Functionalization of 2-Phenylsulfonyl 1,3-Dienes via Cyclopropanation and Epoxidation. Synthesis of Oxabicyclic Systems via BF_3-Induced Rearrangement of Epoxide Derivatives

Claes M. G. Löfström, Anna M. Ericsson, Luc Bourrinet, Seppo K. Juntunen, and Jan-E. Bäckvall*

Department of Organic Chemistry, University of Uppsala, Box 531 S-751 21 Uppsala, Sweden

Received September 14, 1994[⊗]

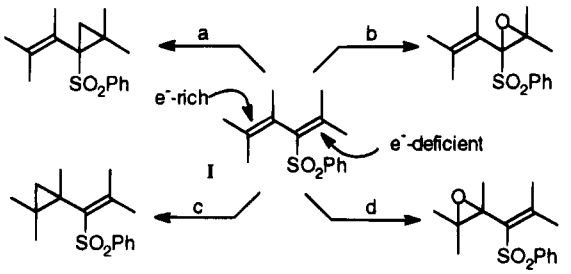
Regioselective cyclopropanation and epoxidation of 2-phenylsulfonyl 1,3-dienes using dimethyloxosulfonium methylide ($(CH_3)_2SOCH_2$) and *m*-chloroperbenzoic acid (*m*-CPBA) gave access to 3,4-epoxy-1,2-methylene-2-phenylsulfonyl alkanes. The Lewis acid-catalyzed rearrangement of these substrates using $BF_3{\cdot}OEt_2$ or $LiClO_4$ was studied. The outcome of the rearrangement appeared to be very much dependent on substrate stereochemistry and substitution pattern, since both ketones and bicyclic ethers (the oxo analogue of the tropa alkaloid skeleton) were isolated. Further functionalization of one of the bicyclic ethers (3-(phenylsulfonyl)-8-oxabicyclo[3.2.1]-2-octene) was undertaken, proceeding with excellent stereoselectivity in all the cases investigated. This opens a way for synthesis of *cis*-2,5-disubstituted tetrahydrofurans.

Introduction

2-Arylsulfonyl 1,3-dienes, **I**, have recently attracted considerable interest, due to their usefulness as synthons in various types of chemistry. Notably they can be utilized in cycloadditions, both with normal and reversed electron demand.[1,2]

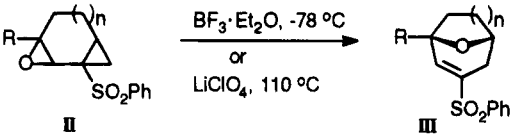
Another interesting feature of these dienes is the difference in electron density between the two double bonds. This allows a number of regioselective reactions to be carried out.[3] In our group we have previously developed regioselective cyclopropanations[4] and epoxidations[5] (Scheme 1).

Scheme 1[a]



[a] Reagents: (a) Me_3SOI, NaH; (b) H_2O_2, NaOH; (c) $CpFe(CO)_2CH_2S(Me)_2^+BF_4^-$; (d) *m*-CPBA.

By consecutive cyclopropanation and epoxidation of 2-(phenylsulfonyl)-1,3-cycloalkadienes compounds with structure **II** were obtained. In this paper we report on their rearrangement to bicyclic ethers of the structure **III** and subsequent synthetic transformations of the latter.



Results and Discussion

Synthesis of Starting Materials. During our investigation of the chemistry of compounds with general structure **I**, we synthesized compound **7a** (Scheme 2). This was done via a cyclopropanation of the electron deficient double bond of **1** according to our previously published procedure,[4] followed by *m*-CPBA epoxidation of the remaining olefinic bond. Interestingly, epoxidation of **4** occurred preferentially syn to the cyclopropane group (syn:anti = 20:1). Apparently, the phenylsulfonyl group exerts a more powerful blocking effect toward the incoming reagent than the cyclopropane. The ratio could be further improved by cooling the reaction mixture with an ice bath. The anti isomer **7b** was synthesized with complete stereoselectivity via the bromohydrin **10** (Scheme 2).

The corresponding reactions were carried out to synthesize **8a** and **8b** from **2** and both isomers (**9a** and **9b**) of the seven-membered epoxycyclopropane from **3**. The *m*-CPBA-epoxidation of the seven-membered vinyl cyclopropane **6** was much slower than that of the six-membered analogue **4**. Furthermore, the stereoselectivity in the epoxidation of **6** was only ~3:1 in favor of the syn isomer **9a**. However, **9a** and **9b** were readily separated by flash chromatography. The bromohydrin method was not applicable for the synthesis of **9b** since **12** could not be formed from **6** (Scheme 2).

The structures of **7a** and **7b** were assigned with the help of NOESY experiments. For **7b** an NOE was observed between the endo hydrogen of the cyclopropane and the epoxy hydrogen closest to the sulfone moiety. No such effect was present for **7a** (Figure 1). Accordingly, **7a** was assigned as the syn and **7b** as the anti isomer.

[⊗] Abstract published in *Advance ACS Abstracts*, May 1, 1995.

(1) (a) Bäckvall, J. E.; Juntunen, S. K. *J. Am. Chem. Soc.* **1987**, *109*, 6396. (b) Bäckvall, J. E.; Plobeck, N. A; Juntunen, S. K. *Tetrahedron Lett.* **1989**, *30*, 2589. (c) Bäckvall, J. E.; Plobeck, N. A. *J. Org. Chem.* **1990**, *55*, 4528. (d) Bäckvall, J. E.; Rise, F. *Tetrahedron Lett.* **1989**, *30*, 5347. (e) Bäckvall, J. E.; Löfström, C.; Maffei, M.; Langer, V. *Ibid.* **1992**, *33*, 2417.

(2) (a) Padwa, A.; Gareau, Y.; Harrison, B.; Norman, B. H. *J. Org. Chem.* **1991**, *56*, 2713. (b) Padwa, A.; Gareau, Y.; Harrison. B.; Rodriguez, A. *Ibid.* **1992**, *57*, 3540. (c) Chou, S. S. P.; Wey, S. J. *Ibid.* **1990**, *55*, 1270.

