Chemical Consequences of Long-Range Orbital Interactions in Norbornane-1,4-diol Monosulfonate Esters

Petrus M. F. M. Bastiaansen, Joannes B. P. A. Wijnberg,* and Aede de Groot*

Laboratory of Organic Chemistry, Agricultural University, Dreijenplein 8, 6703 HB Wageningen, The Netherlands

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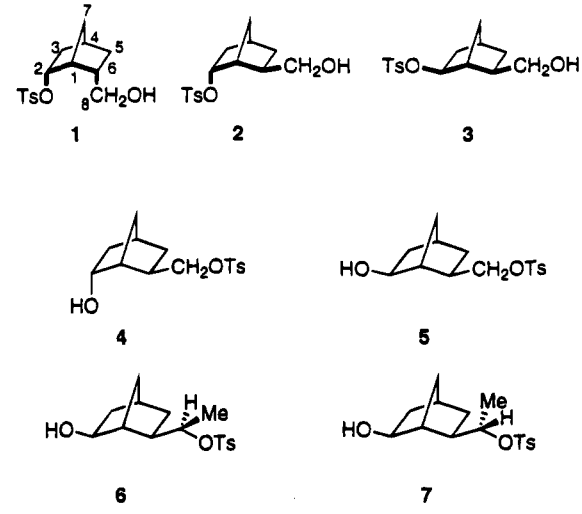
Seven monotosylated 1,4-diols with the rigid norbornane skeleton were treated with a strong base in refluxing benzene to find out whether these compounds react by initial heterolysis of the tosylate ester bond induced by long-range orbital interactions. The tosylates **1**–**7** were designed to investigate the influence of the σ-relay (U-, sickle-, or W-shaped) between the donor and acceptor end of the system, to check whether primary carbocationic ion pairs could act as intermediates, and to study conformational influences on reactivity and product formation. Tosylate **1** with a U-like arrangement of the σ-relay reacted relatively slowly and followed reaction pathways in which no long-range orbital interactions are involved. The reaction outcome of tosylate **2** which possesses a sickle-like arrangement of the σ-relay indicates two competitive processes with and without the involvement of long-range orbital interactions. The secondary tosylates **3**, **6**, and **7** which all possess a W-like arrangement reacted relatively fast and showed predominantly homofragmentation. Although an ideal W-like arrangement is present in the primary tosylates **4** and **5**, no reactions in which long-range orbital interactions are involved were observed. The tosylates **6** and **7** in which the tosylate group is conformationally mobile can give rise to mixtures of products. The ratio in which these products are formed can be rationalized by using the Curtin–Hammett principle.

Introduction

From our previous work on the total synthesis of sesquiterpenes,[1,2] it is known that monosulfonate esters of rigid *trans*-perhydronaphthalene-1,4-diols react smoothly upon treatment with sodium *tert*-amylate in refluxing apolar solvents like benzene or toluene. Long-range orbital interactions are thought to play an important role in these reactions. The theoretical basis for these orbital interactions through bonds (TBI) and through space (TSI), first described by Hoffmann,[3] is well-established by theoretical and experimental studies.[4]

The reactivity of these rigid *trans*-perhydronaphthalene-1,4-diol monosulfonate esters under strongly basic conditions depends on (i) the orientation and position of the sulfonate ester group[5,6] and (ii) the position of the hydroxyl function relative to the sulfonate ester group.[6] The orientation of the hydroxyl group has little or no influence on the reactivity. The extent of the orbital interactions as well as the product composition is strongly determined by the geometry of the relaying σ-bonds between the electron donor (alcoholate) and the electron acceptor (sulfonate ester bond). Homofragmentation, β-elimination, and rearrangement are the main processes observed.

Chart 1



These findings needed confirmation for other rigid 1,4-diol monosulfonate esters. Therefore, we decided to examine the 1,4-diol monotosylate esters **1**–**7** all with a rigid norbornane skeleton (Chart 1). Compared with other rigid systems, these compounds have several advantages: (i) They possess a well-defined geometry of the relaying σ-bonds between the electron donor and the electron acceptor, (ii) their synthesis is not very complicated, and (iii) C(6)-substituted 2-norbornyl sulfonate esters[7] have been extensively studied by Grob et al.,[8] so the spectral and physical data of their products might facilitate the structural assignments of the products found in this study.

As indicated in Chart 1 by the bold bonds, the tosylates **1**, **2**, and **3** all have a different geometry of the σ-relay:

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

(1) Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; Brunekreef, G. A.; de Groot, A. *J. Org. Chem.* **1990**, *55*, 941.

(2) Jenniskens, L. H. D.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1991**, *56*, 6585.

(3) Hoffmann, R.; Imamura, A.; Hehre, W. J. *J. Am. Chem. Soc.* **1968**, *90*, 1499.

(4) For example, see: (a) Hoffmann, R. *Acc. Chem. Res.* **1971**, *4*, 1. (b) Gleiter, R. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 696. (c) Martin, H. D.; Mayer, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 283. (d) Paddon-Row, M. N.; Jordan, K. D. In *Modern Models of Bonding and Delocalization;* Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: New York, 1988; Chapter 3.

(5) Orrū, R. V. A.; Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; de Groot, A. *J. Org. Chem.* **1993**, *58*, 1199.

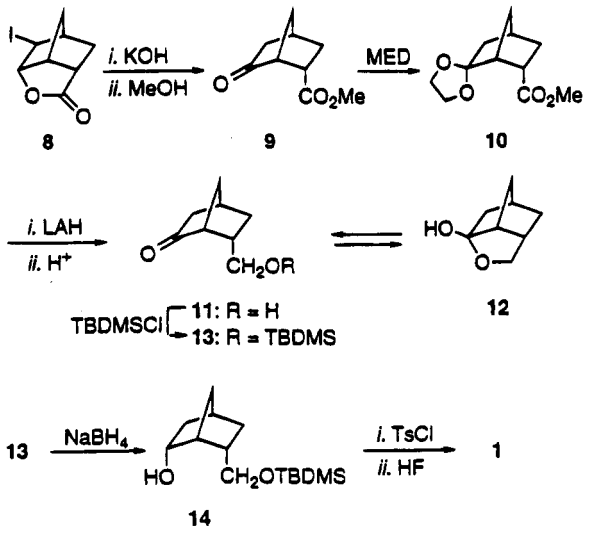
(6) Orrū, R. V. A.; Wijnberg, J. B. P. A.; Bouwman, C. T.; de Groot, A. *J. Org. Chem.* **1994**, *59*, 374.

(7) The numbering system as given in structure **1** will be followed throughout the text of this paper.

(8) For example, see: Grob, C. A. *Angew. Chem.* **1982**, *94*, 87 and references cited therein.

0022-3263/95/1960-4240$09.00/0

Scheme 1



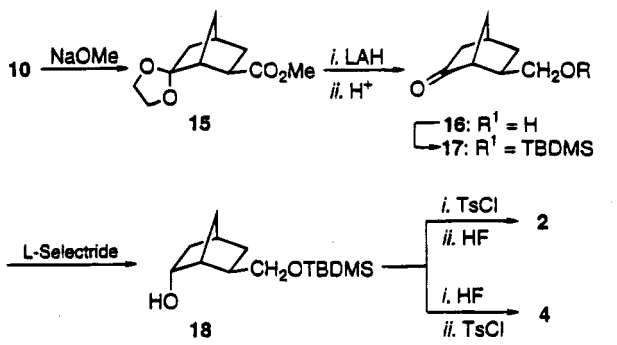
the U-, the sickle-, and the W-like arrangement, respectively. From the reactions of **1**–**3** with sodium *tert*-amylate in refluxing benzene, we expect to obtain information about the influence of these different geometries on the transmission of charge via orbital interactions in these compounds. The reactions of the tosylates **4** and **5** were performed to determine whether the alkoxide function is capable of inducing heterolysis of a primary sulfonate ester group through three intervening C–C bonds. In addition to **4** and **5**, the corresponding secondary tosylates **6** and **7** were also investigated for obvious reasons (primary vs secondary sulfonate esters). Furthermore, the tosylate group of the compounds **4**–**7** can rotate freely about the C(6)–C(8) bond. Therefore, from the experiments with **4**–**7**, we also expect to gather information about the chemical consequences of rotational freedom in these processes.

