Stereochemistry of Addition of Organocopper Reagents and of the Hydride Ion to 1-(Arylsulfonyl)bicyclo[1.1.0]butanes

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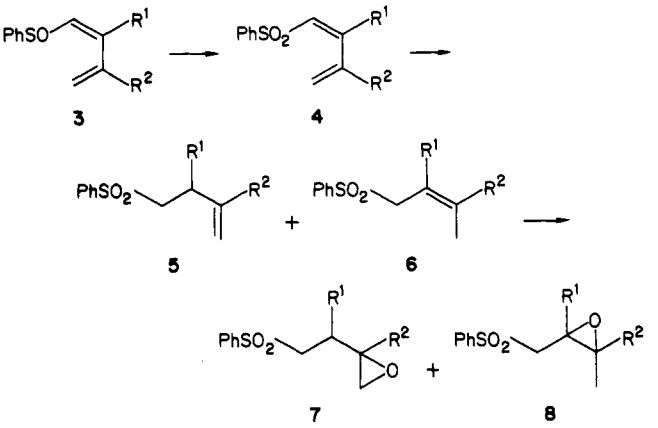
Addition of methylmagnesium iodide/cuprous iodide or of lithium dimethylcuprate to 2-*exo*- and 2-*endo*-methyl-1-(phenylsulfonyl)bicyclo[1.1.0]butane and determination of the relative geometry of the methyls in the 2,3-dimethylcyclobutanes obtained allowed us to establish that addition of the methyl group occurred from the endo side of the bicyclic molecule. Similarly, lithium aluminum hydride reduction of 2-*exo*,3- and 2-*endo*,3-dimethylbicyclobutane was also found to occur by *endo*-addition of the hydride ion at position 3 of the bicyclic system.

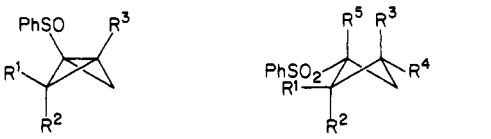
We have recently shown that 1-(phenylsulfonyl)bicyclo[1.1.0]butanes (1) could undergo addition of organocopper reagents or could be reduced with lithium aluminum hydride ($LiAlH_4$) to provide cyclobutane derivatives **2**.[1,2] Although two geometrical isomers of **2** were obtained by addition of alkyl- or alkenylcopper reagents to unsubstituted **1** or by reduction of its 3-methyl derivative,[3] it was assumed that the direction of primary nucleophilic attack on **1** was specifically determined by electronic factors and that scrambling occurred during subsequent protonation of the intermediate α-sulfonyl carbanion. In order to confirm this point and to determine the sense of attack, it was necessary to define the geometry of R^3 or R^4 in the product **2** relative to an already present *exo*-R^1 or *endo*-R^2 substituent at position 2 of the starting material. We now report on the results of these experiments which allow one to conclude that, like in many other reactions of bicyclobutanes with reactive, unsaturated molecules,[4] the primary addition occurs from the endo side of the molecule.

We first observed that in the case of **1a**, which carries a 2-*exo*-methyl substituent, both additon of methylmagnesium iodide (MMI) or lithium dimethylcuprate and reduction by $LiAlH_4$ produced only one **2** isomer. This is probably due to steric factors which impose a preferred trans configuration on the sulfone group relative to the 2-methyl in the intermediate α-sulfonyl carbanion. Subsequent protonation or methylation then proceeds with conservation of this configuration. We also noticed that the 2,3-dimethyl derivative obtained by addition of organocopper reagents to **1a** was different from the corresponding dimethyl derivative obtained by $LiAlH_4$ reduction of **1b**. Since the latter compound failed to crystallize at first, two 1,2,3-trimethyl derivatives were prepared by methylation of the two 2,3-dimethyl isomers with *n*-butyllithium (BuLi) and methyl iodide. The first trimethyl derivative was also formed when addition of MMI to **1a** was carried out in the presence of excess methyl iodide. Both methylations produced only one trimethyl isomer. Since these methylations cannot be expected to change the relative geometry of the 2- and 3-methyls, determination of the structure of the two trimethyl isomers would indicate this geometry.

Scheme I[a]



[a] a, $R^1 = R^2 = Me$; b, $R^1 = Me$; $R^2 = H$.



1a, R^1=Me; R^2=R^3=H
b, R^1=R^3=Me; R^2=H
c, R^1=H; R^2=R^3=Me
d, R^2=Me; R^1=R^3=H

2a, R^1=R^4=Me; R^2=R^3=R^5=H
b, R^1=R^3=Me; R^2=R^4=R^5=H
c, R^1=R^4=R^5=Me; R^2=R^3=H
d, R^1=R^3=R^5=Me; R^2=R^4=H

The molecular structures of the two trimethyl compounds were determined by X-ray analysis and were found to be **2c** for the former (Figure 1) and **2d** for the latter (Figure 2).[5,6] Hence, the structure of the product of addition of MMI or dimethylcuprate to **1a** is **2a**, while that of the product of reduction of **1b** is **2b**. In both cases the nucleophile has, therefore, been added from the endo side of the bicyclic system.

