any starting material (**9**), and elution with an ether gradient yielded a 5:2 ratio of the diastereomers as a red-brown oil (**11**:**12**) (0.169 g, 0.60 mmol, 33%). IR (NaCl): 2013, 1949, 1122, 1116, 1080 cm^{-1}. ^1H NMR ($CDCl_3$): **11**: 5.45 (m, 1H), 4.89 (s, 5H), 3.40 (m, 1H), 3.01 (m, 1H), 2.61 (m, 2H); **12**: 6.25 (dd, *J* = 10.8, 4.4 Hz, 1H), 4.91 (s, 5H), 3.40 (m, 1H), 3.01 (m, 1H), 2.61 (m, 2H). LRMS (FAB) (*m*/*z*): 283 (25) $(M + H)^+$, 254 (9) $(M^+ - CO)$, 226 (100) $(M^+ - 2CO)$. Anal. Calcd For $C_{10}H_{10}FeO_4S$: C, 42.58; H, 3.57. Found: C, 42.67; H, 3.64. Acetonitrile, hexane, and neat SO_2 as solvents were also tried. Yields increased, but diastereoselectivity was decreased (no reaction occurred in hexane): acetonitrile (**9**, 0.175 g, 0.08 mmol yielded **11**:**12**, 0.208 g, 0.07 mmol, 92%, 3:2), neat SO_2 (**9**, 0.140 g, 0.64 mmol yielded **11**:**12**, 0.125 g, 0.44 mmol, 69%, 3:2).

Base/Lewis Acid Aided Synthesis of 11 and 12. The reaction was set up as described above. The Lewis acid (1.2 equiv) was added when the temperature of the iron complex solution reached −78 °C. This was followed by the base (2.0 equiv) addition. Sulfur dioxide (10 mL) was condensed at −78 °C into the reaction mixture. It was allowed to stir at −78 °C for 2 h and then warmed to 25 °C overnight. Saturated aqueous $NaHCO_3$ (50 mL) was added and extracted with ethyl acetate (3 × 30 mL). The combined ethyl acetate extracts were dried over $MgSO_4$ and filtered, and solvent was removed by rotary evaporation to produce a red-brown oil. The crude product was purified by column chromatography on alumina to yield diastereomers **11** and **12**, identical by ^1H NMR comparison to the material reported above.

***anti*- (18) and *syn*-Cyclopentadienyl(*anti*-4-(1,2-dithiol-4-ane 1-oxide))dicarbonyl Iron (19).** The η^1-allyl iron complex **16** (0.19 g, 0.87 mmol) was dissolved in tetrahydrofuran (10 mL), and then 4,5-diphenyl-3,6-dihydro-1,2-dithiin 1-oxide (**17**) (0.31 g, 1.08 mmol) was added. The reaction mixture was allowed to stir at 25 °C overnight and then concentrated under reduced pressure. The crude product was purified on a silica gel prep plate (diethyl ether, R_f = 0.39) yielding metallothiosulfinate ester (**18**) as a light yellow solid, as a 8:1 mixture of *anti* (**18**) to *syn* (**19**) diastereomers (0.17 g, 0.53 mmol, 65% yield), mp 117−120 °C. IR (C_6D_6): 3234, 2014, 1956, 1618, 1456, 1450, 1391, 1337, 1325, 1162, 1074(SO) cm^{-1}. ^1H NMR (*anti*, **18**) (C_6D_6): 3.89 (s, 5H), 3.40 (m, 2H) 3.12 (m, 1H), 2.72 (dd, *J* = 13.3 Hz, 9 Hz, 1H), 2.16 (dd, *J* = 14 Hz, 11.2 Hz, 1H). HRMS EI calcd for $C_{10}H_{10}O_3S_2Fe$: 297.9421; found 297.9421. Anal. Calcd for $C_{10}H_{10}O_3S_2Fe$: C, 40.28; H, 3.39. Found: C, 40.19; H, 3.41.

