Bridgehead Reactivity, Nucleophilic and Radical Additions, and Lithium Aluminum Hydride Reduction of 1-(Arylsulfonyl)bicyclobutanes: General Access to Substituted, Functionalized Cyclobutanes. Syntheses of (±)-Citrilol Acetate, (±)-Junionone, and the Tricyclo[3.3.0.0^{1,4}]octane and Tricyclo[4.3.0.0^{1,7}]nonane Ring Systems

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A general approach to the synthesis of a wide range of substituted cyclobutane derivatives is based on two specific reactions of 1-(arylsulfonyl)bicyclobutanes (1) and on some general reactions of the bicyclobutane ring systems. One specific cyclobutane forming reaction of 1 is the addition of organocopper reagents across the central bond. As tried with methylcuprate reagents, this reaction takes place even with substrates 1 having a quaternary bridgehead carbon. A second specific cyclobutane forming reaction of 1 is the reduction with lithium aluminum hydride. By application of bridgehead substitution reactions to 1, in combination with the above reactions, or by the use of various other radical and anionic addition reactions, a wide array of (arylsulfonyl)cyclobutanes may be obtained. Reductive elimination of the sulfone group, before or after an α-sulfonyl substitution reaction, may complete the cycle of operations. The versatility of this approach is illustrated by the syntheses of the racemic form of the sex pheromone of the citrus mealybug ("citrilol acetate"), of (±)-junionone, and of phenylsulfonyl substituted tricyclo[3.3.0.0^{1,4}]octane and tricyclo[4.3.0.0^{1,7}]nonane.

The high strain energy of the bicyclo[1.1.0]butane ring system, coupled with the olefinic π-bond character of the central bond and with the enhanced acidity of the bridgehead protons, make this systems amenable to a large variety of chemical transformations.[1] Addition reaction of the 1,3-bond,[2] substitution of the bridgehead protons,[3] and metal-catalyzed rearrangements[4] are some of the principal reactions of bicyclobutanes which have been investigated. The reactivity of some tricyclic systems which comprise the bicyclobutane building block, like tricyclo[4.1.0.0^{2,7}]heptane or benzvalene, has also been extensively studied.[5-7]

With 1-(arylsulfonyl)bicyclobutanes being readily available to us from γ,δ-epoxy sulfones,[8] we were looking for specific reactions of these compounds which would be associated with the presence of the sulfone group at the bridgehead position. Two such reactions were found to be the addition of organocopper reagents across the central bond and the reduction of this bond with lithium aluminum hydride ($LiAlH_4$), both reactions leading to cyclobutane derivatives.[9]

With these tools in hand, and with the possibility to apply other relevant reactions of bicyclobutanes to our substrates, we have developed a general approach to the synthesis of substituted, functionalized cyclobutanes.[10] This approach involves occasional substitution at the bridgehead position, hydride addition, or other anionic or radical additions across the central bond, occasional substitution α to the sulfone in the cyclobutane formed, and eventual reductive elimination of the arylsulfonyl group. We have illustrated the versatility of this approach by the syntheses of racemic citrilol acetate[11,12] and juninone,[13] as well as of numerous other cyclobutane derivatives, including isoprenoid compounds and arylsulfonyl derivatives of the condensed tricyclo[3.3.0.0^{1,4}]octane and tricyclo[4.3.0.0^{1,7}]nonane ring systems.

Results and Discussion

Bridgehead Substitutions. The acidity of the bridgehead protons of bicyclobutanes was one of the earliest chemical properties of this system to be recognized and to be utilized in various substitution reactions via formation of the bridgehead anion.[3a]

The corresponding anions of 3-unsubstituted 1-(arylsulfonyl)bicyclobutanes, e.g., **1a-d**, could be readily generated with *n*-butyllithium (BuLi) in tetrahydrofuran (THF). The anionic species were then reacted with a variety of electrophiles, including ethylene oxide and carbonyl compounds, to provide 3-substituted bicyclobutanes, usually in good yields (Table I). Lowering of the yields occasionally occurred by anionic polymerization for which similar basic conditions have been used in the case

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(10) For an exhaustive review on cyclobutane preparations, including transformations of bicyclobutanes, see: Seebach, D. "Methoden der Organischen Chemie (Houben-Weyl)"; Georg Thieme Verlag: Stuttgart, 1971; Vol. 4/4.

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Table I. Reaction Conditions, Yields, and Melting Points of Compounds 1e–t Obtained by Bridgehead Substitution of 1a–d[a]

product	R^1	R^2	Ar[b]	starting material	electrophile	method[c]	yield, %[d]	mp, °C[e]	Anal.[f]
1e	H	$CH(OH)CH_3$	Tol	**1b**	acetaldehyde	B	79	66	$C_{13}H_{16}O_3S$
1f	H	$CH(OH)CH(CH_3)_2$	Tol	**1b**	isobutyraldehyde	A	67	92	$C_{15}H_{20}O_3S$
1g	H	CH(OH)Ph	Tol	**1b**	benzaldehyde	A	62	110	$C_{18}H_{18}O_3S$
1h	H	$C(OH)(CH_3)_2$	Tol	**1b**	acetone	A	59	79	$C_{14}H_{18}O_3S$
1i	H	$C(OH)(CH_3)CH_2CH_3$	Tol	**1b**	2-butanone	A	60	63	$C_{15}H_{20}O_3S$
1j-I[g]	CH_3	$C(OH)(CH_3)CH_2CH_3$	Tol	**1d**	2-butanone	A	84[h]	58	$C_{16}H_{22}O_3S$
1j-II[g]	CH_3	$C(OH)(CH_3)CH_2CH_3$	Tol					50	$C_{16}H_{22}O_3S$
1k[i]	H	CH_3	Ph	**1a**	methyl iodide	A	80		
1l	H	CH_3	Tol	**1b**	methyl iodide	A	78	76	$C_{12}H_{14}O_2S$
1m[j]	CH_3	CH_3	Ph	**1c**	methyl iodide	A			
1n	H	$CH_2CH{=}CH_2$	Ph	**1a**	allyl bromide	B	53[k]	78	$C_{13}H_{14}O_2S$
1o	H	$CH_2CH{=}CH_2$	Tol	**1b**	allyl bromide	B	78	87	$C_{14}H_{16}O_2S$
1p	H	2-cyclohexenyl	Tol	**1b**	3-bromocyclohexene	B	22[l]	87	$C_{17}H_{20}O_2S$
1q	H	CH_2CH_2OH	Tol	**1b**	ethylene oxide	*m*	80	54	$C_{13}H_{16}O_3S$
1r	H	$CH_2CH_2OSO_2CH_3$	Tol	**1b**	ethylene oxide	*n*	75	67	$C_{14}H_{18}O_5S_2$
1s[o,p]	H	$C(CH_3){=}CH_2$	Tol	**1h**			81	85	$C_{14}H_{16}O_2S$
1t[q]	H	$COOC_2H_5$	Tol	**1b**	ethyl chloroformate	*r*	63	64	$C_{14}H_{16}O_4S$

[a] All compounds showed IR absorption bands characteristic of the sulfone group aroung 132° (split in case of *p*-tolyl sulfones) and 1150 cm^{-1}. [b] Ph = phenyl; Tol = *p*-tolyl. [c] Simultaneous addition (A) or sequention addtion (B) of base and electrophile (see Experimental Section). [d] Yields refer to chromatographically and spectroscopically pure compounds. [e] The lower value of a one degree melting range is indicated. [f] Satisfactory analytical data were obtained for all compounds listed in the table (C,H, or, mostly, C,H,S analyses; ±0.4%). [g] The two **1j** diastereomers were formed in ca. 1:1 ratio and were partly separated by chromatography. [h] Total yield. [i] See ref 8. [j] See ref 21. [k] **1b** was recovered in 29%. [l] **1b** was recovered in 26%. [m] BuLi (1.2 equiv) and excess ethylene oxide were added to a solution of **1b** (1 equiv) in THF at −78 °C. The cooling bath was removed and the reaction was worked up after reaching room temperature. [n] The reaction was carried out as described under footnote *m* and was quenched with mesyl chloride. [o] **1s** was prepared by dehydration of **1h** with Burgess' reagent[14] (see Experimental Section). [p] UV λ_{max} (ethanol) 239 (ϵ 16 100) nm; compare with **1b**, λ_{max} 229 (16 750) nm and with $PhSO_2CH{=}C(CH_3)$-$CH{=}CH_2$, λ_{max} 251 (23 200) nm. [q] UV λ_{max} (ethanol) 233 (17 700), 263 (940), 274 (580) nm; compare with $C_7H_7SO_2CH{=}CHCO_2CH_3$ (4) λ_{max} 247 (10 400) nm. [r] See Experimental Section.

Table II. 80-MHz Proton NMR Data of Compounds 1e–t[a]

no.	NMR data
1e	1.30 and 1.37 (two s, *endo*-H, 2), 1.51 (d, 6.6, Me), 2.45 (s, Me), 2.60 (ABq, 6.2, $\Delta\nu$ = 14.3 Hz, *exo*-H, 2), 2.94 (d, 4.0, OH[b]), 4.58 (dq, q after addition of D_2O, 6.6, *CH*OH), 7.35 and 7.81[c]
1f	1.03 and 1.05 (two d, 6.8, two Me), 1.26 and 1.45 (two s, *endo*-H, 2), 1.99 (m, 1), 2.45 (s, Me), 2.62 (ABq, 6.3, $\Delta\nu$ = 20.0 Hz, *exo*-H, 2), 3.14 (d, 2.0, OH[b]), 4.15 (dd, d after addition of D_2O, 5.5, *CH*OH), 7.34 and 7.81[c]
1g	1.36 and 1.49 (two s, *endo*-H, 2), 2.46 (s, Me), 2.78 (ABq, 6.5, $\Delta\nu$ = 21.7 Hz, *exo*-H, 2), 3.56 (d, 2.2, OH[b]), 5.49 (d, s after addition of D_2O, *CH*OH, 7.31–7.53 (m, 7), 7.85 (d, 2).
1h	1.20 (s, *endo*-H, 2), 1.56 (s, two Me), 2.45 (s, Me), 2.55 (s, *exo*-H, 2), 2.80 (s, OH[b]), 7.35 and 7.82[c]
1j-I	0.89 (s, C_4 *endo*-H), 1.02 (t, 7.2, Me), 1.3–1.6 (m and s, A_3B part spectrum of C_2Me and C_2 *endo*-H plus side chain Me), 1.85 (q, side chain CH_2), 2.31 (s, C_4 *exo*-H), 2.45 (s, Me), 2.58 (s, OH[b]), 7.34 and 7.81[c]
1j-II	0.80 (s, C_4 *endo*-H), 1.00 (t, 7.0, Me), 1.2–1.6 (m and s, 7), 1.80 (q, side chain CH_2), 2.39 (s, C_4 *exo*-H), 2.45 (s, Me), 2.65 (s, OH[b]), 7.34 and 7.81[c]
1l	1.29 (s, *endo*-H, 2), 1.87 (s, Me), 2.30 (s, *exo*-H, 2), 2.44 (s, Me), 7.32 and 7.80[c]
1n	1.32 (s, *endo*-H, 2), 2.75 (s, *exo*-H, 2), 2.98 (d, 6.3, allylic H, 2), 5.0–5.4 and 5.8–6.2 (m, vinylic H, 3), 7.5–8.0 (m, 5)
1o	1.29 (s, *endo*-H, 2), 2.32 (s, *exo*-H, 2), 2.44 (s, Me), 2.96 (d, 6.2, allylic H, 2), 5.0–5.4 and 5.8–6.2 (m, 3, vinylic H), 7.33 and 7.81[c]
1p	1.2–1.8 (m) and 1.37 (s, total 9), 2.51 (s, Me), 2.5–2.75 (m, 2), 5.60 (ABq, br, 8.5, 2), 7.35 and 7.85[c]
1q	1.30 (s, *endo*-H, 2), 1.95 (t, OH[b]), 2.35 (s, *exo*-H), 2), 2.44 (s, Me), 2.48 (t, 6.1, CH_2CH_2OH), 3.91 (dt, t after addition of D_2O, 6.1, CH_2CH_2OH), 7.34 and 7.81[c]
1r	1.35 (s, *endo*-H, 2), 2.38 (s, *exo*-H, 2), 2.45 (s, Me), 2.68 (t, 6.3, CH_2CH_2OMs), 3.04 (s, Me), 4.50 (t, 6.3, CH_2CH_2OMs), 7.35 and 7.81[c]
1s	1.38 (s, *endo*-H, 2), 1.98 (s, Me), 2.44 (s, Me), 2.65 (s, *exo*-H, 2), 5.10 (s, $=CH_2$), 7.32 and 7.78[c]
1t	1.29 (t, 7.1, Me), 1.61 (s, *endo*-H, 2), 2.45 (s, Me), 2.99 (s, *exo*-H, 2), 7.33 and 7.79[c]