In order to complete the picture, similar reactions with substrates carrying a 2-*endo*-methyl substituent were carried out. The dimethyl compound **1c** was obtained from epoxide **7a**, prepared according to Scheme I. Sulfoxide **3a**[7] was oxidized with *m*-chloroperbenzoic acid (MCPBA) to sulfone **4a**, which was then reduced with

(1) Gaoni, Y. *Tetrahedron Lett.* **1982**, *22*, 5212–5218.
(2) Gaoni, Y. *Tetrahedron Lett.* **1982**, *22*, 2519–2520.
(3) Copper catalyzed addition of methyl magnesium iodide to unsubstituted **1** or reduction of the 3-methyl derivative of **1** with lithium aluminum hydride were at first thought to yield only one **2** isomer.[1,2] This erroneous conclusion was based on spectral evidence (^1H NMR in $CDCl_3$) and on chromatographic and melting behavior of the mixtures of cis and trans isomers of 1-methyl-3-(phenylsulfonyl)cyclobutane. Proton NMR in benzene-d_6 soon revealed, however, the presence of two isomers by resolution of their superimposed signals. GC–MS analysis, using a capillary, 25-m column coated with SE54, also revealed the presence of two isomers.
(4) Pomerantz, M.; Wilke, R. N.; Gruber, G. W.; Roy, U. *J. Am. Chem. Soc.* **1972**, *94*, 2752–2758 and references cited therein.
(5) X-ray structure determinations were done by Dr. Felix Frolow of this Institute.
(6) See the Experimental Section for analytical methods used and for basic structural data.
(7) Gaoni, Y. *Tetrahedron Lett.* **1977**, 4521–4522.

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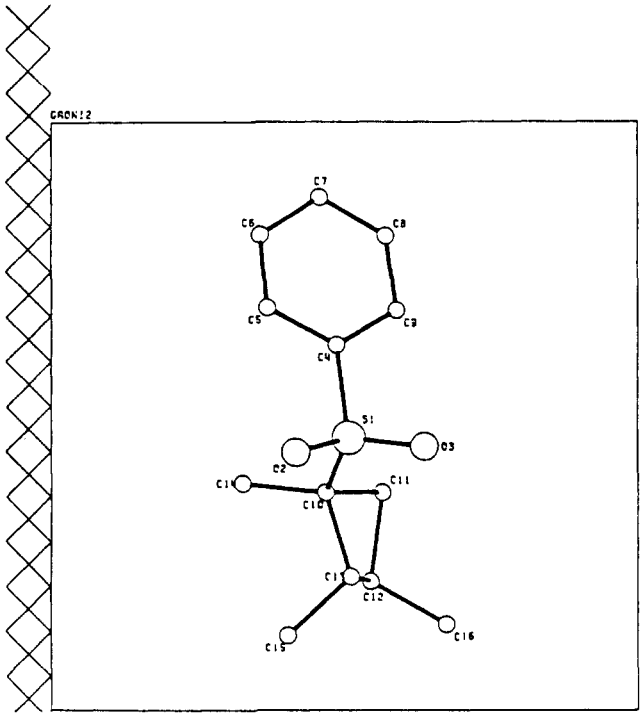


Figure 1. Molecular structure of **2c** derived from **1a** by addition of methyl magnesium iodide and methylation α to the sulfone.

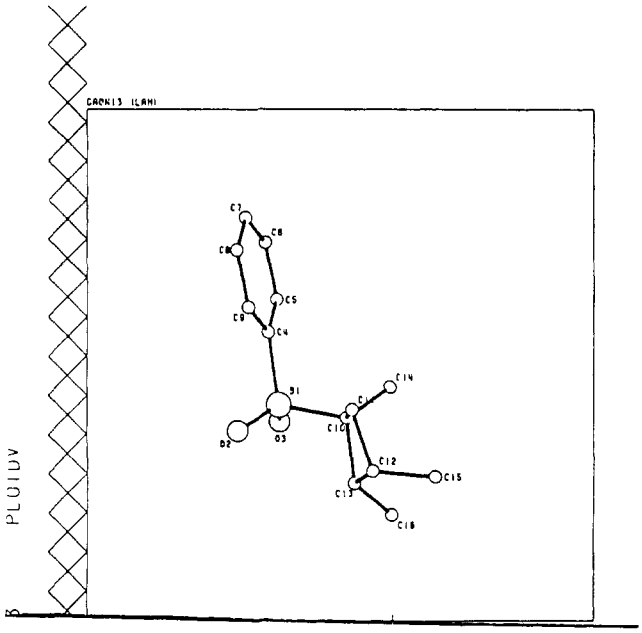
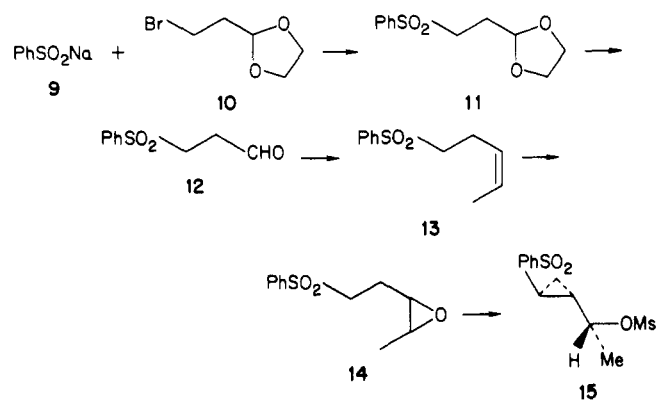


Figure 2. Molecular structure of **2d** derived from **1b** by $LiAlH_4$ reduction and methylation α to the sulfone.

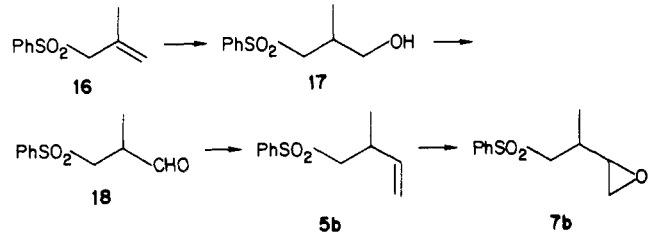
$LiAlH_4$ in tetrahydrofuran (THF) to give a ca. 3:1 mixture of **5a** and **6a** in a total 70% yield. Expoxidation of this mixture produced epoxides **7a** and **8a**, which were chromatographically separated to provide **7a** as a mixture of two diastereomers in 58% yield. Treatment of this mixture with BuLi and mesyl chloride,[8] followed by chromatographic separation, furnished **1b** and **1c** in 20 and 9% yield, respectively.

