129967-20-0; (±)-46, 129967-21-1; methyl crotonate, 623-43-8; 6-methylhept-5-en-2-one, 110-93-0; methyl 4-bromocrotonate, 6000-00-6; 1-iodo-2-methylcyclohexene, 40648-08-6; (*E*)-1-bromo-1-butene, 32620-08-9; 1-bromo-2-methyl-1-propene, 3017-69-4; (*Z*)-1-bromo-1-propene, 590-13-6; 2-bromo-1-propene, 557-93-7; 1-iodocyclohexene, 17497-53-9.

Supplementary Material Available: Experimental details for the preparation of **35–38** and **40–44** (4 pages). Ordering information is given on any current masthead page.

Manganese(III)-Based Asymmetric Oxidative Free-Radical Cyclization of Unsaturated β-Keto Sulfoxides

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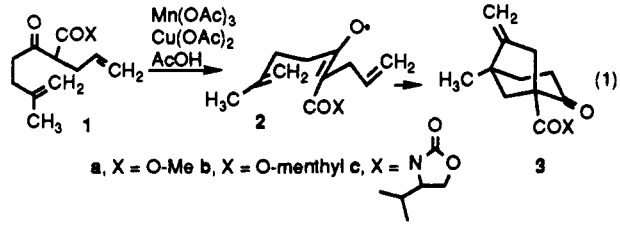
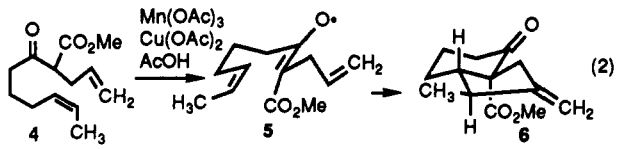
β-Keto sulfoxides and β-keto sulfones can be used as substrates for Mn(III)- and Cu(II)-based oxidative free-radical cyclizations. The sulfoxide chiral center completely controls the stereochemistry of the cyclization. Oxidative cyclization of racemic sulfoxide **8** affords **13** as a single diastereomer. Oxidative cyclization of enantiomerically pure sulfoxide **20** gives **21** as a single enantiomer. The chiral auxiliary can be removed by oxidation with potassium peroxomonosulfate to give the sulfone followed by reduction with sodium amalgam to give bicyclo[3.2.1]octanone **23**. Oxidative cyclization of **26** gives indanone **29**, which spontaneously loses toluenesulfenic acid to give indenone **30**.

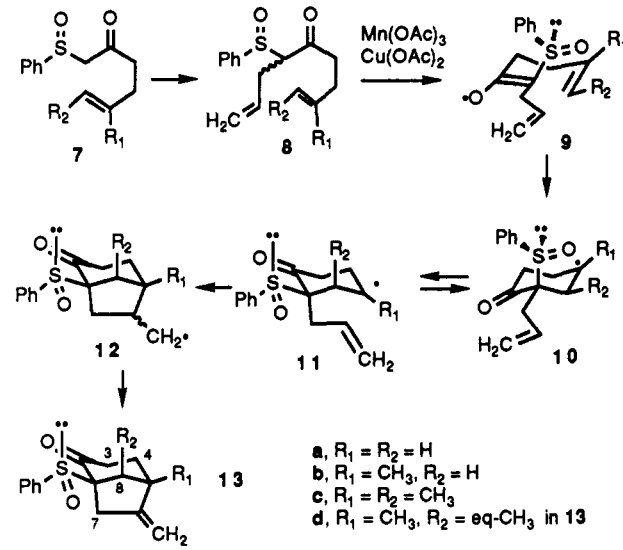
We have recently developed Mn(III)-based oxidative free-radical tandem cyclizations into a general route for the preparation of bicyclo[3.2.1]octan-2-ones **3a** (eq 1) and indenones **6** (eq 2).[1] Since these cyclizations proceed





through achiral radicals **2a** and **5** to produce chiral products **3a** and **6**, we have examined modifications using chiral auxiliaries that would permit these cyclizations to be carried out with asymmetric induction. Initial studies using **1b**, X = *O*-menthyl, were discouraging, affording ≈55:45 mixtures of diastereomers. We next turned our attention to Evans' chiral oxazolidinone, which gives much higher asymmetric induction than chiral esters.[2] Unfortunately, **1c** did not undergo oxidative cyclization on treatment with Mn(III) and Cu(II) in acetic acid. We therefore turned our attention to the oxidative cyclization of β-keto sulfoxides rather than β-keto esters. Sulfoxides have been used successfully in asymmetric carbon–carbon

Scheme I



bond-forming reactions.[3] The proximity of the sulfur chiral center to the radical should lead to a high degree of asymmetric induction if the oxidative cyclization is successful.

Results and Discussion

The requisite β-keto sulfoxides can be easily prepared by standard procedures. Our initial studies were carried out with racemic sulfoxides since the extent of asymmetric induction in the cyclization could be easily determined as

(1) (a) Snider, B. B.; Mohan, R. M.; Kates, S. A. *J. Org. Chem.* **1985**, *50*, 3659. (b) Dombroski, M. A.; Kates, S. A.; Snider, B. B. *J. Am. Chem. Soc.* **1990**, *112*, 2759 and references cited therein. (c) Kates, S. A.; Dombroski, M. A.; Snider, B. B. *J. Org. Chem.* **1990**, *55*, 2427 and references cited therein.

(2) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127.

(3) Posner, G. H. In *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C., Eds.; John Wiley & Sons: Chichester, 1988; pp 823–849. Posner, G. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, pp 225–241. Solladié, G. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, pp 157–199. Barbachyn, M. R., Johnson, C. R. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 4, pp 227–261.

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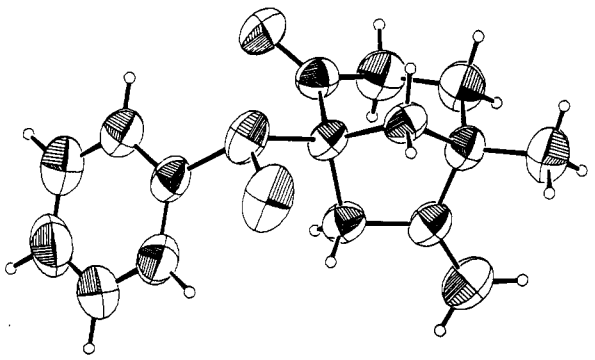


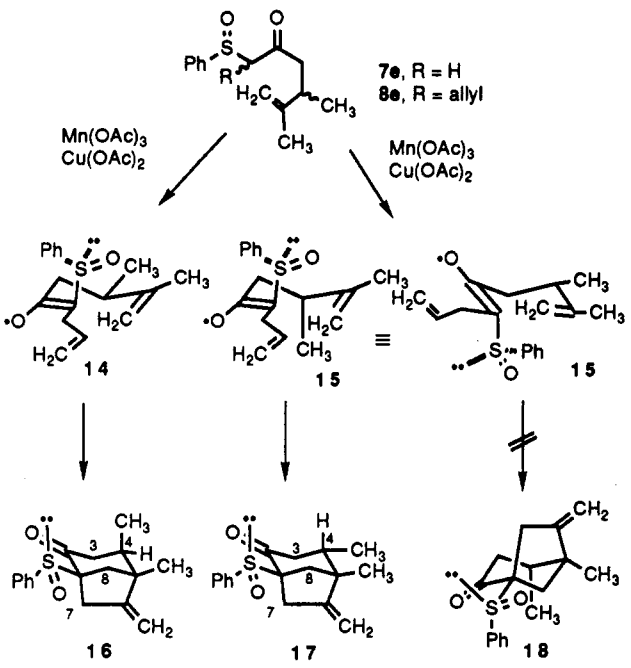
Figure 1. Molecular structure of **13b** showing 50% probability ellipsoids for atoms refined by using anisotropic temperature factors. Hydrogen atoms have been reduced in size for clarity.

diastereomeric excess. Deprotonation of methyl phenyl sulfoxide with LDA and acylation of the anion with the appropriate ester gives **7a** (61%), **7b** (75%), and **7e** (51%).[4] β-Keto sulfoxide **7c** (72%) was prepared by alkylation of the dianion[5] of (phenylsulfinyl)acetone[6] with (*E*)-1-bromo-2-methyl-butene.[7] Alkylation of **7** with sodium hydride and allyl bromide in DMSO[8] for 3 h gives **8a** (50%, 2 diastereomers), **8b** (57%, 2 diastereomers), and **8e** (46%, 4 diastereomers). Phase-transfer-catalyzed alkylation[9] of **7c** affords **8c** (49%) as a mixture of diastereomers. These α-allyl β-keto sulfoxides are not stable. They undergo fragmentation with a half-life of about a week at room temperature to give a conjugated dienone and benzenesulfenic acid.[10]

Reaction of **8a** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of $Cu(OAc)_2 \cdot H_2O$ in acetic acid for 14 h at 25 °C gives 40% of **13a** (Scheme I). The ^1H and ^{13}C NMR spectra clearly demonstrate that only a single diastereomer is present, indicating that the sulfoxide chiral center completely controls the two newly introduced chiral centers. Similarly, oxidative cyclization of **8b** affords 44% of **13b**, mp 103–103.5 °C, as a single diastereomer. While the NMR spectra clearly indicate that **13a** and **13b** are diastereomerically pure, they do not permit assignment of stereochemistry. Although the yields of **13a** and **13b** are only moderate, none of the other diastereomer could be detected by careful analysis of the NMR spectra of the crude product and other column fractions.