[a] Spectra were taken in $CDCl_3$. Chemical shifts are given in δ values. Multiplicities, coupling constants (Hz), proton assignments, and occasional relative integrations are given in parentheses. [b] Exchangeable with D_2O. [c] AB-like system of the four aromatic *p*-tolyl protons.

of 1-cyanobicyclobutane.[2b] The polymerization could be partly or totally avoided by simultaneous addition of the base and the electrophile to a solution of **1**.

All bicyclobutane derivatives could be readily identified on the basis of their ^1H NMR spectral properties, and particularly the lack of coupling of the exo and endo protons and the relatively strong deshielding of the former (Table II). A differentiation of the two endo and the two exo protons appeared, however, in the case of the secondary alcohols **1e–g**, with the result that a long-range exo–exo coupling of ca. 6.5 Hz could be observed.

The known effect of electronic conjugation of the central bond and the bridgehead substituents[1,15,16] could be observed in some **1** derivatives. It was qualitatively compared with some vinylic sulfones, such as 2-methyl-1-(phenylsulfonyl)-1,3-butadiene (obtained by oxidation of the corresponding sulfoxide[17]) or with methyl β-(phenylsulfonyl)acrylate (**4**;[18] see Table I).

Upon trying to prepare ester **1t** from **1b** using 1.5 equiv of BuLi and excess ethyl carbonate, the thiopyrone derivative **2** and ketone **3** were obtained in 28 and 56% yield, respectively. With 2 equiv of BuLi, **2** was obtained in 70% yield. Compound **2** results from an intramolecular condensation of the primary reaction product **1t** via abstraction of an aromatic proton by the base in excess.

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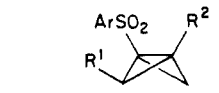
Table III. Cyclobutyl Sulfones Obtained by $LiAlH_4$ Reduction of Bicyclobutyl Sulfones[a-c]

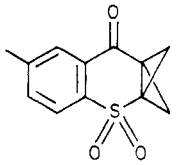
product	yield, %	starting material	mp, °C	Anal.[d]
5a	94	**1a**	45–46	$C_{10}H_{12}O_2S$
5b[e,f]	80	**1k**	113–114[g]	$C_{11}H_{14}O_2S$
5d[e,h]	50	**1o**		$C_{14}H_{18}O_2S$[h]
5e[e]	83	**1h**	79–83	$C_{14}H_{20}O_3S$
6a	95	**1c**	62–63	$C_{11}H_{14}O_2S$
6b[i]				
7a	93	**15b**[j]	57–58	$C_{12}H_{16}O_2S$
8[k]	90	**10**[i]	128–129	$C_{14}H_{18}O_2S$

[a] See Experimental Section for the general conditions of the reduction reaction. [b] See footnotes *a,d*, Table I. [c] ^1H NMR data (see footnote *a*, Table II) for **5a**: 1.8–2.8 (m, 6), 3.82 (pentuplet, 8.0, 1), 7.5–8.0 (m, 5). For **5b**: 1.09 (d, resolved for about half height, 5.2, Me), 1.7–2.8 (m, 5), 3.4–3.8 (m, 1), 7.5–8.0 (m, 5); NMR in benzene-d_6 resolved the methyl doublet into two doublets at δ 0.67 (J = 6.7) and 0.80 (J = 5.6) in a ratio of ca. 3:2, and the methine signal at 3.6 into two, partly superimposed multiplets. For **5d**: 2.0–3.0 (m, 7), 2.43 (s, Me), 3.5–3.75 (m, 1), 4.87–5.07 and 5.5–5.8 (m, 3), 7.32 and 7.34 (aromatic H, 4). For **5e**: 1.11 (s, two Me), 1.24 (s, OH), 2.1–2.7 (m, 5), 2.44 (s, Me), 3.63 (m, 1), 7.32 and 7.79 (4). For **6a**: 0.95 (d, 6.6, Me), 1.4–3.0 (m, 5), 3.37 (q, 8.0, 1), 7.5–8.0 (m, 5). For **7a**: 1.17 (s, Me), 1.48 (s, Me), 1.5–2.6 (m, 4), 3.40 (t, 8.4, 1), 7.5–8.0 (m, 5). For **8**: 0.9–3.0 (m, 12), 3.68 (q, 8.5, 1), 7.5–8.0 (m, 5). [d] See footnote *f*, Table I. [e] Obtained as a mixture of cis and trans isomers. [f] Ratio of isomers ca. 3:2 (GC–MS). [g] Recrystallization from ethanol. [h] Ratio of isomers ca. 3:1, with a molecular weight of 250 for both (GC–MS analysis, chemical ionization). [i] Cis or trans 2,3-dimethyl isomer, according to starting material; see ref 21. [j] Reference 8. [k] The endo addition of the hydride ion[21] should yield (1*RS*, 6*RS*, 7*RS*)-7-(phenylsulfonyl)bicyclo[4.2.0]octane (**8**).

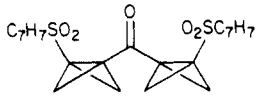
Ketone **3** results from an intermolecular condensation between **1b** anion and ester **1t**. The structure of the two compounds could be readily determined by their analytical and spectral properties. In particular, a one-proton singlet and a two-proton AB quartet appeared in the aromatic region of the ^1H NMR spectrum of **2**. This compound also showed an IR carbonyl absorption at 1693 cm^{-1} and UV absorptions with λ max 216, 248, and 288 nm (ϵ 23 900, 6400, 1620). Ketone **3** showed an IR carbonyl absorption at 1720 cm^{-1} and a UV absorption with λ max 245 nm (ϵ 27 100).



1a, $R^1 = R^2 = H$, Ar = Ph
b, $R^1 = R^2 = H$, Ar = *p*-tolyl
c, R^1 = Me, $R^2 = H$, Ar = Ph
d, R^1 = Me, $R^2 = H$, Ar = *p*-tolyl



2



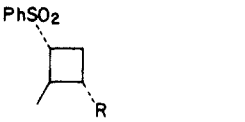
3

Several of the bicyclobutanes described up to here and a few others have been used in further transformations into cyclobutanes as is described below. Similar transformations should be applicable to the other **1** compounds.

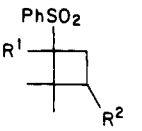
$LiAlH_4$ Reductions. All compounds **1** to which the reaction has been applied could be reduced with excess $LiAlH_4$ in THF to cyclobutyl sulfones, usually in high yields.[9b] The reaction seems to be specific to the 1-(arylsulfonyl)bicyclobutanes, which behave in this respect like α,β-unsaturated sulfones.[19] Lithium in primary amines is otherwise needed in order to reduce the 1,3-bond of bicyclobutanes.[20] $LiAlH_4$ reduction of 1-methoxycarbonyl-[1a] or 1-cyano-bicyclobutane[2a] produced only the corresponding hydroxymethyl or aminomethyl derivatives.

Hydride addition to **1** has been shown to occur from the endo side of the bicyclic system, with formation of one or two geometrical isomers of **5** or **6** according to the presence or absence of a 2-substituent.[21,22]

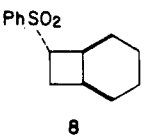
5a, R = H; Ar = Ph
b, R = Me; Ar = Ph
c, R = Me; Ar = *p*-tolyl
d, $R = CH_2CH{=}CH_2$; Ar = *p*-tolyl
e, $R = C(OH)(CH_3)_2$; Ar = *p*-tolyl
f, $R = C(CH_3){=}CH_2$; Ar = *p*-tolyl
g, $R = CH{=}CMe_2$; Ar = *p*-tolyl
h, R = *n*-Bu; Ar = Ph
i, R = OMe; Ar = *p*-tolyl.



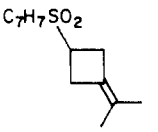
6a, R = H
b, R = Me
c, R = *n*-Bu



7a, $R^1 = R^2 = H$
b, $R^1 = CH(OH)CH_2C(CH_3)OCH_2CH_2O$; $R^2 = H$
c, $R^1 = CH(OH)CH_2COCH_3$; $R^2 = H$
d, $R^1 = H$; $R^2 = C(CH_3){=}CH_2$
e, $R^1 = CH_2OH$; $R^2 = C(CH_3){=}CH_2$.



8



9

The results of $LiAlH_4$ reductions are summarized in Table III.

Reduction of **1h** and dehydration of **5e** were carried out as a potential additional method for the introduction of an isopropenyl group at position 3, besides the use of isopropenyl copper reagents (see below). The reduction itself was, however, relatively very slow and needed an extra large excess of $LiAlH_4$. Moreover, dehydration of **5e** with Burgess' reagent[14] produced a mixture of two **5f** isomers and of the isopropenylidene derivative **9**, in about equal amounts.

Conjugate Addition of Organocopper Reagents. Both alkyl- and alkenylmagnesium halides, with cuprous salts catalysis, and lithium dialkyl- and dialkenylcuprates were found to add across the central bond of **1**, producing cyclobutane derivatives in good yields.[9a] The addition was shown to take place from the endo side of the bicyclic system.[21] system.[21] Two geometrical 1,3-isomers were formed in the absence of a 2-substituent[22] and mainly one isomer when a 2-methyl group was present.

The reaction seems to be specific to the 1-(arylsulfonyl)bicyclobutanes which behave here again like α,β-unsaturated sulfones.[23]

(19) Russel, G. A.; Sabourin, E.; Mikol, G. J. *J. Org. Chem.* **1966**, *31*, 2854–2858.

(20) Moore, W. R.; Hall, S. S.; Largmann, C. *Tetrahedron Lett.* **1969**, 4353–4356.

(21) See the preceding paper in this issue.

(22) See the footnote in the preceding paper in this issue concerning our first erroneous conclusion about the specificity of $LiAlH_4$ reduction and of organocopper reagents addition to some **1** derivatives.