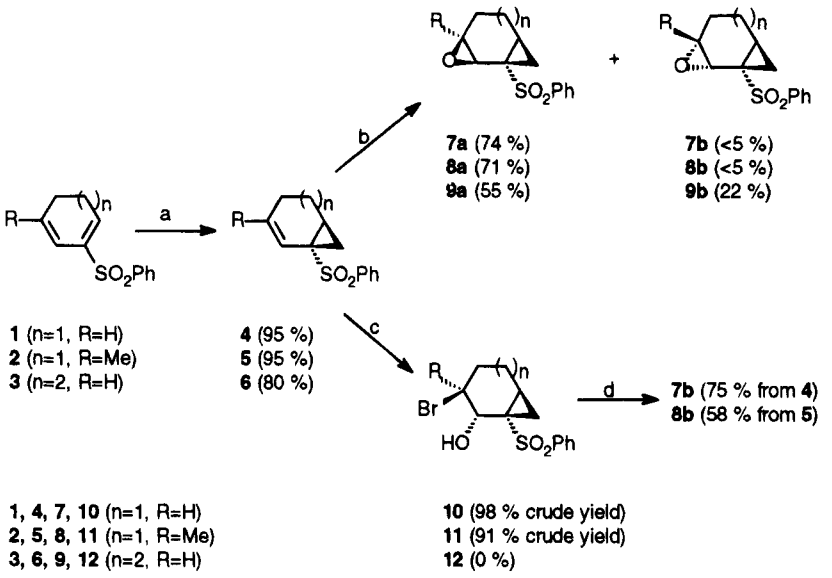
(3) For regioselective nuclephilic additions, see ref 1a and; Sellén M.; Bäckvall, J. E.; Helquist, P. *J. Org. Chem.* **1991**, *56*, 835.

(4) Bäckvall, J. E.; Löfström, C.; Juntunen, S. K.; Mattson, M. *Tetrahedron Lett.* **1993**, *34*, 2007.

(5) (a) Bäckvall, J. E.; Juntunen, S. K. *J. Org. Chem.* **1988**, *53*, 2398. (b) Bäckvall, J. E.; Ericsson, A. M.; Juntunen, S. K.; Nájera, C.; Yus, M. *Ibid.* **1993**, *58*, 5221.

0022-3263/95/1960-3586$09.00/0

Scheme 2[a]



[a] Reagents: (a) Me_3SOI, NaH; (b) *m*-CPBA; (c) NBS, H_2O; (d) 2 M NaOH.

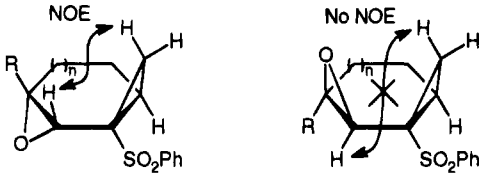


Figure 1.

The same method was used to assign the isomers of **8** and **9**, respectively, the corresponding NOE effects being present in **8b** and **9b** but not in **8a** and **9a**.

Rearrangement Reactions. When **7a** was reacted with $BF_3{\cdot}Et_2O$ it did not undergo the expected rearrangement to ketone **16** in any appreciable yield.[6] Instead the bicyclic tetrahydrofuran **13** was formed as the major product (Table 1, entry 1). A related type of rearrangement of some open-chain epoxycyclopropanes has previously been observed.[7] In the same manner methyl analogue **8a** rearranged to the oxabicyclic product **14** (Table 1, entry 4). Compound **18**, an open chain epoxycyclopropane synthesized in the same manner as **7a, 8a**, and **9a** did not give **19** (Table 1, entry 9). The anti isomer **7b** yielded **16** as the only identifiable product, while **8b** gave **17** (Table 1, entries 3 and 6).

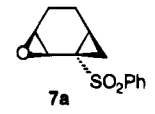
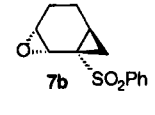
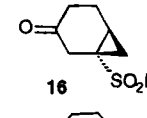
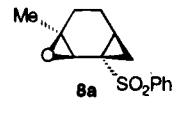
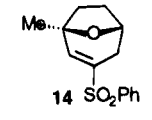
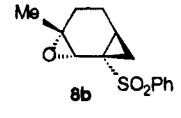
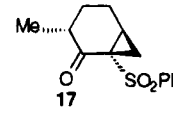
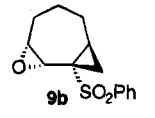
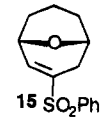
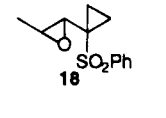
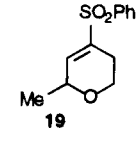
For the seven-membered ring, the syn epoxycyclopropane **9a** gave only a complex mixture of products under the reaction conditions. However, the anti isomer **9b** rearranged to oxabicyclic product **15** in moderate yield (Table 1, entry 7). No detectable amount of ketone (cf. **16**) was present in the crude product from either **9a** or **9b**.

The mechanism for the rearrangement of **7a** to **13** is not fully elucidated. The reaction does not seem to be concerted, since a mixture of **20** and **21** was obtained when the reaction was carried out in the presence of acetic anhydride. The stereochemistry of **20** was assigned from its ^1H NMR spectrum.

(6) This well known isomerisation is mentioned in several standard textbooks. See for example: Carey, F. A.; Sundberg, R, J. *Advanced Organic Chemistry*, 3rd ed., Plenum Press: New York, 1990; p 635.

(7) (a) Donnelly, J. A.; Hoey J. G.; O'Brien, S.; O'Grady, J. *J. Chem. Soc., Perkin Trans 1* **1973**, 2030. (b) Donnelly, J. A.; Hoey J. G. *Ibid.* **1975**, 2364.

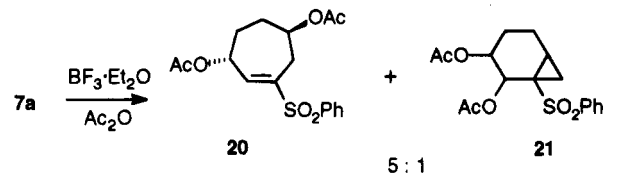
Table 1. Rearrangement Reactions of 3,4-Epoxy-1,2-methylene-2-(phenylsulfonyl)alkanes

entry	starting material	method[a]	reaction product	yield, %
1	 **7a**	A	 **13**	60
2	**7a**	B	**13**	47
3	 **7b**	A	 **16**	45
4	 **8a**	A	 **14**	50
5	**8a**	B	**14**	35
6	 **8b**	A	 **17**	58
7	 **9b**	A	 **15**	35
8	**9b**	B	**15**	30
9	 **18**	A	 **19**	0

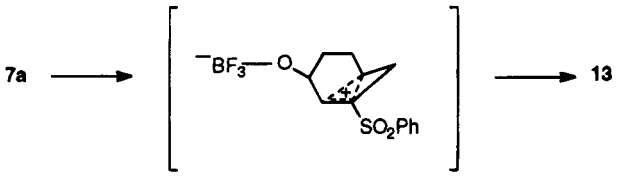
[a] Method A: $BF_3{\cdot}Et_2O$, −78 °C → rt; method B: $LiClO_4$, 110 °C.