Cyclopentadienyl(4-(1,2-dithiol-4-ane-5-methyl-1-oxide))dicarbonyl Iron (23, 24, 25, 26). The iron allyl complex (**22**) (0.048 g, 0.20 mmol) was dissolved in THF (15 mL) and then treated with 4,5-diphenyl-3,6-dihydro-1,2-dithiin 1-oxide (**17**) (1.24 equiv). The reaction mixture was allowed to stir for 55 h at 25 °C. The solvent was removed by rotary evaporation, and the residue was purified by column chromatography on alumina. Pentane removed any unreacted starting materials and impurities, and elution with an ether gradient yielded an 8:3:1:1 ratio of diastereomers (**23**, **24**, **25**, **26**) as a red-brown oil (0.023 g, 0.074 mmol, 35%). IR (NaCl): 2960, 2917, 2853, 1999, 1949, 1066 cm^{-1}. ^1H NMR ($CDCl_3$) (only diagnostic peaks for each diastereomer are reported): **23** 4.94 (s, 5H), 0.99 (d, *J* = 6.0 Hz, 3H); **24** 4.89 (s, 5H), 1.73 (d, *J* = 6.0 Hz, 3H); **25** 4.86 (s, 5H), 1.61 (d, *J* = 6.0 Hz, 3H); **26** 4.82 (s, 5H), 1.49 (d, *J* = 6.0 Hz, 3H). LRMS (FAB): Calcd for $C_{11}H_{12}FeO_3S_2Li$ $(M + Li)^+$ 319.1; found, 319.1.

General Procedure for the Synthesis of Manganese Allyl Complexes. The manganese carbonyl dimer $[Mn_2(CO)_{10}]$ (2.0 g, 5.13 mmol) was dissolved in toluene. Dimethylphenyl phosphine (1.42 g, 10.3 mmol) was added to the reaction mixture, which was degassed. The solution was refluxed for 6 h, and then the resulting orange solution was poured into pentane (100 mL) and cooled to −78 °C. The yellow precipitate $[(Me_2PhP)Mn(CO)_4]_2$ was vacuum filtered and vacuum dried (2.56 g, 4.2 mmol, 82%).[13] The manganese anion was generated by stirring a THF solution of $[(Me_2PhP)Mn(CO)_4]_2$ over a 1% sodium amalgam for 5 h. The anion was then added using a

(8) Bucheister, A.; Klemarczyk, P.; Rosenblum, M. *Organometallics* **1982**, *1*. 1679.
(9) (a) Green, M. L. H.; Nagy, P. L. I. *J. Chem. Soc.* **1963**, 189. (b) Downs, R. L.; Wojcicki, A. *Inorg. Chim. Acta* **1978**, *27*, 91.
(10) Palmer, G. T.; Basolo, F. *J. Am. Chem. Soc.*, **1985**, *107*, 3122.
(11) Cutler, A.; Fish, R. W.; Giering, W. P.; Rosenblum, M. *J. Am. Chem. Soc.* **1972**, *94*, 4354.
(12) Brookhart, M.; Studabaker, W. B.; Husk, G. R. *Organometallics* **1987**, *6*, 1141.
(13) Wawersik, H.; Basolo, F. *Inorg. Chim. Acta* **1969**, *3*, 113.

double-ended needle to a THF solution of the appropriate allyl chloride (2.1 equiv) cooled to −78 °C. This mixture was stirred at −78 °C for 2 h and then allowed to warm to 25 °C overnight. The solvent was removed by rotary evaporation. The remaining residue was dissolved in pentane (25 mL) and filtered through Celite, and the flask was placed in a liquid nitrogen bath. The yellow pentane solution was decanted away from impurities. The pentane was removed by rotary evaporation and high vacuum, and the allyl complexes (**27a**,**b**) were used immediately without any other further purification.