The relative stereochemistry of **13b** could be assigned, as shown in Figure 1, from an X-ray structure determination. The structure clearly indicates that the relative stereochemistry is as shown in **13b**. The dihedral angle between the sulfoxide oxygen and carbonyl carbon of 177° corresponds closely to the calculated[11] minimum of 179°. The dihedral angle between the sulfoxide oxygen and the phenyl CH of 14.6° is close to the calculated[11] minimum of 32°. Crystal packing forces are probably not responsible for the conformation of **13b** since the geometry corresponds well with the conformational minimum calculated by MM2.

Scheme II



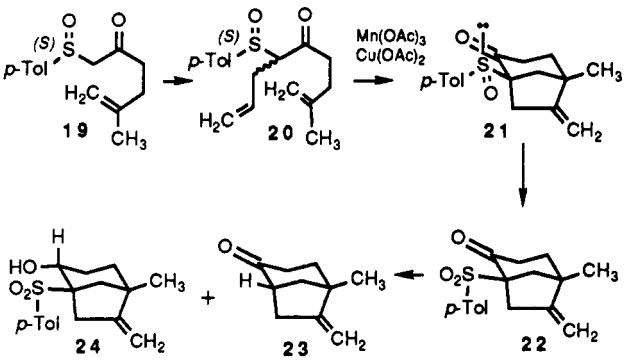
The stereochemistry of **13b** suggests that this oxidative cyclization is proceeding as shown in Scheme I. Oxidation of β-keto sulfoxide **8b** gives enol radical **9b** in which the sulfoxide is the only chiral center in the molecule. Radical **9b** adopts an extended conformation as we have previously demonstrated for radicals **2** and **5** obtained from β-keto esters.[1] Cyclization occurs with complete selectivity from the less hindered face, since a lone pair is much smaller than a phenyl group, to give cyclohexyl radical **10b**. Chair inversion gives cyclohexyl radical **11b**, which undergoes a second cyclization to give **12b**. Cyclopentanemethyl radical **12b** reacts with Cu(II) to give **13b**.

Oxidative cyclization of **8c** was examined to demonstrate unequivocally that the initial cyclization proceeds similarly to those of the β-keto esters through extended enol radical **9**. As predicted, we obtained 43% of a 10:1 mixture of **13c** and the epimer **13d** with an equatorial methyl group. The predominant formation of **13c** with an axial methyl group provides further support for the mechanism shown in Scheme I. The minor isomer **13d** may be formed by an initial cyclization proceeding through a boat transition state.

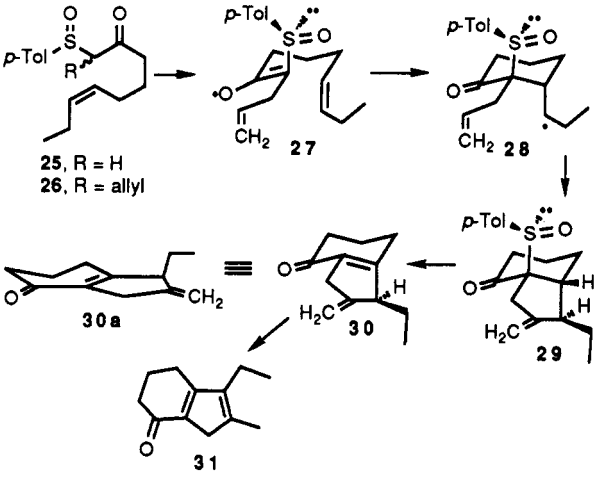
The oxidative cyclization of **8e** was examined to determine the relative ability of the sulfoxide chiral center and a methyl group to control the stereochemistry in the cyclization. We have previously shown in the oxidative cyclization of β-keto esters that, as expected, methyl groups prefer to adopt an equatorial position in the initial cyclization. Since there is a chair inversion prior to the second cyclization, the methyl groups end up primarily axial (>5:1) in the final bicyclo[3.2.1]octan-2-one. Oxidation of **8e** will give enol radicals **14** and **15** (Scheme II). Enol radical **14** should give **16** exclusively. This is the matched case. The initial cyclization can occur from the least hindered face of the enol radical with an equatorial methyl group. Enol radical **15** could give either **17** or **18**. This is the mismatched case. The initial cyclization can occur from the least hindered face of the enol radical with an axial methyl group to give **17** or from the more hindered face of the enol radical with an equatorial methyl group

(4) Solladié, G.; Demailly, G.; Greck, C. *J. Org. Chem.* **1985**, *50*, 1552. Solladié, G. *Synthesis* **1981**, 185.
(5) Grieco, P. A.; Pogonowski, C. S. *J. Org. Chem.* **1974**, *39*, 732. Kuwajima, I.; Iwasawa, H. *Tetrahedron Lett.* **1974**, 107.
(6) Iriuchijima, S.; Tsuchihashi, G.-I. *Synthesis* **1975**, 401.
(7) Edelson, J.; Skinner, C. G.; Ravel, J. M.; Shive, W. *J. Am. Chem. Soc.* **1959**, *81*, 5150.
(8) Gassman, P. G.; Richmond, G. D. *J. Org. Chem.* **1966**, *31*, 2355. Bravo, P.; Piovosi, E.; Resnati, G.; De Munari, S. *Gazz. Chim. Ital.* **1988**, *118*, 115.
(9) Pohmakotr, M.; Chancharunee, S. *Tetrahedron Lett.* **1984**, *25*, 4141.
(10) Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.
(11) Model version KS 2.94 and KS 2.95 obtained from Prof. K. Steliou, University of Montreal, was used for MM2 minimizations and conformational searching.

Scheme III



Scheme IV



to give **18**. Only **16** and **17** are isolated, establishing that the facial selectivity induced by the sulfoxide center can overcome the equatorial preference of the methyl group.

The stereochemistry of **13c**, **13d**, **16**, and **17** can be easily established by examination of their ^1H and ^{13}C NMR spectra. The structure of **13c** follows from the ^1H NMR absorption of H8 at δ 2.49 (dq, 1, J = 2, 7.4). Decoupling experiments established that the unexpected coupling constant is a four-bond W coupling with H4-endo, indicating that H8 is equatorial. The ^{13}C NMR spectrum confirms the stereochemical assignment. C4 is shifted upfield by the γ axial methyl group from δ 40.7 in **13b** and δ 41.6 in **13d** to δ 32.8 in **13c**. The axial methyl group in **13c** absorbs at δ 8.6 while the equatorial methyl group in **13d** absorbs at δ 12.7. C7 is shifted upfield to δ 28.5 in **13d** by the γ equatorial methyl group from δ 34.0 in **13b** and δ 34.3 in **13c**.

The stereochemistry of **16** and **17** was assigned on the basis of analysis of the ^1H and ^{13}C NMR spectra. The equatorial methine proton H4 of **16** is coupled to H3-endo with J = 8 Hz, to H3-exo with J = 0 Hz, and to H8 with a four-bond W coupling of 2 Hz. These values are only consistent with an equatorial H4. The axial methine proton H4 of **17** is coupled to H3-endo with J = 14 Hz and to H3-exo with J = 4.5 Hz. These values are only consistent with an axial H4. The ^{13}C NMR spectrum of **16** shows shifts from that of **13b** as expected for introduction of an axial methyl group on C4: C3 (8.1), C4 (2.5), C5 (2.6), and C8 (−5.1). The ^{13}C NMR spectrum of **17** shows shifts from that of **13b** as expected for introduction of an equatorial methyl group on C4: C3 (9.8), C4 (1.5), C5 (2.9), and C8 (0.1). The upfield shift of C8 by an axial methyl group of **16**, but not by the equatorial methyl group of **17**, is particularly significant.

The formation of **13a** and **13b** as a single diastereomer suggests that the sulfur chiral center is completely controlling the stereochemistry of these oxidative cyclizations. For this process to be synthetically useful, optically pure acyclic β-keto sulfoxide **8** must be readily available and the sulfoxide must be easily removed from the product **13**. Acylation[4] of methyl (*S*)-tolyl sulfoxide[12] as described above affords 56% of **19** (Scheme III). Phase-transfer-catalyzed alkylation[9] of **19** affords 79% of **20** of a mixture of two diastereomers. Oxidative cyclization of **20** as described above affords 44% of **21** as a single stereoisomer. Examination of the ^1H and ^{13}C NMR spectra establishes that only a single diastereomer is present. Examination of the ^1H NMR spectra in CCl_4 in the presence of 3 equiv of the chiral solvating agent (*R*)-2,2,2-trifluoro-1-(9-anthryl)ethanol[13] establishes that only a single enantiomer is present. This technique is suitable for determination of the enantiomeric purity of **21**, since the methyl group of racemic **13b** absorbs as two singlets at δ 1.17 and 1.13 in the presence of the chiral solvating agent. The selective formation of **21** as a single enantiomer establishes that the sulfoxide is not epimerizing prior to cyclization.