Reduction of **1c** with $LiAlH_4$ cleanly produced the same *trans*-dimethyl derivative **2a** as that obtained by organocuprates addition to **1a**. Addition of the hydride ion had again occured from the endo side of the bicyclic system,

Scheme II



Scheme III



without, however, bringing about an inversion of the sulfone group relative to the *trans*-2-methyl.

Preparation of the 2-*endo*-methyl derivative **1d** proved to be rather elusive. Our first approach was to use *cis*-epoxide **14** which would necessarily lead to **1d** according to the general scheme of bicyclobutane formation.[8] This epoxide was therefore prepared as shown in Scheme II.

Reaction of sodium benzene sulfinate **9** with bromo ketal **10** provided sulfone **11** which was deketalized to aldehyde **12** and treated with ethylidenetriphenylphosphorane to furnish the cis-γ,δ-unsaturated sulfone **13**. Epoxidation with MCPBA gave the *cis*-epoxide **14** in 26% overall yield. Sulfones **13** and **14** were different from the corresponding trans compounds prepared according to our general procedure[8] from crotyl bromide and methyl phenyl sulfone. An attempt to directly convert **14** into a bicyclic derivative[8] failed to yield any such compound. Mesylate **15**, which is the last intermediate in the formation of the bicyclobutane, was then prepared from epoxide **14**. It was found to be different from mesylate **15a** prepared from the corresponding *trans*-epoxide (see Experimental Section). Both mesylates were submitted to the action of BuLi in THF. Mesylate **15a** was highly reactive and provided **1a** after a reaction time of 1 min in 76% yield. Mesylate **15** was highly unreactive and was recovered unchanged after a reaction time of 5 h.

Our next approach to **1d** was based on that depicted in Scheme I. Reduction of sulfone **4b** failed, however, to provide any of the desired **5b**. In fact, no monomeric product was recovered from this reaction.

The bicyclic sulfone **1d** was finally obtained, together with **1a**, from the diastereomeric epoxides **7b**, prepared according to Scheme III.

Hydroboration[9] of sulfone **16** provided alcohol **17** which was oxidized with pyridinium chlorochromate[10] (PCC) to aldehyde **18**. The crude aldehyde, containing unreacted **17** in varying amounts, was treated with methylenetriphenylphosphorane in ether or THF to provide **5b** in

(8) Gaoni, Y. *J. Org. Chem.* **1982**, *47*, 2564–2571.

(9) Lane, C. F. *J. Org. Chem.* **1974**, *39*, 1437–1438.
(10) Corey, E. J.; Suggs, W. J. *Tetrahedron Lett.* **1975**, 2647–2650.

18–28% yield (40% yield relative to chromatography purified aldehyde). Epoxidation gave a 2:1 ratio of two **7b** epoxides in 83% yield. The usual treatment[8] then provided a mixture of **1a** and **1d** in 36% yield, from which **1d** could be separated in 23% yield.

The complete lack of reactivity of mesylate **15** toward displacement by the α-sulfonyl anion results most probably from a transition geometry which, while directing the mesyloxy group to point away from the negative charge for a backside displacement to occur,[8] also compresses the methyl group against the cyclopropane ring. When the methyl is not directly involved in the closure of the second ring, as in the case of epoxide **7b**, it does not seem to interfere with this cyclization.

The change in geometry of the 2-methyl from **1a** and **1b** to **1d** and **1c** is clearly seen in the ^{1}H NMR spectra. The deshielded *exo*-methyl protons of **1a** and **1b** have the same chemical shifts as the 2-*endo* proton and as a consequence, a complex A_3B pattern is observed for this four-proton system. The *endo*-methyl protons of **1d** and **1c**, on the other hand, are shielded by the second cyclopropane ring and are shifted to a much higher field. The whole spectrum is then simplified to a first-order spectrum.

Addition of MMI to **1d** was slower than the addition to **1a** and produced a less pure product. The major component (86–90%) was, however, **2b**. The accompanying isomeric product (GC–MS) was not **2a**, as could be established by ^{1}H NMR. Moreover, methylation of the mixture furnished only the trimethyl derivative **2d**, isolated in 66% yield. A secondary product, methylated also on the aromatic ring and formed because excess BuLi and methyl iodide have been used, was isolated in 20% yield. Its NMR chemical shifts and splitting patterns were, however, very similar to those of **2d**.

Addition of dimethylcuprate to **1d** also furnished a not very pure **2b**, with similar GC–MS analysis. The presence of **2a**, could, however, again be excluded on the basis of the ^{1}H NMR spectrum. The minor isomeric product in the last two reactions is believed to be epimeric with **1b** on the carbon bearing the sulfone groups.

It can thus be concluded that in the presence of a 2-endo substituent, the incoming methyl is again added from the endo side of the bicyclic system. There is here, however, practically no accompanying change in the relative geometry of the sulfone group and the 2-methyl group which continue to keep their trans relationship.

Experimental Section

General Procedures. Melting points were taken on a Fisher-Johns apparatus and were not corrected. Infrared spectra were measured in chloroform with a Perkin-Elmer 457A grating spectrometer. Proton NMR spectra were measured in deuteriochloroform with a Varian FT-80A spectrometer. Chemical shifts are reported in δ units downfield from internal Me_4Si, and the J values are given in hertz. Combined gas chromatographic–mass spectral analyses (GC–MS) were performed with a Finnigan automated spectrometer.

THF was dried by distillation from sodium diphenyl ketyl. Reactions with commercial BuLi in hexane were carried out under argon atmosphere. Workup included quenching with aqueous ammonium chloride solution, rotoevaporation of most of the THF, partitioning between ether and water, drying the combined ether extracts, and rotoevaporation of the ether.