Tetracarbonyl(2-methyl-2-propenyl)(dimethylphenylphosphine)manganese (27b). The manganese anion was generated from $[(Me_2PhP)Mn(CO)_4]_2$ (1.00 g, 1.60 mmol) and then added to a THF solution of methallyl chloride (0.31 g, 3.44 mmol) using the procedure outlined above. The product was obtained as an orange oil (**27b**) (1.085 g, 3.01 mmol, 77%). IR (NaCl): 3060, 2912, 2044, 1957, 1955, 1607 cm^{-1}. ^1H NMR ($CDCl_3$): 7.50−7.39 (m, 5H), 4.50 (d, J = 2.1 Hz, 1H), 4.23 (d, J = 2.1 Hz, 1H), 1.74 (d, J = 8.3 Hz, 6H), 1.72 (s, 3H), 1.33 (d, $J(^{31}P-^1H)$ = 7.4 Hz, 2H). ^{13}C NMR (C_3D_6O): 206.08, 156.11 (d, $J(^{31}P-^{13}C)$ = 6.3 Hz), 138.00 (d, $J(^{31}P-^{13}C)$ = 40.5 Hz), 130.57 (d, $J(^{31}P-^{13}C)$ = 2.4 Hz), 130.02 (d, $J(^{31}P-^{13}C)$ = 8.8 Hz), 129.47 (d, $J(^{31}P-^{13}C)$ = 9.3 Hz), 102.32, 24.25, 17.78 (d, $J(^{31}P-^{13}C)$ = 9.5 Hz), 15.95 (d, $J(^{31}P-^{13}C)$ = 28.7 Hz). APT (C_3D_6O): 156.11 (C), 138.00 (C), 130.57 (CH), 130.02 (CH), 129.47 (CH), 103.22 (CH_2), 24.25 (CH_3), 17.78 (CH_2), 15.95 (CH_3). LRMS EI: calcd for $C_{15}H_{18}MnO_3P$ $(M - CO)^+$ 332.0; found, 332.1. LRMS FAB: calcd for $C_{15}H_{19}MnO_3P$ $(M + H - CO)^+$ 333.0; found, 333.0 (100), 305 (41) $(M + H - 2CO)^+$, 277-(27) $(M + H - 3CO)^+$.

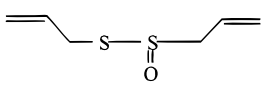
$(Me_2PhP)(CO)_4Mn(SO_2-CH_2CH=CH_2)$ (28a). The manganese allyl complex (**27a**) (0.185 g, 0.53 mmol) was dissolved in THF, purged with nitrogen, and then cooled to −78 °C. Sulfur dioxide (15 mL) was condensed at −78 °C into the reaction mixture, which was allowed to stir at −78 °C for 2 h and then warmed to 25 °C overnight. The solvent was removed by rotary evaporation, and the remaining residue was vacuum dried. Recrystallization from acetone/pentane afforded a bright yellow solid (**28a**) (0.210 g, 0.51 mmol, 96%), mp 87−90 °C. IR (NaCl): 2099, 2082, 2012, 1953, 1037 cm^{-1}. ^1H NMR (C_3D_6O): 7.86−7.49 (m, 5H), 6.13−5.92 (m, 1H), 5.39 (d, J = 10.5 Hz, 1H), 5.38 (d, J = 17.1 Hz, 1H), 3.60 (d, J = 6.9 Hz, 2H), 2.21 (d, J = 10.3 Hz, 6H). Anal. Calcd for $C_{15}H_{16}O_6$-MnPS: C, 43.92; H, 3.93. Found: C, 43.81; H, 4.02.

$(Me_2PhP)(CO)_4Mn(S_2O-CH_2CH=CH_2)$ (28b). The manganese allyl complex **27a** (0.122 g, 0.35 mmol) was dissolved in THF. The 4,5-diphenyl-3,6-dihydro-1,2-dithiin 1-oxide (**17**) (0.125 g, 0.44 mmol) was added, and the reaction mixture was allowed to stir for 24 h. The solvent was removed by rotary evaporation. The crude product was purified by column chromatography on silica. Pentane eluted the 2,3-diphenyl-1,3-butadiene side product of S_2O generation, and elution with an ether gradient yielded an orange oil (**28b**) (0.095 g, 0.224 mmol, 64%). IR (NaCl): 3054, 2982, 2911, 2071, 1993, 1991, 1950, 1617, 1045, 910 cm^{-1}. ^1H NMR ($CDCl_3$): 7.56−7.38 (m, 5H), 6.02−5.90 (m, 1H), 5.33 (d, J = 16.1 Hz, 1H), 5.35 (d, J = 9.4 Hz, 1H), 3.79 (q, J_{AB} = 16.3 Hz, 2H), 1.93 (d, J = 7.2 Hz, 3H), 1.89 (d, J = 7.3 Hz, 3H). ^{13}C NMR (C_3D_6O): 206.22, 137.31 (d, $J(^{31}P-^{13}C)$ = 43.8 Hz), 131.08 (d, $J(^{31}P-^{13}C)$ = 2.4 Hz), 130.29 (d, $J(^{31}P-^{13}C)$ = 9.0 Hz), 129.56 (d, $J(^{31}P-^{13}C)$ = 9.8 Hz), 125.98, 121.63, 67.84 (d, $J(^{31}P-^{13}C)$ = 10.7 Hz), 15.54 (d, $J(^{31}P-^{13}C)$ = 7.8 Hz), 14.92 (d, $J(^{31}P-^{13}C)$ = 8.0 Hz). APT (C_3D_6O): 137.31 (C), 131.08 (CH), 130.29 (CH), 129.56 (CH), 125.98 (CH), 121.63 (CH_2), 67.84 (CH_2), 15.54 (CH_3), 14.92 (CH_3). LRMS FAB: calcd for $C_{15}H_{16}MnO_5PS_2$ $(M)^+$ 426.0; found, 426.0.