Results and Discussion

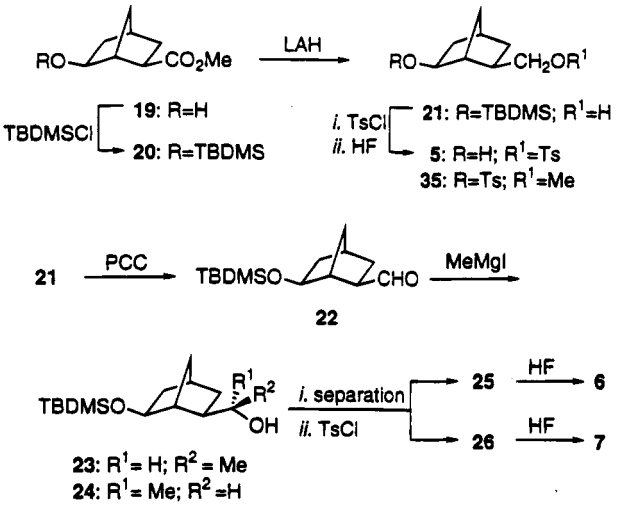
The tosylate **1** was prepared from the readily available iodo lactone **8**. Via a modified version of a known procedure, **8** was converted into the keto ester **9**[9] (Scheme 1). Protection of the keto group as its ethylene acetal (**9** → **10**) was successively followed by reduction and hydrolysis to give the keto alcohol **11**. The ^{13}C NMR spectral data of **11** show the presence of lactol **12** in about 40%. Probably, the keto alcohol **11** exists in equilibrium with its cyclic hemiacetal form **12**. Treatment of this equilibrium mixture with TMSCl in pyridine at 0 °C afforded a mixture of the corresponding silyl ethers. On the other hand, the use of the more bulky TBDMSCl in combination with imidazole in DMF at room temperature afforded selectively the silyl ether **13**. Apparently, TBDMSCl reacts only with the primary hydroxyl group of **11** and not with the tertiary one of **12**. Reduction of **13** with $NaBH_4$ gave the endo alcohol **14** as the sole product. Further transformation of **14** to the tosylate **1** was performed according to standard procedures. In this respect, it should be mentioned that the tosylation of **14** required an elevated temperature (80 °C). With iodo lactone **8** as starting material, the overall yield of **1** amounted to 16%.

The ethylene acetal **10** was also used in the synthesis of the known tosylate **2**.[10] Epimerization of the endo ester group in **10** to the exo position was achieved with NaOMe in dry MeOH to give the exo ester **15** in 62% yield (Scheme 2).

Scheme 2



Scheme 3



In an analogous fashion as outlined above, i.e., **15** → **16** → **17** → **18** → **2**, the exo ester **15** gave the tosylate **2** in an overall yield of 53%. In this reaction sequence, L-Selectride (Aldrich) was used instead of $NaBH_4$ because the reduction of **17** with $NaBH_4$ produced an inseparable mixture of the endo and exo alcohol. The endo alcohol **18** was also converted into the known tosylate **4**[11] according to standard procedures (overall yield 41%).

The tosylate **3** was synthesized according to a known procedure.[12] An intermediate in this synthesis, i.e., hydroxy ester **19**, was used as starting material in the preparation of the tosylates **5**–**7** (Scheme 3). After protection of the hydroxyl group of **19**, reduction of the resulting silyl ether **20** gave the primary alcohol **21** in high yield. Tosylation and desilylation of **21** afforded the tosylate **5** in 68% overall yield from **19**. Oxidation of the primary alcohol function in **21** with PCC produced the aldehyde **22**. Treatment of this aldehyde with an excess of MeMgI in dry ether at 0 °C afforded a 1:1 mixture of the diastereoisomeric secondary alcohols **23** and **24**. After separation by column chromatography, both alcohols were tosylated to give the compounds **25** and **26**. Finally, desilylation of the latter two compounds provided the tosylates **6** and **7** in overall yields of 31 and 33%, respectively, from **19**.

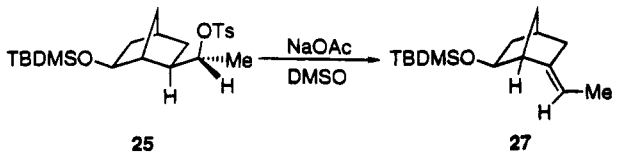
(9) Nakazaki, M.; Naemura, K.; Kondo, Y. *J. Org. Chem.* **1976**, *41*, 1229.

(10) Fischer, W.; Grob, C. A.; von Sprecher, G.; Waldner, A. *Helv. Chim. Acta* **1980**, *63*, 816.

(11) Menger, F. M.; Chow, J. F.; Kaiserman, H.; Vasquez, P. C. *J. Am. Chem. Soc.* **1983**, *105*, 4996.

(12) Fischer, W.; Grob, C. A.; von Sprecher, G. *Helv. Chim. Acta* **1980**, *63*, 806.

Scheme 4



25 27

Table 1. Reactions of the Tosylates 1–7 with Sodium *tert*-Amylate[a]

entry	tosylate	reaction time[b]	products[c] (%)	recovery[d]
1	**1**	10	**28** (22) + **29** (22) + **30** (12)	15
2	**2**	10	**31** (19) + **32** (4)	21
3	**3**	1	**31** (78)[e] + **33** (3)[e]	0
4	**4**	10	**36** (28)[e]	4
5	**5**	10	[f]	48
6	**5**	1	**16** (5) + **37** (5) + **38** (3)	72
7	**6**	1	**39** (51)[g]	0
8	**7**	1	**40**, **41**, and **42**[h] (42)[g] + **43** (6)	24
9	**7**	1	**40** (53) + **43** (11)	12

[a] All reactions were performed in refluxing benzene with ca. 5 equiv of sodium *tert*-amylate, except for entry 9 in which ca. 5 equiv of sodium *tert*-amylate and 1 equiv of 15-crown-5 were used. [b] Reaction time in min. [c] Isolated yield in parentheses. [d] Percentage of recovered starting material. [e] Yield was determined with capillary GC using ethylbenzene as an internal standard. [f] Complex product mixture. [g] Yield is somewhat diminished due to aldol condensations under the influence of sodium *tert*-amylate. [h] These compounds were obtained in a ratio of 15:4:1, respectively.

The *R*- and *S*-configuration of **6** and **7**, respectively, followed from a thermodynamically controlled elimination experiment in which the protected tosylate **25** was treated with NaOAc in DMSO[13,14] (Scheme 4). The geometry of the elimination product **27** was ascertained by ^{1}H NOE difference spectroscopy. Irradiation of the multiplet for the olefinic H at δ 5.36 gives a strong NOE with H-1 at δ 2.48; no NOE was observed between the methyl group and H-1. These data are consistent with the structural assignment for **27**. Since this elimination is assumed to proceed in an anti fashion, tosylate **6** must have the *R*-configuration at C(8), and consequently, tosylate **7** will have the *S*-configuration.

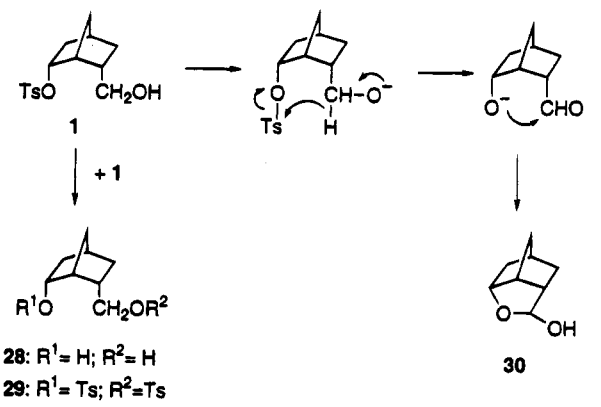
In order to obtain comparable data about the reactivity of the tosylates **1**–**7**, all these compounds were subjected to standard reaction conditions. The reactions were run in benzene at reflux temperature with ca. 5 equiv of sodium *tert*-amylate. Depending on the reaction rate, a reaction time of 1 or 10 min was maintained. By comparing the quantities of recovered starting material, a rough estimate of the relative reaction rates could be obtained. The results of these studies are collected in Table 1.