Epoxidations were done with commercial, ~90% MCPBA in dichloromethane room temperature by using 210 mg of acid and 4 mL of solvent per mmol of substrate. Workup involved cooling the reaction flask in ice, filtration of precipitated acid, rotoevaporation of most of the solvent, dissolving in ether, washing with aqueous sodium sulfite and sodium carbonate, drying, and evaporating the solvent. Alternatively, the reaction flask was cooled in ice and ammonia gas was passed over the stirred reaction mixture for 10–15 min. The precipitated salts were filtered and the solvent evaporated to yield the crude epoxide.

TLC was done on Merck Kieselgel 60-F254 precoated aluminum plates. Silica gel for column chromatography was Merck Kieselgel 60 (70–230 mesh).

Elemental analyses were performed by Eng. R. Heller of this Institute or at the Microanalytical Laboratory of the Hebrew University, Jerusalem.

2-*exo*-Methyl-1-(phenylsulfonyl)bicyclo[1.1.0]butane (1a). 1-(Phenylsulfonyl)-*trans*-3-pentene was prepared in 70% yield from methyl phenyl sulfone and crotyl bromide as described:[8] NMR δ 1.59 (d, Me, J = 4.8), 2.42 (m, 2), 3.12 (m, 2), 5.39 (m, 2) 7.5–8.0 (m 5); IR 1305, 1145, 1087 cm^{-1}. Epoxidation furnished 1-(phenylsulfonyl)-*trans*-3,4-epoxypentane in 89% yield: NMR δ 1.26 (d, Me, J = 4.9), 1.7–2.2 (m, 2), 2.74 (t, 2), 3.22 (t, 2, J = 7.8), 7.5–8.0 (m, 5); IR 1305, 1148, 1087 cm^{-1}. Consecutive treatment of the latter epoxide in THF with BuLi, methanesulfonyl chloride (MsCl), and BuLi,[8] followed by chromatographic purification provided **1a** in 65% yield: mp 44–45 °C (pentane); NMR δ 1.12 (dd, 1, C_4 *endo*-H), 1.37-1.70 (m, 4, A_3B part-spectrum of C_2 Me and C_2 *endo*-H), 2.32 (dd, 1, J^1 = 1.3, J^2 = 3.7, C_4 *exo*-H), 2.63 (dt, 1, C_3 H), 7.5–8.0 (m, 5); IR 1310, 1150, 1083 cm^{-1}. Anal. ($C_{11}H_{12}O_2S$) C, H.

2-*exo*,3-Dimethyl-1-(phenylsulfonyl)bicyclo[1.1.0]butane (1b). A solution of lithium diisopropylamide (LDA) was prepared in THF (3 mL) at 0 °C from 2 mL of a 2 N solution of diisopropylamine in THF (4.0 mmol) and 2.4 mL of a 1.56 N solution of BuLi in hexane (3.7 mmol). The LDA solution was introduced into a solution of **1a** (500 mg, 2.4 mmol) in THF (7 mL) kept at 0 °C, with the simultaneous dropwise addition of excess methyl iodide (0.5 mL in 3 mL of THF). Workup and recrystallization of the crude solid product from pentane provided **1b** (440 mg, 82% yield): mp 60–61 °C (pentane); NMR δ 1.06 (s, 1, C_4 *endo*-H), 1.38–1.45 (m, 4, A_3B part-spectrum of C_2 Me and C_2 *endo*-H), 1.82 (s, Me), 2.15 (s, 1, C_4 *exo*-H); IR 1317, 1155, 1100 cm^{-1}. Anal. ($C_{12}H_{14}O_2S$) C, H, S.

(*Z*)-2,3-Dimethyl-1-(phenylsulfonyl)-1,3-butadiene (4a). Sulfoxide **3a**[7] (10 g) was oxidized in dichloromethane (150 mL) at 0 °C with MCPBA (10 g) for 2 h. Extractive workup and chromatography on silica gel (40 g, hexane–ether 3:2) provided **4a** (9.04 g, 84% yield): NMR δ 1.80 (d, Me, J = 0.9), 1.94 (d, Me, J = 1.4), 4.74, 4.97, 6.21 (three br s, 1 H each), 7.5–8.0 (m, s); IR 1616, 1315, 1155, 1095, 910 cm^{-1}; GC–MS (chemical ionization, CI), m/e 223 [(M + 1)$^+$, $C_{12}H_{14}O_2S$, M_r 222].

1,2-Epoxy-2,3-dimethyl-4-(phenylsulfonyl)butane (7a). To a stirred solution of **4a** (6.5 g) in THF (150 mL), cooled to 0 °C was added powdered $LiAlH_4$ (1 g) all at once, followed by another equal portion after 15 min. After stirring for another 15 min, ether (150 mL) was added to the reaction mixture, followed by dropwise addition of a saturated aqueous sodium sulfate solution until a well-separated precipitate was formed. Filtration of the precipitate and evaporation of the solvent gave, after chromatography on silica gel (120 g, hexane–ether 3:1), a mixture of **5a** and **6a** (4.6 g, 71% yield) in a ratio of 3:1, respectively, as determined by GC–MS (CI), m/e 225 for both isomers [(M + 1)$^+$, $C_{12}H_{16}O_2S$, M_r 224].

Epoxidation of the above mixture (2.15 g) followed by chromatography on Florisil (40 g, hexane–ether 7:3) provided two epoxides.

2,3-Epoxy-2,3-dimethyl-1-(phenylsulfonyl)butane (**8a**, 0.28, 12% yield): mp 74–75 °C (hexane); NMR δ 1.16 (s, Me), 1.31 (s, Me), 1.58 (s, Me), 3.41 (ABq, 2, J = 14.4, $\Delta\nu$ = 25.4 Hz), 7.5–8.0 (m, s). Anal. ($C_{12}H_{16}O_3S$) C, H, S.