(23) (a) Posner, G. H.; Brunelle, D. J. *J. Org. Chem.* **1973**, *38*, 2747–2756. (b) De Chirico, G.; Fiandanese, V.; Marchese, G.; Naso, F.; Sciacovelli, O. *J. Chem. Soc., Chem. Commun.* **1981**, 523–524.

Table IV. Reaction Conditions, Yields, and Physical Properties of Cyclobutyl Sulfones Obtained by Addition of Organocopper Reagents to Bicyclobutyl Sulfones[a-c]

entry	product	starting material	reagent[d]	Cu^I salt[d]	reaction time, h; temp, °C	solvent	yield, %[e]	Anal.[f]
1	**5b**[g,h]	**1a**	methyl magnesium iodide (5.3)	CuI[i] (0.3)	3; 20	ether	85[j]	
2	**5f**[g]	**1b**	isopropenyl magnesium bromide (4)	CuBr (0.23)	1; 20	THF	61[j,k]	$C_{14}H_{18}O_2S$[l,m]
3	**5f**[g,i]	**1b**	bis(isopropenyl)copper lithium (5)	CuI[i]	0.5; −15 0.5; →20	ether–THF	27[j,k]	
4	**5g**[g,i,n]	**1b**	isobutenyl magnesium bromide (4)	$CuBr{\cdot}Me_2S$[o]	1; 20	THF	77[j,k]	$C_{15}H_{20}O_2S$[p]
5	**5h**[b]	**1b**	di-*n*-butylcopper lithium (1.6)	$CuBr{\cdot}Me_2S$	0.3; 0	ether–Me_2S	86[j]	*q*
6	**6c**	**1c**	di-*n*-butylcopper lithium (1.6)	$CuBr{\cdot}Me_2S$	0.75; 0	ether–Me_2S	73	*r*
7	**11a**	**1l**	dilithium dimethylcyanocuprate (2)	CuCN	2; 0	ether	67	$C_{13}H_{18}O_2S$[s]
8	**11a**	**1l**	dimethylcopper lithium (2)	CuI[i]	24; 20	THF	45	
9	**11b**[g]	**1o**	dilithium dimethyl cyanocuprate (2)	CuCN	14; 20	ether	62[j,k]	$C_{15}H_{20}O_2S$[t]
10	**11c**[u]	**1m**	dimethylcopper lithium (2)	CuI[i]	40; 20	THF	66	$C_{13}H_{18}O_2S$
11	**11c**,**12**[v]	**1m**	dimethylcopper lithium (1.2)	$CuBr{\cdot}Me_2S$	1; 20	ether–Me_2S	36	
12	**13**,**14**[w]	**10**[x]	dimethylcopper lithium	$CuBr{\cdot}Me_2S$	0.5; 20	ether–Me_2S	52[j]	$C_{15}H_{20}O_2S$[y] $C_{15}H_{18}O_2S$[z]

[a] See ref 21 for typical experimental procedures. [b] See footnote *a*, Table I. [c] ^1H NMR data (see footnote *a*, Table II) for **5b**, see Table III. For *trans*-**5f**: 1.66 (s, Me), 2.0–3.2 (m, 5), 2.44 (s, Me), 3.67 (m, 1), 4.68 and 4.77 (two br s, $=CH_2$), 7.33 and 7.77 (4), For *cis*-**5f**: 1.66 (s, Me), 2.2–2.8 (m, s), 2.44 (s, Me), 3.64 (pentuplet, 8.8, 1), 4.69 and 4.77 (two br s, $=CH_2$), 7.33 and 7.75 (4). For *trans*-**5g**: 1.53 (s, Me), 1.64 (s, Me), 1.7–3.9 (m, 6), 2.44 (s, Me), 5.27 (br d, 8.0, 1), 7.32 and 7.74 (4). For *cis*-**5g**: 1.55 (s, Me), 1.66 (s, Me), 2.29 (t, 9.0, 4), 2.43 (s, Me), 2.95 (m, 1), 3.60 (pentuplet, 9.0, 1), 5.16 (br d, 8.0, 1), 7.32 and 7.74 (4). For **5h**: 0.86 (t, Me), 1.0–2.7 (m, 11), 2.43 (s, Me), 3.60 (m, 1), 7.33 and 7.73 (4). For **6c**: 0.86 (t, Me), 0.93 (d, 6.6, Me), 1.23 (br, 6), 1.4–2.4 (m, 4), 3.22 (q, 8.3, 1), 7.5–8.0 (m, 5). For **11a**: 1.13 (s, two Me), 1.7–2.4 (m, 4), 2.43 (s, Me), 3.70 (pentuplet, 8.6, 1), 7.31 and 7.74 (4). For **11b**: 1.12 (s, Me), 1.8–2.5 (m, 6), 2.43 (s, Me), 3.69 (pentuplet, 8.2, 1), 4.9–5.15 and 5.3–6.0 (m, 3), 7.32 and 7.74 (4). For **11c**: 0.79 (d, Me), 0.97 (s, Me), 1.08 (s, Me), 1.6–2.7 (m, 3), 3.31 (q, 1), 7.5–8.0 (m, 5). ^1H NMR with 270 MHz: 0.79 (d, 7.0, Me), 0.97 (s, Me), 1.08 (s, Me), 1.81 (dd, 11.3, 8.3, C_4 H), 2.17 (dd, 11.3, 9.4, 1), 2.54 (pentuplet, C_2 H), 3.29 (q, 8.6, C_3 H), 7.5–7.7 (m, 3), 7.85–7.9 (m, 2). For **14** (solid isomer, 270 MHz): 1.10 (s, Me), 1.03–1.65 (m, 8), 1.75 and 2.10 (dd and t, AB part of an ABX system, 10.6, 10.6, 7.7, C_8 H, 2), 2.60 (m, C_6 H, 1), 3.61 (apparent q, 9.0, C_7H, 1), 7.5–7.7 (m, 3), 7.85–7.9 (m, 2). For **13**: 1.12 (s, Me), 1.2–1.8 (m, 8), 2.69 (t, 4.4, C_6 H, 1), 6.71 (s, C_8 H, 1), 7.5–8.0 (m, 5). [d] The molar ratio of reagent to substrate is indicated in parenthesis. [e] See footnote *d*, Table I. [f] Solid products were analyzed by combustion analysis (see footnote *f*, Table I). Liquid products were analyzed by gas chromatographic–mass spectral analysis (GC–MS), usually with chemical ionization (CI). [g] Obtained as a mixture of cis and trans isomers. [h] The composition of the mixture was similar to that of the reduction product (Table III). [i] The cuprous iodide was purified by Soxhlet washings with THF. [j] Total yield. [k] The ratio of trans to cis isomer was ca. 1:2. [l] The products were separated/purified by chromatography on silica gel (hexane–ether, 4:1). [m] GC–MS (CI), *m/e* 251 for both isomers [$(M + 1)^+$, molecular weight, M_r 250]. [n] mp of solid *cis*-**5g**, 60–61 °C. See Experimental Section for X-ray crystal data of this isomer. [o] The complex was prepared according to ref 25. [p] GC–MS (CI) for *trans*-**5g**, *m/e* 265 (M_r 264). [q] GC–MS (EI) analysis showed two isomers in a ratio of 7:3; *m/e* 157, 139, 111, 110, 91, 81, 69. [r] GC–MS (EI) analysis showed one isomer; *m/e* 143, 125, 83, 77, 69. [s] GC–MS (CI) analysis showed one product, *m/e* 239 (M_r 238). [t] GC–MS (CI), *m/e* for both isomers 265 (M_r 264). [u] A unique isomer is obtained, with the sulfone group trans to the 2-methyl (see ref 21). It crystallizes from pentane in two crystalline forms and has a melting range of 57–80 °C; the resolidified melt melts sharply at 57–58 °C. (A similar behavior has been observed for the corresponding *cis*-1,2-dimethyl derivative[21]). The absence of an isomeric product was shown by identity of the ^1H NMR spectra of the recrystallized product and the residue from the mother liquors of crystallization. [v] Impure sulfone **12** was isolated in ca. 5% yield during chromatographic purification of **11c**. It was 80% pure by GC–MS (CI) analysis, with *m/e* for the major product 237 [$(M + 1)^+$; $C_{13}H_{16}O_2S$, M_r 236]. ^1H NMR δ 1.03 (d, Me), 1.06 (s, Me), 1.14 (s, Me), 6.67 (s, vinylic H), 7.5–8.0 (m, 5). [w] The mixture of reaction products is constituted of two **14** isomers, namely, the major, solid isomer (1*RS*,6*RS*,7*RS*)-1-methyl-7-(phenylsulfonyl)bicyclo[4.2.0]octane, mp 78–79 °C, the corresponding 7*SR* isomer, and compound **13**. Similar results were obtained under conditions described in entries 8 and 9. See text. [x] See ref 8. [y] C, H, S analysis of solid **14**. [z] GC–MS (CI) analysis of **13**, *m/e* 263 (M_r 262).

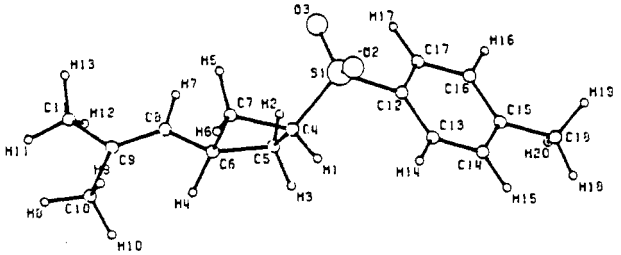


Figure 1. Molecular structure of *cis*-**5g**.

The conditions and results of various addition experiments are summarized in Table IV. Chromatographic separation of the cis and trans isomers was readily achieved with products having vinylic substituents, such as **5f** and **5g**. The molecular structure of the crystalline, more polar **5g** isomer was determined by X-ray analysis and found to have the cis configuration (Figure 1).[24]

Several cis and trans 1,3-isomers of the general structure **5** had the common feature of showing better resolved ^1H NMR spectra for the more polar, usually more abundant isomer, especially as far as the α-sulfonyl proton was concerned. This proton appeared then usually as a well-resolved pentuplet, having almost equal coupling constants with all four neighboring protons. This observation was also valid for *cis*-**5g**. On this basis we have assigned a cis configuration to the more polar **5f** isomer, as well as to a few other 3-substituted cyclobutyl sulfones which showed similar ^1H NMR characteristics.

A particular feature of the cuprate addition reaction is the possibility to directly introduce a methyl group at a quaternary bridgehead carbon of the bicyclic substrate, with formation of a new quaternary carbon. Here, again, the similarity of the central bond of **1** to a double bond is apparent. Various methyl copper reagents were used in this reaction, sometimes with significant variations in yields and usually with large variation in reaction rates (Table IV, entries 7–12). Dilithium dimethylcyanocuprate[26] seems to have the advantage of producing clean, relatively fast reactions.

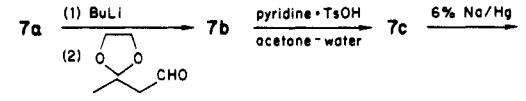
A cyclobutene sulfone was obtained as a secondary product in reaction of **1m** and **10**. A three-component

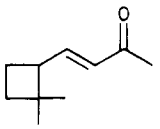
(24) X-ray analyses have been carried out by Dr. F. Frolow of this Institute.

(25) House, H. O.; Chu, C. Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460–1469.

(26) Lipshutz, B. H.; Wilhelm, K. S.; Kozlowski, J. *Tetrahedron Lett.* **1982**, *23*, 3755–3758.