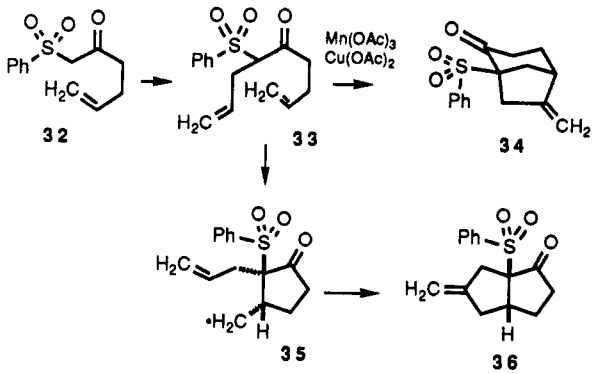
Although β-keto sulfoxides can usually be reduced readily to ketones, reductive cleavage of **21** was expected to be difficult since the enolate of the bicyclic ketone **23** is inaccessible. As expected, reductive cleavage of the product β-keto sulfoxide with aluminum amalgam was unsuccessful. Since sulfones are more easily reduced than sulfoxides, we developed a two-step approach for reduction of the sulfoxide. Oxidation of **21** with potassium peroxomonosulfate[14] affords 88% of β-keto sulfone **22**. Reduction of **22** with Na_2HPO_4-buffered sodium amalgam[15] provides 63% (87% based on recovered **22** and **24**) of **23** and 30% of a 4.3:1 mixture of the equatorial sulfone alcohol **24** and recovered **22**. Oxidation of **24** with Collins' reagent regenerates **22**.[16] The absolute stereochemistry of **23** is assigned as shown on the basis of the relative stereochemistry determined in the X-ray crystal structure of **13b** and the stereochemistry of the starting sulfoxide. The positive Cotton effect provides independent confirmation that the stereochemistry of **23** is as shown.[17]

Oxidative cyclization of **26** was examined to develop a route to optically pure indenones. Acylation of methyl-(*S*)-tolyl sulfoxide[12] with *N*-methoxy-*N*-methyl-*cis*-5-octenamide[18] affords 67% of **25**. Phase-transfer-catalyzed alkylation[9] of **25** affords 67% of **26** as a mixture of two diastereomers. To our surprise, the only product that is obtained from oxidative cyclization of **26** is indenone **30** (15%), which no longer contains a tolylsulfinyl group. Oxidation affords extended enol radical **27**, which presumably cyclizes to monocyclic radical **28**. The second cyclization and oxidative termination by reaction with Cu(II) will give **29**. Elimination of toluenesulfenic acid will give **30** (Scheme IV).

Loss of toluenesulfenic acid at room temperature is unusual but not unprecedented.[10] This elimination can proceed only if indenone **29** is formed with a cis ring fusion.

(12) Zhao, S. H.; Samuel, O.; Kagan, H. B. *Org. Synth.* **1989**, *68*, 49.
(13) Pirkle, W. H.; Beare, S. D. *J. Am. Chem. Soc.* **1968**, *90*, 6250.
(14) Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 1287.
(15) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, *39*, 3477.
(16) Ichikawa, Y.; Isobe, M.; Goto, T. *Tetrahedron Lett.* **1984**, *25*, 5049.
(17) For the application of the Cotton effect to the assignment of stereochemistry to bicyclo[3.2.1]octan-2-one, see: Walborsky, H. M.; Baum, M. E.; Youssef, A. A. *J. Am. Chem. Soc.* **1961**, *83*, 988.
(18) Turner, J. A.; Jacks, W. S. *J. Org. Chem.* **1989**, *54*, 4229.

Scheme V



However, cyclization of the analogous radical **5** from β-keto ester **4** affords trans-fused indenone **6**. The stereochemistry of **6** is determined in the initial cyclization, which proceeds to give a chair cyclohexane with an equatorial alkyl group. We had anticipated, apparently incorrectly, that the cyclization of **27** would occur analogously. Presumably, the phenylsulfinyl group is larger than an ester so that the alkyl group adopts an axial conformation in the transition state leading to **28** to avoid interactions with the sulfoxide. Alternative explanations based upon different geometries of the enol radical can be excluded, since the extended geometry of the enol radical shown in **27** has been established in the cyclization of **8c**.

Indenone **30** is optically active. It shows a positive Cotton effect at 336 nm for the R-band and a negative Cotton effect at 247 nm for the K-band as expected for conjugated enones.[19] The MM2 minimized conformation[11] for **30** is shown in **30a**. The enantiomer shown, with the ring methylene down on the left and the ethyl group up on the right, is predicted to have a positive R-band Cotton effect, since the octant rule for the R-band of conjugated ketones is the reverse of the octant rule for saturated ketones.[19] The assignment of the expected absolute stereochemistry to **30** supports the mechanistic hypothesis proposed to account for its formation.

Although indenone **30** is optically active, we are unable to determine its optical purity. Spectroscopic methods were precluded by the lack of sharp absorptions in the ^1H NMR spectrum. Chemical methods were limited by the instability of **30**; it decomposes on storage, even at −20 °C. The ^1H NMR spectrum of the ketal obtained from (2*R*,3*R*)-2,3-butanediol could have been analyzed to determine optically purity.[20] Unfortunately, this reaction was unsuccessful, giving a complex mixture containing some of the achiral cyclopentadiene **31**.

We briefly examined the oxidative cyclization of unsaturated β-keto sulfones. Alkylation of the dianion of (phenylsulfonyl)acetone with allyl bromide gives 61% of **32** and 10% of **33**. Alkylation of **32** with sodium hydride and allyl bromide in DMF affords 50% of **33**. Oxidative cyclization of **33** affords 20% of **34** and 4% of **36** (Scheme V). The formation of bicyclo[3.2.1]octanone **34** is analogous to the formation of **13a** and requires no further comment. The formation of **36** is unexpected, since we have not seen analogous products in the cyclization of β-keto esters.[1] In 5-exo cyclizations of enol radicals derived from β-keto esters, the side chain is formed selectively cis to the ester. The selectivity increases with larger alkyl groups in the α-position, suggesting that an ester is smaller than an alkyl group. Apparently, sulfones are larger than an allyl group since the primary alkyl radical **35** is formed with the side chain trans to the sulfone so that a second cyclization can occur to give **36**. The formation of **36** supports our contention that enol radical **27** cyclizes to give **28** with the side chain trans to the sulfoxide.

These results demonstrate that β-keto sulfoxides and β-keto sulfones can be used as substrates for Mn(III)- and Cu(II)-based oxidative free-radical cyclizations. The sulfoxide chiral center completely controls the stereochemistry of the cyclization so that these reactions can be used for the efficient preparation of optically active bicyclo[3.2.1]octanones. Cyclizations of α-sulfinyl radicals may prove to be a general procedure for controlling absolute stereochemistry in radical cyclizations.

Experimental Section

General. NMR spectra were recorded at 300 MHz in $CDCl_3$ unless otherwise indicated. Chemical shifts are reported in δ; coupling constants are reported in hertz. Ester precursors to **7b** and **7e** were prepared by orthoester Claisen rearrangements.

1-(Phenylsulfinyl)-5-hexen-2-one (7a). A mixture of diisopropylamine (0.31 mL, 2.20 mmol), *n*-BuLi (0.74 mL, 2.7 M solution in hexane, 2.00 mmol), and 3 mL of THF was stirred at 0 °C for 30 min. The mixture was cooled to −78 °C and a solution of methyl phenyl sulfoxide (274 mg, 1.95 mmol) in 5 mL of THF was added slowly. The solution was stirred at −78 °C for 30 min, and a solution of ethyl 4-pentenoate (275 mg, 2.14 mmol) was added. The resulting mixture was stirred at −78 °C for 90 min and then at 0 °C for 1 h. It was quenched (saturated NH_4Cl solution), acidified (5% HCl), and extracted with CH_2Cl_2. The organic phase was then washed (brine), dried ($MgSO_4$), and evaporated to give a waxy white solid (488 mg). Flash chromatography on silica gel (49:2 CH_2Cl_2–CH_3OH) gave 245 mg (61%) of **7a**[5] as a white solid: mp 68–68.5 °C (ether); ^1H NMR 7.62–7.67 (m, 2), 7.52–7.57 (m, 3), 5.71 (ddt, 1, *J* = 17.1, 10.3, 6.5), 5.00 (br dd, 1, *J* = 17.1, 1.6), 4.98 (br dd, 1, *J* = 10.3, 1.6), 3.87 (d, 1, *J* = 13.6), 3.77 (d, 1, *J* = 13.6), 2.58–2.64 (m, 2), 2.25–2.33 (m, 2); ^{13}C NMR 210.1, 143.3, 136.6, 132.0, 130.0 (2 C), 124.4 (2 C), 116.1, 68.4, 44.4, 27.4; IR (CH_2Cl_2) 3075, 1713, 1644, 1085, 1043 cm^{-1}.