Epoxide **7a** (1.35 g, 58% yield) was obtained as a ca. 1:1 mixture of two isomers: NMR δ 1.14, 1.19, 1.22, 1.25 (Me signals, 6), 2.05 (m, 1), 2.59 (s, 2), 2.7–3.3 (m, 2), 7.5–8.0 (m, 5); GC–MS (CI), m/e 241 for both isomers [(M + 1)$^+$, $C_{12}H_{16}O_3S$, M_r 240].

2-*endo*,3-Dimethyl-1-(phenylsulfonyl)bicyclo[1.1.0]butane (1c). The epoxide mixture **7a** (1.1 g) was treated in THF (30 mL) at 0 °C with BuLi, MsCl, and BuLi[8] to provide a mixture of **1b** and **1c**. Chromatography on silica gel (70 g, hexane–ether 17:3) separated first **1b** (200 mg, 20% yield) then mixed fractions of **1b** and **1c** (86 mg) and then pure **1c** (90 mg, 9% yield). Sulfone **1c**: mp 52–53 °C (pentane); NMR δ 0.90 (d, C_2 Me, J = 6.0), 1.85 (s, C_3 Me), 1.93 (d, 1, C_4 *endo*-H, J = 1.8), 2.50 (dd, 1, C_4 *exo*-H, J^1 = 1.8, J^2 = 4.3), 3.05 (m, 1, C_2 *exo*-H), 7.5–8.0 (m, 5); IR 1312, 1155, 1110, 1090, 975, 920 cm^{-1}. Anal. ($C_{12}H_{14}O_2S$) C, H, S.

2-[2-(Phenylsulfonyl)ethyl]-1,3-dioxolane (11). A mixture of sodium sulfinate (**9**, 12.4 g, 75 mmol) and 3-bromopropionaldehyde ethylene acetal (**10**, 13.7 g, 75 mmol) in dry DMF (70 mL) was warmed at 80 °C for 12 h. The cooled mixture was partitioned between ether and water and the combined ether extracts were dried and evaporated. Chromatography on Florisil (130 g, hexane–ethyl acetate 5:2) furnished **11** (14.8 g, 81% yield): mp 62–63 °C (hexane); NMR δ 2.08 (m, 2), 3.23 (m, 2), 3.86 (m, 4), 4.95 (t, 1, J = 3.9), 7.5–8.0 (m, 5); IR 1315, 1150, 1095 cm^{-1}. Anal. ($C_{11}H_{14}O_4S$) C, H, S.

3-(Phenylsulfonyl)propanal (12). To a solution of **11** (8.5 g) in acetone (120 mL) was added 15% sulfuric acid (120 mL) and the mixture was refluxed for 1 h. Most of the acetone was rotoevaporated and the remaining solution was neutralized with solid sodium bicarbonate and extracted with ether. Chromatography on silica gel (100 g, dichloromethane–hexane–ethyl acetate 20:15:3) provided **12** (5.1 g, 72% yield): NMR δ 2.96 and 3.42 (AA'BB' spectrum, 4), 7.5–8.0 (m, 5), 9.74 (s, 1); IR 1730, 1327, 1320, 1157, 1150, 1054 cm^{-1}; GC–MS (CI), m/e 199 [(M + 1)$^+$, $C_9H_{10}O_3S$, M_r 198].

***cis*-1-(Phenylsulfonyl)-3-pentene (13).** Ethylidenetriphenylphosphorane was prepared in THF (40 mL) by stirring ethyltriphenylphosphonium bromide (2.78 g, 7.5 mmol) with BuLi (6.75 mmol) for 3 h at 0 °C. Aldehyde **12** (1.5 g, 7.5 mmol) dissolved in THF (3 mL) was then introduced dropwise and stirring was continued for 0.5 h. Workup and chromatography on silica gel (75 g, dichloromethane–hexane–ethyl acetate 20:15:4) provided **13** (0.78 g, 49% yield): IR 1315, 1150, 1093 cm^{-1}; NMR δ 1.56 (d, Me, J = 5.0), 2.50 (m, 2), 3.11 (m, 2), 5.40 (m, 2), 7.5–8.0 (m, 5). ^{1}H NMR in benzene-d_6 showed a shifted, similar spectrum but upon addition of the *trans*-3-pentene isomer (see above) to the solution, three peaks, due to the two compounds, were observed in the methyl region, as well as additional absorptions in the olefinic region. Sulfone **1e** was thus shown to be originally free of the trans isomer and this was also confirmed by GC–MS (CI), one peak, m/e 211 [(M + 1)$^+$, $C_{11}H_{14}O_2S$, M_r 210].

1-(Phenylsulfonyl)-*cis*-3,4-epoxypentane (14). Epoxidation of **13** (625 mg, 3.0 mmol) and chromatography on silica gel (15 g, dichloromethane–hexane–ethyl acetate 20:15:3) furnished **14** (570 mg, 92% yield): NMR δ 1.23 (d, Me, J = 5.4), 1.8–2.1 (m, 2), 2.9–3.4 (m, 4), 7.5–8.0 (m, 5); IR 1315, 1155, 1095 cm^{-1}; GC–MS (CI), m/e 227 [(M + 1)$^+$, $C_{11}H_{14}O_3S$, M_r 226].

***trans*-1-[(1*RS*)-1-[(Methylsulfonyl)oxy]ethyl]-(2*SR*)-2-(phenylsulfonyl)cyclopropane (15), *trans*-1-[(1*SR*)-1-[(Methylsulfonyl)oxy]ethyl]-(2*SR*)-2-(phenylsulfonyl)cyclopropane (15a), and Their Reaction with BuLi.** Mesylate **15** and its diastereomer **15a** were prepared from the *cis*-**14** and from the *trans*-epoxide, respectively, by treatment in THF with 1.2 equiv of BuLi and 1.2 equiv of MsCl.[8]

Mesylate **15** was chromatographed on silica gel (30 times the weight of the crude product, dichloromethane–hexane–ethyl acetate 20:15:3) to provide the pure compound in 50% yield: mp 101–102 °C (dichloromethane–pentane); NMR δ 1.0–2.1 (m, 3, C_2 and C_3 ring protons), 1.46 (d, Me, J = 6.4), 2.6–2.8 (m, 1, C_2 H), 2.84 (s, Me), 4.36 (pentuplet, 1, $J \simeq 6.5$), 7.5–8.0 (m, s); IR 1330, 1315 (broad band), 1185, 1160, 1095 cm^{-1}. Anal. ($C_{12}H_{16}O_5S_2$) C, H, S.