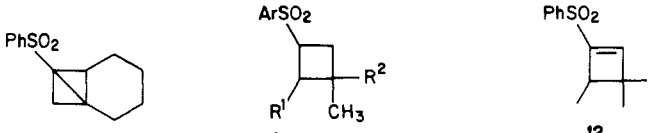
Scheme I





21

mixture was indeed obtained from **10** with various methylcopper reagents. It was constituted of **13** and two **14** isomers in an approximate ratio of 3:6:2, respectively (GC–MS analysis). The major **14** isomer could be isolated as a solid and fully characterized. The second **14** isomer could not be obtained free of the major one but the ^{1}H NMR spectrum of the mixture was very similar to that of solid **14**, with just one additional methyl signal at δ 1.08. It is considered to have the sulfone group cis to the 2-methylene and trans to the 3-methyl. The steric hindrance of the 2-substituent is probably less important here than that of a 2-methyl group, where a high preference for a trans configuration has been observed (e.g., **11c**, Table IV).



10 12

11a, R^1=H, R^2=Me; Ar=*p*-tolyl
b, R^1=H; R^2=$CH_2CH{=}CH_2$; Ar=*p*-tolyl
c, R^1=R^2=Me; Ar=Ph

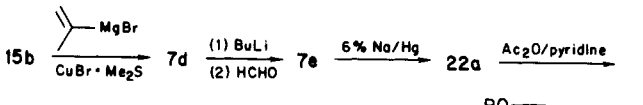
13 14

The cyclobutene derivatives seem to be ene reaction products, by analogy to other numerous reactions of bicyclobutanes with active molecules.[2c] The cyclobutene was formed in the reactions of the more hindered substrates, namely **1m** and **10**. This would suggest that it results from a competitive side reaction when methylation is relatively slow. No constructive mechanistic suggestion can be advanced at this stage, especially since the mechanism of methyl transfer by cuprate reagents is itself not well established.[27]

Other Nucleophilic Additions to 1. Besides the above described specific reactions of **1**, a few of the common reactions of the central bond of bicyclobutanes have been applied to these substrates, leading to products in high yields. Such were the additions of sodium methylate,[2b,g] sodium thiophenolate,[2f] and thiophenol itself, under radical addition conditions (air atmosphere).[5a] (See Table V).

Another radical addition reaction which occured readily with **1b** and **15a** was the addition of tri-*n*-butyltin hydride in warm benzene, activated by azobis(isobutyronitrile) (Table V). This is to be contrasted with the behavior of the vinylic sulfone **18** which did not yield any product after a 10-fold longer reaction time. The tin derivatives **17a** could be further elaborated by oxidation or by treatment with iodine. Thus, oxidation with chromic anhydride/pyridine,[28] under nonoptimized conditions, produced ketone **19** in 60% yield relative to unrecovered starting material. Iodine in benzene cleaved the tin–carbon bonds unselectively and the two **20** isomers were obtained in a total 30% yield.

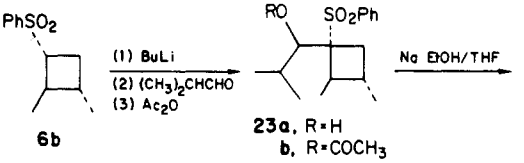
Scheme II[a]



22b

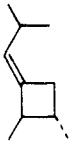
[a] **22a**, R = H; **b**, R = $COCH_3$.

Scheme III

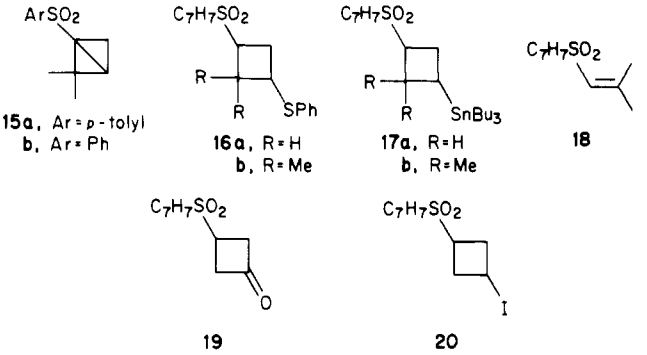


6b

23a, R=H
b, R=$COCH_3$



24



15a, Ar=*p*-tolyl
b, Ar=Ph

16a, R=H
b, R=Me

17a, R=H
b, R=Me

18 19 20

Synthetic Elaborations of the Intermediate Cyclobutyl Sulfones. The substituted, funtionalized cyclobutane derivatives obtained from the bicyclobutyl sulfones **1** by one of the reactions or sequence of reactions described above, may be further elaborated by substitution α to the sulfone and eventual reductive elimination of this group. Two natural products, namely, junionone (**21**)[13] and citrilol acetate (*cis*-**22b**),[11,12] could be synthesized by this route.[9] The two syntheses were mainly meant to be illustrative and no optimization of yields was really tried.

The synthesis of junionone proceeded according to Scheme I.[9b] Pure junionone was obtained by preparative GC and found to have spectral properties identical with those of an authentic sample.[13] Full details are given in the Experimental Section.

The synthesis of citrilol acetate (*cis*-**22b**) proceeded according to Scheme II.[9a] The *cis*- and *trans*-**22b** isomers could be separated by preparative GC and were found to have spectral properties identical with those described for authentic samples.[12]

The synthesis of a large number of nonnatural isoprenoid compounds may be envisaged by the above sequence

(27) Carruthers, W. In "Comprehensive Organometallic Chemistry"; Pergamon Press: Oxford, 1982; Vol. 7, pp 661–729.

(28) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836–4838.

Table V. Cyclobutyl Sulfones Obtained by Anionic and Radical Additions to Bicyclobutyl Sulfones. Reaction Conditions and Physical Properties[a,b]

product[c]	starting material	reagent and conditions	yield, %[d]	mp, °C	Anal.[e]
5i	**1b**	CH_3ONa[f]	95		$C_{12}H_{16}O_3S$[g]
16a	**1a**	$PhSNa$[h]	78	116–117[i]	$C_{17}H_{18}O_2S_2$
				61–63[j]	$C_{17}H_{18}O_2S_2$
16a	**1a**	$PhSH$[k]	52		
16b	**15a**[l]	$PhSNa$[m,n]	78	61–62[i]	$C_{19}H_{22}O_2S_2$
				55–56[j]	$C_{19}H_{22}O_2S_2$
17a	**1b**	$(n\text{-}Bu)_3SnH$[o]	91		
17b	**15a**[l]	$(n\text{-}Bu)_3SnH$[p]	80		

[a] See footnote *a*, Table I. [b] ^1H NMR data (see footnote *a*, Table II) for **5i**-I: 2.05–2.4 (m, 2), 2.44 (s, Me), 2.6–3.05 (m, 2), 3.22 (s, Me), 3.5–3.8 (m, 1), 4.15 (pentuplet, 6.0, 1), 7.34 and 7.79 (4). For **5i**-II: 2.2–2.8 (m, 4), 2.44 (s, Me), 3.0–3.4 (m, 1), 3.22 (s, Me), 3.77 (pentuplet, 7.0, 1), 7.34 and 7.75 (4). For *trans*-**16a**: 2.0–2.5 (m, 2), 2.44 (s, Me), 2.88–3.3 (m, 2), 3.7–4.2 (7, 2), 7.26 (s, 5), 7.32 and 7.75 (4). For *cis*-**16a**: 2.43 (s, Me), 2.56 (t, 8.3, 4), 3.66 (pentuplet, 2), 7.25 (s, 5), 7.31 and 7.70 (4). For *trans*-**16b**: 1.26 (s, Me), 1.55 (s, Me), 1.9–2.3 (m, 1), 2.43 (s, Me), 2.7–3.0 (m, 1), 3.50 (dd, 7.3, 8.4, C_3H, 1), 7.25 (s, 5), 7.31 and 7.74 (4). For *cis*-**16b**: 1.20 (s, Me), 1.53 (s, Me), 2.4–2.6 (m, 2), 2.43 (s, Me), 3.36 (two partly superimposed t, C_1 and C_3H, 2), 7.26 (s, 5), 7.32 and 7.73 (4). For *trans*-**17a**: 0.7–1.7 (m, 27), 2.1–2.5 (m, 3), 2.44 (s, Me), 2.7–3.1 (m, 2), 3.78 (q, 7.6, 1), 7.32 and 7.76 (4). For *cis*-**17a**: 0.5–196 (m, 27), 2.0–2.65 (m, 5), 2.43 (s, Me), 3.97 (q, 7.9, 1), 7.32 and 7.73 (4). For **17b**: 0.8–2.5 (m), 2.42 (s, Me), 3.02 and 3.56 (m and dd, 1), 7.31 and 7.8 (d and two superimposed d, 4). [c] All products were obtained as mixtures of cis and trans isomers, mostly separable by column chromatography (SiO_2, hexane–ether). [d] Total yield. See also footnote *d*, Table I. [e] See footnote *f*, Table I. [f] **1b** (1 mmol) was added to a CH_3ONa solution (0.2 g of sodium in 4 mL of methanol) and kept at 50 °C for 1.5 h. Extractive workup with ether and chromatographic separation furnished isomers **5i**-I and II in a ratio of 15:4. [g] GC–MS (CI) *m/e* for both isomers 241 (M_r 240). [h] PhSNa was prepared in THF (10 mL) under an argon atmosphere from PhSH (0.5 mL) and NaH (120 mg); **1a** (5 mmol) was added and the reaction was run at room temperature for 1 h. The ratio of trans to cis isomer was ca. 2:5. [i] Trans isomers. [j] Cis isomer. [k] **1a** (1 mmol) was stirred in THF (5 mL) with 0.16 mL of PhSH at room temperature and under air atmosphere for 1 h. The ratio of trans to cis isomer was 2:3. [l] See Experimental Section. [m] See footnote *h* above; reaction time: 4 h. The ratio of trans to cis isomer was ca. 3:2. [n] Similar results were obtained with PhSH/air (footnote *k*); reaction time: 19 h. [o] **1b** (1.8 mmol) was refluxed in benzene (5 mL) with $(n\text{-}Bu)_3SnH$ (2 mmol) and a trace of azobis(isobutyronitrile) for 0.5 h. Evaporation of the solvent and chromatographic separation (SiO_2, hexane–ether 9:1) provided *trans*- and *cis*-**17a** in a ratio of ca. 1:5. [p] Same reaction conditions as described under footnote *o*. The isomers were not separable by column chromatography.

of reactions. One example, in which the steric course was controlled by the nature of the starting material, begins with *trans,trans*-**6b**[21] and proceeds according to Scheme III.

Sequential treatment of lithiated **6b** with isobutyraldehyde and acetic anhydride produced a mixture of two diastereomeric acetates **23b** and residual unacetylated diastereomeric alcohols **23a**.[29a] The major acetate isomer separated as a solid from the reaction mixture. Treatment of the recrystallized product with sodium and ethanol in THF[30] produced hydrocarbon **24** as a unique isomer to which the *E* configuration is tentatively assigned on the basis of steric considerations. The elimination of the two functional groups with formation of a double bond, which has been formerly achieved with 6% sodium amalgam,[29]

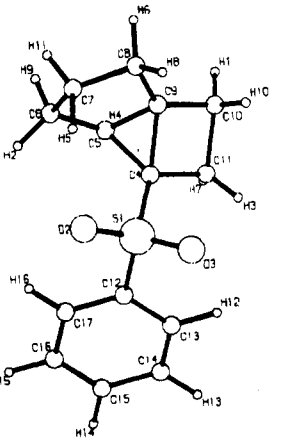


Figure 2. Molecular structure of **32**.