5-Methyl-1-(phenylsulfinyl)-5-hexen-2-one (7b) was prepared as described above for **7a** from methyl phenyl sulfoxide (300 mg, 2.14 mmol) and ethyl 4-methyl-4-pentenoate (330 mg, 2.32 mmol). Sulfoxide **7b** (240 mg, 48%, 75% based on recovered sulfoxide) was isolated as a yellowish oil: ^1H NMR 7.65–7.68 (m, 2), 7.52–7.59 (m, 3), 4.71 (br s, 1), 4.61 (br s, 1), 3.95 (d, 1, *J* = 13.6), 3.73 (d, 1, *J* = 13.6), 2.53–2.73 (m, 2), 2.24 (br t, 2, *J* = 7.5), 1.70 (s, 3); ^{13}C NMR 201.0, 143.6, 142.9, 131.6 (2 C), 129.4, 124.0 (2 C), 110.6, 68.0, 43.1, 30.7, 22.5; IR (neat) 1716, 1650, 1055, 1048, 890 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82; S, 13.57. Found: C, 66.10; H, 6.85; S, 13.48.

***(E)*-5-Methyl-1-(phenylsulfinyl)-5-hepten-2-one (7c).** Addition of (phenylsulfinyl)acetone[6] (1.00 g, 5.49 mmol) in 10 mL of THF to a solution of LDA (10.98 mmol) in 20 mL of THF at 0 °C produced a dark red mixture of the dianion. (*E*)-1-Bromo-2-methyl-2-butene[7] (0.90 g, 6.04 mmol) in 5 mL of THF was added, and the reaction was quenched 5 min later with 10% HCl. The layers were separated and the aqueous layer was extracted (CH_2Cl_2). The combined organic layers were washed (saturated $NaHCO_3$), dried ($MgSO_4$), and evaporated in vacuo to produce 1.7 g of a yellow oil. Flash chromatography on silica gel (1:1 hexane–EtOAc) afforded 0.98 g (72%) of **7c** as a yellow oil: ^1H NMR 7.68–7.63 (m, 2), 7.55–7.52 (m, 3), 5.32 (br q, 1, *J* = 6.4), 3.95 (d, 1, *J* = 13.7), 3.73 (d, 1, *J* = 13.7), 2.65–2.48 (m, 2), 2.25–2.17 (m, 2), 1.55 (s, 3), 1.54 (br d, 3, *J* = 6.4); ^{13}C NMR 201.4, 143.0, 133.4, 131.5, 129.3 (2 C), 123.9, (2 C), 119.4, 68.0, 43.4, 32.6, 15.6, 13.3; IR (neat) 1725, 1455, 1095, 1055, 750 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_2S$: C, 67.16; H, 7.25; S, 12.81. Found: C, 67.15; H, 7.20; S, 12.91.

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4,5-Dimethyl-1-(phenylsulfinyl)-5-hexen-2-one (7e) was prepared as described above for **7a** from methyl phenyl sulfoxide (350 mg, 2.5 mmol) and ethyl 3,4-dimethyl-4-pentenoate (380 mg, 2.4 mmol). Sulfoxide **7e** (154 mg, 25%, 51% based on recovered sulfoxide) was isolated as a yellow oil, which was a 1:1 mixture of two diastereomers: ^{1}H NMR 7.63–7.68 (m, 2), 7.50–7.58 (m, 3), 4.69 (m, 1), 4.67 (m, 1), 3.88 (d, 1, J = 13.7), 3.77 (d, 0.5 × 1, J = 13.7), 3.76 (d, 0.5 × 1, J = 13.7), 2.37–2.73 (m, 3), 1.68 (dd, 0.5 × 3, J = 0.8, 0.8), 1.67 (dd, 0.5 × 3, J = 0.8, 0.8), 1.01 (d, 0.5 × 3, J = 6.8), 0.98 (d, 0.5 × 3, J = 6.9); ^{13}C NMR 200.8, 148.3, (142.8, 142.9), 131.4, (129.2 (0.5 × 2 C), 129.3 (0.5 × 2 C)), (123.8 (0.5 × 2 C), 123.9 (0.5 × 2 C)), 109.9, (68.1, 68.3), (50.3, 50.4), (35.9, 36.0), 19.4, 19.3; IR (neat) 1735, 1715, 1088, 1048 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_2S$: C, 67.16; H, 7.25. Found: C, 67.56; H, 7.02.

4-(Phenylsulfinyl)-1,8-nonadien-5-one (8a). To a flame-dried round-bottom flask containing NaH (18 mg, 60% oil dispersion, 0.45 mmol) at 25 °C was added a solution of **7a** (100 mg, 0.45 mmol) in 2.5 mL of DMSO. After the formation of hydrogen bubbles subsided (about 15 min), the mixture was treated with allyl bromide (0.04 mL, 0.46 mmol) and stirred at 25 °C for 3 h. The reaction mixture was then quenched (5% HCl) and the aqueous layer was extracted (1:4 CH_2Cl_2–Et_2O). The layers were separated and the organic phase was washed (water, brine), dried (Na_2SO_4), and evaporated in vacuo to afford 197 mg of a yellowish liquid. Flash chromatography on deactivated silica gel (1:1 hexane–EtOAc) gave 59 mg (50%) of **8a** as a yellowish liquid that is a ≈1:1 mixture of two diastereomers: ^{1}H NMR 7.50–7.62 (m, 5), 5.51–5.79 (m, 2), 4.84–5.18 (m, 4), 3.78 (dd, 0.5 × 1, J = 10, 5), 3.70 (dd, 0.5 × 1, J = 10, 5), 2.65–3.00 (m, 1), 2.45–2.63 (m, 2), 2.15–2.40 (m, 1), 2.00–2.15 (m, 2); ^{13}C NMR (202.7, 203.8), (140.8, 141.2), (136.4, 136.6), (132.4, 132.6), (131.8 (0.5 × 2 C), 131.9 (0.5 × 2 C)), (129.2, 129.3), (124.8 (0.5 × 2 C), 124.9 (0.5 × 2 C)), (118.9, 119.0), (115.4, 115.5), (73.9, 75.9), (44.3, 44.8), (29.8, 30.8), (26.7, 26.9); IR (neat) 1710, 1643, 1085, 1048, 998, 915 cm^{-1}.

2-Methyl-6-(phenylsulfinyl)-1,8-nonadien-5-one (8b) was prepared from **7b** (183 mg, 0.78 mmol) as described above for **8a**. Flash chromatography on silica gel (65:35 hexane–EtOAc) gave 64 mg of recovered **7b** and 88 mg (41%, 57% based on recovered **7b**) of **8b** as a yellowish liquid that is a ≈1:1 mixture of two diastereomers: ^{1}H NMR 7.51–7.62 (m, 5), 5.57–5.77 (m, 1), 5.12 (m, 2), 4.70 (br s, 0.5 × 1), 4.65 (br s, 0.5 × 1), 4.51 (br s, 0.5 × 1), 3.81 (dd, 0.5 × 1, J = 4.8, 9.8), 3.74 (dd, 0.5 × 1, J = 5.3, 9.7), 1.93–2.83 (m, 6), 1.60 (s, 0.5 × 3), 1.67 (s, 0.5 × 3); ^{13}C NMR (202.9, 204.0), (143.5, 143.8), (140.8, 141.2), (132.4, 132.5), (131.7 (0.5 × 2 C), 131.9 (0.5 × 2 C)), (129.1, 129.2), (124.7 (0.5 × 2 C), 124.8 (0.5 × 2 C)), (118.8, 118.9), (110.3, 110.4), (73.3, 76.0), (43.4, 43.9), (30.4, 30.7), (29.8, 30.2), (22.4, 22.5); IR (neat) 1710, 1652, 1645, 1084 cm^{-1}.

(*E*)-8-Methyl-4-(phenylsulfinyl)-1,8-decadien-5-one (8c) was prepared as described below for **20** from sulfoxide **7c** (0.80 g, 3.20 mmol). Flash chromatography on silica gel (5:1 hexane–EtOAc) afforded 0.45 g (49%) of **8c** as a ≈1:1 mixture of two diasteromers: ^{1}H NMR 7.67–7.47 (m, 5), 5.76–5.58 (m, 1), 5.19–4.96 (m, 3), 3.78 (dd, 0.5 × 1, J = 9.7, 4.8), 3.72 (dd, 0.5 × 1, J = 9.3, 5.7), 2.82–2.64 (m, 2), 2.58–2.43 (m, 2), 2.18–2.20 (m, 2), 1.68–1.48 (m, 3), 1.54 (br s, 0.5 × 3), 1.44 (br s, 0.5 × 3); ^{13}C NMR (204.3, 203.2), (141.4, 140.8), (133.7, 133.5), (132.6, 132.5), (131.9, 131.7), (129.2, (0.5 × 2 C), 129.2 (0.5 × 2 C)), (124.9, (0.5 × 2 C), 124.7 (0.5 × 2 C)), (119.3, 119.3), (118.8, 118.8), (76.1, 73.9), (44.4, 43.8), (32.4, 32.2), (30.8, 29.6), (15.6, 15.5), (13.3, 13.3); IR (neat) 1705, 1075, 1040, 990, 910 cm^{-1}.