$(Me_2PhP)(CO)_4Mn(S_2O-CH_2C(Me)=CH_2)$ (28c). The manganese allyl complex **27b** (0.087 g, 0.24 mmol) was dissolved in THF. The 4,5-diphenyl-3,6-dihydro-1,2-dithiin 1-oxide (**17**) (0.086 g, 0.30 mmol) was added, and the reaction mixture was allowed to stir for 48 h. The reaction was worked up using the procedure outlined above for **28b** to yield an orange oil (**28c**) (0.042 g, 0.095 mmol, 36%). IR (NaCl): 2921, 2918, 2852, 1992, 1988, 1952, 1901, 1559, 1051, 942, 912 cm^{-1}. ^1H NMR ($CDCl_3$): 7.52−7.25 (m, 5H), 5.03 (s, 2H), 3.78 (q, J_{AB} = 12.8 Hz, 2H), 1.97−1.93 (m, 6H), 1.88 (s, 3H). LRMS FAB: calcd for $C_{16}H_{18}MnO_5PS_2Li$ $(M + Li)^+$ 447.0; found, 446.3.

Results and Discussion

We have been interested in the preparation of compounds containing unusual organosulfur functional groups because they have been identified as the biologically active components of many plants with traditional medicinal applications. The −S−S(O)− (thiosulfinate ester) functional group is present in a number of these compounds, and thiosulfinate esters have been isolated or synthesized which have biological activities as antibacterials,[14] antifungals[14] (allicin (**4**), garlic), antivirals,[15] plant growth regulators[16] (asparagusic acid *S*-oxides (**5**), R=CO_2H, asparagus; brugeriol and isobrugeriol (**6**), R=OH, mangroves), platelet aggregation inhibitors[17] (garlic), tumor growth inhibitors,[18] and anticarcinogenic enzyme inducers.[19] This potential cancer chemopreventive activity has attracted increasing attention over the past few years, and a variety of organosulfur compounds (thiosulfinate esters and dithiolthiones primarily) that are anticarcinogenic enzyme inducers (particularly glutathione *S*-transferase inducers) have now been isolated or prepared.[19] This anticarcinogenic activity coupled with the recently reported HIV-1 replication inhibition activity of 1,2-dithiolanes[7] forms the basis for our continuing interest in the synthesis of five-membered-ring sulfur-containing heterocycles.



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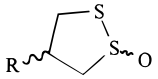


5 R=CO_2H

6 R=OH

Reaction of $CpFe(CO)_2$(cyclopropyl),[11] $CpFe(CO)_2$-(allyl),[20] and $(PR_3)(CO)_4Mn$(allyl)[21] complexes with sulfur dioxide (SO_2) has been reported previously, so most of the current study deals with the reactions of these complexes with disulfur monoxide (S_2O). Initially, we prepared the simplest $CpFe(CO)_2$ cyclopropyl **9** by reaction of $CpFe(CO)_2^-Na^+$ (**7**) with cyclopropyl bro-

(14) For a recent review on organosulfur compounds that have been isolated from garlic, onions, and related plants and their biological activities see: Block, E. *Angew. Chem., Intl. Ed. Engl.* **1992**, *31*, 1135−78, and references therein.

(15) Frolov, A. F.; Mishenkova, E. L. *Mikrobiol. Zh. Kiev* **1970**, *32*, 628; *Chem. Abstr.* **1971**, *74*, 74916c.

(16) (a) Yanagawa, H.; Kato, T.; Kitahara, Y. *Tetrahedron Lett.* **1973**, 1073. (b) Yanagawa, H.; Kato, T.; Kitahara, Y. *Tetrahedron Lett.* **1972**, 2549. (c) Yanagawa, H.; Kato, T.; Sagami, H.; Kitahara, Y. *Synthesis* **1973**, 607. (d) Yanagawa, H.; Kato, T.; Kitahara, Y. *Tetrahedron Lett.* **1973**, 1073. (e) Kato, A.; Takahashi, J. *Phytochemistry* **1976**, *15*, 220. (f) Kato, A.; Okutani, T. *Tetrahedron Lett.* **1972**, 2959.