The reactions of the tosylates **1**–**3** were performed to investigate the influence of the geometry of the relaying σ-bonds between the hydroxyl and the tosylate group on the reaction rate and product composition.

The tosylate **1** gave a mixture of three compounds: diol **28** (22%), ditosylate **29** (22%), and lactol **30** (12%) (entry 1). The quantity of regained starting material after 10 min reaction time amounted to 15%.

Treatment (10 min) of the tosylate **2** afforded nortricyclene **31** (19%), together with a small amount of the ditosylate **32** (4%) and recovered **2** (21%) (entry 2). Because of the high volatility of nortricyclene, the isolation of this compound from the reaction mixture was troublesome. Therefore, the yield and identity of nortricyclene were determined in the crude extract by means of capillary GC using ethylbenzene as internal standard and GC/MS analysis, respectively. For that purpose, an authentic sample of nortricyclene was prepared according to a known procedure.[15]

Scheme 5



No starting tosylate **3** was recovered from the reaction even in 1 min runs (entry 3). On the basis of GC analysis, the major product was nortricyclene (**31**) (78%). A small amount (3%) of the known cyclic ether **33**[16] was also formed. It should be noted that tosylate **3** entirely reacted at room temperature within 10 min to yield **31** (55%) and **33** (6%). On the other hand, the reactivity of the methyl ether **35**[17] of tosylate **3** was extremely low. Under the standard conditions, this compound did not give any detectable reaction product and was regained almost quantitatively. This proves again that the presence of a free hydroxyl group is crucial in these reactions. It is also noteworthy that all attempts to obtain the TBDMS ether of tosylate **3** in pure form via column chromatography on silica gel failed because its silyl ether bond appeared to be very sensitive to hydrolysis. The silyl ether bonds in other TBDMS ethers, for instance in the TBDMS ether of tosylate **2**, were much more stable to hydrolysis.[18]

These results clearly show that the reaction rate of the tosylates **1**–**3** strongly depends on the geometry of their σ-relays. The tosylates **1** and **2** with a U- and sickle-like arrangement, respectively, react very slowly compared with tosylate **3** which possesses a W-like arrangement. The question arises, however, whether the tosylates **1**–**3** all react according to a mechanism in which orbital interactions control their reactivity and product composition. Especially in case of tosylate **1**, everything points to ordinary intra- and intermolecular substitution reactions without any participation of TBI or other long-range orbital interactions (Scheme 5). The formation of diol **28** and ditosylate **29** can easily be explained by an intermolecular nucleophilic reaction between two molecules of **1** via an attack of the primary alkoxide of one molecule on the tosylate sulfur atom of the other.[19] The formation of lactol **30** probably proceeds via an intramolecular

(13) Bartsch, R. A.; Read, R. A.; Larsen, D. T.; Roberts, D. K.; Scott, K. J.; Rae Cho, B. B. A. *J. Am. Chem. Soc.* **1979**, *101*, 1176.

(14) The ^{1}H NMR data and GC analysis of olefin **27** revealed the presence of the TBDMS ether of **43** (ca. 5%).

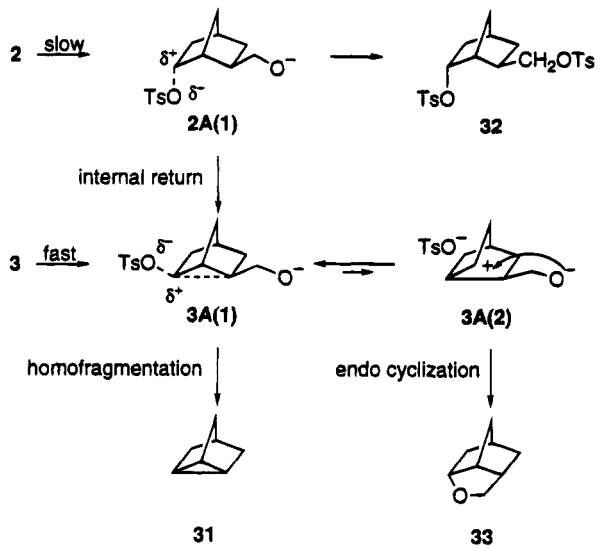
(15) Roberts, J. D.; Trumbell, E. R.; Bennet, W.; Armstrong, R. *J. Am. Chem. Soc.* **1950**, *72*, 3116.

(16) An authentic sample of the cyclic ether **33** was prepared following a previously described procedure.[9]

(17) The O-methylated tosylate **35** was obtained by treatment of the primary alcohol **21** with NaH and MeI in dry DMF to give the corresponding methyl ether **34**, followed by cleavage of the silyl ether bond and tosylation (see Experimental Section).

(18) We assume that orbital interactions are responsible for the remarkable instability of the silyl ether bond in the TBDMS ether of tosylate **3**.

Scheme 6

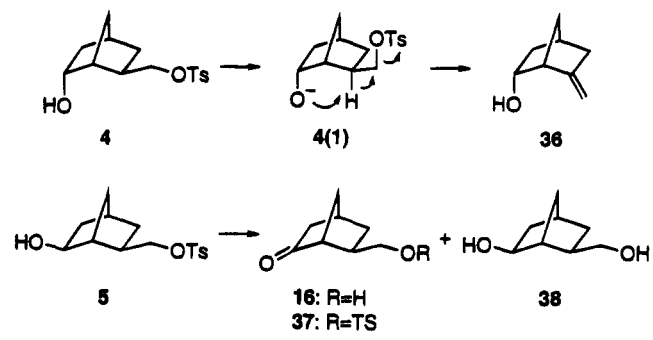


hydride transfer from C(8) bearing the alkoxide function to the sulfur atom of the tosylate group.[20] This results in the cleavage of the S–O bond to give an intermediate oxygen anion which then cyclizes to lactol **30**.

The reaction outcome of tosylate **2** indicates two competitive processes (Scheme 6). One involves the intramolecularly induced heterolysis of the tosylate group to form nortricyclene (**31**); the other, leading to ditosylate **32**, must proceed intermolecularly in a similar way as described above for the formation of **29** from tosylate **1**. In the heterolysis step of **2**, σ-participation is not very likely because no C–C bond is antiperiplanar to the tosylate ester bond.[21] A similar stereochemical requirement (no C–H bond antiperiplanar to the C–OTs bond) prevents σ-(C–H) participation. As a consequence, the heterolysis of tosylate **2** induced by orbital interactions will be relatively slow and intermolecular processes in which no long-range orbital interactions are involved can compete successfully with the homofragmentation pathway leading to **31**. The formation of **31** from **2** probably proceeds via an internal return with inversion of the stereochemistry of the tosylate group at C(2).[5] Because all reactions are performed in benzene, contact ion pairs are most likely involved in the intramolecularly induced departure of the tosylate group. In the contact ion pair **2A(1)**, 1,3-bridging is inhibited by the tosylate anion that is located on the endo side.[22] Internal return can lead to the more stable bridged intermediate **3A(1)** which subsequently homofragments into **31** and formaldehyde. Unfortunately, it is not possible to demonstrate this internal return (**2** → **2A(1)** → **3A(1)** → **3**) because tosylate **3** reacts extremely fast under the influence of sodium *tert*-amylate (vide infra).