2,3-Dimethyl-6-(phenylsulfinyl)-1,8-nonadien-5-one (8e) was prepared from **7e** (107 mg, 0.43 mmol) as described above for **8a**. Flash chromatography on silica gel (7:3 hexane–EtOAc) afforded 57 mg (46%) of **8e** as a mixture of four diastereomers in roughly equal amounts: ^{1}H NMR 7.40–7.73, (m, 5), 5.56–5.77 (m, 1), 5.02–5.17 (m, 2), 4.55–4.71 (m, 2), 3.78 (dd, 0.5 × 1, J = 9.7, 4.6), 3.74 (dd, 0.25 × 1, J = 9.2, 5.6), 3.73 (dd, 0.25 × 1, J = 9.6, 5.2), 1.96–2.82 (m, 5), 1.66 (d, 0.25 × 3, J = 0.8), 1.62 (d, 0.25 × 3, J = 0.7), 1.55 (br s, 0.5 × 3), 0.80 (d, 0.25 × 3, J = 6.8), 0.92 (d, 0.25 × 3, J = 6.8), 0.94 (d, 0.25 × 3, J = 7.0), 0.95 (d, 0.25 × 3, J = 7.0); ^{13}C NMR (202.50, 202.53, 203.49, 203.72), (148.80, 148.60, 148.70, 148.75), (140.60, 140.77), (132.45, 132.51, 132.53), (131.69, 131.22, 131.83, 131.86), (129.10, 129.15, 129.17, 129.20), (124.80, 124.85, 124.95, 125.02), 118.86, (109.44, 109.50, 109.56, 109.68), (73.86, 73.98, 75.65, 75.70), (50.88, 51.05, 51.19, 51.30), (35.08, 35.31, 35.40, 35.45), (29.53, 29.61, 30.53, 30.69), (20.06, 20.14, 20.17), (19.24, 19.37, 19.40, 19.45); IR (neat) 1715, 1665, 1085, 1050 cm^{-1}.

(1*S,5*S**)-6-Methylene-1(*R**)-(phenylsulfinyl)bicyclo-[3.2.1]octan-2-one (13a).** A mixture of **8a** (51 mg, 0.19 mmol), manganese(III) acetate (101 mg, 0.38 mmol), and copper(II) acetate (40 mg, 0.20 mmol) in 2 mL of glacial acetic acid was stirred at 25 °C for 14 h. Water (20 mL) was added, and a 10% $NaHSO_3$ solution was added dropwise until the brownish solution turned light blue. The aqueous solution was extracted with CH_2Cl_2. The organic layer was washed (saturated $NaHCO_3$, brine), dried (Na_2SO_4), and evaporated in vacuo to give 50 mg of a viscous yellow oil. Flash chromatography (deactivated silica gel, 7:3 hexane–EtOAc) provided 8 mg of recovered **8a** followed by 17 mg (33%, 40% based on recovered **8a**) of **13a** as a waxy solid: ^{1}H NMR 7.77–7.81 (m, 2), 7.44–7.47 (m, 3), 5.10 (br s, 1), 5.00 (br s, 1), 3.10 (m, 1, H5), 2.90 (ddd, 1, J = 16.9, 2.4, 2.2, H7), 2.64 (ddd, 1, J = 11.7, 5.2, 2.5, H8), 2.32–2.40 (m, 2), 1.86–2.00 (m, 3), 1.80 (br d, 1, J = 16.9, H7); ^{13}C NMR 208.9, 148.4, 141.3, 130.9 (2 C), 128.5, 126.0 (2 C), 108.6, 74.0 (C1), 42.6 (C5), 39.5 (C8), 37.0 (C3), 33.7 (C7), 33.0 (C4); IR (neat) 3070, 1711, 1042 cm^{-1}. Anal. Calcd for $C_{15}H_{16}O_2S$: C, 69.20; H, 6.20. Found: C, 69.30; H, 6.60.

(1*S,5*S**)-5-Methyl-6-methylene-1(*R**)-(phenylsulfinyl)bicyclo[3.2.1]octan-2-one (13b).** Oxidative cyclization of **8b** (88 mg, 0.32 mmol) for 22 h produced 101 mg of crude product. Flash chromatography on silica gel (65:35 hexane–EtOAc) afforded 39 mg (44%) of **13b** as a yellowish oil, which solidified on standing: mp 103–103.5 °C (from hexane); ^{1}H NMR 7.77–7.80 (m, 2), 7.28–7.48 (m, 3), 5.01 (m, 2), 2.99 (ddd, 1, J = 17.0, 2.7, 2.7, H7), 2.48, (dd, 1, J = 12.0, 3.4, H8), 2.23–2.40 (m, 2), 1.98 (dd, 1, J = 12.0, 2.7, H8), 1.65–1.92 (m, 3), 1.30 (s, 3); ^{13}C NMR 209.2, 151.9, 141.1, 130.9 (2 C), 126.0 (2 C), 106.9, 74.7 (C1), 45.8 (C8), 45.7 (C5), 40.7 (C4), 37.6 (C3), 34.0 (C7), 22.5 (5-Me); IR (neat) 3058, 1713, 1080, 1040 cm^{-1}. The structure was confirmed by X-ray crystallographic analysis.

***syn*- and *anti*-5,8-Dimethyl-6-methylene-1-(phenylsulfinyl)bicyclo[3.2.1]octan-2-one (13c and 13d).** Oxidative cyclization of sulfoxide **8c**, (0.45 g, 1.6 mmol) for 18 h provided 0.41 g of crude product. Flash chromatography on silica gel (3:1 hexane–EtOAc) afforded 0.20 g (43%) of a 10:1 mixture of **13c** and **13d** (^{1}H NMR), which solidified upon standing: mp 94.5–95.5 °C (from hexane); ^{1}H NMR (**13c**) 7.79–7.76 (m, 2), 7.46–7.43 (m, 3), 5.06 (dd, 1, J = 3.0, 2.1), 5.00 (dd, 1, J = 2.5, 1.8), 2.94 (ddd, 1, J = 17.1, 3.0, 2.5, H7), 2.49 (dq, 1, J = 2, 7.4 H8), 2.26–2.20 (m, 2, H3), 1.90 (m, 1, H4), 1.83 (ddd, 1, J = 17.1, 2.1, 1.8, H7), 1.56–1.46 (m, 1, H4), 1.18 (s, 3), 1.14 (d, 3, J = 7.4); ^{1}H NMR (C_6D_6) (**13c**) 8.03 (m, 2), 7.10–6.96 (m, 3), 4.75 (dd, 1, J = 3.0, 2.2), 4.66 (dd, 1, J = 2.5, 1.9), 3.03 (ddd, 1, J = 17.0, 3.0, 2.5, H7), 2.60 (dq, 1, J = 1.8, 7.0, H8), 1.84 (ddd, 1, J = 15.6, 6.6, 0.8 H3), 1.65 (dddd, 1, J = 15.6, 12.7, 8.8, 1.3, H3), 1.62 (ddd, 1, J = 17.0, 2.2, 1.9, H7), 1.33 (ddd, 1, J = 12.7, 12, 6.6, H4), 0.93–0.88 (m, 1, H4), 0.92 (d, 1, J = 7.0, 8-methyl exo), 0.76 (s, 3); ^{1}H NMR (**13d** determined from the mixture) 5.14 (dd, 1, J = 2.1, 2.1), 3.54 (ddd, 1, J = 17.5, 2.6, 2.6, H7 endo), 1.19 (d, 3, J = 7.5), 1.14 (s, 3); ^{1}H NMR (C_6D_6) (**13d** determined from the mixture) 4.85 (dd, 1, J = 1.9, 1.9), 3.63 (ddd, 1, J = 17.8, 2.5, 2.5, H7), 1.19 (d, 3, J = 7.4), 0.68 (s, 3); ^{13}C NMR (**13c**) 209.8 (C=O), 152.1 (C), 140.7 (C), 130.6 (CH), 128.4 (2 CH), 125.9 (2 CH), 106.8 (CH_2), 78.4 (C1), 47.8 (C8), 47.1 (C5), 37.2 (C3), 34.3 (C7), 32.8 (C4), 20.8 (5-Me), 8.6 (8-ax-Me); (**13d**) 151.4 (C), 142.0 (C), 130.8 (CH), 128.0 (2 CH), 127.3 (2 CH), 108.0 (CH_2), 54.2 (C8), 50.0 (C5), 41.6 (C4), 38.1 (C3), 28.5 (C7), 19.8 (5-Me), 12.7 (8-eq-Me) (two carbons not observed); IR (neat) 1710, 1440, 1040, 895, 880 cm^{-1}. Anal. Calcd for $C_{17}H_{20}O_2S$: C, 70.80; H, 6.29; S, 11.12. Found: C, 70.72; H, 6.38; S, 11.06.