(17) Block, E.; Ahmad, S.; Catalfamo, J. L.; Jain, M. K.; Apitz-Castro, R. *J. Am. Chem. Soc.* **1986**, *108*, 7045.

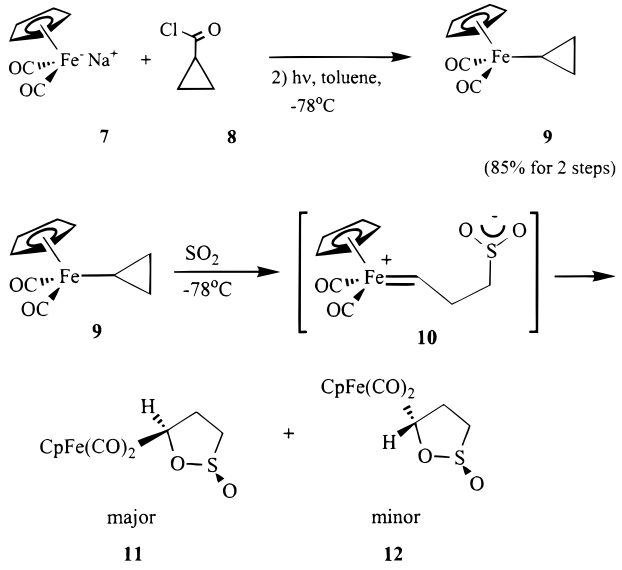
(18) (a) Hirsh, A. F.; Piantadosi, C.; Irvin, J. L. *J. Med. Chem.* **1965**, *8*, 10. (b) DePaulo, J. A.; Carruthers, C. *Cancer Res.* **1960**, *20*, 431.

(19) (a) Kohlmeier, L.; Su, S. R. *FASEB J.* **1997**, *11*, A369. (b) Prochaska, J. J.; Santaria, A. B.; Talalay, P. *Proc. Natl. Acad. Sci. U.S.A.* **1992**, *89*, 2394.

(20) (a) Chen, L. S.; Su, S. R.; Wojcicki, A. *J. Am. Chem. Soc.* **1974**, *96*, 5655. (b) Chen, L. S.; Su, S. R.; Wojcicki, A. *Inorg. Chim. Acta* **1978**, *27*, 79.

(21) (a) Hartman, F. A.; Wojcicki, A. *Inorg. Chim. Acta* **1968**, *2*, 289. (b) Hartman, F. A.; Wojcicki, A. *Inorg. Chim. Acta* **1968**, *2*, 351.

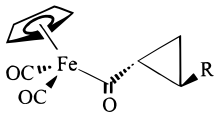
mide[11] and reaction of $CpFe(CO)_2Br$ with cyclopropyllithium.[11] However, isolated yields of **9** were always in the 20−30% range, and we found reaction of $CpFe(CO)_2^-Na^+$ (**7**) with cyclopropylcarbonyl chloride (**8**) followed by decarbonylation to be a high-yield route to **9**.[22] Cyclopropyl complex **9** had been previously reported to cyclize with SO_2 to an unspecified diastereomeric mixture of sultines (**10**),[11] so we decided to first repeat this reaction before moving on to more substituted cyclopropyl complexes and S_2O. We found that complex **9** reacted with SO_2 in toluene at −78 °C to produce a 2.5:1 mixture of diastereomers in 33% yield. The isolated yield of the **11**/**12** mixture improved to 69% in neat SO_2; however use of SO_2 in the polar aprotic solvent acetonitrile proved optimal, and we isolated the **11**/**12** mixture in 92% yield. Diastereoselectivity (**11**:**12**) was decreased slightly to 1.5:1 by the solvent change. We assigned the relative stereochemistry of the major (**11**) and minor (**12**) diastereomers using the method of Yanagawa, Kato, and Kitahara.[16a,b] They had reported differences in the methine chemical shifts upon treatment of methyl esters of natural products (**5**, R = CO_2-Me) with $Eu(FOD)_3$. We found that when the **11**/**12** mixture was treated with 0.4 equiv of $Eu(FOD)_3$ ($CDCl_3$), the methine proton in the minor diastereomer (δ 6.25) shifted downfield more than the major diastereomer (δ 5.45). On the basis of this chemical shift difference, we propose the *syn* (**11**) and *anti* (**12**) relationships for the major and minor diastereomers.