The high reactivity of tosylate **3** and the selective formation of nortricyclene **31** observed for the reaction of **3** can be attributed to the fast formation of intermediate **3A(1)** as a result of a combined action of TBI, σ-participation, and 1,3-bridging.[6] The formation of a small amount of cyclic ether **33** in this reaction suggests

Scheme 7



that, when **3A(1)** is formed, some of it rearranges to give **3A(2)** before it can collapse to **31**. Endo cyclization[23] of the unbridged intermediate **3A(2)** will give **33**. The simultaneous occurrence of homofragmentation and rearrangement in this reaction also suggests that homohyperconjugation[24,25] in these norbornane systems is somewhat less effective than in the corresponding *trans*-perhydronaphthalene derivatives.[26]

In order to determine whether an alcoholate function can intramolecularly induce the heterolysis of a primary sulfonate ester group through three intervening C–C bonds, the tosylates **4** and **5** were treated with sodium *tert*-amylate in refluxing benzene for 10 min. After reaction of tosylate **4**, the known olefinic alcohol **36**[11] (28%) was the only detectable product. A small amount (4%) of starting material **4** was recovered (entry 4). The determination of the yield and identity of the relatively volatile **36** was performed in a manner identical to that of nortricyclene. A complex mixture of (decomposition) products and a relatively large amount (48%) of unreacted starting material was obtained from the reaction with tosylate **5** (entry 5). A reaction time of 1 min provided more information about the course of this reaction. After workup, small amounts of the carbonyl compounds **16** (5%) and **37** (5%) and the diol **38** (3%) could be isolated in addition to 72% of the starting material (entry 6).[27]

The formation of olefinic alcohol **36** from tosylate **4** is most likely the result of an anti E2 mechanism in which the 2-*endo*-alcoholate acts as an intramolecular catalyst[11] as depicted by structure **4(1)** (Scheme 7). In tosylate **5** with the hydroxyl group in the exo position, such an intramolecular catalysis is not possible and, therefore, **5** will react more slowly than **4** (entries 4 and 5). It is very much open to question whether orbital interactions through the intervening C–C bonds participate in the reactions of **4** and **5** because none of the products which resulted from the 1 min reaction of tosylate **5** (entry 6) can be explained with initial heterolysis of the sulfonate ester bond. The formation of the ketones **16** and **37** must be attributed to an alkoxide-induced intermolecular hydride shift,[28] while S–O bond cleavage by either a hydride or an alkoxide attack on the sulfur atom of the tosylate group in **5** accounts for the formation of diol **38**.

(19) Competing S–O bond scission often occurs upon treatment of tosylate esters with O-nucleophiles. For example, see: Netscher, T. *Tetrahedron Lett.* **1988**, *29*, 455.

(20) It is also possible that S–O bond scission occurs by an intermolecular alkoxide attack[19] instead of an intramolecular hydride attack.

(21) Fischer, W.; Grob, C. A.; von Sprecher, G.; Waldner, A. *Tetrahedron Lett.* **1979**, 1905.

(22) Grob, C. A. *Acc. Chem. Res.* **1983**, *16*, 426.

(23) Fischer, W.; Grob, C. A.; Hanreich, R.; von Sprecher, G.; Waldner, A. *Helv. Chim. Acta* **1981**, *64*, 2298.

(24) Adcock, W.; Kok, G. B. *J. Org. Chem.* **1987**, *52*, 356.

(25) Grob, C. A.; Gründel, M.; Sawlewitz, P. *Helv. Chim. Acta* **1988**, *71*, 1502.

(26) *trans*-Perhydronaphthalene-1,4-diol monosulfonate esters possessing the ideal W-like arrangement only show homofragmentation.[6]

(27) Similar (side) reactions can also occur with the other tosylates.

(28) Oxidation of secondary alcohols by hydride transfer under the influence of alkali–metal alkoxides in benzene has been reported in the literature. For example, see: Warnhoff, E. W.; Reynolds-Warnhoff, P. *J. Org. Chem.* **1963**, *28*, 1431.

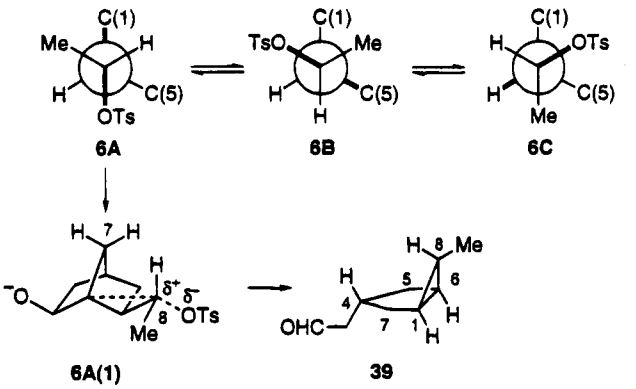
Since **4** and **5** have the same geometry of the σ-relay, it is therefore justified to conclude that orbital interactions only play a secondary role in the reactivity of both compounds. Possibly in combination with a restraining effect of free rotation about the C(6)–C(8) bond, the formation of an unstable primary carbocation at C(8) probably impedes the heterolysis of the sulfonate ester bond induced by orbital interactions in these compounds.[29]

The reactions of the secondary tosylates **6** and **7** were performed to find out whether the presence of the primary sulfonate ester group in the tosylates **4** and **5** constitutes the major obstacle for effective transmission of TBI in these compounds. A short treatment (1 min) of tosylate **6** afforded the cyclopropane derivative **39** in 51% yield as the sole product (entry 7). No starting material could be detected. It should be noted that longer reaction times diminished the yield of **39** by aldol condensation reactions.[30] The presence of a cyclopropane ring in **39** was concluded from the proton-coupled ^{13}C NMR spectrum. The signals of the tertiary cyclopropane carbon atoms appear at δ 14.01 (d, J_{CH} = 158.6 Hz) and 25.14 (2d, J_{CH} = 165.0 Hz). The stereochemistry of **39** was established by NOE-difference and 2D $^{1}H-^{13}C$ chemical shift correlation measurements. Irradiation of H-8 at δ 0.58 gives a NOE with the three-proton signal at δ 1.80–2.07. One of these protons proves to be H-4; the other two are β-H-5 and β-H-7. According to molecular mechanics calculations using the MM2(87) force field program,[31] the NOE signal probably originates from an interaction between H-4 and H-8. However, it still remains uncertain from which signal the NOE arises. Notwithstanding, these data unequivocally confirm our structural assignments for **39**.

Tosylate **7** reacted more slowly than **6**. After a reaction time of 1 min, the quantity of regained **7** amounted to 24%. As products, a 15:4:1 mixture (42%) of the three aldehydes **40**, **41**, and **42**, respectively, and the olefin **43** (6%) were obtained (entry 8). Because it was not possible to separate the mixture of aldehydes by column chromatography, analytical samples of **40**, **41**, and **42** were produced by preparative GC. In the ^{13}C NMR spectrum of **40**, the signals due to the tertiary cyclopropane carbon atoms appear at δ 13.93 (d, J_{CH} = 151.8 Hz) and 25.14 (2d, J_{CH} = 165.4 Hz). The orientation of H-8 was established by a NOE signal between this proton and the other cyclopropane protons at C(1) and C(6). Furthermore, no NOE was observed between H-8 and H-4 or between H-8 and the β protons at C(5) and C(7). Consequently, this compound possesses the stereochemistry as shown in structure **40**. More selectivity was observed when **7** was treated with a mixture of sodium *tert*-amylate and 15-crown-5 (entry 9). This reaction gave, next to recovered **7** (12%), the aldehyde **40** (53%) and the olefin **43** (11%). The other two aldehydes **41** and **42** could not be detected in the product mixture.

The results of these studies on **4**–**7** clearly show that the presence of a secondary sulfonate ester is a prerequisite for effective transmission of orbital interactions in these systems. Furthermore, it turns out from the fast reaction of **6** that the free rotation about the C(6)–C(8) bond has no significant influence on the reactivity.