Decoupling in $CDCl_3$ of **13c** established that the small long range coupling of 2.0 Hz in H8 at δ 2.49 is due to H4e at δ 1.56 and not to either H7 at δ 2.94 or 1.83.

***exo*- and *endo*-(1*S**,5*R**)-4,5-Dimethyl-6-methylene-(*R**)-(phenylsulfinyl)bicyclo[3.2.1]octan-2-one (16 and 17).** Oxidative cyclization of **8e** (57 mg, 0.20 mmol) for 22 h produced 62 mg of crude **16** and **17**. Flash chromatography on silica gel (7:3 hexane–EtOAc) afforded 48 mg (83%) of a 1:1 mixture of **16** and **17**. Recrystallization from hexane afforded 5 mg of a 4:1 mixture of **16** and **17**. Evaporation of the mother liquor gave 22 mg (47% combined recrystallized yield) of a 2.5:1 mixture of **17** and **16**. The data were determined from the mixtures: mp

(crystalline 4:1 mixture of **16** and **17**) 131–135 °C. Anal. Calcd for $C_{17}H_{20}O_2S$: C, 70.80; H, 6.99; S, 11.11. Found: C, 70.63; H, 6.99; S, 11.01.

Data for **16**: ^{1}H NMR 7.70–7.80 (m, 2), 7.45–7.50 (m, 3), 5.02 (dd, 1, J = 3.0, 1.9), 4.98 (ddd, 1, J = 2.5, 1.9, 0.7), 3.00 (ddd, 1, J = 3.0, 2.5, H7), 2.57 (dd, 1, J = 14.8, 8, H3), 2.26 (dd, 1, J = 12, 2, H8), 2.20 (dd, 1, J = 12, 2, H8), 2.03 (d, 1, J = 14.8, H3), 1.93 (ddq, 1, J = 8, 2, 6.8, H4), 1.85 (ddd, 1, J = 17, 1.9, 1.9, H7), 1.24 (s, 3), 1.02 (d, 3, J = 6.8); ^{13}C NMR 154.4, 141.1, 130.9 (2 C), 128.5, 125.9 (2 C), 106.7, 75.5 (C1), 48.3 (C5), 45.7 (C3), 43.2 (C4), 40.7 (C8), 33.6 (C7), 20.9 (5-Me), 16.1 (4-ax-Me), (carbonyl carbon not detected).

Data for **17**: ^{1}H NMR 7.76–7.82 (m, 2), 7.44–7.53 (m, 3), 5.10 (ddd, 1, J = 1.8, 1.8, 0.6), 4.91 (ddd, 1, J = 2.9, 2.1), 2.98 (ddd, 1, J = 17, 2.9, 1.8, H7), 2.53 (d, 1, J = 11.9, H8), 2.31 (dd, 1, J = 14, 4.5, H3), 2.00 (dd, 1, J = 11.9, 2.4, H8), 1.92 (m, 1), 1.83 (dd, 1, J = 14, H3), 1.82 (m, 1), 1.20 (s, 3), 0.86 (d, 3, J = 6); ^{13}C NMR 208.7, 147.8, 141.1, 130.9 (2 C), 128.5, 125.9 (2 C), 109.6, 74.9 (C1), 48.6 (C5), 47.4 (C3), 45.9 (C8), 42.4 (C4), 33.9 (C7), 20.5 (5-Me), 15.0 (4-eq-Me).

(−)-(*S*)-5-Methyl-1-(*p*-tolylsulfinyl)-5-hexen-2-one (19) was prepared as described above for **7a** from (−)-(*S*)-methyl *p*-tolyl sulfoxide[12] (1.10 g, 7.1 mmol) and ethyl 4-methyl-4-pentenoate (1.00 g, 7.1 mmol). Workup as described above afforded 1.77 g of crude product. Flash chromatography on silica gel (3:2 hexane–EtOAc) afforded 1.00 g (56%) of **19** as a light yellow oil, which solidified to give flat, colorless crystals: mp 58–58.5 °C (hexane); ^{1}H NMR 7.55 (d, 2, J = 8.3), 7.34 (d, 2, J = 8.3), 4.71 (br s, 1), 4.62 (br s, 1), (d, 1, J = 13.5), 3.72 (d, 1, J = 13.5), 2.73–2.52 (m, 2), 2.42 (s, 3), 2.28–2.17 (br t, 2), 1.69 (s, 3); ^{13}C NMR 200.8, 143.8, 142.1, 139.6, 130.0 (2C), 124.0 (2C), 110.5, 68.0, 43.1, 30.6, 22.4, 21.3; IR (neat) 1710, 1460, 1035, 880, 800 cm^{-1}; $[\alpha]^{29}_D$ −234° (c = 0.15 acetone). Anal. Calcd for $C_{14}H_{18}O_2S$: C, 67.16; H, 7.25; S, 12.81. Found: C, 67.04; H, 7.20; S, 12.77.

(6*RS*)-2-Methyl-6(*S*)-(*p*-tolylsulfinyl)-1,8-nonadien-5-one (20). A solution of sulfoxide **19** (0.25 g, 1.0 mmol), benzyltriethylammonium chloride (0.25 g, 1.1 mmol), allyl bromide (0.13 g, 1.1 mmol), and 50% NaOH (0.058 mL, 1.1 mmol) in 15 mL of CH_2Cl_2 was stirred at 25 °C.[9] The solution was stirred for 3 h and 10% HCl was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo. Flash chromatography on silica gel (5:1 hexane–EtOAc) afforded 0.23 g (79%) of **20** as a ≈1:1 mixture of two diastereomers: ^{1}H NMR 7.46 (d, 0.5 × 2, J = 8.3), 7.44 (d, 0.5 × 2, J = 8.3), 7.32 (d, 0.5 × 2, J = 8.3), 7.30 (d, 0.5 × 2, J = 8.3) 5.78–5.59 (m, 1), 5.13 (br d, 0.5 × 1, J = 17), 5.10 (br d, 0.5 × 1, J = 17), 5.08 (br d, 1, J = 11), 4.72 (br s, 0.5 × 1), 4.66 (br s, 0.5 × 1), 4.61 (br s, 0.5 × 1), 4.52 (br s, 0.5 × 1), 3.80 (dd, 0.5 × 1, J = 9, 5), 3.72 (dd, 0.5 × 1, J = 9, 5), 2.75–1.90 (m, 6), 2.44 (s, 0.5 × 3), 2.42 (s, 0.5 × 3), 1.69 (s, 0.5 × 3), 1.60 (s, 0.5 × 3); ^{13}C NMR (203.9, 203.1), (143.9, 143.7), (142.6, 142.4), (137.9, 137.5), (132.7, 132.6), (129.9 (0.5 × 2 C), 129.9 (0.5 × 2 C)), (124.9 (0.5 × 2 C), 124.7 (0.5 × 2 C), (118.7, 118.7), (110.4, 110.4), (75.9, 74.0), (44.5, 44.0), (30.8, 30.5), (30.3, 29.7), (22.5, 22.4), (21.4, 21.4); IR (neat) 1660, 1045, 995, 920, 890, 810 cm^{-1}.

(−)-(1*S*,5*S*)-5-Methyl-6-methylene-1(*R*)-(*p*-tolylsulfinyl)bicyclo[3.2.1]octan-2-one (21). Oxidative cyclization of sulfoxide **20** (0.69 g, 2.3 mmol) for 15 h produced 0.48 g of crude product. Flash chromatography on silica gel (2:1 hexane–EtOAc) afforded 0.29 g (44%) of **21** as a light yellow oil: ^{1}H NMR 7.66 (br d, 2, J = 8.3), 7.26 (br d, 2, J = 8.3), 5.00 (br s, 2), 3.00 (ddd, 1, J = 17.1, 2.7, 2.7, H7), 2.47 (dd, 1, J = 11.6, 3.3, H8), 2.39 (s, 3), 2.39–2.30 (m, 2), 1.96 (dd, 1, J = 11.6, 2.2, H8), 1.90 (dddd, 1, J = 17.1, 2.0, 2.0, 2.0, H7), 1.85–1.66 (m, 2), 1.29 (s, 3); ^{13}C NMR 209.3, 152.1, 141.3, 137.8, 129.3 (2 C), 126.0 (2 C), 106.8, 74.6 (C1), 45.8 (C8), 45.7 (C5), 40.8 (C4), 37.6 (C3), 33.9 (C7), 22.5 (5-Me), 21.3; IR (neat) 1710, 1040, 915 cm^{-1}; $[\alpha]^{29}_D$ −59.2° (c = 0.21, ether). Anal. Calcd for $C_{17}H_{20}O_2S$: C, 70.80; H, 6.99; S, 11.12. Found: C, 70.91; H, 6.97; S, 11.15.