This result suggests a stepwise reaction, where the initial step would consist of a Lewis acid supported cleavage of the carbon−oxygen bond in the 3-position to produce an intermediate cyclopropyl carbinyl cation.[8]

The difference in reactivity between **7a** and **7b** is surprising but can be explained by considering the

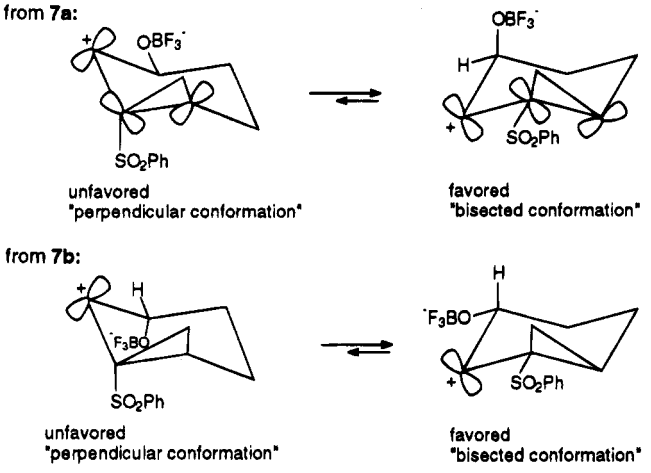


conformations necessary for ring closure. The different conformations for the cyclopropyl carbinyl cations from



7a and **7b** are given in Scheme 3. In each case there is an unfavored "perpendicular conformation" and a favored "bisected conformation" of the cation.[8] The latter con-

Scheme 3. Conformation of Cyclopropyl Carbinyl Cation from 7a and 7b



formation is stabilized by an overlap between the empty p-orbital and the cyclopropyl ring. For the carbocation from **7a** the conformation necessary for ring closure is the favored conformation whereas for the carbocation from **7b** it is the unfavored conformation.

The analogous arguments are valid for **9a** and **9b**. The favored "bisected conformation"[8] of the cyclopropyl carbinyl cation from **9a** and **9b** is given in Figure 2. In

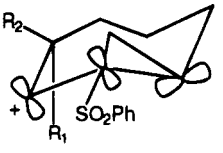
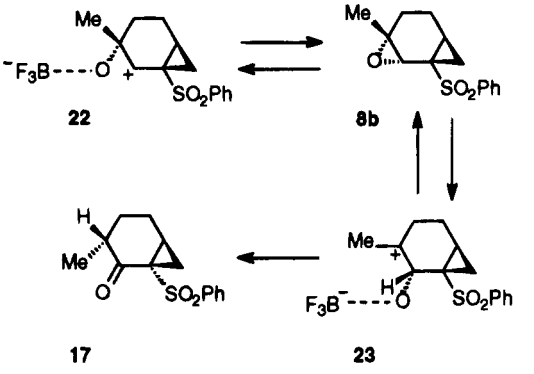


Figure 2. Favored "bisected conformation" of cyclopropyl carbinyl cation from **9a** or **9b** (from **9a**, $R_1 = H$, $R_2 = OBF_3^-$; from **9b**, $R_1 = OBF_3^-$, $R_2 = H$).

the conformation necessary for ring closure, oxygen is trans to the cyclopropyl ring ($R_1 = OBF_3^-$) and this is the carbocation obtained from **9b**.

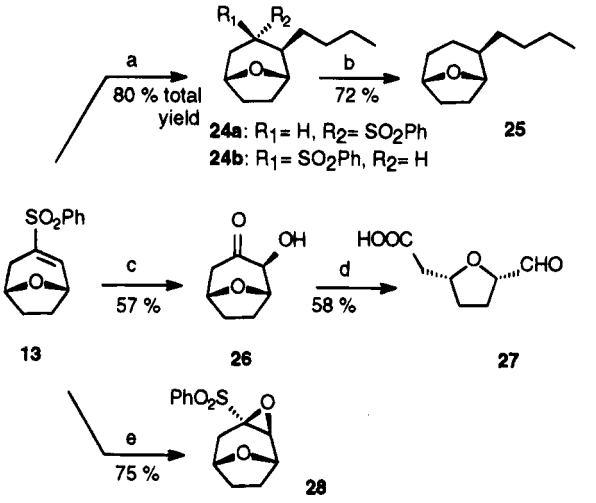
The difference in regioselectivity between the reactions of **7b** and **8b** to give ketones **16** and **17**, respectively, is interesting and can be explained by considering the structures of epoxide-opened intermediates **22** and **23**. In intermediate **22** there is no possibility of a hydrogen rearrangement to form a product corresponding to **16**. In **23**, however, there is a hydrogen available for a migration which gives compound **17**. Moreover, the opening of **8b** to **23** should proceed with reasonable ease, since the cationic center formed is tertiary.



The rearrangement of epoxide to ketone with lithium perchlorate in refluxing benzene as an alternative reagent to BF_3-etherate has been described.[9] This approach was also effective for our rearrangement, although the yields were lower than with BF_3 (Table 1, entries 2, 5, and 8).

Synthetic Transformations. As expected[10] it was possible to carry out a Michael-type cuprate addition to **13**. The product consisted of two isomers (**24a** and **24b**) in a ratio of ~3:2 (Scheme 4). However, the cuprate had

Scheme 4[a]



[a] Reagents: (a) CuI, BuLi; (b) Na(Hg), Na_2HPO_4; (c) OsO_4 NMO; (d) $NaIO_4$; (e) H_2O_2, NaOH.

attacked exclusively from the exo side of **13**, the endo side apparently being too hindered. The presence of two isomers is a result of low selectivity in the protonation of the initially formed phenylsulfonyl-stabilized carbanion. It was possible to separate the two isomers by column chromatography. Reductive desulfonylation[11] of

(8) (a) Buss, V.; Gleiter, R.; Schleyer, P. v. R. *J. Am. Chem Soc.* **1971**, *93*, 3927. (b) Richey, H. G. Jr. in *Carbonium Ions* Vol. III, Eds. Olah, G. A.; Schleyer, P. v. R., Wiley, New York, 1972, pp 1201–1294. (c) Poulter, C. D.; Spillner, C. J. *J. Am. Chem Soc.* **1974**, *96*, 7591.

(9) Rickborn, B.; Gerkin, R. M. *J. Am. Chem Soc.* **1971**, *93*, 1693.

(10) Fuchs, P. L.; Braish, T. F. *Chem. Rev.* **1986**, *86*, 903 and references cited therein. See also ref 1a.

(11) (a) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, *17*, 3477. (b) Trost, B. M; Weber, L; Strege, P.; Fullerton, T. J; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3426.

the isomeric mixture yielded **25** as the only product (Scheme 4), confirming the high stereoselectivity of the initial cuprate attack.