7 **8** **9** **10** **11** **12**

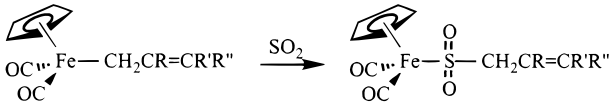
If proposed intermediate **10** is present, the diastereoselectivity of the ring closure might be influenced by Lewis acid additives. However, knowing that these types of iron complexes are also particularly sensitive to trace protic acid, we decided to perform the SO_2 cyclization of **9** in the presence of Lewis acids and bases. We performed these cyclizations in toluene and found that while isolated yields of **11**:**12** improved with additives, diastereoselectivity was little effected ($MgBr_2$/$NaHCO_3$, **11**:**12** 1.5:1, 60%; $MgBr_2$/Et_3N, **11**:**12** 2:1, 74%; Et_3Al/$NaHCO_3$, **11**:**12** 1:1, 62%).

We next wanted to look at this cycloaddition with substituted cyclopropyl complexes; however, we were thwarted here by an inability to prepare the complexes. Preparation of carbonylated cyclopropyls (**13**) proceeded cleanly as before via reaction of the appropriate acid chloride (R = Me;[23] R = Ph) with $CpFe(CO)_2^-Na^+$ (**7**). The same photolysis conditions that worked well for the decarbonylation to produce **9** resulted in rapid decomposition of both of these substituted cyclopropyls (**13**). Attempts to do modified Simmons−Smith type cyclopropanations[24] on CpFe(CO)(vinyl) phosphine and phosphite complexes in hopes of producing more stable cyclopropyls also were unsuccessful. Treatment of **9** with our previously reported "S_2O" source, 4,5-diphenyl-3,6-dihydro-1,2-dithiin 1-oxide (**17**)[2a] in THF at 25 °C, also resulted in decomposition of **9**, so we turned our attention to the 3 + 2 cycloadditions of metal allyls with S_2O.



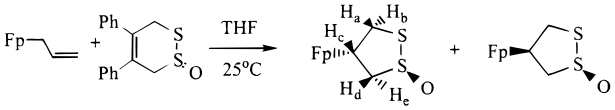
13

Treatment of a variety of $CpFe(CO)_2$(allyl) complexes with SO_2 has been reported previously by Wojcicki and co-workers. Whereas the unsubstituted allyl (**14**, R = R′ = R″ = H) can provide a cyclized product upon rapid removal of SO_2, all other $CpFe(CO)_2$ allyl complexes (**14**) yielded insertion (**15**) rather than 3 + 2 cycloaddition products when treated with SO_2.[20]



14 **15**

In chemistry related to this, we have found that **16** reacts with S_2O source **17** to yield **18** and **19** in 65% yield as a 8:1 (**18**:**19**) mixture of diastereomers. The assignment of relative positions of Fp (Fp = $CpFe(CO)_2$) and O in **18** was based on ^1H NMR coupling constants, NOE experiments, and shift reagent experiments described below. The metallothiosulfinate ester had a characteristic S=O stretch in the IR at 1074 cm^{-1}. The ^1H NMR spectra (C_6D_6) of **18** and **19** showed the expected double doublets for the protons of $-CH_2-$ groups of the sulfur ring. Upon irradiation of a major diastereomer one-proton multiplet at 3.12 ppm, all other major peaks were simplified; therefore, this peak was assigned to H_c of **18**. H_a and H_d absorb around 3.4 ppm, and H_b and H_e are below 3.0 ppm. Vicinal coupling constants of **18** are analogous to those seen in the known *anti* diastereomer of the methyl ester of asparagusic acid *S*-oxide (**5**, R = CO_2Me): J_{ac} = 5.0 Hz, J_{bc} = 9.0 Hz, J_{dc} = 3.3 Hz, J_{ec} = 11.2 Hz.[16]



16 **17** **18** **19**

(22) Jones et al. have previously reported this method as a good route to related iron cyclopropyls: Trace, R. L.; Jones, W. M. *J. Organomet. Chem.* **1989**, *376*, 103, and references therein.