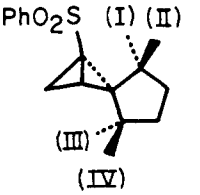
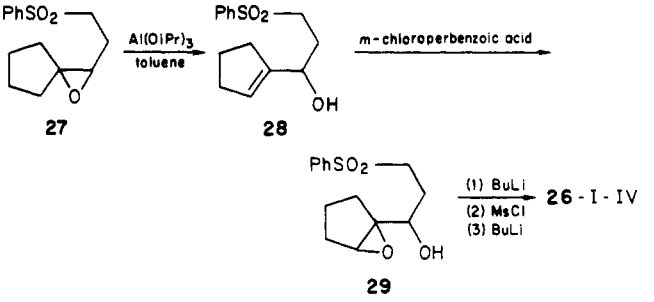


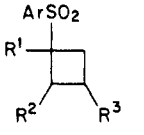
Figure 3. Configurational assignments for alcohols **26**. The OH group is alternatively placed in one of the positions I–IV.

Scheme IV



can thus be realized under the convenient modified Bouveault–Blanc reduction conditions.

Several other reactions of the lithiated cyclobutyl sulfones were carried out as preliminary experiments or as control experiments yielding the α-sulfonyl substituted compound **25** (Table VI).



25a, R^1 = $CH(OH)CH_3$; R^2 = R^3 = H; Ar = Ph
b, R^1 = CO_2Et; R^2 = R^3 = H; Ar = Ph
c, R^1 = $CH_2CH{=}C(CH_3)_2$; R^2 = H; R^3 = Me; Ar = Ph
d, R^1 = CH_2OH; R^2 = H; R^3 = $C(CH_3){=}CH_2$; Ar = *p*-tolyl
e, R^1 = CH_2OH; R^2 = Me; R^3 = H; Ar = Ph
f, R^1 = $CH(OCOCH_3)CH_2CH(CH_3)_2$; R^2 = Me; R^3 = H; Ar = Ph

A particular case of α-sulfonyl substitution was the intramolecular ring-forming reaction of two spirocyclobutyl sulfones, which produced the novel tricyclo[3.3.0.$0^{1,4}$]octane and tricyclo[4.3.0.$0^{1,7}$]nonane ring systems. These two systems are representaetives of a class of difusotricyclic compounds which have been briefly discussed theoretically in regard to strain energy or to a strategy of bond disconnections.[31,32] The four isomeric alcohols **26** (Figure 2)

(29) (a) Kocienski, P. J.; Lythgoe, B.; Ruston, S. *J. Chem. Soc. Perkin, Trans. 1* **1978**, 829–834. (b) Julia, M.; Paris, J. M. *Tetrahedron Lett.* **1973**, 4833–4836.

(30) Fujita, Y.; Ishiguro, M.; Onishi, T.; Nishida, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1325–1326.

(31) Gund, P.; Gund, T. M. *J. Am. Chem. Soc.* **1981**, *103*, 4458–4465.

Table VI. Reaction Conditions, Yields, and Physical Properties of Compound 25[a-c]

product	starting material	electrophile	yield, %[d]	mp, °C	Anal.[e]
25a	**5a**	acetaldehyde	77	52–53	$C_{12}H_{16}O_3S$
25b	**5a**	diethyl carbonate	72	79–80	$C_{13}H_{16}O_4S$
25c[f]	**5b**	prenyl bromide	86		
25d[g]	*cis*-**5f**	formaldehyde	55		$C_{15}H_{20}O_3S$[h]
25d[g]	*trans*-**5f**	formaldehyde	57		$C_{15}H_{20}O_3S$[h]
25e[i]	**6a**	formaldehyde	78	71–73	$C_{12}H_{16}O_3S$
25f[j]	**6a**	isovalenaldehyde/ acetic anhydride	49[k]		$C_{18}H_{26}O_4S$[l]

[a] See footnote *a*, Table I. [b] See Experimental Section, preparations of **7b**, **7e**, and **23b** for representative procedures. [c] ^1H NMR data (see footnote *a*, Table II) for **25a**: 1.36 (d, 6.4, Me), 1.8–2.5 (m, 6), 3.40 (s, OH), 4.03 (q, 6.5, 1), 7.5–8.0 (m, 5). For **25b**: 1.15 (t, 7.1, Me), 2.0–3.0 (m, 6), 4.11 (q, 7.1, 2), 7.5–8.0 (m, 5). For **25c** (mixture of isomers): 1.09 (d, 5.4, Me), 1.52 (s, Me), 1.68 (s, Me), 1.7–2.7 (m, 7), 5.15 (br t, 1), 7.5–8.0 (m, 5). For **25d**-I: 1.63 (s, Me), 1.9–2.2 (m, 2), 2.44 (s, Me), 2.6–3.0 (m, 4), 3.67 (s, 2), 4.67 and 4.77 (two br s, 2), 7.35 and 7.80 (4). For **25d**-II: 1.67 (s, Me), 2.0–2.2 (m, 2), 2.46 (s, Me), 2.5–2.9 (m, 3), 3.02 (t, OH), 3.84 (d, 6.2, 2, singlet after addition of D_2O), 4.71 and 4.80 (two br s, 2), 7.35 and 7.75 (4). For **25e**: 0.77 (d, 7.1, Me), 1.5–3.2 (resolved m, 5 and OH), 3.89 (narrow ABq after addition of D_2O, 2), 7.5–8.0 (m, 5). For **25f** (mixture of isomers): 0.82 (d, Me), 0.91 (d, *gem*-dimethyl), 1.20 (d, Me), 1.53 (Me), 1.1–3.6 (m), 5.50 (m, 1), 7.5–8.0 (m, 5). [d] See footnote *d*, Table I. [e] See footnote *f*, Table I. [f] Nonseparated mixture of two isomers, MS, *m/e* 137 ($M^+ - PhSO_2$), 136 (base peak), 121, 107, 95, 94, 93, 81. [g] A separable 1:2 mixture of two isomers was obtained from either cis or trans **5f**. [h] MS (CI) analysis of the separated isomers, *m/e* 281 (M_r 280). [i] One isomers is obtained, assigned the *cis*-1-(hydroxymethyl)-2-methyl configuration (see ref 21). [j] A mixture of two diastereomeric acetates and of unacetylated alcohols was obtained. [k] Yield of the diastereomeric acetates **25f** obtained as a solid mixture by crystallization of the chromatographically purified total reaction product from hexane, mp 70–100 °C. [l] GC-MS (CI) analysis; two isomers in a ratio of 2:1, *m/e* 339 $(M + 1)^+$, 279, 155, 143, 137 (base peak) for both isomers.

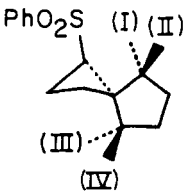
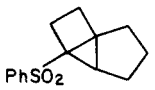


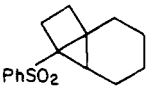
Figure 4. Possible configurations of alcohols **30** and mesylates **31**.

were prepared according to Scheme IV by a slight modificatioin of the route previously described.[8] (For full details see Experimental Section.)

$LiAlH_4$ reduction of alcohols **26** either individually or in various isomer mixtures, produced alcohols **30** (Figure 3) as liquid products. These were only roughly purified and converted into methanesulfonyl derivatives **31**. Only two mesylates could, however, be derived from the reduction products of the four **26** alcohols and these were assigned the transoid structures III and IV in Figure 3, the sulfone group presumably assuming a trans relationship relative to the bulkier substituent. Of the two isomers, only one reacted readily with BuLi to provide the tricyclic compound **32** in 80% yield. It is assigned configuration IV which allows for a backside displacement by the α-sulfonyl anion. The second mesylate isomer was recovered practically unchanged from treatment with BuLi and was assigned configuration III.



32



33

Structure **32** was in full agreement with the spectral and analytical properties of the compound and was also confirmed by X-ray analysis[24] (Figure 4).

The strain inherent in system **32** was reflected in the ease of hydrogenolysis of skeletal bonds accompanying the reductive elimination of the phenylsulfonyl group. Three methods were used for the latter reaction, namely, 6% sodium amalgam in ethanol,[23a] lithium in ethylenediamine/pentane at room temperature,[33] and sodium–ethanol/THF[30] at −13 to 0 °C. The reaction products were analyzed by GC–MS and found to consist in large proportion of one or two C_8H_{14} hydrocarbons (90–97%) and two minor C_8H_{12} hydrocarbons. The major C_8H_{14} compound was tentatively identified as *cis*-octahydropentalene by a very good fit with the MS of an authentic sample, as retrieved by the instrument. The second C_8H_{14} isomer, formed only in the sodium–ethanol reduction, was not identified. The minor C_8H_{12} compounds have the molecular formula of the parent hydrocarbon, tricyclo-[3.3.0.$0^{1,4}$]nonane, but none has thus far been isolated.

The tricyclic system **33** was prepared by a reaction sequence similar to that described for **32**, starting with the six-membered ring analogue of **27**.[8] Sulfone **33** was obtained in a low overall yield, resulting from low yields in several of the intermediate steps. The last reactive mesylate (**34**), the six-membered ring homologue of **31**-IV, was, however, obtained as a pure solid and was converted into **33** in 70% yield. Comparison of the analytical and spectral data of **33** with those of **32** allowed us to assign to it the indicated structure.

Experimental Section

See the preceding paper in this issue concerning general procedure.

1-(*p*-Tolylsulfonyl)bicyclo[1.1.0]butane (1b) was prepared as described for **1a**:[8] mp 91–92 °C (hexane); NMR δ 1.36 (s, 2, *endo*-H), 2.44 (s, Me), 2.50 (s, 3, C_3 H and *exo*-H), 7.34 and 7.82 (4); IR 1323, 1313, 1168, 1152, 1116, 1093, 1084 cm^{-1}; UV (ethanol) λ_{max} 229 (ϵ 10 750), 263 (620), 274 (380) nm. Anal. ($C_{11}H_{12}O_2S$) C, H.

2-*exo*-Methyl-1-(*p*-tolylsulfonyl)bicyclo[1.1.0]butane (1d) was prepared as described for **1c**:[21] mp 111–112 °C (hexane); NMR δ 1.08 (t, 1, J = 1.5, C_4 *endo*-H), 1.3–1.7 (m, 4, A_3B part-spectrum of C_2 Me and C_2 *endo*-H), 2.32 (m, 1 C_4 *exo*-H), 2.44 (s, Me), 2.57 (m, 1, C_3H), 7.32 and 7.81 (4); IR 1323, 1312, 1155, 1093 cm^{-1}. Anal. ($C_{12}H_{14}O_2S$) C, H, S.

Bridgehead Substitution Reactions. Method A. Simultaneous Addition of the Base and the Electrophile. Commercial BuLi in hexane (1.5 mmol) was diluted in THF (4 mL) and added through a dropping funnel into an ice-cooled solution of the bicyclic sulfone (1 mmol) in THF (10 mL), while a solution

(32) Corey, E. J.; Howe, W. J.; Orf, H. W.; Pensak, D. A.; Peterson, G. *J. Am. Chem. Soc.* **1975**, *97*, 6116–6124.