Attempts to cleave the double bond in **13** with ozone were unsuccessful, a complex mixture of products being obtained. Compound **13** could, however, be subjected to catalytic dihydroxylation with osmium tetroxide and NMO (Scheme 3).[12] Predictably,[13] the sulfone moiety was spontaneously eliminated from the initially formed diol to give the α-ketol **26**. This reaction, like the cuprate addition, proceeded with complete stereoselectivity from the exo side of the molecule. Compound **26** was ring opened by sodium periodate to give the *cis*-2,5-disubstituted tetrahydrofuran **27** (Scheme 4). Compound **27** is of potential synthetic interest, since 2,5-disubstituted tetrahydrofurans are frequently found in nature, *e.g.* as one of the dominant building blocks in polyether antibiotics.[14]

We also converted **13** into the epoxide **28** (Scheme 4). Only one isomer resulted. This was assigned as the expected exo epoxide on basis of the coupling constants.

Conclusions

In conclusion, we have discovered that several compounds of structure **II** rearrange to form **III** as the dominant products. The reaction is dependent on the configuration of the initially formed epoxide-opened cyclopropyl carbinyl cation intermediate. The reaction product can be transformed synthetically in several ways in a highly stereoselective manner. Notably, *cis*-2,5 disubstituted tetrahydrofurans can be synthesized.

Experimental Section

General Methods. NMR spectra were recorded on a 300 MHz spectrometer, ^{1}H at 300 MHz and ^{13}C at 74.5 MHz using $CDCl_3$ as solvent and internal standard (7.26 ppm, ^{1}H; 77 ppm, ^{13}C). IR spectra were recorded on an FT-IR spectrophotometer using a 0.1 mm KBr cell with $CDCl_3$ or CCl_4 as solvent. Only the strongest and structurally most important peaks are listed (ν_{max}, cm^{-1}). Elemental analyses were performed by Analytische Laboratorien, Gummersbach, Germany. Reaction solvents were dried and distilled under nitrogen using standard procedures. Merck silica gel 60 (230–400 mesh) was employed for flash chromatography. The sulfonyl dienes (general structure **I**) used were synthesized according to previously published procedures.[15]

1,2-Methylene-2-(phenylsulfonyl)-3-cyclohexene (4). Trimethylsulfoxonium iodide (15.54 g, 70.6 mmol) and NaH (80% in paraffin oil, 2.23 g, 74 mmol) were dissolved in dry DMSO (80 mL) and stirred at room temperature under a nitrogen atmosphere. After 20 min the evolution of hydrogen had stopped and 2-(phenylsulfonyl)-1,3-cyclohexadiene (**1**) (10.13 g, 46.0 mmol), dissolved in THF (25 mL) was added during 30 min via a dropping funnel. After an additional 1 h of stirring at room temperature, the reaction mixture was quenched by the addition of saturated NH_4Cl solution (40 mL). Ether (50 mL) was added and the phases were separated. The aqueous phase was extracted with ether (2 × 50 mL), and the combined organic phases were washed with brine (3 × 50 mL). After drying ($MgSO_4$), the solvent was evaporated, giving 11.1 g of crude product. Flash chromatography (EtOAc/hexane = 20/80) afforded 10.20 g (95%) of **4** as a colorless solid: mp 52–54 °C; IR ($CDCl_3$), 3060, 3036, 1447, 1304, 1142 cm^{-1}; ^{1}H NMR δ 7.86–7.80 (m, 2H), 7.62–7.46 (m, 3H), 6.08 (dd, J = 10, 3.5 Hz, 1H), 5.66–5.57 (m, 1H), 2.30–2.20 (m, 1H), 1.96–1.82 (m, 3H), 1.73–1.58 (m, 1H), 1.50–1.37 (m, 1H), 1.18 (dd, J = 7, 5 Hz, 1H); ^{13}C NMR δ 139.1, 133.1, 128.9, 128.0, 127.4, 121.5, 40.0, 21.8, 19.7, 18.5, 17.0. Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found: C, 66.37, H, 6.01.

4-Methyl-1,2-methylene-2-(phenylsulfonyl)-3-cyclohexene (5). Prepared according to the method used for the synthesis of **4**. Flash chromatography EtOAc/hexane = 20/80, 95% yield: IR ($CDCl_3$) 3063, 3011, 2969, 2864, 1447, 1300, 1206, 1185, 1143, 1091 cm^{-1}; ^{1}H NMR δ 7.89–7.83 (m, 2H), 7.65–7.49 (m, 3H), 5.72 (s, 1H), 2.25–2.15 (m, 1H), 1.91 (dd, J = 9.5, 5 Hz, 1H), 1.93–1.53 (m, 4H), 1.61 (s, 3H), 1.09 (dd, J = 7, 5 Hz, 1H); ^{13}C NMR δ 139.4, 136.4, 133.1, 129.0, 128.2, 115.0, 40.8, 25.2, 23.8, 20.3, 19.0, 18.6.

1,2-Methylene-2-(phenylsulfonyl)-3-cycloheptene (6). Prepared according to the method used for the synthesis of **4**. Flash chromatography EtOAc/hexane = 20/80, 80% yield: mp 65–67 °C; IR ($CDCl_3$) 2933, 2867, 1447, 1303, 1140 cm^{-1}; ^{1}H NMR δ 7.88–7.81 (m, 2H), 7.66–7.58 (m, 3H), 5.71–5.52 (m, 2H), 2.23–2.11 (m, 1H), 2.11–1.83 (m, 4H), 1.47–1.34 (m, 1H), 1.34–1.17 (m, 1H), 1.04–0.89 (m, 1H), 0.71 (dd, J = 7, 5 Hz, 1H); ^{13}C NMR δ 138.3, 135.6, 133.1, 128.6, 128.5, 121.0, 44.3, 27.4, 27.1, 24.1, 21.4, 20.3. Anal. Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49. Found: C, 67.51; H, 6.46.