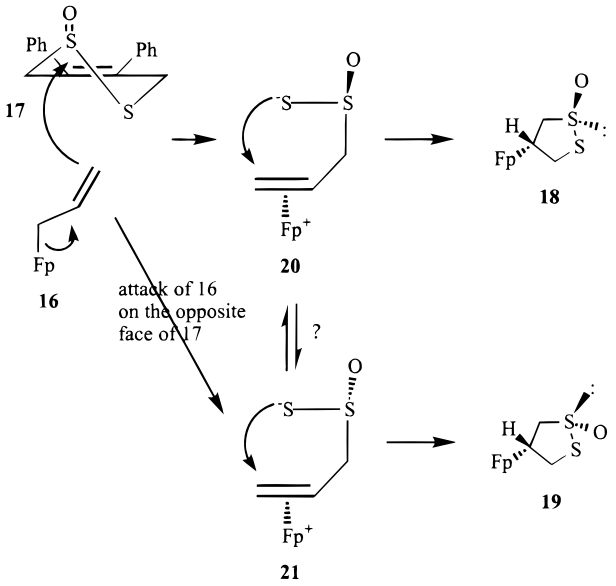
(23) Conti, N. J.; Crowther, D. J.; Tivakornpannarai, S.; Jones, W. M. *Organometallics* **1990**, *9*, 175.

(24) Ambler, P. W.; Davies, S. G. *Tetrahedron Lett.* **1988**, *29*, 6979.

Additional confirmation of relative stereochemistry **18** for the major diastereomer comes from shift reagent experiments and NOE experiments. As mentioned above, Yanagawa, Kato, and Kitahara had reported differences in the methine (H_c) chemical shifts upon treatment of methyl esters of natural products (**5**) with $Eu(FOD)_3$.[16a,b] When the **18**/**19** mixture was treated with 0.4 equiv of $Eu(FOD)_3$, H_c in the major diastereomer shifted downfield by an amount similar to that reported previously for the natural product (**5**).[16a,b] Last, irradiation of H_a and H_d produced a 4.4% NOE enhancement of H_c. However, when H_e was irradiated, only a 0.9% NOE enhancement was seen at H_c. Taken together, these three pieces of evidence strongly implicate structure **18** for the major diastereomer.

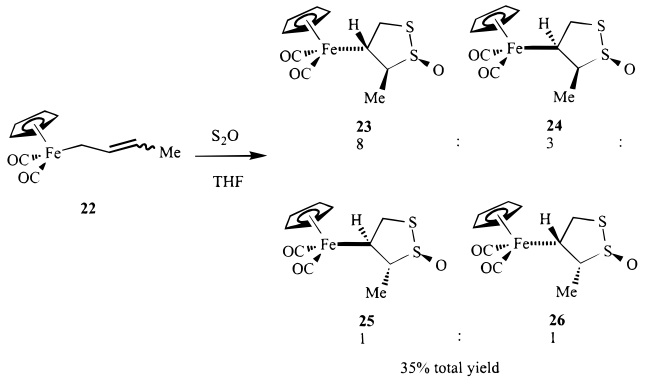
Formation of the *anti* diastereomer **18** can be explained via a mechanistic model analogous to ones proposed by Rosenblum, Wojcicki, and us to explain prior cyclizations with SO_2 and S_2O.[1] The initial step of this mechanism would involve nucleophilic attack by the electrons of the C=C double bond from **16** on the sulfoxide sulfur of **17**. The conformation of **17** with the sulfoxide oxygen in an axial position is about 3 kcal/mol more stable than its equatorial counterpart.[25]

The compound **17** then undergoes electrocyclic ring opening to generate cationic alkene iron intermediates (**20** and **21**) and 2,3-diphenylbutadiene. Intramolecular ring closure from **20** or **21** would then explain the products. It is possible that this observed **18**:**19** ratio is a kinetic result arising from approach of **16** toward the least hindered face of the electrophilic sulfur in **17** as depicted. However, **20** and **21** are potentially interconvertible by a known thiosulfinate ester racemization mechanism,[26] so we cannot rule out the possibility that this ratio is determined by ring closure rates of **20** and **21** regardless of which face of **17** reacts with **16**.



If a divalent coordinating metal is added to the reaction mixture, the *syn* (**19**) product could be the major product[27] if the coordinating metal will bind with the oxygen of sulfur and the oxygen of one of the carbonyls on iron. When the divalent coordinating alkali metal ($MgBr_2$) was added to the reaction mixture, we observed a 6:1 mixture of diastereomers of the product, *anti* (**18**): *syn* (**19**), respectively. This observation of more *syn* product is consistent with this coordination argument; however, the *syn* diastereomer could not be formed predominantly. Attempts to use other cations ($SnCl_2$, $ZnCl_2$) resulted only in rapid decomposition of **17**.