(33) See Bodeker, C.; de Waard, E. R.; Huisman, H. O. *Tetrahedron.* **1981**, *37*, 1233–1235.

of the electrophile (1.5 mmol in 4 mL of THF) was added via syringe at a similar rate with a short lag of time. Workup followed after 0.25 h and chromatographic purification was done on silica gel (8–12 g per mmol of substrate). Recrystallizations were done mostly from pentane or hexane.

Method B. BuLi (1 mmol) was added to the bicyclic sulfone (1 mmol) in THF (8 mL) at 0 °C, followed immediately by the alkylating agent (in excess of 1 mmol). Workup followed after a reaction time of 5 min and the products were chromatographically purified.

Other methods were occasionally used and these are described further below.

3-(1-Methylethenyl)-1-(*p*-tolylsulfonyl)bicyclo[1.1.0]butane (1s). A solution of **1h** (532 mg, 2.0 mmol) and Burgess' reagent[14] (5.0 mmol) in benzene (35 mL) was refluxed for 10 min. It was then cooled down to room temperature, washed with water, dried, and evaporated. Chromatography on silica gel (15 g, hexane–ether 2:3) provided **1s** (400 mg, 81% yield) as a thermally unstable, polymerizing solid, mp 85–86 °C (hexane).

5-Methyl-1*H*,7*H*-dihydro-1a,7a-methanebenzo[*b*]cyclopropa[*e*]thiopyran-7-one 2,2-Dioxide (2) and Bis[3-(*p*-tolylsulfonyl)bicyclo[1.1.0]but-1-yl] Ketone (3). A solution of **1b** (208 mg, 1 mmol) in THF (10 mL) was treated at 0 °C with BuLi (1.5 mmol) and, after 1 min, with diethyl carbonate (0.2 mL, ca. 2 mmol). Extractive workup with dichloromethane was carried out after 3 min. Chromatography on silica gel (8 g, hexane–dichloromethane–ethyl acetate 15:20:3) separated **2** (66 mg, 28% yield) from **3** (123 mg, 56% yield).

Compound **2**: mp 181–182 °C (benzene–hexane); NMR δ 2.13 (dd, 2, J^1 = 1.6, J^2 = 2.2, *endo*-H), 2.49 (s, Me), 2.99 (dd, 2, same J values, *exo*-H), 7.62 and 7.94 (ABq, 2), 7.67 (s, 1); IR 1693, 1328, 1165, 1155, 1138 cm^{-1}; UV (ethanol) λ_{max} 216 (ϵ 23 900), 248 (6400), 288 (1620) nm. Anal. ($C_{12}H_{10}O_3S$) C, H, S.

Ketone **3**: mp 223–224 °C (ethanol); NMR δ 1.71 (s, 4, *endo*-H), 2.43 (s, 6, two Me), 3.20 (s, 4, *exo*-H), 7.35 and 7.81 (8); IR 1720, 1320, 1310, 1150 cm^{-1}; UV (ethanol) λ_{max} 245 nm (ϵ 27 100). Anal. ($C_{23}H_{22}O_5S_2$) C, H, S.

When 2 equiv of BuLi were used in the above reaction, only small, undetermined amounts of **3** were formed, while **2** was isolated in 70% yield.

Ethyl 3-(*p*-Tolylsulfonyl)bicyclo[1.1.0]butanecarboxylate (1t). BuLi (3.9 mmol) was added to **1b** (624 mg, 3 mmol) in THF (40 mL) at −35 °C and the solution was stirred at −35 to −30 °C for 20 min. It was then transfered via a side arm and a connecting tube into a stirred solution of ethyl chloroformate (1.5 mL, ca. 15 mmol) in THF (10 mL) kept at −30 °C. Extractive workup with ether–dichloromethane followed after 10 min, during which time the temperature was allowed to rise to −20 °C. The crude product obtained after evaporation of the solvents was taken in ether (5 mL) and a solid precipitate was filtered and found to consist of practically pure **3** (TLC and mp, 95 mg, 14% yield). Chromatography of the remaining product on silica gel (15 g, hexane–ether 7:3) furnished **1t** (530 mg, 63% yield).

Reduction of Bicyclobutyl Sulfones with $LiAlH_4$. General Procedure. A solution of **1** in THF (5 mL per mmol) was kept under a blanket of inert gas and cooled to 0 °C. Powdered $LiAlH_4$ (80% by weight of **1**) was added all at once to the stirred solution and stirring was continued at 0 °C until the presence of **1** could not be detected by TLC (from 0.25 h to a few hours). An equal volume of ether was then added to the mixture, followed by controlled addition of a saturated sodium sulfate solution. This was continued until a well separated white precipitate had formed. Anhydrous potassium carbonate was then added for drying. Filtration and evaporation of the solvents yielded the crude reduced product which could be directly recrystallized or else filtered on a short column of silica gel and then recrystallized.

1-Isopropylidene-3-(*p*-tolylsulfonyl)cyclobutane (9) and Sulfones (5f). A solution of **5e** (211 mg, 0.78 mmol) and Burgess' reagent[14] (2.0 mmol) in benzene (13 mL) was refluxed for 10 min, cooled back to room temperature, extracted with water, dried, and evaporated. Chromatography on silica gel separated a mixture of *trans*-**5f** (Table IV) and **9** (156 mg) from *cis*-**5f** (28 mg, total yield 94%). Rechromatography on the first mixture on alumina (activity III, 10% silver nitrate, 25 g, hexane–ether 1:1) separated **9** (71 mg) from *trans*-**5f** (66 mg). Sulfone **9**: NMR δ 1.49 (s, two Me), 2.44 (s, Me), 2.5–3.3 (m, 4), 3.71 (m, 1), 7.32 and 7.78 (4); IR 1318, 1307, 1293, 1150, 1085 cm^{-1}; GC–MS (CI), m/e 251 [(M + 1)$^+$, $C_{14}H_{18}O_2S$, M_r 250].

X-ray Crystal Data of *cis*-5g. Crystals of *cis*-**5g** are monoclinic, space group $P2/c$, a = 17.069 (3) Å, b = 5.831 (1) Å, c = 17.299 (3) Å, β = 60.83 (3)°, V = 1503.4 Å^3, Z = 4, calculated density 1.18 g cm^{-3}.

A crystal of *cis*-**5g** was centered on a CAD-4 diffractometer. The intensities of all reflections were measured according to $\alpha - \theta$ technique with a scan range of 1.0° and constant scan speed of 1.5° per min. A total of 2024 reflections were measured (1832 observed) by using Mo Kα radiation (0.7114 Å) up to θ 23°.

The structure was solved by direct-phase determination. The non-hydrogen atoms were refined anisotropically. The coordinates of the hydrogen atoms were calculated after each cycle of least squares and the overall isotropic temperature factor was refined (final U = 0.16 Å). Final R values are R = 0.092, R_w = 0.093.

A final difference Fourier map possessed no special features.

2,2-Dimethyl-1-(*p*-tolylsulfonyl)bicyclo[1.1.0]butane (15a) was prepared as described for **15b**:[8] mp 73–74 °C; NMR δ 0.93 (s, Me), 1.52 (s, Me), 1.78 (t, 1, J = 2.3, C_4 *endo*-H), 2.43 (s, 4, Me and C_4 *exo*-H), 2.59 (dd, 1, J^1 = 2.5, J^2 = 1.4, C_3 H), 7.32 and 7.84 (4); IR 1322, 1312, 1296, 1155, 1094 cm^{-1}. Anal. ($C_{13}H_{16}O_2S$) C, H.

3-(*p*-Tolylsulfonyl)cyclobutanone (19). Chromic anhydride (4 g, 40 mmol) was added to a stirred solution of dichloromethane (100 mL) and pyridine (6.3 g, 80 mmol). After 0.25 h, a mixture of *cis*- and *trans*-**17a** (1.66 g, 3.3 mmol) dissolved in dichloromethane (5 mL) was added to the oxidizing solution and stirring was continued at room temperature for 5 h. After addition of ether (200 mL), the supernatant was decanted from a precipitated thick gum and was washed with 5% hydrochloric acid and 5% sodium bicarbonate. Chromatography on silica gel (15 g, hexane–water 4:1) furnished 750 mg of recovered **17a** (TLC, NMR) and then 250 mg of **19** (61% yield relative to unrecovered **17a**): mp 66–67 °C (hexane–ether); NMR δ 2.43 (s, Me), 3.0–4.0 (m, 5), 7.38 and 7.82 (4); IR 1800, 1318, 1303, 1150, 1087 cm^{-1}. Anal. ($C_{11}H_{12}O_3S$) C, H.

***cis*- and *trans*-1-Iodo-3-(*p*-tolylsulfonyl)cyclobutane (20).** A solution of iodine (250 mg) in benzene (13 mL) was added to a refluxing solution of **17a** (480 mg, 0.96 mmol) in the same solvent (5 mL) until persistence of color and at the approximate rate of absorption. Ether was added to the cooled solution which was then washed with 5% sodium hydroxide solution and water, dried, and evaporated. Chromatography on silica gel (20 g, hexane–ether 7:3 and 1:1) furnished *trans*- and *cis*-**20** (50 mg each, 31% yield).

trans-**20**: mp 92–93 °C (hexane); NMR δ 2.44 (s, Me), 2.5–2.9 (m, 2), 3.05–3.4 (m, 2), 3.8–4.2 (m, 1), 4.4–4.8 (m, 1), 7.35 and 7.76 (4); IR 1327, 1316, 1300, 1287, 1160, 1097 cm^{-1}. Anal. ($C_{11}H_{13}IO_2S$) C, H.

cis-**20**: mp 161–162 °C (hexane–dichloromethane); NMR δ 2.44 (s, Me), 2.6–3.3 (m, 4), 3.71 (q, 1), 4.28 (q, 1), 7.35 and 7.73 (4); IR 1330, 1315, 1300, 1284, 1255, 1162, 1097 cm^{-1}. Anal. ($C_{11}H_{13}IO_2S$), C, H.

Synthesis of (±)-Junionone (21, cf. Scheme I). 1-[(1-Hydroxy-3,3-ethylenedioxy)butyl]-2,2-dimethyl-1-(phenylsulfonyl)cyclobutane (7b). BuLi (1.87 mmol) was added to a solution of **7a** (350 mg, 1.50 mmol) in THF (9 mL) at −15 °C, followed after 10 min by 3,3-(ethylenedioxy)butyraldehyde (300 mg, 2.3 mmol) in THF (2 mL). Workup after an additional 10 min and chromatography on silica gel (20 g, hexane–ether 3:2) provided recovered **7a** (122 mg) and then a mixture of two diastereomeric **7b** (297 mg, 82% yield relative to unrecovered **7a**). Rechromatography of this mixture effected partial separation of the isomers.

Isomer **7b**-I: mp 143–144 °C (hexane); NMR δ 1.27, 1.43 and 1.60 (three methyl s), 1.6–2.6 (m, 6), 3.45 (d, 1, J = 2.4, OH), 3.91 (m, 4), 4.11 and 4.22 (dt, 1, dd after addition of D_2O, J^1 = 9.3, J^2 = 2.0), 7.5–8.0 (m, 5); IR 3540 (br), 1295, 1140 cm^{-1}. Anal. ($C_{18}H_{26}O_5S$) C, H.