The enantiomeric purity of **21** was established by analysis of the ^{1}H NMR spectra in CCl_4 in the presence of approximately 3 molar equiv of the chiral solvating agent (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.[13] The 5-methyl resonance of racemic **13b** appears as a singlet at 1.33 ppm without solvating agent and as two equally intense resonances at 1.17 and 1.13 ppm with solvating agent. The *p*-tolylmethyl and 5-methyl resonances of **21** appear as singlets at 2.39 ppm and 1.32 ppm, respectively, without solvating agent and as singlets at 2.38 and 1.13, respectively, with solvating agent.

(+)-(1*S*,5*S*)-5-Methyl-6-methylene-1-(*p*-tolylsulfonyl)bicyclo[3.2.1]octan-2-one (22). To a solution of sulfoxide **21** (0.19 g, 0.66 mmol) in 2 mL of CH_3OH at 0 °C was added $KHSO_5$ (0.40 g, 1.3 mmol) in 2 mL of water.[14] The solution was warmed to 25 °C, stirred for 6 h, and poured into CH_2Cl_2 (30 mL). The organic layer was separated, dried ($MgSO_4$), and evaporated in vacuo to give 0.18 g (88%) of **22** as colorless crystals: mp 187–188 °C (CH_2Cl_2–hexane); ^{1}H NMR 7.95 (d, 2, J = 8.4), 7.32 (d, 2, J = 8.4), 5.11 (ddd, 1, J = 2.2, 2.2, 0.6), 5.06 (dd, 1, J = 3.0, 2.1), 3.51 (ddd, 1, J = 17.1, 3.0, 2.2, H7), 2.71 (dddd, 1, J = 17.1, 2.2, 2.1, 1.8, H7), 2.61 (dd, 1, J = 11.6, 3.2, H8), 2.44 (s, 3), 2.40–2.25 (m, 2), 1.96 (dd, 1, J = 11.6, 1.8, H8), 1.77–1.63 (m, 2), 1.30 (s, 3); ^{13}C NMR 203.0, 151.8, 144.8, 135.1, 130.5, (2 C), 129.1 (2 C), 107.3, 76.0, 45.2, 45.1, 39.9, 38.5, 37.0, 22.8, 21.6; IR (neat) 1720, 1280, 1140, 890 cm^{-1}; $[\alpha]^{29}_D$ +72.8° (c = 0.35, CH_2Cl_2). Anal. Calcd for $C_{17}H_{20}O_3S$: C, 67.07; H, 6.62; S, 10.53. Found: C, 66.91; H, 6.50; S, 10.59.

(+)-(1*R*,5*S*)-5-Methyl-6-methylenebicyclo[3.2.1]octan-2-one (23). To a slurry of 6% Na(Hg) (159 mg, 0.416 mmol) and disodium hydrogen phosphate (59 mg, 0.416 mmol) in 5 mL of methanol was added sulfone **22** (31.3 mg, 0.104 mmol) in 1 mL of THF.[15] The solution was stirred for 1 h and additonal Na(Hg) (10 mg) was added. After 0.5 h, the mixture was diluted with water (25 mL), acidified with 10% HCl, and extracted with CH_2Cl_2 (25 mL). The organic layer was dried ($MgSO_4$) and evaporated in vacuo to provide 19.7 mg of a mixture of **23**, **22**, and **24**. Flash chromatography on silica gel (10:1 pentane–ether) afforded 9.7 mg (63%, 87% based on recovered material) of **23** as a colorless oil, followed by 9.1 mg of a 4.3:1 mixture of **24** and **22**.

Data for **23**: ^{1}H NMR 5.04 (ddd, 1, J = 1.9, 1.7, 0.6), 4.98 (dd, 1, J = 2.5, 2.1), 2.75–2.63 (m, 2), 2.50 (br d, 1, J = 16.8, H7), 2.38 (dddd, 1, J = 16, 12, 8.6, 0.8, H3), 2.23 (br dd, 1, J = 16, 6.3, H3), 1.87 (ddd, 1, J = 12, 3.5, 3.5, H8), 1.79 (br d, 1, J = 12, H8), 1.75 (ddd, 1, J = 12, 12, 6.3, H4), 1.64 (dddd, 1, J = 12, 8.6, 3.2, 1.5, H4), 1.22 (s, 3); ^{13}C NMR 213.6, 155.0, 105.5, 48.8, 45.0, 43.5, 40.5, 37.3, 35.6, 23.0; IR (neat) 1700 cm^{-1}; $[\alpha]^{29}_D$ +36° (c = 0.201, CH_2Cl_2); CD $\Delta\epsilon_{286}$ = +1.46 (c = 0.068 g/dm^3, CH_2Cl_2). Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 79.92; H, 9.50.

(−)-(*S*)-1-(*p*-Tolylsulfinyl)-(*Z*)-6-nonen-2-one (25). To LDA (5.2 mmol) in 30 mL of THF at −78 °C was added (−)-(*S*)-methyl *p*-tolyl sulfoxide (0.81 g, 5.2 mmol). The solution was stirred for 30 min and *N*-methoxy-*cis*-5-octenamide[16] (0.97 g, 5.2 mmol) was added. The solution was stirred for 2 h, warmed to 25 °C, and stirred for 3 h. Workup as described above afforded 1.00 g (67%) of **25** as a pale yellow oil, which solidified to colorless crystals: mp 38.5–39.0 °C (hexane); ^{1}H NMR 7.54 (d, 2, J = 8.3), 7.34 (d, 2, J = 8.3), 5.43–5.17 (m, 2), 3.92 (d, 1, J = 13.5), 3.69 (d, 1, J = 13.5), 2.51–2.37 (m, 2), 2.42 (s, 3), 2.05–1.96 (m, 4), 1.61–1.56 (m, 2), 0.94 (t, 3, J = 7.5); ^{13}C NMR 201.6, 142.1, 139.7, 132.7, 130.2, (2 C), 127.6, 124.0 (2 C), 68.2, 44.3, 26.0, 22.9, 21.4, 20.4, 14.3; IR (neat) 1710, 1035, 805 cm^{-1}; $[\alpha]^{29}_D$ −196° (c = 0.482, acetone). Anal. Calcd for $C_{16}H_{22}O_2S$: C, 69.02; H, 7.97; S, 11.52. Found: C, 69.07; H, 8.06; S, 11.54.

(4*RS*)-4(*S*)-(*p*-Tolylsulfinyl)-(*E*)-1,9-dodecadien-5-one (26) was prepared as described above for **20** from sulfoxide **25** (0.150 g, 0.539 mmol). Flash chromatography on silica gel (5:1 hexane–EtOAc) afforded 0.12 g (67%) of **26** as a ≈1:1 mixture of two diastereomers: ^{1}H NMR 7.47 (d, 0.5 × 2, J = 8.1), 7.46 (d, 0.5 × 2, J = 8.1), 7.33 (d, 0.5 × 2, J = 8.1), 7.31 (d, 0.5 × 2, J = 8.1), 5.76–5.56 (m, 1), 5.42–5.16 (m, 2), 5.16–5.04 (m, 2), 3.77 (dd, 0.5 × 1, J = 9, 5), 3.69 (dd, 0.5 × 1, J = 9, 5), 2.80–2.42 (m, 2.5), 2.41 (s, 3), 2.22 (ddd, 0.5 × 1, J = 18.0, 9.0, 6.5), 2.06–1.76 (m, 5), 1.58–1.24 (m, 2), 0.95 (t, 0.5 × 3, J = 7.5), 0.93 (t, 0.5 × 3, J = 7.5); ^{13}C NMR (204.5, 203.6), (142.5, 142.3), (138.0, 137.5), (132.7, 132.6), (132.5, 132.5), (129.9 (0.5 × 2 C), 129.8 (0.5 × 2 C)), (127.8, 127.7), (124.9 (0.5 × 2 C), 124.7 (0.5 × 2 C)), (118.7, 118.7), (75.9, 73.9), (45.1, 44.6), (30.8, 29.6), (26.1, 26.0), (22.8, 22.6), (21.4, 21.4), (20.4, 20.4), (14.2, 14.2); IR (neat) 1720, 1050, 920, 810 cm^{-1}.