***t*-3,4-Epoxy-*t*-1,2-methylene-*r*-2-(phenylsulfonyl)cyclohexane (7a).** **4** (8.0 g, 34.1 mmol) was dissolved in CH_2Cl_2 (100 mL). The solution was stirred on an ice bath for 20 min. Then *m*-CPBA (50–60%, 27.5 g, 79.5–95.6 mmol) was added in small portions during another 20 min while the cooling was continued. The reaction mixture was allowed to warm up to room temperature while stirring for 16 h. The reaction mixture was filtered and then again cooled on an ice bath, and saturated Na_2SO_3 solution (30 mL) was carefully added. The phases were separated, and the CH_2Cl_2 phase was washed with saturated Na_2SO_3 solution (20 mL), saturated Na_2CO_3 (2 × 20 mL), 2 M NaOH (20 mL), and brine (3 × 20 mL). Drying and evaporation gave 10.0 g of crude product. Flash chromatography (EtOAc/hexane = 30/70) yielded 6.30 g (74 %) of **7a**: mp 79–81 °C; IR ($CDCl_3$), 3070, 3012, 2935, 1480, 1306, 1148 cm^{-1}; ^{1}H NMR δ 7.97–7.90 (m, 2H), 7.72–7.52 (m, 3H), 3.70 (dd, J = 4.5, 1 Hz, 1H), 3.10–3.04 (m, 1H), 1.96–1.85 (m, 2H), 1.85–1.75 (m, 2H), 1.75–1.61 (m, 1H), 1.61–1.48 (m, 1H), 1.25 (dd, J = 7, 5 Hz, 1H); ^{13}C NMR δ 139.3, 133.6, 129.1, 128.3, 52.0, 49.8, 41.4, 20.1, 18.7, 15.9, 14.6. Anal. Calcd for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64. Found: C, 62.22; H, 5.53.

***t*-3,4-Epoxy-*t*-1,2-methylene-*c*-4-methyl-*r*-2-(phenylsulfonyl)cyclohexane (8a).** Prepared according to the method used for the synthesis of **7a**. Flash chromatography EtOAc/hexane = 30/70, yield 71%): IR ($CDCl_3$) 3074, 2927, 2864, 1583, 1478, 1441, 1426, 1384, 1358, 1301, 1206, 1185, 1143, 1080 cm^{-1}; ^{1}H NMR δ 7.95–7.89 (m, 2H), 7.69–7.52 (m, 3H), 3.57 (s, 1H), 1.92–1.63 (m, 5H), 1.52–1.40 (m, 1H), 1.21 (s, 3H), 1.22–1.14 (m, 1H); ^{13}C NMR δ 139.4, 135.5, 129.0, 128.2, 57.8, 56.5, 41.7, 24.1, 22.8, 19.7, 17.0, 14.6.

Compounds 9a and 9b. Were prepared according to the method described for **7a**, employing a reaction time of 24 h. Separation with flash chromatography (EtOAc/hexane = 30/70) afforded pure samples of **9a** and **9b**.

***t*-3,4-Epoxy-*t*-1,2-methylene-*r*-2-(phenylsulfonyl)cycloheptane (9a):** 55% yield; mp 103–104 °C; IR ($CDCl_3$), 3060, 2931, 2860, 1443, 1305, 1256, 1178, 1147 cm^{-1}; ^{1}H NMR δ 7.91–7.85 (m, 2H), 7.70–7.52 (m, 3H), 3.74 (d, J = 4 Hz, 1H), 3.09 (dd, J = 6, 3 Hz, 1H), 2.12–1.96 (m, 2H), 1.91–1.74 (m, 2H), 1.70–1.48 (m, 2H), 1.44–1.28 (m, 2H), 1.11–0.95 (m, 1H); ^{13}C NMR δ 139.0, 133.6, 129.2, 128.3, 59.7, 55.5, 42.5, 25.9, 25.2, 24.6, 21.2, 17.8.

***c*-3,4-Epoxy-*t*-1,2-methylene-*r*-2-(phenylsulfonyl)cycloheptane (9b):** 22% yield; mp 94–99 °C; IR ($CDCl_3$), 3060, 2989, 2931, 2860, 1578, 1478, 1449, 1378, 1288, 1268, 1177, 1148 cm^{-1}; ^{1}H NMR δ 8.03–7.96 (m, 2H), 7.67–7.49 (m, 3H), 3.22 (dd, J = 4, 1 Hz, 1H), 2.92 (dt, J = 6.5, 4 Hz, 1H), 2.30–

(12) Van Rheenen, V.; Cha, D. Y.; Hartley, W. M. *Organic Syntheses;* Wiley: New York, 1988; Col Vol. VI, p 342.

(13) See for example: Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon Press: New York, 1993; p 338–340.

(14) (a) Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309. (b) Solladié, G.; Dominguez, C. *J. Org. Chem.* **1994**, *59*, 3898 and references cited therein.

(15) (a) Andell, O. S.; Bäckvall, J. E. *Tetrahedron Lett.* **1985**, *26*, 4555. (b) Bäckvall, J. E.; Juntunen, S. K.; Andell, O. S. *Org. Synth.* **1989**, *68*, 148. (c) Bäckvall, J. E.; Nájera, C.; Yus, M. *Tetrahedron Lett.* **1988**, *29*, 1455.

2.17 (m, 1H), 2.05–1.86 (m, 3H, H-1), 1.76–1.61 (m, 1H), 1.51–1–22 (m, 2H), 1.11–0.95 (m, 1H), 0.76 (dd, J = 7, 5 Hz, 1H); ^{13}C NMR δ 139.9, 133.4, 128.9, 128.7, 53.9, 52.7, 43.3, 27.9, 27.0, 23.2, 20.2, 19.9. Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10. Found: C, 63.48; H, 6.08.

***c*-3,4-Epoxy-*t*-1,2-methylene-*r*-2-(phenylsulfonyl)cyclohexane (7b).** To a solution of **4** (976 mg 4.17 mmol) in DMSO (16 mL) were added NBS (1.58 g, 8.88 mmol) and water (200 μL, 11.08 mmol). The reaction mixture spontaneously warmed somewhat and turned orange. After 16.5 h of stirring at room temperature the color was pale yellow and water (40 mL) was added. The resulting mixture was extracted with ether (3 × 50 mL), and the combined ethereal phases were washed with brine (3 × 30 mL), dried ($MgSO_4$) and concentrated in vacuo, yielding 1.36 g (98%) of crude **10**. No attempt was made to purify this product further.

The crude **10** was dissolved in CH_2Cl_2 (20 mL) and 2 M NaOH (5.5 mL) was added. After a total of 24 h of stirring at room temperature, water (50 mL) and CH_2Cl_2 (30 mL) were added. The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). After drying ($MgSO_4$), evaporation of the solvent afforded 846 mg of crude **7b**. Flash chromatography (EtOAc/hexane = 30/70) gave 783 mg (75%) of pure **7b**: mp 102–104 °C; IR (CCl_4), 3067, 3009, 2942, 2846, 1446, 1427, 1321, 1312, 1283, 1173, 1144, 1086 cm^{-1}; ^{1}H NMR δ 7.94–7.87 (m, 2H), 7.70–7.55 (m, 3H), 3.64–3.61 (br d, J = 4 Hz, 1H), 3.02 (br t, J = 3.5 Hz, 1H), 1.90–1.70 (m, 3H), 1.65–1.57 (m, 1H), 1.52–1.39 (m, 1H), 1,32–1.20 (m, 1H), 1.03 (dd, J = 6, 5 Hz, 1H); ^{13}C NMR δ 139.0, 133.7, 129.3, 128.2, 50.5, 48.2, 38.8, 21.3, 16.8, 16.0, 13.6. Anal. Calcd for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64. Found: C, 62.26; H, 5.51.