Isomer **7b**-II: mp 116–117 °C (hexane); NMR δ 1.27, 1.35 and 1.59 (three methyl s), 1.6–2.2 (m, 6), 2.27 (d, 1, J = 2.3, OH), 3.89 (m, 4), 4.25 and 4.35 (dt, 1, dd after addition of D_2O, J^1 = 8.2, J^2 = 3.0), 7.5–8.0 (m, 5); IR 3540 (br), 1290, 1138 cm^{-1}. Anal. ($C_{18}H_{26}O_5S$) C, H.

A mixture of the two **7b** isomers (436 mg) was refluxed in acetone (13 mL), containing three drops of water and 95 mg of

pyridinium tosylate,[34] for 3 h. Extractive workup with ether provided a crude mixture of two ketones **7c** (420 mg) with methyl signals at δ 1.11, 1.39, 2.10, and 2.21. A portion of this mixture (260 mg) was treated without further purification with 6% sodium amalgam (1.28 g, 4 equiv of sodium) in methanol (7 mL) for 2 h at room temperature. A few drops of aqueous ammonium chloride solution were added and the solution was decanted from the mercury with ether washings. The solvents were distilled at atmospheric pressure to a residual volume of ca. 2 mL. Saturated sodium chloride solution was added and the mixture was extracted with ether.

The crude product (140 mg) was composed of a ca. 1:1 mixture of **7b** and **21**, besides minor impurities (^{1}H NMR and GC analyses). The yield of **21** was estimated at 25–30%. Preparative GC was carried out with an Aerograph A-90-P instrument by using 20 ft × 0.5 in. column of 15% Carbowax on Chromosorb W at 195 °C. Pure **21** could thus be obtained for spectroscopic identification and was found to have a ^{1}H NMR spectrum which matched exactly the one described for an authentic sample:[13] IR 1670, 1620 cm^{-1}.

Synthesis of (±)-Citrilol Acetate (*cis*-22b, cf. Scheme II). 2,2-Dimethyl-1-(1-methylethenyl)-3-(phenylsulfonyl)cyclobutane (7d). Addition of isopropenylmagnesium bromide to **15b** (1.74g) was carried out as described (see Table IV and ref 21). A dark-colored reaction mixture was obtained which was chromatographed on silica gel (70 g, hexane–ethyl acetate 17:3) to provide one **7d** isomer (455 mg, 22% yield) as the only well-defined product: NMR δ 1.24 and 1.26 (two close methyl s), 1.65 (br s, Me), 1.8–2.7 (m, 3), 3.2–3.4 (m, 1), 4.70 and 4.91 (two br s, 2), 7.5–8.0 (m, 5); MS, *m/e* 123 (base peak, M$^+$ – $C_6H_5SO_2$, $C_{15}H_{20}O_2S$, M_r 264).

***cis*- and *trans*-1-(Hydroxymethyl)-2,2-dimethyl-3-(1-methylethenyl)-1-(phenylsulfonyl)cyclobutane (7e).** BuLi (2.1 mmol) was added to a solution of **7d** (490 mg, 1.86 mmol) in THF (10 mL) at 0 °C. After 5 min the solution was cooled to −15 °C and a stream of formaldehyde, obtained by depolymerization of paraformaldehyde at 150 °C, was passed over the stirred solution for 5 min. Workup and chromatography on silica gel (20 g, hexane–ether 3:1) provided two **7e** isomers.

Isomer **7e**-I (49 mg, 9% yield): mp 122–123 °C (hexane); NMR δ 1.24, 1.72 and 1.77 (three methyl s), 1.6–2.3 (m, 2), 3.3–3.7 (m, 4, 3 after addition of D_2O), 4.49 and 4.87 (two br s, 2), 7.5–8.0 (m, 5). Anal. ($C_{16}H_{22}O_3S$) C, H.

Isomer **7e**-II (348 mg, 54% yield): mp 88–89 °C (hexane); NMR δ 1.27, 1.37 and 1.67 (three methyl s), 1.7–1.82 (m, 1), 2.5–2.8 (m, 2), 3.08 (OH, 1), 3.57 and 4.13 (ABq, 2, *J* = 13.2), 4.72 and 4.94 (two br s, 2), 7.5–8.0 (m, 5). Anal. ($C_{16}H_{12}O_3S$) C, H.

***cis*- and *trans*-1-(Acetoxymethyl)-2,2-dimethyl-3-(methylethenyl)cyclobutane (22b).** Isomer **7e**-II (250 mg, 0.85 mmol) was stirred in methanol (10 mL) with 6% sodium amalgam (1.3 g, 3.4 equiv of sodium) at 0 °C for 2.5 h. Workup was carried out as described for **7c**, and the crude product was acetylated with acetic anhydride (1.5 mL) in pyridine (2 mL) for 20 h. The crude acetylation product was composed mainly of *cis*- and *trans*-**22b** in a ratio of ca. 2:1, respectively (GC and NMR analysis, 120 mg, 72% yield). Preparative GC was carried out as described for **21** and provided pure samples of *cis*-**22b** (citrilol acetate) and *trans*-**22b**. The ^{1}H NMR spectra of the two isomers matched exactly those published for authentic samples,[12] except for the lower-field methyl signal of the *gem*-dimethyl group of *cis*-**22b** which appeared at δ 1.19 instead of the reported value of δ 1.12.

Synthesis of (*E*)-*trans*-1,2-Dimethyl-3-(2-methylpropylidene)cyclobutane (24, cf. Scheme III). *r*-1-[1-(Acetyloxy)-2-methylpropyl]-*c*-2-methyl-*t*-3-methyl-1-(phenylsulfonyl)cyclobutane (23b). BuLi (5.74 mmol) was added to a solution of *trans,trans*-**6b**[21] (1157 mg, 5.17 mmol) in THF (40 mL) at 0 °C. Isobutyraldehyde (0.75 mL) and acetic anhydride were then added at 10-min intervals. Extractive workup after further 10 min provided a crude mixture from which a solid product precipitated upon trituration with pentane. Recrystallization from hexane provided 665 mg (38% yield) of one pure **23b** isomer: mp 121–122 °C; NMR δ 0.63 (d, *J* = 7.1, Me), 0.90 (d, *J* = 6.9, Me), 1.11, 1.17 and 1.20 (two partly superimposed methyl d), 1.50 (s, Me), 1.7–2.8 (m, 5), 5.07 (d, 1, *J* = 5.2), 7.5–8.0 (m, 5); IR 1740, 1310, 1290, 1148 cm^{-1}. Anal. ($C_{18}H_{26}O_4S$).

Chromatography of the residual material on silica gel (20 g, hexane–ether 7:3) furnished 696 mg of a mixture of two diastereomeric acetates **23b** (additional doublet at δ 5.12) and two diastereomeric alcohols **23a**. One pure **23a** isomer was obtained in the last chromatography fractions (112 mg, 7% yield).

***r*-1-(1-Hydroxy-2-methylpropyl)-*c*-2-methyl-*t*-3-methyl-1-(phenylsulfonyl)cyclobutane (23a):** mp 131–132 °C (hexane); NMR δ 0.79 (d, *J* = 5.8, Me), 1.02 (d, *J* = 6.8, Me), 1.08 (d, *J* = 7.1, *gem*-dimethyl), 1.7–2.8 (m, 5), 2.31 (d, *J* = 7.8, OH), 3.77 (dd, 1, d after addition of D_2O, *J* = 2.1), 7.5–8.0 (m, 5); IR 3550, 1300, 1245 cm^{-1}. Anal. ($C_{16}H_{24}O_3S$) C, H, S.

Reductive Elimination of 23b. Sodium pieces (210 mg) were added to a solution of recrystallized **23b** (382 mg) in THF (4 mL)–ethanol (0.8 mL) kept at 10–15 °C. After stirring for 1.5 h, ethanol was added to destroy excess sodium and the solution was partitioned between ether and water. The solvents were then evaporated under atmospheric pressure until a bath temperature of 150 °C was reached. At this stage there remained behind 155 mg of over 90% pure **24** (GC–MS analysis). This residue was distilled at a bath temperature of 155 °C and two fractions were collected, which were constituted by **24** and residual THF (120 mg, ca. 70% yield). A 20-mg residue from the distillation was also constituted by practically pure **24**. The distilled product was evaporated a reduced pressure, with a great loss of material, to provide solvent-free 24: NMR δ 0.92 (d, *J* = 6.6, *gem*-dimethyl), 1.05 (d, *J* = 6.7, Me), 1.09 (d, *J* = 6.5, Me), 1.2–2.6 (m, 5), 4.89 (d, with fine allylic splitting, 1, *J* = 8.6); IR 2900–3000 (very strong), 1455, 1375, 985 cm^{-1}; GC–MS, *m/e* (relative intensity) 138 (M$^+$, 5.1), 123 (26.4), 109 (22.2), 96 (10.2), 95 (20.6), 82 (18.6), 81 (64.7), 79 (15.7), 67 (100).

1,2-Epoxy-1-[1-hydroxy-3-(phenylsulfonyl)propyl]cyclopentane (29a). Epoxide **27**[8] (1 mol equiv) was refluxed in toluene with aluminum isopropoxide (1.1 mol equiv) for 24 h.[35] Isomerization was usually not complete by this time, but the reaction mixture was cooled down, filtered on Celite, and evaporated. The crude residual product was epoxidized with *m*-chloroperbenzoic acid in the usual way.[21] Chromatography on silica gel (ten times by weight of product, hexane–ethyl acetate 3:5) separated **27** (up to 45% recovery) from **29a** (up to 75% yield).

Epoxide **29a** was obtained as a slowly solidifying mixture of two diastereomers: mp 89–91 °C (ethanol); NMR δ 1.45–2.15 (m, 8), 2.44 (OH), 3.15–3.45 (m, 3), 3.89 (pentuplet, 1), 7.5–8.0 (m, 5). Anal. ($C_{14}H_{18}O_4S$) C, H.

Chromatographically pure alcohol **28** could be obtained as a liquid from the isomerization mixture before epoxidation: NMR δ 1.75–2.4 (m, 9), 3.19 (apparent t, 2, *J* = 8), 4.29 (br t, 1), 7.5–8.0 (m, 5); IR 3500 (br), 1320, 1308, 1150, 1090 cm^{-1}.

(1*RS*,4*RS*,5*SR*)-5-[(Methylsulfonyl)oxy]-1-(phenylsulfonyl)spiro[3.4]octane (31-III) and (1*RS*,4*RS*,5*RS*)-5-[(Methylsulfonyl)oxy]-1-(phenylsulfonyl)spiro[3.4]octane (31-IV). Epoxides **29a** were treated in THF (8 mL per mmol) at 0 °C by 1 equiv of BuLi, followed by 1 equiv of mesyl chloride, and then by 3 equiv of BuLi. Workup after 1 h and chromatography on silica gel provided alcohols **26** in a total 50% yield.[8]

Alcohols **26** were reduced with $LiAlH_4$ in THF, either individually or in various mixtures, according to the general procedure. The reduced alcohols **30** were roughly purified by filtration on silica gel and converted into their mesylates with mesyl chloride in dichloromethane–triethylamine. Only two mesylates were obtained from the various reduced alcohols **26**.

Mesylate **31**-III was isolated as an unstable solid, in 49% yield, from the product of reduction of **26**-III: mp 103–104 °C dec (ethanol); NMR δ 1.6–2.4 (m, 10), 3.09 (s, Me), 4.09 (t, 1, *J* = 8), 4.88 (t, 1, *J* = 4), 7.5–8.0 (m, 5). Anal. ($C_{15}H_{20}O_5S_2$) C, H.