Mesylate **15a**, derived from the *trans*-epoxide (see above), was equally purified by chromatography and obtained in 62% yield: mp 78–79 °C (dichloromethane–pentane); NMR δ 1.32 (d, Me, J = 6.3), 1.3–1.75 (m, 2), 1.8–2.1 (m, 1), 2.4–2.6 (m, 1), 2.98 (s, Me), 4.41 (pentuplet, 1, $J \simeq 6.5$), 7.5–8.0 (m, 5); IR 1367, 1330, 1315 (broad band), 1183, 1160, 1096 cm^{-1}. Anal. ($C_{12}H_{16}O_5S_2$) C, H, S.

Treatment of **15a** (494 mg, 1.63 mmol) in THF (15 mL) at 0°C with BuLi (1.80 mmol) for 1 min, followed by workup and chromatographic puirification provided sulfone **1a** in 76% yield. Similar treatment of **15** for 5 h gave only starting material.

2-Methyl-1-(phenylsulfonyl)-3-butene (5b) and Epoxide 7b. Hydroboration of sulfone **16** (5.88 g) with boron hydride–dimethyl sulfide complex was carried out in dichloromethane according to a described procedure.[9] The crude alcohol **17** (6.2 g, 96% yield) had an NMR spectrum practically identical with that of a purified sample and was used directly for oxidation. Purified 1-hydroxy-2-methyl-3-(phenylsulfonyl)propane (**17**) could be obtained by chromatography on Florisil (hexane–ether 1:3): NMR δ 1.08 (d, Me, J = 6.9), 1.98 (t, 1, OH, exchanged with D_2O), 2.25 (m, 1), 2.8–3.7 (m, 4), 7.5–8.0 (m, 5); IR 3520 br, 1315, 1156, 1094 cm^{-1}; GC–MS (CI), m/e 215 [(M + 1)$^+$, $C_{10}H_{14}O_3S$, M_r 214].

Oxidation of **17** was carried out with pyridinium chlorochromate (PCC) in methylene chloride[10] with 2 mol of reagent per mol of alcohol. Some unreacted **17** was usually observed in the crude reaction product even under these conditions. The crude aldehyde **18** could, however, be used in the subsequent Wittig olefination reaction. Purified 2-methyl-3-(phenylsulfonyl)propanal (**18**) could be obtained by chromatography on silica gel (hexane–ether 1:1): NMR δ 1.34 (d, Me, J = 7.1), 2.8–3.2 (m, 2), 3.6–3.9 (m, 1), 7.5–8.0 (m, 5), 9.60 (s, 1); IR 1735, 1320, 1160, 1097 cm^{-1}.

Crude aldehyde **18** (3.0 g, less than 14.1 mmol) in THF (8 mL) was added to methylenetriphenylphosphorane, prepared in THF (100 mL) by treatment of methyltriphenylphosphonium bromide (10 g, 28 mmol) by BuLi (26 mmol) at 0 °C for 1.5 h. The mixture was then stirred at room temperature for 20 h. Workup and chromatography on silica gel (20 g, hexane–ether 4:1) furnished sulfone **5b** (0.84 g, 28% yield relative to crude **18**): NMR δ 1.18 (d, Me, J = 6.5), 2.7–3.2 (m, 3), 4.9–5.1 and 5.5–5.9 (m, 3), 7.5–8.0 (m, 5); IR 1317, 1158, 1093, 998, 930 cm^{-1}; GC–MS (CI), m/e 211 [(M + 1)$^+$, $C_{11}H_{14}O_2S$, M_r 210].

Epoxidation of **5b** (0.91 g) was carried out at room temperature for 48 h. Workup and chromatography on silica gel (15 g, hexane–ether 1:1) furnished **7b** (817 mg, 83% yield) as a mixture of two diastereomers: NMR δ 1.16 and 1.22 (two d, Me), 2.17 (m, 1), 2.5–3.4 (m, 5), 7.5–8.0 (m, 5); IR 1315, 1155, 1093 cm^{-1}; GC–MS (CI) two isomers in a ratio of 2:1, m/e 227 for both [(M + 1)$^+$, $C_{11}H_{14}O_3S$, M_r 226].

2-*endo*-Methyl-1-(phenylsulfonyl)bicyclo[1.1.0]butane (1d). A mixture of epoxides **7b** (810 mg) was treated in THF at 0 °C with BuLi and mesyl chloride[8] to yield a crude mixture of **1a** and **1d**. Separation on silica gel (40 g, hexane–ether 17:3) provided first **1a** (61 mg), then mixed fraction (21 mg), and then pure **1d** (140 mg, 23% yield, total yield 36%). Sulfone **1d** did not solidify but was pure by GC–MS (CI), m/e 209 [(M + 1)$^+$, $C_{11}H_{12}O_2S$, M_r 208]; NMR δ 0.93 (d, Me, J = 6.0), 2.03 (t, 1, C_4 *endo*-H, J = 2.5), 2.49 and 2.67 (two m, 2, C_3 H and C_4 *exo*-H), 3.30 (m, 1, C_2 *exo*-H), 7.5–8.0 (m, 5); IR 1315, 1155 cm^{-1}.