Scheme 8



The formation of the homofragmentation product **39** from tosylate **6** requires an all-trans arrangement of the participating σ-bonds.[6,32] This means that the C(8)–OTs bond in **6** must adopt an orientation antiperiplanar to the C(1)–C(6) bond as indicated by the Newman projection formula **6A** along the C(6)–C(8) bond (Scheme 8). Deprotonation of **6A** will lead to the bridged intermediate **6A(1)** which can homofragment to give the aldehyde **39**.

The formation of the main aldehyde **40** from tosylate **7** proceeds analogously to that of **39** and must originate from conformation **7A** (Scheme 9). In conformation **7B**, the C(5)–C(6) bond and the C(8)–OTs bond are properly aligned (antiperiplanar) for skeletal rearrangement. The initially formed dipolar intermediate **7B(1)** rearranges to **7B(2)** which can undergo a Grob fragmentation to give the aldehyde **41**. The formation of aldehyde **42** from conformation **7C** proceeds in a similar way, i.e., via **7C-(1)** and **7C(2)**, but now a 1,2-H shift (C(6) → C(8)) precedes the Grob fragmentation. The olefin **43** is probably formed by an intermolecularly base-assisted anti elimination from the conformations **7A**–**7C** as the reaction path **7D** → **7D(1)** → **43** shows.[33,34]

Although these mechanisms provide a good explanation for the formation of these different products from **6** and **7**, no answer is given why the diastereomeric compounds **6** and **7** show differences in selectivity and reactivity. As depicted in Schemes 8 and 9, the products **39** and **40**–**42** must be derived from the staggered conformations **6A** and **7A**–**7C**, respectively, and can therefore be considered as the chemical consequences of conformational isomerism.

In order to explain the different chemical behavior of **6** and **7**, the Curtin–Hammett (C–H) principle is very useful.[35] The reaction of **6** to form **39** through conformation **6A**[36] in which the σ-relay has adopted the W-like arrangement is the only product-forming route. Consequently, the lowest energy transition state must be the one leading to the bridged intermediate **6A(1)**, assuming that heterolysis (or ion pair formation) is the rate-determining step.[1] This is consistent with the trans rule, which predicts that the extent of orbital interactions through σ-bonds is maximized for an all-trans (W-like)

(29) Menger[11] also came to the conclusion that, in the base-induced formation of **36** from (2-*endo*,6-*exo*)-6-(bromomethyl)bicyclo[2.2.1]-heptan-2-ol, "long-distance catalysis appears unlikely". The remark that "through-bond inductive effects are, in any event, attenuated by three intervening carbons" to support this conclusion is not really essential in this respect as follows from our work presented here.

(30) See ref 5 and references cited therein.

(31) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (b) The QCPE MM2(87) program was used.

(32) Paddon-Row, M. N. *Acc. Chem. Res.* **1982**, *15*, 245.

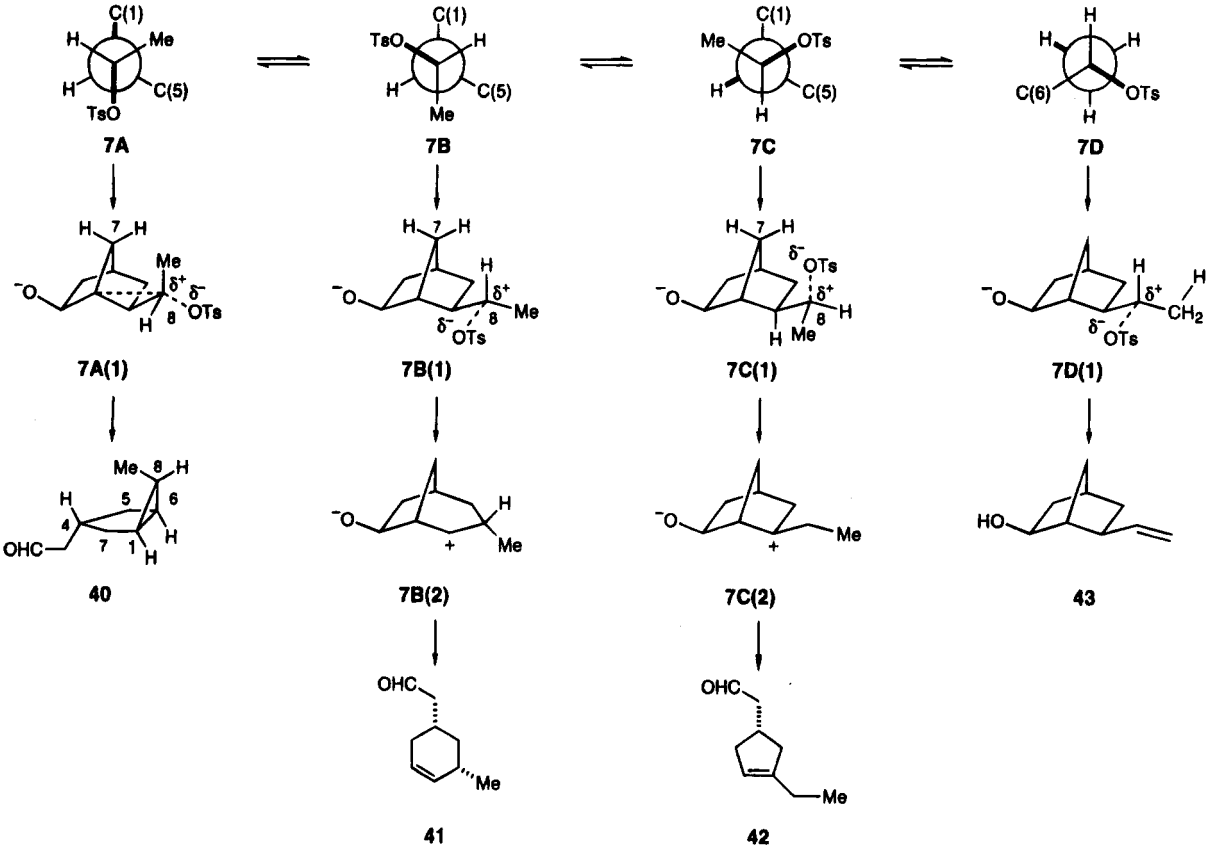
(33) The Newman projection formula **7D** is viewed along the C(8)–CH_3 bond.

(34) A minor statistical factor should also be considered as there are three equivalent conformations **7D** which may be interconverted by 120° rotation about the C(8)–CH_3 bond.

(35) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83.

(36) Because of the relatively small steric repulsion between syn H-7 and H-8, this staggered conformation is probably the most stable one.

Scheme 9



arrangement of the σ-bonds,[32] and is supported by our earlier findings.[6]

The reaction outcome of tosylate **7** is more complicated to explain. Of the three staggered conformations of **7** leading to products, conformation **7B**[36] must have the lowest energy. If the product ratio was directly equated to the ground state conformational preferences,[37] one would expect aldehyde **41** as the main product and not, as found in this reaction, **40**. The 15:4:1 ratio of the products **40**, **41**, and **42**, respectively, must therefore be controlled by the differences in free energy of the three transition states leading to the respective intermediates **7A(1)**, **7B(1)**, and **7C(1)**. The lower energy of the transition state leading to the bridged intermediate **7A-(1)** and the higher energies of the other two transition states can be attributed to the W-like arrangement of the σ-relay in conformation **7A** and the sickle-like arrangements of the σ-relay in the conformations **7B** and **7C**. The difference in steric repulsion between syn H-7 and H-8 (more favorable) in the transition state to **7B(1)** and between syn H-7 and the tosylate group (less favorable) in the transition state to **7C(1)** can explain the different formation rate of the aldehydes **41** and **42**.