Mesylate **31**-IV was obtained in 60% yield from the product of reduction of **26**-IV: mp 125–126 °C (ethanol); NMR δ 1.6–2.5 (m, 10), 3.03 (s, Me), 3.86 (t, 1, *J* = 8.2), 4.82 (t, 1, *J* = 6.3), 7.5–8.0 (m, 5). Anal. ($C_{15}H_{20}O_5S_2$) C, H.

The mesylate obtained from **26**-I by the same sequence was identical with **31**-III and the mesylate obtained from **26**-II was identical with **31**-IV (mp's and NMR's).

(34) Sterzycki, R. *Synthesis*. **1979**, 724–725.

(35) Terao, S.; Shiraishi, M.; Kato, K. *Synthesis*. **1979**, 467–468.

4-(Phenylsulfonyl)tricyclo[3.3.0.0^{1,4}]octane (32). Mesylate **31**-IV (430 mg, 1.25 mmol) was treated with BuLi (1.35 mmol) in THF (15 mL) at 0 °C for 10 min. Workup and chromatography on silica gel (15 g, hexane–ethyl acetate 7:3) provided **32** (250 mg, 80% yield): mp 110–111 °C (ethanol); NMR δ 1.4–2.6 (m, 11), 7.5–8.0 (m, 5); IR 1310, 1295, 1150, 1088 cm^{-1}; MS, *m/e* (relative intensity) 248 (M$^+$, 11), 125 (39), 107 (35), 105 (17), 95 (16), 91 (55), 79 (100). Anal. ($C_{14}H_{16}O_2S$) C, H.

X-ray Crystal Data. Crystals of **32** are monoclinic, space group $P2_1/c$, a = 11.851 (1) Å, b = 9.276 (3) Å, c = 11.553 (4) Å β = 91.62 (4)°, V = 1269.51 Å^3, Z = 4.

A total 2698 reflections (one gradient) were measured by using Ni-filtered Cu Kα radiation (1.5418 Å) up to θ 65°. Intensities were corrected for Lorentz polarization factors yielding 2267 independent reflections with $F_0 > 3F_0$. The structure was solved with direct methods, and refined to R = 0.042. All hydrogen atoms were found on a difference Fourier map and refined with overall temperature factor. A final difference map possessed no special features.

Reductive Elimination of 32. (A) Sodium Amalgam in Ethanol. Sulfone **32** (39 mg, 0.16 mmol) was refluxed in ethanol (3 mL) in the presence of 6% sodium amalgam (0.77 g, 2 equiv of sodium) for 5 h. Addition of water and extraction with pentane was followed by GC–MS (CI) analysis. One major peak (90% of total) showed a molecular weight of 110 and two minor peaks (7% of total), a molecular weight of 108 each.

(B) Sodium and Ethanol in THF.[30] Sodium (30 mg) was added to a solution of **32** (29 mg) in THF (0.5 mL) and ethanol (0.1 mL) kept at −13 °C. The mixture was stirred 1 h at that temperature and 1 h at 0 °C. Pentane (5 mL) was added and the solvents were decanted from residual sodium and washed with water. GC–MS analysis showed two major peaks (41% and 56% of total) with M_r 110 and two minor peaks (2.5%) of M_r 108.

(C) Lithium in Ethylenediamine. Sulfone **32** (35 mg) was stirred in a mixture of pentane (2 mL), ethylenediamine (2 mL), and excess lithium until the color of the mixture turned blue. Solid ammonium chloride and then aqueous ammonium chloride were added and the product was extracted with pentane. The pentane extract was washed with 25% aqueous potassium hydroxide and dried. The results of the GC–MS analysis were very similar to those of the sodium amalgam reduction.

(1*RS*,4*RS*,5*RS*)-5-[(Methylsulfonyl)oxy]-1-(phenylsulfonyl)spiro[3.5]nonane (34). The same sequence of reactions described above for **31** were carried out on the six-membered ring homologue of **27**,[8] without full characterization of the intermediates, except for **34** which precipitated from the total mesylation product of a mixture of reduced alcohols. Recrystallization from ethanol provided pure **34**: mp 162–163 °C; NMR δ 1.2–2.6 (m, 12), 3.09 (s, Me), 3.96 (t, 1, J = 8), 4.56 (m, 1), 7.5–8.0 (m, 5). Anal. ($C_{16}H_{22}O_5S$) C, H.

7-(Phenylsulfonyl)tricyclo[4.3.0.0^{1,7}]nonane (33). Treatment of **34** (35 mg) with BuLi as described for **31**-IV provided **33** (18 mg after trituration with cold ethanol, 70% yield) which was recrystallized from ethanol: mp 98–99 °C; NMR δ 1.1–2.5 (m, 13), 7.5–8.0 (m, 5); IR 1310, 1160, 1140, 1092 cm^{-1}; MS, *m/e* (relative intensity) 262 (M$^+$, 22), 245 (33), 137 (19), 126 (24), 125 (76), 121 (88), 120 (13), 119 (14), 105 (25), 95 (29), 93 (60), 91 (84), 81 (12), 79 (100). Anal. ($C_{15}H_{18}O_2S$) C, H.

Registry No. **1a**, 80989-84-0; **1b**, 86537-30-6; (±)-**1c**, 96744-29-5; (±)-**1d**, 96667-16-2; (±)-**1e**, 96667-17-3; (±)-**1f**, 96667-18-4; (±)-**1g**, 96667-19-5; **1h**, 96667-20-8; (±)-**1i**, 96667-21-9; (±)-**1j**-I, 96667-22-0; (±)-**1j**-II, 96745-00-5; **1k**, 80989-89-5; **1l**, 96667-23-1; (±)-**1m**, 96667-24-2; **1n**, 86537-49-7; **1o**, 96667-25-3; (±)-**1p**, 96667-26-4; **1q**, 96667-27-5; **1r**, 96667-28-6; **1s**, 96667-29-7; **1t**, 96667-30-0; **2**, 96667-31-1; **3**, 96688-78-7; **5a**, 78710-80-2; *cis*-**5b**, 96667-37-7; *trans*-**5b**, 96667-32-2; *cis*-**5d**, 96667-38-8; *trans*-**5d**, 96667-33-3; *cis*-**5e**, 96667-39-9; *trans*-**5e**, 96667-34-4; *cis*-**5f**, 86537-37-3; *trans*-**5f**, 86537-38-4; *cis*-**5g**, 86537-35-1; *trans*-**5g**, 86537-36-2; *cis*-**5h**, 96667-43-5; *trans*-**5h**, 96667-42-4; *cis*-**5i**, 96667-52-6; *trans*-**5i**, 96667-51-5; (±)-**6a**, 96667-35-5; (±)-**6b**, 96667-68-4; (±)-**6c**, 96744-30-8; (±)-**7a**, 96667-36-6; (±)-(*R**,*R**)-**7b**, 96667-65-1; (±)-(*R**,*S**)-**7b**, 96667-64-0; (±)-(*R**,*R**)-**7c**, 96667-66-2; (±)-(*R**,*S**)-**7c**, 96667-67-3; **7d**, 86537-39-5; (±)-*cis*-**7e**, 86537-40-8; (±)-*trans*-**7e**, 86537-41-9; (±)-**8**, 96745-01-6; **9**, 96667-41-3; (±)-**10**, 96667-40-2; **11a**, 96667-44-6; *cis*-**11b**, 96667-46-8; *trans*-**11b**, 96667-45-7; (±)-*trans*-**11c**, 96667-47-9; (±)-**12**, 96667-48-0; (±)-**13**, 96667-49-1; (±)-**14** (major), 96667-50-4; (±)-**14** (minor), 96744-31-9; (±)-**15a**, 96667-60-6; (±)-**15b**, 81583-37-1; *cis*-**16a**, 96667-53-7; *trans*-**16a**, 96667-54-8; (±)-*cis*-**16b**, 96667-55-9; (±)-*trans*-**16b**, 96667-56-0; *cis*-**17a**, 96688-79-8; *trans*-**17a**, 96667-57-1; (±)-*cis*-**17b**, 96667-58-2; (±)-*trans*-**17b**, 96667-59-3; **19**, 96667-61-7; *cis*-**20**, 96667-62-8; *trans*-**20**, 96667-63-9; (±)-**21**, 86562-53-0; (±)-*cis*-**22a**, 86537-44-2; (±)-trans-**22a**, 86537-45-3; (±)-*cis*-**22b**, 86562-51-8; (±)-*trans*-**22b**, 86562-52-9; (±)-**23a**(isomer 1), 96667-70-8; (±)-**23a**(isomer 2), 96745-03-8; (±)-**23b** (isomer 1), 96745-02-7; (±)-**23b** (isomer 2), 96667-69-5; (±)-**24**, 96667-71-9; (±)-**25a**, 96667-72-0; **25b**, 86537-54-4; *cis*-**25c**, 96667-73-1; *trans*-**25c**, 96667-74-2; *cis*-**25d**, 96667-75-3; *trans*-**25d**, 96667-76-4; (±)-*trans*-**25e**, 96667-77-5; (±)-**25f**(isomer 1), 96667-78-6; (±)-**25f** (isomer 2), 96744-32-0; (±)-**25f** (alcohol, isomer 1), 96667-79-7; (±)-**25f** (alcohol, isomer 2), 96744-33-1; (±)-**26-I**, 81624-16-0; (±)-**26-II**, 81602-47-3; (±)-**26-III**, 81602-49-5; (±)-**26-IV**, 81602-51-9; (±)-**27**, 81583-01-9; (±)-**27** (6-membered ring homologue), 81583-02-0; (±)-**28**, 96667-80-0; (±)-**29a** (isomer 1), 96667-81-1; (±)-**29a** (isomer 2), 96744-34-2; (±)-**30-I**, 96667-82-2; (±)-**30-II**, 96744-35-3; (±)-**30-III**, 96744-36-4; (±)-**30-IV**, 96744-37-5; (±)-**31-III**, 96667-83-3; (±)-**31-IV**, 96744-38-6; (±)-**32**, 96667-84-4; (±)-**33**, 96667-86-6; (±)-**34**, 96667-85-5; CH_3CHO, 75-07-0; $(CH_3)_2CHCHO$, 78-84-2; PhCHO, 100-52-7; CH_3COCH_3, 67-64-1; $CH_3COCH_2CH_3$, 78-93-3; $ClCOOC_2H_5$, 541-41-3; $CH_2{=}C(Br)CH_3$, 557-93-7; $(CH_2{=}C(CH_3))_2CuLi$, 21329-14-6; $(CH_3)_2C{=}CHBr$, 3017-69-4; $(n\text{-}Bu)_2CuLi$, 24406-16-4; $Me_2(CN)CuLi_2$, 80473-70-7; Me_2CuLi, 15681-48-8; $(CH_3)_2C{=}CHCH_2Br$, 870-63-3; $(CH_3)_2CHCH_2CHO$, 590-86-3; 3-bromocyclohexene, 1521-51-3; ethylene oxide, 75-21-8; 3,3-(ethylenedioxy)butyraldehyde, 18871-63-1; *cis*-octahydropentalene, 1755-05-1.

Supplementary Material Available: Tables of atom coordinates, anisotropic temperature factors, calculated hydrogen atom coordinates, bond lengths, and bond angles for compounds *cis*-**5g** and **32** (10 pages). Ordering information is given on any current masthead page.