***r*-2-Methyl-*t*-3-methyl-*t*-1-(phenylsulfonyl)cyclobutane (2a) and *r*-2-Methyl-*c*-1-methyl-*t*-3-methyl-1-(phenylsulfonyl)cyclobutane (2c).** (a) Addition of MMI to **1a**. MMI was prepared in ether (12 mL) from magnesium (250 mg, 10.29 mmol) and methyl iodide (1.6 g, 11.26 mmol). Cuprous iodide (120 mg, 0.63 mmol) was then added, followed after 10 min of stirring by a solution of **1a** (500 mg, 2.40 mmol) in ether (2 mL). The mixture was stirred at room temperature for 6 h and was then quenched by adding ether (20 mL) and pouring on aqueous ammonium chloride solution. Chromatography on silica gel (30 g, hexane–ether 3:1) separated first **2c** (160 mg, 28% yield) then **2a** (290 mg, 54% yield).

Sulfone **2a**: mp 52–53 °C (pentane); NMR δ 0.91 (d, Me, J = 6.5), 1.07 (d, Me, J = 5.8), 1.7–2.4 (m, 4), 3.20 (q, 1, $J \simeq 8$), 7.50–8.0 (m, 5); IR 1320, 1160, 1100 cm^{-1}. Anal. ($C_{12}H_{16}O_2S$) C, H.

Sulfone **2c**: mp 78–79 °C (hexane); NMR δ 0.82 (d, Me, J = 6.9), 1.09 (d, Me, J = 5.8), 1.30 (s, Me), 1.6–2.8 (m, 4), 7.5–8.0 (m, 5); IR 1310, 1300, 1145, 1095 cm^{-1}. Anal. ($C_{13}H_{18}O_2S$) C, H.

(b) Addition of lithium dimethylcuprate to **1a**. To a suspension of cuprous ioide (1.55 g, 8.1 mmol) in THF (40 mL) was added at 0 °C a solution of methyllithium in ether (14.8 mmol) and the mixture was stirred until a clear solution was obtained. Sulfone **1a** (1.3 g, 6.25 mmol) was then added as a solid and stirring was continued for 3 h. Workup and chromatography on silica gel (20 g, hexane–ether 4:1) provided pure **2a** (1.27 g, 90% yield).

X-ray crystal data: Crystals of **2c** are monoclinic, space group $P2_1/n$, a = 8.125 (4) Å, b = 12.913 (9) Å, c = 11.703 (7) Å, β = 85.42 (4)°, V = 1318.8 Å^3, Z = 4; Calculated density 1.18 g cm^{-3}.

A crystal of **2c** was optically centered on ENRAF-NONIUS CAD-4 diffractometer. The intensities of all reflections were measured according to $w - \theta$ technique by using a scan range of 1.0° and constant scan speed of 1.5° per min. A total of 1830 reflections were measured (1260 observed) with Ni-filtered Cu Kα radiation (1.5418 Å) up to θ 60°.

The structure was solved by direct-phase determination. The non-hydrogen atoms were refined anisotropically. The positions of hydrogen atoms were calculated after each cycle of least squares

and the overall temperature factor was refined (final U = 0.12 Å^2). Final R values are R = 0.11, R_w = 0.11. The phenyl ring and adjacent hydrogens were refined as a rigid body with constraint to ideal geometry.

Presentation of structure factors is omitted and can be obtained upon request.

A final difference Fourier map possessed no special features.

***r*-2-Methyl-*c*-3-methyl-*t*-1-(phenylsulfonyl)cyclobutane (2b).** (a) $LiAlH_4$ reduction of **1b**. Excess powdered $LiAlH_4$ (160 mg, 4.2 mmol) was added all at once to a stirred solution of **1b** (200 mg, 0.9 mmol) in THF (5 mL) kept at 0 °C. Stirring was continued at that temperature until TLC monitoring showed the disappearance of starting material (ca. 2.5 h). Workup was done as described above for **5a**. The proton NMR spectrum of crude **2b** was identical with that of the chromatographically pure compound (silica gel, 10 g, hexane–ether 3:1; 195 mg, 97% yield), which eventually solidified. Upon recrystallization from pentane or hexane it precipitated usually in two crystalline forms, with a melting range from 55 to ca. 75 °C. Occasionnally only the lower melting form was obtained from hexane, mp 55–56 °C. The resolidified melt of the mixed solids also melted sharply at the temperature. In its pure or mixed form, **2b** had one and the same NMR spectrum and the absence of **2a** was established by measuring the spectrum in benzene-d_6 or by a 270-MHz spectrum: NMR δ 0.85 (d, Me, J = 7.0), 1.00 (d, Me, J = 7.0), 1.70 (m, 1), 2.50 (m, 2), 2.90 (m, 1), 3.34 (q, 1, J = 8.0), 7.5–8.0 (m, 5); NMR (270) δ 0.85 (d, Me, J = 7.1), 1.00 (d, Me, J = 7.1), 1.69 (ddd, 1, C_4 β-H), 2.46 (m, 1, C_3 H), 2.58 (dt, 1, C_4 α-H), 2.97 (sextet, 1, C_2 H), 3.43 (q, 1, C_1 H), 7.51–7.63 (m, 3), 7.85–7.89 (m, 2); IR 1310, 1286, 1150, 1090 cm^{-1}. Anal. ($C_{12}H_{16}O_2S$) C, H, S.