***c*-3,4-Epoxy-*t*-1,2-methylene-*r*-2-(phenylsulfonyl)-*t*-4-methylcyclohexane (8b).** The synthesis was carried out from **5** via **11** using a reaction sequence analogous to that giving **7b** from **4** via **10.** The overall yield was 53% (198 mg of **5** gave 111 mg of **8b**) after flash chromatography (EtOAc/hexane = 20/80): IR ($CDCl_3$) 3072, 2943, 2872, 1449, 1320, 1302, 1179, 1143, 1091 cm^{-1}; ^{1}H NMR δ 7.90–7.85 (m, 2H), 7.71–7.55 (m, 3H), 3.45 (s, 1H), 1.87–1.77 (m, 1H), 1.78–1.63 (m, 2H), 1,58–1.52 (m, 1H), 1.26–1.15 (m, 2H), 1.16 (s, 3H), 1.08–1.04 (m, 1H); ^{13}C NMR δ 139.1, 133.6, 129.1, 128.1, 56.8, 54.8, 40.3, 27.2, 21.5, 18.4, 16.7, 14.0.

3-(Phenylsulfonyl)-8-oxabicyclo[3.2.1]-2-octene (13) (Method A). **7a** (700 mg, 2.8 mmol) was dissolved in CH_2Cl_2 (30 mL). A nitrogen atmosphere was established, and the solution was cooled down to −78 °C. BF_3·Et_2O (1 mL, 8.1 mmol) was added with a syringe, and the reaction mixture was allowed to stir at −78 °C for 1.5 h. The temperature was then allowed to rise slowly to room tempereature during 20 h, and the reaction mixture was poured into a mixture of CH_2Cl_2 (50 mL) and water (20 mL). The phases were separated, and the organic phase was filtered through a short plug of silica gel. Drying ($MgSO_4$) and evaporation gave 700 mg of crude product. This was purified by flash chromatography (EtOAc/hexane 20/80), leaving 422 mg (60%) of pure **13**: mp 88–90 °C; IR ($CDCl_3$) 3060, 2954, 2860, 1713, 1447, 1316, 1158 cm^{-1}; ^{1}H NMR δ 7.81–7.75 (m, 2H), 7.60–7.44 (m, 3H), 7.11 (dt, J = 4.5, 2 Hz, 1H), 4.67–4.60 (br t, J = 5 Hz, 1H), 4.56 (br t, J = 6.5 Hz, 1H), 2.54 (dd, J = 17.5, 7.5 Hz, 1H), 2.13–1.85 (m, 4H), 1.60–1.48 (m, 1H); ^{13}C NMR δ 140.7, 138.5, 136.5, 133.4, 129.2, 128.0 , 72.6, 72.4, 34.4, 32.1, 29.3. Anal. Calcd for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64. Found: C, 62.26; H, 5.58.

1-Methyl-3-(phenylsulfonyl)-8-oxabicyclo[3.2.1]-2-octene (14): 50% yield; IR (CCl_4) 3072, 2978, 2872, 1708, 1449, 1378, 1314, 1155, 1126, 1090 cm^{-1}; ^{1}H NMR δ 7.85–7.77 (m, 2H,), 7.63–7.47 (m, 3H), 7.04–7.00 (m, 1H), 4.65–4.56 (m, 1H), 2.51 (dm, J = 17 Hz, 1H), 2.25–2–10 (m, 2H), 2.01 (d, J = 17 Hz, 1H), 1.75–1.50 (m, 2H), 1.47 (s, 3H); ^{13}C NMR δ 143.5, 138.6, 136.5, 133.4, 129.2, 127.9, 78.4, 73.4, 41.1, 31.7, 30.6, 22.1.

3-(Phenylsulfonyl)-9-oxabicyclo[3.3.1]-2-nonene (15): 35% yield; IR ($CDCl_3$), 3060, 2931, 2860, 1725, 1447, 1305, 1155 cm^{-1}; ^{1}H NMR δ 7.91–7.85 (m, 2H), 7.64–7.50 (m, 3H), 7.07 (dt, J = 4.5, 2 Hz, 1H), 4.57 (br t, J = 4.5 Hz, 1H), 4.25 (br t, J = 6 Hz, 1H), 2.56 (dd, J = 18, 7.5, Hz, 1H), 2.12 (d, J = 18 Hz, 1H), 2.00–1.85 (m, 2H), 1.70–1.42 (m, 4H); ^{13}C NMR δ 139.6, 138.7, 138.6, 133.5, 133.5, 129.2, 128.1, 67.4, 31.5, 26.9, 26.9, 14.8. Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.01; H, 6.10. Found: C, 63.38; H, 5.97.

1,2-Methylene-2-(phenylsulfonyl)cyclohexane-4-one (16). The reaction was carried out in the same way as the BF_3-promoted rearrangement of **7a** to **13**. A 200 mg amount of **7b** gave 90 mg (45%) of **16** after flash chromatography (EtOAc/hexane = 50/50): IR ($CDCl_3$) 3064, 2938, 2875, 1715, 1449, 1417, 1350, 1309, 1151, 1092 cm^{-1}; ^{1}H NMR δ 7.85–7.79 (m, 2H), 7.69–7.51 (m, 3H), 2.92 (dd, 1/2 AB, J = 18, 1.5 Hz, 1H), 2.53 (d, 1/2 AB, J = 18 Hz, 1H), 2.37–2.17 (m, 3H), 2.12–1.95 (m, 2H), 1.78 (ddd, J = 10, 6, 1.5 Hz, 1H), 0.99 (t, J = 6 Hz, 1H); ^{13}C NMR δ 206.4, 137.6, 133.8, 129.3, 128.5, 39.6, 38.1, 34.8, 19.9, 17.5, 15.0. Anal. Calcd for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64. Found: C, 62.21; H, 5.55.