The same steric effects which give rise to the formation of three different products in the reaction of **7** can also explain the selectivity in the reaction of **6**. The adverse steric repulsion between syn H-7 and C(8)-Me, which is present in the transition state to the bridged intermediate **7A(1)**, is absent in the transition state to **6A(1)**. As a result, 1,3-bridging in the transition state to **6A(1)** will be lower in energy than in the case of the reaction of **7A** to **7A(1)**. On the other hand, the transition state derived from conformation **6B** (see Scheme 8) is assumed to be higher in energy (more steric repulsion) than the transition state in the reaction of **7B** to **7B(1)**, while the transition state originated from **6C** will lie close in energy to the one involved in the reaction of **7C** to **7C(1)** (about the same steric repulsion). As a consequence, the absolute differences in free energies of the three transition states will be smaller in the reaction of **7** than they are assumed to be in the reaction of **6**. In other words, homofragmentation is the preferred (and only) pathway by which **6** reacts, while in the case of **7**, different product-forming reactions (homofragmentation, rearrangement, and 1,2-H shift) can take place at the same time.

The relative energies of transition states are also used to explain the more selective reaction of **7** upon treatment with sodium *tert*-amylate in combination with 15-crown-5. Since the use of 15-crown-5 leads to a "naked" alkoxide[39] which is a better electron donor, 1,3-bridging will be strengthened, and this may be the principal factor in the increased stabilization of the transition state to **7A(1)** compared with two other transition states, leading to **7B(1)** and **7C(1)**, in which no 1,3-bridging can occur.[37]

Concluding Remarks

As these and earlier experiments show, the reactivity of rigid 1,4-diol monosulfonate esters under strongly basic conditions is directly related to the geometry of the relaying C–C bonds (trans rule), irrespective of the

(37) It might be possible that stereoelectronic effects also influence the conformational equilibrium position of the deprotonated conformations of **7**,[38] but this has no influence on the product ratio as long as the rate of interconversion remains much faster than the rate of product formation.

(38) The possible influence of orbital interactions on the relative energies of conformations was suggested by Hoffmann et al.: Gleiter, R.; Stohrer, W.-D.; Hoffmann, R. *Helv. Chim. Acta* **1972**, *55*, 893. The first experimental verification of this effect was reported in 1989: Krijnen, B.; Beverloo, H. B.; Verhoeven, J. W.; Reiss, C. A.; Goubitz, K.; Heijdenrijk, D. *J. Am. Chem. Soc.* **1989**, *111*, 4433.

(39) Bartsch, R. A. *Acc. Chem. Res.* **1975**, *8*, 239.

structural features of the substrate. It also appears that the reactivity of these compounds initially depends on whether the sulfonate ester group is primary or secondary (the energy gap between primary and secondary carbocations is ~20 kcal/mol).[40] Secondary monosulfonate esters of rigid 1,4-diols show typical reactions in which orbital interactions are involved, whereas the corresponding primary sulfonate esters probably react via processes in which orbital interactions only play a minor role.[41]

Compounds in which the sulfonate ester group is conformationally mobile can give rise to mixtures of different products. The ratio in which these products are formed can be very well-analyzed with the C−H principle. Conformations in which the σ-relay has the W-like arrangement are (much) more reactive than conformations with a sickle-like arrangement, just as the trans rule predicts.

Experimental Section[42]

Materials. All reagents were purchased from Aldrich or Janssen and were used without further purification unless otherwise stated. A stock solution of sodium *tert*-amylate (3.2 M in toluene) was prepared by the procedure of Conia[43] and stored under an Ar atmosphere in a refrigerator. The tosylate **3**[12] and the starting materials **8**[9] and **19**[12] were prepared following previously described procedures. The compounds **4**,[11] **9**,[11] **20**[12] **29**,[9] **31**,[15] and **36**[11] have been characterized before.

***endo*-6-Carbomethoxybicyclo[2.2.1]heptan-2-one (9).** To a solution of 84 g of KOH (1.49 mol) in 150 mL of MeOH and 600 mL of H_2O was added 137.68 g (0.522 mol) of iodo lactone **8**. The solution was stirred at rt for 72 h, acidified with concd HCl, and extracted with five 200 mL portions of EtOAc. The combined organic layers were washed with 100 mL of brine and dried. After evaporation under reduced pressure, the remaining residue was dissolved in 800 mL of dry MeOH and 200 mL (1.576 mol) of TMSCl was added. The mixture was stirred at rt for 4 h and then carefully neutralized with 4 N aqueous NaOH. After removal of MeOH under reduced pressure, the remaining aqueous solution was extracted with three 150 mL portions of EtOAc. The combined organic layers were washed successively with 100 mL of saturated aqueous $NaHCO_3$ and 100 mL of brine and dried. After evaporation, the resulting product was purified via flash chromatography on silica gel (3:1 petroleum ether (bp 40−60 °C)/EtOAc) to yield 65.86 g (75%) of **9**. The spectroscopic data for **9** were identical with those reported in the literature.[11]

***endo*-6′-Carbomethoxyspiro[1,3-dioxolane-2,2′-bicyclo-[2.2.1]heptane] (10).** To a solution of 57.56 g (0.343 mol) of **9** in a mixture of 525 mL of CH_2Cl_2 and 340 mL (2.745 mol) of MED were added catalytic amounts of ethylene glycol and $TsOH·H_2O$. The reaction mixture was stirred at rt for 65 h, after which time 7 mL of Et_3N was added. The reaction mixture was then diluted with 500 mL of CH_2Cl_2 and washed with 300 mL of brine. The organic layer was dried and evaporated, and the crude dioxolane was chromatographed on basic alumina (activity II) (3:1 petroleum ether (bp 40−60 °C)/EtOAc) to afford 58.68 g (81%) of **10**: ^{1}H NMR δ 1.38 (m, 1 H), 1.51−1.92 (m, 5 H), 2.27 (m, 1 H), 2.57−2.73 (m, 2 H), 3.63 (s, 3 H), 3.67−3.92 (m, 4 H); ^{13}C NMR δ 29.43 (t), 34.96 (d), 39.06 (t), 42.05 (d), 43.26 (t), 46.95 (d), 51.11 (q), 63.72 (t), 64.57 (t), 115.10 (s), 174.45 (s); MS *m*/*z* (relative intensity) 212 (M^+, 59), 181 (15), 153 (100), 127 (38), 126 (32), 114 (12), 100 (23), 87 (12), 82 (13), 74 (20); HRMS calcd for $C_{11}H_{16}O_4$ (M^+) 212.1048, found 212.1047. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 61.95; H, 7.52.

***endo*-6-(Hydroxymethyl)bicyclo[2.2.1]heptan-2-one (11).** A solution of 23.11 g (0.109 mol) of **10** in 100 mL of dry THF was added dropwise to a stirred solution of 4.96 g of LAH (0.131 mol) in 50 mL of dry THF at −78 °C. The reaction mixture was stirred at −78 °C for 1 h and was allowed to come to rt, and stirring was continued for an additional 16 h. The excess LAH was carefully quenched with a small amount of saturated aqueous Na_2SO_4. After the addition of 200 mL of EtOAc, the reaction mixture was dried and evaporated to yield 18.71 g (93%) of a crude hydroxy ethylene acetal. This product was dissolved in 50 mL of acetone, and 350 mL of 1 N HCl was added. The reaction mixture was stirred at rt for 72 h and then neutralized with 4 N aqueous NaOH. After concentration under reduced pressure, the residue was taken up in 100 mL of H_2O and extracted with five 100 mL portions of CH_2Cl_2. The combined organic layers were dried and evaporated. The resulting product was flash chromatographed (1:1 petroleum ether (bp 40−60 °C)/EtOAc) to give 12.73 g (83%) of **11**: MS *m*/*z* (relative intensity) 140 (M^+, 40), 122 (15), 111 (30), 110 (17), 97 (18), 96 (23), 82 (70), 81 (100), 80 (47), 67 (60); HRMS calcd for $C_8H_{12}O_2$ (M^+) 140.0837, found 140.0836. The ^{13}C NMR spectrum of **11** revealed the presence of its cyclic hemiacetal **12** in about 40%.

11: ^{13}C NMR (main peaks) δ 30.32 (t), 40.64 (d), 45.76 (t), 52.36 (d), 64.14 (t), 217.98 (s).