(−)-(1*S*)-1-Ethyl-1,2,3,5,6,7-hexahydro-2-methylene-4*H*-inden-4-one (30). Oxidative cyclization of sulfoxide **26** (0.43 g, 1.35 mmol) buffered with potassium acetate (0.53 g, 5.4 mmol) for 17 h at 40 °C gave 0.55 g of crude product. Flash chroma-

tography on silica gel (30:1 CH_2Cl_2–ether) afforded 37 mg (15%) of **30** as a light yellow oil, which decomposed on standing: ^1H NMR 5.12 (dddd, 1, J = 2.2, 2.2, 2.2, 0.6), 4.99 (dddd, 1, J = 2.2, 2.2, 2.2, 0.6), 3.36 (m, 1), 3.21 (dddd, 2, J = 2.6, 2.6, 2.6, 2.6), 2.43–2.39 (m, 2), 2.34–2.25 (m, 2), 2.09–2.01 (m, 2), 1.80–1.60 (m, 2), 0.80 (t, 3, J = 7.4); ^{13}C NMR 197.4, 166.1, 149.4, 136.6, 108.4, 54.4, 37.8, 35.8, 25.0, 24.9, 23.4, 9.2; IR (neat) 1670, 890 cm^{-1}; $[\alpha]^{29}_D$ −52° (c = 0.37, CH_2Cl_2); CD $\Delta\epsilon_{336}$ = +0.023 (c = 0.115 g/dm^3, CH_2Cl_2), $\Delta\epsilon_{247}$ = −0.56 (c = 4.60 × 10^{-4} g/dm^3, CH_2Cl_2).

1-Ethyl-3,5,6,7-tetrahydro-2-methyl-4*H*-inden-4-one (31). A solution of **30** (17 mg, 0.10 mmol), (2*R*,3*R*)-(−)-2,3-butanediol (11 mg, 0.012 mmol) and a trace of pyridinium *p*-toluenesulfonate in 20 mL of benzene was heated at reflux for 21 h on a Dean–Stark apparatus. The reaction mixture was washed (water), dried ($MgSO_4$), and evaporated in vacuo to give 12 mg of a dark orange oil, which contained mainly **31**: ^1H NMR 3.12 (t, 2, J = 1.2), 2.57–2.50 (m, 2), 2.45–2.39 (m, 2), 2.35–2.26 (m, 2), 2.07 (br q, 2, J = 7.0), 2.04 (s, 3), 1.03 (t, 3, J = 7.0).

1-(Phenylsulfonyl)-5-hexen-2-one (32). To a suspension of NaH (100 mg, 60% oil dispersion, 2.5 mmol) in 5 mL of THF at 0 °C was added (phenylsulfonyl)acetone (500 mg, 2.5 mmol) in 8 mL of THF. The mixture was stirred at 0 °C for 30 min and *n*-BuLi (1.1 mL, 2.4 M in hexane, 2.6 mmol) was added. The orange-yellow solution was stirred for 30 min and allyl bromide (0.02 mL, 2.5 mmol) was added via syringe. The mixture was stirred at 25 °C for 2 h, quenched (saturated NH_4Cl solution), acidified (10% HCl), and extracted with CH_2Cl_2. The organic layer was washed (brine), dried (Na_2SO_4), and evaporated in vacuo to give 687 mg of a yellow oil. Flash chroamtography on silica gel (1:1 hexane–EtOAc) yielded 372 mg (61%) of **32** and 10% of the dialkylated product **33**. The ^1H NMR and IR data of **32** are identical with those previously reported.[21]

4-(Phenylsulfonyl)-1,8-nonadien-5-one (33). To a suspension of NaH (50 mg, 60% oil dispersion, 1.25 mmol) in 1 mL of DMF was added a solution of **32** (300 mg, 1.26 mmol) in 2 mL of DMF. The mixture was stirred at 25 °C for 15 min and allyl bromide (0.14 mL, 1.60 mmol) was added via syringe. The reaction was stirred for 2 h, quenched (saturated NH_4Cl and 5% HCl), and extracted with CH_2Cl_2. The organic layer was washed (brine), dried (Na_2SO_4), and evaporated in vacuo. Flash chromatography on silica gel (4:1 hexane–EtOAc) gave 158 mg (50%) of **33**: ^1H NMR 7.75–7.80 (m, 2), 7.65–7.75 (m, 1), 7.52–7.65 (m, 2), 5.77 (ddt, 1, J = 17.1, 10.3, 6.5), 5.56 (ddt, 1, J = 17.5, 9.6, 6.4), 4.97–5.09 (m, 4), 4.16 (dd, 1 J = 10.5, 4.5), 2.83–3.02 (m, 2), 2.52–2.70 (m, 2), 2.26–2.37 (m, 2); ^{13}C NMR 200.8, 136.3, 134.4, 131.6, 129.5, 129.1, 119.2, 115.7, 74.2, 44.3, 31.3, 27.0 (one aromatic peak coincided with one of the peaks for the aromatic/alkenyl carbons); IR (neat) 3085, 1727, 1648, 1325, 1312, 1152, 1088, 1000, 920 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_3S$: C, 64.72, H, 6.52; S, 11.52. Found: C, 64.89; H, 6.48; S, 11.63.

6-Methylene-1-(phenylsulfonyl)bicyclo[3.2.1]oct-2-one (34) and 7-Methylene-1-(phenylsulfonyl)bicyclo[3.3.0]octan-2-one (36). Oxidative cyclization of **32** (37 mg, 0.13 mmol) at 55 °C for 22 h produced 25 mg of crude product. Flash chromatography on silica gel (1:1 hexane–EtOAc) afforded 6.4 mg of **34** (20%) followed by 1.2 mg of **36** (4%).

Data for **34**: ^1H NMR 8.06–8.09 (m, 2), 7.61–7.66 (m, 1), 7.51–7.56 (m, 2), 5.17 (m, 1), 5.09 (m, 1), 3.40 (ddd, 1, J = 17, 2.6, 2.6), 3.10 (m, 1), 2.78 (ddd, 1, J = 11.7, 5.2, 2.5), 2.65 (ddd, 1, J = 17, 2, 1), 2.28–2.50 (m, 2), 1.99 (dd, 1, J = 11.7, 2.0), 1.76–1.90 (m, 2); ^{13}C NMR 148.1, 138.1, 133.8, 130.5, 128.5, 109.1, 78.1, 41.9, 38.6, 37.6, 36.4, 32.7 (carbonyl carbon not observed); IR (neat) 3073, 1723, 1305, 1145, 723, 686 cm^{-1}. Anal. Calcd for $C_{15}H_{16}O_3S$: 276.0821. Found: 276.0834.

Data for **36**: ^1H NMR 7.78–7.83 (m, 2), 7.68–7.78 (m, 1), 7.56–7.68 (m, 2), 4.90 (s, 1), 4.80 (s, 1), 3.60 (m, 1), 2.91 (br d, 1, J = 16.5), 2.85 (dd, 1, J = 15.3, 8.5), 2.55–2.80 (m, 1), 2.43 (br d, 1, J = 16.5), 2.35–2.40 (m, 3), 2.20 (br d, 1, J = 15); ^{13}C NMR 134.6, 130.6, 129.1, 109.4, 40.5, 39.2, 39.1, 30.0, 25.3 (four quaternary carbons not observed); IR (neat) 3065, 1745, 1305, 1150, 718, 686 cm^{-1}. Anal. Calcd for $C_{15}H_{16}O_3S$: 276.0821. Found: 276.0842.

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Supplementary Material Available: Experimental details for the X-ray diffraction study of **13b**, and tables of (i) atomic coordinates, (ii) anisotropic thermal parameters, (iii) bond lengths and angles, and (iv) hydrogen atom positions, and (v) ORTEP diagram showing atom numbers (9 pages). Ordering information is given on any current masthead page.

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Efficient C-21 Deoxygenation of 21-Alkoxy-20-keto Corticoid Steroids with Trimethylsilyl Iodide in the Presence of Methanol

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Reaction of 21-alkyl ethers **1**, **4–6**, **8**, and **9** with a large excess of trimethylsilyl iodide (TMSI) produced the deoxygenated products **3** and **11** in low to moderate yields along with a small amount of 21-alcohols **2** and **10**. The deoxygenation reaction in the presence of 1.5 molar equiv of MeOH gave the products in much higher yields than those without MeOH, except the reaction of the ethyl and *n*-propyl ethers **4** and **5**. Treatment of **1** and **8** with trimethylsilyl chloride/NaI in the presence of MeOH gave similar results to those with TMSI. Compound **3** was also produced in high yields by reaction of **1** and **4** with HI under mild conditions. On the other hand, treatment of 17α-ketol **7** with TMSI in the presence of MeOH yielded 17aβ-methyl D-homo steroid **15**. The results along with deuterium-labeling experiments with MeOD and IR and ^1H NMR spectral analysis during the reaction with TMSI suggest that dealkylation of the 21-alkyl ethers precedes the deoxygenation, in which HI produced in situ by reaction of MeOH with TMSI would be involved.

Introduction

The use of organosilicon reagents in organic synthesis has become widespread during recent years. Trimethylsilyl iodide (TMSI), which was developed independently in Olah's[1] and Jung's[2] laboratories, has gained importance for the cleavage of esters,[1,2a] lactones,[3] ethers,[2b,3] ketals,[4] and cabamates[5] as well as for the conversion of alcohols[6]

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