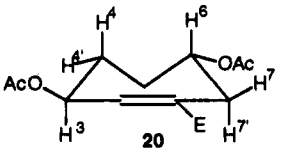
***t*-1,2-Methylene-*r*-2-(phenylsulfonyl)-*c*-4-methylcyclohexan-3-one (17).** The reaction was carried out in the same way as the BF_3-promoted rearrangement of **7a** to **13**. A 100 mg amount of **8b** gave 58 mg (58%) after flash chromatography (EtOAc/hexane = 30/70): IR ($CDCl_3$) 3072, 2966, 2931, 2872, 1702, 1449, 1349, 1308, 1192, 1152, 1073 cm^{-1}; ^{1}H NMR δ 8.00–7.94 (m, 2H), 7.66–7.49 (m, 3H), 2,85–2.76 (tdm, J = 6.5, 3.5 Hz, 1H), 2.18–2.01 (m, 3H), 1.78 (dd, J = 9.5, 6 Hz, 1H), 1.76–1.70 (m, 1H), 1.50 (br t, J = 6.5 Hz, 1H, 1.26 (br qd, J = 13, 6 Hz, 1H), 1.03 (d, J = 7 Hz, 3H); ^{13}C NMR δ 202.0, 140.2, 133.4, 129.2, 128.7, 50.1, 43.8, 24.8, 22.7, 21.0, 15.1, 15.0. Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10. Found: C, 63.47; H, 6.03.

3-(Phenylsulfonyl)-8-oxabicyclo[3.2.1]-2-octene (13) (Method B). **7a** (101 mg, 0.40 mmol) was dissolved in toluene (5 mL). $LiClO_4$ (150 mg, 1.41 mmol) was added. The reaction mixture was heated at reflux for 23 h. After cooling, the toluene was evaporated and the residue dissolved in CH_2Cl_2 (15 mL) and water (15 mL). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (15 mL). The combined organic phases were dried ($MgSO_4$), and the solvent was evaporated affording a residue of 100 mg. After flash chromatography (EtOAc/hexane = 20/80) 47 mg (47 %) of **13** remained.

***trans*-3,6-Diacetoxy-1-(phenylsulfonyl)-1-cycloheptene (20). 1,2-Cyclopropyl-3,4-diacetoxy-2-(phenylsulfonyl)cyclohexane (21).** **7a** (200 mg, 0.80 mmol) and Ac_2O (1.0 mL, 10.2 mmol) was dissolved in CH_2Cl_2 (10mL) and cooled down to −78 °C. BF_3·Et_2O (300 μL, 2.4 mmol) was added, and the reaction mixture was allowed to warm slowly to room temperature during 13 h. K_2CO_3 (sat, 15 mL) was added, and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic phases were dried ($MgSO_4$) and evaporated. In the crude product (260 mg) **20** and **21** were present in a ratio of ~5:1. Flash chromatography (EtOAc/hexane = 30/70) failed to separate the two products, but yielded a purified mixture (160 mg, 56%) of **20** and **21** in a ratio of ~8:1. After a change of flash solvent to Et_2O/pentane = 65/35 a pure sample of **20** was obtained.

IR ($CDCl_3$) 3060, 2954, 2861, 1737, 1449, 1367, 1320, 1308, 1237, 1155, 1078, 1032 cm^{-1} ; ^{1}H NMR δ 7.89–7.83 (m, 2H), 7.68–7.52 (m, 3H), 7.24–7.20 (m, 1H), 5.51–5.42 (m, 1H), 4.47–4.36 (m, 1H), 2.73 (br d, 1/2 AB, J = 15.5 Hz, 1H), 2.52 (ddt, 1/2 AB, J = 15.5, 10, 1.5 Hz, 1H), 2.20–2.05 (m, 1H), 2.11 (s, 3H), 1.98–1.83 (m, 1H), 1.93 (s, 3H), 1.83–1.68 (m, 2H); ^{13}C NMR δ 170.0, 169.5, 144.8, 138.3, 137.8, 133.7, 129.4, 128.3, 71.9, 69.2, 32.6, 32.3, 29.3, 21.1, 21.0.

The stereochemical assignment of **20** is based on the large value of the coupling constants for $J_{6,7'}$ and $J_{3,4}$ obtained from the ^{1}H NMR spectrum (see below).



20 E = SO_2Ph

$J_{6,7'}$ = 10 Hz, $J_{3,4}$ = 10 Hz

***c*-2-Butyl-*c*-3-(phenylsulfonyl)-*r*-8-oxabicyclo[3.2.1]-octane (24a).** *c*-2-Butyl-*t*-3-(phenylsulfonyl)-*r*-8-oxabicyclo-[3.2.1]octane (24b). **13** (200 mg, 0.80 mmol) was dissolved in dry THF (10 mL), and 220 mg (1.16 mmol) of CuI was added. A nitrogen atmosphere was established and the slurry was cooled to −78 °C. BuLi (1.6 M in hexane, 2.0 mL, 3.2 mmol) was added via syringe, and the reaction mixture was allowed to stir at −78 °C for 1 h. The cooling bath was removed and the stirring continued for 1.5 h. The reaction mixture was then quenched with saturated NH_4Cl solution (10 mL). Ether (15 mL) was added, and the phases were separated. The aqueous phase was extracted with ether (2 × 15 mL), and the combined organic phases washed with brine (2 × 15 mL). After drying ($MgSO_4$) and evaporation of the solvent, 237 mg of crude product remained. This consisted of both **24a** and **24b,** but the two isomers proved to be separable with flash chromatography (EtOAc/hexane = 20/80).

24a: 132 mg (54%); IR ($CDCl_3$) 3060, 2955, 2931, 2861, 1466, 1449, 1331, 1302, 1290, 1143, 1084, 996 cm^{-1}; ^1H NMR δ 7.90−7.85 (m, 2H), 7.68−7.52 (m, 3H,), 4.33 (br t, J = 7 Hz, 1H), 4.16 (d, J = 7 Hz, 1H), 3.00 (dt, J = 10, 3.5 Hz, 1H), 2.20−1.85 (m, 7H), 1.62−1.48 (m, 1H,), 1.42−1.29 (m, 1H), 1.20−1.02 (m, 4H), 0.76 (t, J = 7 Hz, 3H); ^{13}C NMR δ 138.5, 133.5, 129.2, 128.7, 76.5, 72.0, 60.2, 39.0, 35.6, 29.0, 28.9, 28.9, 27.1, 22.4, 13.9. Anal. Calcd for $C_{17}H_{24}O_3S$: C, 66.20; H, 7.84. Found: C, 65.93, H, 7.68.

24b: 63 mg (26%); IR ($CDCl_3$) 3072, 2954, 2931, 2872, 1467, 1449, 1308, 1149, 1085, 985 cm^{-1}; ^1H NMR δ 7.88−7.83 (m, 2H), 7.67−7.50 (m, 3H), 4.46−4.37 (m, 2H), 3.31 (dt, J = 13, 4 Hz, 1H), 2.23 (td, J = 13, 3.5 Hz, 1H), 2.06−1.79 (m, 5H), 1.62−1.13 (m, 7H), 0.90 (t, J = 7 Hz, 3H); ^{13}C NMR δ 139.4, 133.5, 129.1, 128.3, 75.8, 73.6, 58.7, 40.1, 29.4, 28.4, 28.2, 28.0, 25.2, 22.6, 14.1. Anal. Calcd. for $C_{17}H_{24}O_3S$: C, 66.20; H, 7.84. Found: C, 65.97; H, 7.99.