12: ^{13}C NMR (main peaks) δ 38.19 (d), 46.64 (t), 50.20 (d), 70.65 (t), 112.21 (s).

***endo*-6-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-bicyclo[2.2.1]heptan-2-one (13).** To a solution of 5.08 g (36.2 mmol) of **11** in 50 mL of DMF were added 4.41 g (64.8 mmol) of imidazole and 5.48 g (36.3 mmol) of TBDMSCl. The reaction mixture was stirred at rt for 24 h, poured into 80 mL of H_2O, and then extracted with five 50 mL portions of CH_2Cl_2. The combined organic layers were washed with 50 mL of brine, dried, and evaporated. The resulting product was flash chromatographed (20:1 petroleum ether (bp 40−60 °C)/EtOAc) to yield 8.20 g (89%) of **13** as a clear oil: ^{1}H NMR δ −0.02 (s, 3 H), −0.01 (s, 3 H), 0.83 (s, 9 H), 1.12 (m, 1 H), 1.58−2.08 (m, 5 H), 2.29 (m, 1 H), 2.52−2.62 (m, 2 H), 3.43 (dd, J = 6.2, 10.1 Hz, 1 H), 3.46 (dd, J = 6.8, 10.1 Hz, 1 H); ^{13}C NMR δ −5.78 (2q), 18.03 (s), 25,63 (3q), 30.53 (t), 34.66 (d), 38,35 (t), 40.84 (d), 45,33 (t), 52.66 (d), 64.49 (t), 216.08 (s); MS *m*/*z* (relative intensity) 239 (M^+ − 15, 3.8), 199 (5), 198 (17), 197 (100), 106 (9), 92 (5), 90 (5), 80 (7), 67 (23), 74 (10), 60 (4); HRMS calcd for $C_{13}H_{23}O_2Si$ (M^+ − 15, 3.8) 239.1467, found 239.1467.

***endo,endo*-6-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-methyl]bicyclo[2.2.1]heptan-2-ol (14).** To a stirred solution of 2.71 g (10.7 mmol) of **13** in 75 mL of EtOH was added 0.60 g (15.9 mmol) of $NaBH_4$. The reaction mixture was stirred at 50 °C for 90 min and then quenched with an excess of saturated aqueous NH_4Cl. After concentration under reduced pressure, the resulting residue was taken up in 30 mL of H_2O and extracted with four 25 mL portions of EtOAc. The combined organic layers were washed with 25 mL of brine, dried, and evaporated. The remaining product was flash chromatographed (20:1 petroleum ether (bp 40−60 °C)/EtOAc) to give 2.62 g of **14** (96%) as a clear oil: ^{1}H NMR δ 0.07 (s, 6 H), 0.83 (m, 1 H), 0.89 (s, 9 H), 1.18−1.42 (m, 3 H), 1.65 (m, 1 H), 1.92−2.24 (m, 4 H), 3.78 (dd, J = 2.4, 10.9 Hz, 1 H), 3.90 (dd, J = 5.3, 10.9 Hz, 1 H), 4.09 (m, 1 H), 4.88 (d, J = 10.2 Hz, OH); ^{13}C NMR δ −5.84 (q), −5.76 (q), 18.05 (s), 25.57 (3q), 31.19 (t), 36.98 (d), 38.78 (d), 39.12 (t), 41.22 (d), 46.66 (d), 63.30 (t), 73.95 (d); MS *m*/*z* (relative intensity) 241 (M^+ − 15, 1.9), 199 (55), 32 (19), 108 (74), 106 (19), 92 (10), 82 (22), 81 (29), 80 (68), 76 (100); HRMS calcd for $C_{13}H_{25}O_2Si$ (M^+ − 15) 241.1624, found 241.1624.

***endo,endo*-6-[(4-Methylbenzenesulfonyl)oxy]bicyclo-[2.2.1]heptane-2-methanol (1).** To a stirred solution of 1.24 g (4.8 mmol) of alcohol **14** in 25 mL of dry pyridine were added 1.715 g (9.0 mmol) of TsCl and 2.01 g (16.5 mmol) of DMAP. The reaction mixture was stirred at 80 °C for 52 h and then concentrated under reduced pressure. The resulting mixture was taken up in 100 mL of EtOAc and washed successively with two 25 mL portions of saturated aqueous $NaHCO_3$ and one 25 mL portion of brine. The organic layer was dried and

(40) Schultz, J. C.; Houle, F. A.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 3917.

(41) In the related Wharton reaction, a few primary sulfonate esters give products which can only be explained as the result of the chemical consequences of orbital interactions: Caine, D. *Org. Prep. Proced. Int.* **1988**, *20*, 1.

(42) For a general description of the experimental procedures employed in this research, see ref 2. Column chromatography was performed using Merck silica gel 60 (70−230 mesh) and ICN alumina B-Super I (activity grade II).

(43) Conia, M. J.-M. *Bull. Soc. Chim. Fr.* **1950**, *17*, 537.

evaporated, and the crude product was flash chromatographed (50:1 petroleum ether (bp 40–60 °C)/EtOAc) to give 0.858 g (44%) of pure *endo,endo*-6-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]bicyclo[2.2.1]heptan-2-ol 4-methylbenzenesulfonate: ^{1}H NMR δ 0.05 (s, 6 H), 0.91 (s, 9 H), 1.04 (m, 1 H), 1.18 (m, 1 H), 1.27–1.46 (m, 2 H), 1.86–2.30 (m, 4 H), 2.39–2.50 (m, 1 H), 2.46 (s, 3 H), 3.74 (dd, J = 8.5, 10.2 Hz, 1 H), 3.83 (dd, J = 6.0, 10.2 Hz, 1 H), 4.84 (dddd, J = 1.7, 4.3, 4.3, 10.2 Hz, 1 H), 7.35 (d, J = 8.2 Hz, 2 H), 7.80 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ −5.46 (2q), 18.20 (s), 21.37 (q), 25.74 (3q), 34.89 (t), 36.33 (d), 36.73 (t), 37.78 (t), 43.17 (d), 43.34 (d), 66.10 (t), 83.23 (d), 127.46 (2d), 129.49 (2d), 134.01 (s), 144.23 (s); MS m/z (relative intensity) (M^+ − 57, 0.3), 231 (8), 230 (14), 229 (100), 149 (4), 107 (19), 91 (9), 79 (6), 75 (4), 73 (6); HRMS calcd for $C_{17}H_{25}O_4SSi$ (M^+ − 57) 353.1243, found 353.1248. To a solution of 0.680 g (1.49 mmol) of this TBDMS ether in 10 mL of acetonitrile was added 10 drops of 40% aqueous HF. The reaction mixture was stirred at rt for 30 min and then poured into 50 mL of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with three 25 mL portions of EtOAc, after which the combined organic layers were dried and evaporated. The crude product was flash chromatographed (5:1 petroleum ether (bp 40–60 °C)/EtOAc) which afforded 0.457 g (92%) of **1** as an oil: ^{1}H NMR δ 0.99 (m, 1 H), 1.16 (m, 1 H), 1.32–1.65 (m, 2 H), 1.83–2.12 (m, 2 H), 2.21–2.53 (m, 3 H), 2.47 (s, 3 H), 2.63 (m, 1 H), 3.75 (dd, J = 7.4, 11.1 Hz, 1 H), 3.91 (dd, J = 8.5, 11.1 Hz, 1 H), 4.92 (m, 1 H), 7.37 (d, J = 8.2 Hz, 2 H), 7.82 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 21.41 (q), 33.53 (t), 36.22 (d), 36.28 (t), 37.82 (t), 42.74 (2d), 64.99 (t), 83.56 (d), 127.49 (2d), 129.66 (2d), 133.24 (s), 144.65 (s); MS m/z (relative intensity) 266 (M^+ − 30, 5), 125 (59), 107 (25), 96 (38), 95 (100), 92 (91), 82 (28), 81 (74), 80 (55), 68 (38), 67 (38); HRMS calcd for $C_{14}H_{18}O_3S$ (M^+ − 30) 266.0977, found 266.0974. Anal. Calcd for $C_{15}H_{20}O_4S$: C, 60.78; H, 6.80. Found: C, 60.57; H, 6.86.