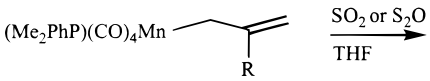
Cyclopentadienyl iron dicarbonyl crotonyl complex **22** (E:Z, 4:1) also reacts with **17** to produce thiosulfinate ester products. This cyclization reaction now generates three chiral centers so there are four possible diastereomers. By ^1H NMR, we saw four products (**23**, **24**, **25**, **26**) in a 8:3:1:1 ratio. Once again, we determined the stereochemistry using $Eu(FOD)_3$ shift reagent experiments and compared our results to the data reported on the natural products, asparagusic acid *S*-oxides (**5**),[16a,b] brugeriol, and isobrugeriol (**6**).[16d,e] We found that when the **23**/**24**/**25**/**26** mixture was treated with 0.4 equiv of $Eu(FOD)_3$, the methyl doublets of **23** and **24** moved downfield 2.9 ppm each, while this doublet only shifted downfield by 2.2 ppm in **25** and 2.1 ppm in **26**. The $Eu(FOD)_3$ shift reagent experiment results were also used to determine the stereochemistry at the chiral center attached to the Fp group. The Cp singlet ^1H NMR resonances of **23** and **26** did not move downfield (0.65 ppm) as much as the analogous resonances of **24** and **25** (2.0 ppm). We can infer from these data that the E isomer of **22** cyclized with a 8:1 (**23**:**25**) selectivity as we saw for **16**, whereas the Z isomer cyclized with a reduced 3:1 selectivity (**24**:**26**).



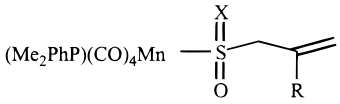
Last, $(PMe_2Ph)(CO)_4$ manganese allyl complexes **27a** and **27b** were also treated with SO_2 for **27a** and S_2O precursor **17** for **27a** and **27b**. The reaction of $(CO)_5Mn$-CH_2−CH=CH_2 with SO_2 has previously been reported to yield the SO_2 insertion product analogous to **28a**.[21] We prepared **28a** here so that its spectroscopic properties could be compared to those of **28b** and **28c** since S_2O insertion products have not been reported previously by our group. The alkenyl portion of the ^1H NMR of **28a** is very similar to that of **27a**, as expected. However, the CH_2 resonance of **28a** (C_3D_6O, δ 3.60, d, J = 6.9 Hz) is easily distinguished from the CH_2 resonance of **27a** (C_3D_6O, δ 1.33, t, J ^1H = ^{31}P = 8.0 Hz) and is comparable to the ^1H NMR CH_2 resonance previously reported for $(CO)_5MnSO_2CH_2$−CH=CH_2 ($CDCl_3$, δ 3.75, d, J = 8 Hz).[21a]

(25) Juaristi, E.; Guzman, J.; Kane, V. V.; Glass, R. S. *Tetrahedron* **1984**, *40*, 1477.
(26) Mikolajczyk, M.; Drabowicz, J. *Top. Stereochem.* **1982**, *13*, 333.
(27) Ozin, G. A.; Gil, C. *Chem. Rev.* **1989**, *89*, 1749.

Similarly, **27a** and **27b** reacted with S_2O precursor (**17**) to yield new complexes **28b** and **28c** with alkenyl ^{1}H NMR resonances comparable to those seen in **27a** and **27b** but with CH_2 ^{1}H NMR resonances shifted downfield to δ 3.79 and 3.78, respectively ($CDCl_3$). Unlike **28a**, the central sulfur in complexes **28b** and **28c** is a chiral center[26] and the CH_2 protons of both of these complexes are diastereotopic (J_{AB} = 16 Hz in **28b**, 13 Hz in **28c**).



27a R=H
27b R=Me



28a R = H, X = O, 96%
28b R=H, X = S, 64%
28c R=Me, X = S, 36%

In conclusion, we have effected diastereoselective 3 + 2 cycloaddition reactions of $CpFe(CO)_2$ cyclopropyl with SO_2 and $CpFe(CO)_2$ allyl complexes with S_2O and determined the relative stereochemistry of the major diastereomers formed. In contrast, related phosphine tetracarbonyl manganese allyl complexes reacted with S_2O to yield insertion rather than cycloaddition products. Biological screening data of sulfur heterocycles generated by demetalation of these and related iron complexes will be reported in due course.

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