***c*-2-Butyl-*r*-8-oxabicyclo[3.2.1]octane (25).** A crude mixture of **24a** and **24b** (210 mg, 0.68 mmol) was dissolved in a dry mixture of MeOH (3 mL) and THF (3 mL), and the solution was cooled on an ice bath. Na_2HPO_4 (378 mg, 2.66 mmol) and freshly prepared Na(Hg) (6% Na, 378 mg, 2.2 mmol Na) were added quickly and a nitrogen atmosphere was established. The reaction mixture was stirred for 19 h. During this time the temperature was allowed to slowly increase to room temperature. The reaction mixture was filtered through Celite, which was then thoroughly washed with ether. Water (10 mL) was added, and the two phases were separated. The aqueous phase was extracted with ether (2 × 15 mL), and the combined organic phases were washed with brine (2 × 15 mL). After drying ($MgSO_4$) and evaporation, 97 mg of crude **25** remained. After flash chromatography (ether/pentane = 20/80), 70 mg (72%) of **25** was isolated: IR ($CDCl_3$) 2941, 2876, 2858, 1467, 1453, 1230, 1007, 980 cm^{-1}; ^1H NMR δ 4.32−4.25 (m, 1H), 4.13 (br d, J = 7 Hz, 1H), 2.04−1.55 (m, 7H), 1.51−1.10 (m, 8H), 0.89 (m, app t, J = 7 Hz, 3H); ^{13}C NMR δ 78.0, 75.2, 39.5, 31.1, 30.1, 29.3, 27.8, 27.7, 22.9, 20.0, 14.1.

***c*-2-Hydroxy-*r*-8-oxabicyclo[3.2.1]octane-3-one (26). 13** (305 mg, 1.22 mmol) was dissolved in water (3 mL) and acetone (3 mL). OsO_4 (2.5% in *t*-BuOH, 83 mg, 8.16 μmol) and *N*-methylmorpholine *N*-oxide (427 mg, 3.64 mmol) were added. After 45 h of stirring at room temperature, saturated $NaHSO_4$ (10 mL) was added. After 30 min of stirring, this mixture was filtered through Celite which was then thoroughly washed with acetone. The resulting solution was acidified with concentrated H_2SO_4, and the acetone was evaporated. The aqueous residue was extracted with EtOAc (5 × 15 mL), the combined organic phases were dried (Na_2SO_4), and the solvent was evaporated yielding 120 mg of crude product. This was subjected to flash chromatography (EtOAc/hexane = 50/50) giving 99 mg (57%) of **26** as a clear oil which turned into a white gum upon standing: IR ($CDCl_3$) 3577, 3409, 2958, 2917, 2885, 1725, 1468, 1379, 1321, 1222, 1075 cm^{-1}; ^1H NMR δ 4.67 (t, J = 5.5 Hz, 1H), 4.53 (d, J = 7.5 Hz, 1H), 3.59 (d, J = 8.5 Hz, 1H), 3.43 (d, J = 8.5 Hz, 1H), 3.02 (dd, J = 15.5, 5.5 Hz, 1H), 2.15 (d, J = 15.5 Hz, 1H), 2.10−1.92 (m, 2H), 1.72−1.52 (m, 2H); ^{13}C NMR 206.4, 79.3, 76.6, 75.0, 46.2, 28.1, 24.2.

2-(*cis*-2-Formyltetrahydrofuran-5-yl)acetic acid (27). **26** (100 mg, 0,70 mmol) was dissolved in methanol (3 mL) and pH 7 phosphate buffer (3 mL). $NaIO_4$ (159 mg, 0.74 mmol) was added, and the reaction mixture was allowed to stir at room temperature for 15 h. It was then diluted with water (15 mL) and extracted with EtOAc (8 × 10 mL). The combined organic phases were dried (Na_2SO_4), and the solvent was evaporated, giving 65 mg (58%) of **27**: ^1H NMR δ 9.68 (d, J = 2 Hz, 1H) 4.53−4.41 (m, 1H), 4.40−4.33 (m, 1H), 2.72 (dd, 1/2 AB, J = 10, 4.5 Hz, 1H), 2,62 (dd, 1/2 AB, J = 10, 3.5 Hz, 1H), 2.27−2.07 (m, 3H), 1.15−1.02 (m, 1H); ^{13}C NMR δ 202.4, 176.0, 83.2, 76.8, 40.1, 30.7, 27.4. Due to its instability, this compound was charactarized by NMR only.

***c*-2,3-Epoxy-*t*-3-(phenylsulfonyl)-*r*-8-oxabicyclo[3.2.1]-octane (28). 13** (250 mg, 1.0 mmol) was dissolved in MeOH (5 mL). H_2O_2 (30% in water, 300 μL, 3 mmol) was added, followed by 2 M NaOH (0.5 mL, 1 mmol). After 15 h the reaction mixture was poured into ether (10 mL) and water (10 mL). The phases were separated, and the aqueous phase was extracted with ether (3 × 15 mL). The combined organic phases were dried ($MgSO_4$), and the solvent was evaporated affording 227 mg of crude **28**. After flash chromatography (EtOAc/hexane = 30/70) 200 mg (75%) of pure **28** remained: mp 109−110 °C; IR (CCl_4) 3060, 2966, 2884, 1449, 1331, 1161, 1126, 1084, 1055 cm^{-1}; ^1H NMR δ 7.92−7.83 (m, 2H), 7.72−7.52 (m, 3H), 4.54 (d, J = 5.5 Hz, 1H), 4.36 (tm, J = 8 Hz, 1H), 3.58 (s, 1H), 2.22 (d, J = 15 Hz, 1H), 2.20−1.95 (m, 4H), 1.85−1.70 (m, 1H); ^{13}C NMR δ 135.5, 134.4, 129.3, 129.2, 70.9, 70.8, 67.7, 55.6, 30.2, 27.7, 26.8. Anal. Calcd for $C_{13}H_{14}O_4S$: C, 58.63; H, 5.30. Found: C, 58.54; H, 5.22.

Acknowledgment. The Swedish Natural Science Research Council is gratefully acknowledged for financial support. We thank Professor Paul Helquist and Docent David Tanner for valuable scientific discussions and Docent Adolf Gogoll for assistance with structural elucidation problems.

Supplementary Material Available: ^1H NMR spectrum of compound **8b**, ^{13}C NMR spectra of compounds **5**, **8a**, **9a**, **14**, **20**, **25**, **26** and **27** (11 pages). This material is contained in libraries on microfiche, immediatley follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO941574N