(b) Addition of MMI to **1d**. To a solution of MMI prepared from magnesium (150 mg, 6.17 mmol) and methyl iodide (0.3 mL, 4.8 mmol) in ether (3 mL) were added cuprous iodide (30 mg, 0.16 mmol) and, 10 min later, a solution of **1d** (130 mg, 0.63 mmol) in ether (3 mL). The reaction mixture was stirred at room temperature for 20 h. Workup and chromatography on silica gel (10 g, hexane–ether 7:3) furnished first mixed fractions containing starting material and product (27 mg) and then a mixture constituted mainly of **2b** (65 mg). The NMR spectrum of this mixture was mainly that of **2b**, with two extra singlets at δ 1.33 and 1.42, integrating together for ca. one proton (relative to a methyl signal of the main product), and an extra multiplet at δ 2.3, also integrating for about one proton. No absorption due to **2a** was observed in the methyl region or around δ 2.0. The IR spectrum of the mixture was practically identical with that of **2b**: GC–MS (CI), m/e 215 for the two components of the mixture [(M + 1)$^+$, ratio ca. 9:1, $C_{12}H_{16}O_2S$, M_r 214].

(c) Addition of lithium dimethylcuprate to **1d**. The reaction was carried out as described above for **1a** by using the same amount of cuprate reagent for 140 mg (0.67 mmol) of **1d**. Chromatography separated recovered **1d** (16 mg, 11%) from **2b** (50 mg) of similar quality to that obtained by MMI addition. Crystallization from pentane gave pure **2b** (^{1}H NMR), mp 55–70 °C, remelting at 55–56 °C.

***r*-2-Methyl-*c*,*c*-1,3-dimethyl-1-(phenylsulfonyl)cyclobutane (2d).** (a) An ice cooled solution of **2b** (155 mg, 0.7 mmol, obtained by $LiAlH_4$ reduction of **1b**) in THF (5 mL) was treated for 5 min with BuLi (1 mmol) and then with methyl iodide (0.2 mL, excess) for 1 min. Workup and chromatography on silica gel (10 g, hexane–ether 3:1) provided **2d** (132 mg, 80% yield): mp 65–66 °C (hexane); NMR δ 0.83 (d, Me, J = 7.4), 1.03 (d, Me, J = 7.2), 1.34 (s, Me), 1.50 (m, 1), 2.5–3.5 (m, 3), 7.5–8.0 (m, 5); IR 1310, 1800, 1150, 1097 cm^{-1}. Anal. ($C_{13}H_{18}O_2S$) C, H, S.

(b) The mixture obtained by addition of MMI to **1d** (see above) and composed mainly of **2b** (60 mg, 0.27 mmol) was treated with BuLi (0.46 mmol) and excess methyl iodide. Chromatography on silica gel (8 g, hexane–ether 4:1) separated first a mixture composed of ca. 80% (GC–MS) of a product identified as *r*-2-methyl-*c*,*c*-1,3-dimethyl-1-(*o*-tolylsulfonyl)cyclobutane (16 mg, ca. 24% yield); NMR δ 0.88 (d, Me, J = 7.4), 1.05 (d, Me, J = 7.3), 1.34 (s, Me), 1.46 (m, 1), 2.4–3.5 (m, 3), 2.69 (s, Me), 7.15–7.55 (m, 3), 7.7–7.9 (m, 1); GC–MS (CI), m/e 253 for the main peak [(M + 1)$^+$, $C_{14}H_{20}O_2S$, M_r 252. The minor components of the mixture were not isomeric with **2d**]. This was followed by fractions containing pure **2d** (42 mg, 66% yield).

X-ray crystal data: crystals of **2d** are monoclinic, space group $P2_1/n$, a = 6.529 (1) Å, b = 13.933 (1) Å, c = 14.554 (1) Å, β = 88.95 (1)°, V = 1323.7 Å^3, Z = 4, calculated density 1.18 g cm^{-3}.

Measurements were carried out as described for **2c**, with a total of 2314 reflections measured (2117 observed), max θ = 70°.

Solution of the structure followed the method described for **2c** (final overall temperature factor for hydrogens U = 0.10 Å). Final R values are R = 0.072 and R_w = 0.081.

A final difference Fourier map possessed no special features.

Registry No. 1 (unsubstituted), 80989-84-0; 1 (3-methyl derivative), 80989-89-5; **1a**, 86537-31-7; **1b**, 96745-04-9; **1c**, 96745-05-0; **1d**, 96745-07-2; **2a**, 96745-08-3; **2b**, 96745-09-4; **2c**, 96689-29-1; **2d**, 96745-10-7; **3a**, 66464-01-5; **4a**, 95199-54-5; **5a**, 96689-20-2; **5b**, 96689-27-9; **6a**, 84602-85-7; **7a** (isomer 1), 96689-22-4; **7a** (isomer 2), 96689-23-5; **7b** (isomer 1), 96689-28-0; **7b** (isomer 2), 96689-31-5; **8a**, 96689-21-3; **9**, 873-55-2; **10**, 18742-02-4; **11**, 56161-51-4; **12**, 83802-85-1; *trans*-**13**, 96689-19-9; *cis*-**13**, 96689-24-6; *trans*-**14**, 78710-70-0; *cis*-**14**, 78710-69-7; **15**, 96689-25-7; **15a**, 96745-06-1; **16**, 49639-05-6; **17**, 96689-26-8; **18**, 83802-87-3; MMI, 917-64-6; methyl phenyl sulfone, 3112-85-4; crotyl bromide, 4784-77-4; ethylidenetriphenylphosphorane, 1754-88-7; ethyltriphenylphosphonium bromide, 1530-32-1; methylenetriphenylphosphorane, 3487-44-3; methyltriphenylphosphonium bromide, 1779-49-3; lithium dimethyl cuprate, 15681-48-8; *r*-2-methyl-*c*,*c*-1,3-dimethyl-1-(*o*-tolylsulfonyl)cyclobutane, 96689-30-4; *cis*-1-methyl-3-(phenylsulfonyl)cyclobutane, 96667-37-7; *trans*-1-methyl-3-(phenylsulfonyl)cyclobutane, 96667-32-2.

Supplementary Material Available: Tables of atom coordinates, anisotropic temperature factors, calculated hydrogen atom coordinates, bond lengths, and bond angles for compounds **2c** and **2d** (10 pages). Ordering information is given on any current masthead page.