***exo*-6′-Carbomethoxyspiro[1,3-dioxolane-2,2′-bicyclo[2.2.1]heptane] (15).** To a solution of 18.75 g (88.44 mmol) of dioxolane **10** in 175 mL of dry MeOH was added 100 mL of 0.45 M NaOMe in dry MeOH. The solution was refluxed under a N_2 atmosphere for 68 h, allowed to come to rt, and then poured into 400 mL of ice–water and 150 mL of brine. The aqueous layer was extracted with three 200 mL portions of EtOAc. The combined organic layers were washed with 150 mL of brine, dried, and evaporated. The resulting oil was flash chromatographed (3:1 petroleum ether (bp 40–60 °C)/EtOAc) to give 11.61 g (62%) of **15** as a clear oil: ^{1}H NMR δ 1.37–1.63 (m, 4 H), 1.71–1.93 (m, 2 H), 2.27 (m, 1 H), 2.37 (m, 1 H), 2.87 (dd, J = 5.1, 9.8 Hz, 1 H), 3.62 (s, 3 H), 3.77–4.00 (m, 4 H); ^{13}C NMR δ 32.65 (t), 35.10 (d), 35.53 (t), 39.05 (d), 42.44 (t), 47.51 (d), 51.51 (q), 63.76 (t), 64.34 (t), 115.14 (s), 176.09 (s); MS m/z (relative intensity) 212 (M^+, 35), 154 (9), 153 (100), 127 (33), 126 (15), 114 (8), 100 (19), 82 (10), 74 (16), 28 (33); HRMS calcd for $C_{11}H_{16}O_4$ (M^+) 212.1048, found 212.1047. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 61.97; H, 7.68.

***exo*-6-(Hydroxymethyl)bicyclo[2.2.1]heptan-2-one (16).** The keto alcohol **16** was prepared from **15** (8.59 g, 40.49 mmol) as described for the synthesis of **11**. Workup and flash chromatography (3:1 petroleum ether (bp 40–60 °C)/EtOAc) afforded 4.82 g (85%) of pure **16**: ^{1}H NMR δ 1.28 (m, 1 H), 1.50–2.09 (m, 6 H), 2.55 (m, 1 H), 2.60 (m, 1 H), 2.90 (br s, OH), 3.34–3.53 (m, 2 H); ^{13}C NMR δ 31.52 (t), 34.11 (t), 35.00 (d), 38.85 (d), 44.52 (t), 51.70 (d), 64.60 (t), 217.87 (s); MS m/z (relative intensity) 140 (M^+, 78), 109 (49), 96 (100), 82 (89), 81 (35), 80 (69), 79 (42), 68 (61), 42 (30), 28 (75); HRMS calcd for $C_8H_{12}O_2$ (M^+) 140.0839, found 140.0838.

***exo*-6-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]bicyclo[2.2.1]heptan-2-one (17).** The silyl ether **17** was prepared from **16** (3.00 g, 21.43 mmol) as described for the silylation of **11**. Workup and flash chromatography (20:1 petroleum ether (bp 40–60 °C)/EtOAc) afforded 5.30 g (97%) of **17**: ^{1}H NMR δ 0.01 (s, 6 H), 0.86 (s, 9 H), 1.33 (m, 1 H), 1.50–2.12 (m, 6 H), 2.56 (m, 1 H), 2.63 (m, 1 H), 3.38–3.54 (m, 2 H); ^{13}C NMR δ −5.58 (2q), 18.04 (s), 25.65 (3q), 31.34 (t), 34.13 (t), 35.07 (d), 38.57 (d), 44.54 (t), 51.99 (d), 65.02 (t), 217.35 (s); MS m/z (relative intensity) 239 (M^+ − 15, 3.4), 198 (17), 197 (100), 132 (6), 118 (8), 106 (21), 90 (6), 80 (24), 76 (41), 74 (12); HRMS calcd for $C_{13}H_{24}O_2Si$ (M^+ − 15) 239.1467, found 239.1467.

(2-*endo*,6-*exo*)-6-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]bicyclo[2.2.1]heptan-2-ol (18). To 10.8 mL of 1 M L-Selectride in THF was slowly added dropwise a solution of 2.50 g (9.84 mmol) of **17** in 100 mL of dry THF at −78 °C. The solution was stirred at −78 °C for 15 min and was allowed to come to rt, and stirring was continued for 16 h. Then a mixture of 12.5 mL of H_2O and 37.5 mL of EtOH was carefully added to the reaction mixture. Stirring was continued at rt for 20 min, after which time a mixture of 12.5 mL of 4 M aqueous NaOH and 25 mL of 30% H_2O_2 was added. Stirring was continued for 5 h, and then the reaction mixture was concentrated under reduced pressure. To the remaining residue was added 100 mL of H_2O, and the aqueous layer was extracted with four 75 mL portions of EtOAc. The combined organic layers were dried and evaporated, and the crude product was flash chromatographed (20:1 petroleum ether (bp 40–60 °C)/EtOAc) to yield 2.24 g (89%) of **18** as a clear oil: ^{1}H NMR δ 0.03 (s, 6 H), 0.83 (m, 1 H), 0.88 (s, 9 H), 1.00–1.52 (m, 4 H), 1.61 (br s, OH), 1.95 (m, 1 H), 2.10–2.22 (m, 2 H), 2.34 (m, 1 H), 3.37 (dd, J = 8.6, 10.0 Hz, 1 H), 3.42 (dd, J = 6.8, 10.0 Hz, 1 H), 4.22 (m, 1 H); ^{13}C NMR δ −5.28 (2q), 18.36 (s), 25.96 (3q), 33.90 (d), 34.09 (t), 34.49 (t), 37.12 (d), 38.71 (t), 44.64 (d), 66.47 (t), 72.70 (d); MS m/z (relative intensity) 241 (M^+ − 15, 1.3), 199 (37), 132 (21), 108 (72), 106 (21), 82 (14), 80 (75), 78 (9), 76 (100), 28 (37); HRMS calcd for $C_{13}H_{25}O_2Si$ (M^+ − 15) 241.1624, found 241.1624.

(2-*exo*,6-*endo*)-6-[(4-Methylbenzenesulfonyl)oxy]bicyclo[2.2.1]heptane-2-methanol (2). The alcohol **18** (0.508 g, 1.98 mmol) was treated with TsCl for 8 h as described for the tosylation of **14**. After workup, the crude product was purified by flash chromatography (20:1 petroleum ether (bp 40–60 °C/EtOAc) to afford 0.643 g (79%) of (2-*endo*,6-*exo*)-6-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]bicyclo[2.2.1]heptan-2-ol 4-methylbenzenesulfonate: ^{1}H NMR δ −0.03 (s, 6 H), 0.82 (s, 9 H), 0.99–1.19 (m, 3 H), 1.29–1.46 (m, 2 H), 1.84 (m, 1 H), 2.06–2.30 (m, 3 H), 2.38 (s, 3 H), 3.26 (d, J = 6.9 Hz, 2 H), 4.71 (ddd, J = 4.0, 4.0, 10.3 Hz, 1 H), 7.27 (d, J = 8.2 Hz, 2 H), 7.73 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ −5.57 (2q), 18.01 (s), 21.36 (q), 25.67 (3q), 33.30 (t), 33.77 (t), 34.07 (d), 35.79 (t), 36.11 (d), 43.01 (d), 65.65 (t), 82.10 (d), 127.50 (2d), 129.49 (2d), 134.03 (s), 144.16 (s); MS m/z (relative intensity) 353 (M^+ − 57, 0.2), 131 (9), 130 (16), 129 (100), 181 (9), 108 (17), 92 (9), 80 (17), 76 (12), 74 (8); HRMS calcd for $C_{17}H_{25}O_4SSi$ (M^+ − 57) 353.1242, found 353.1238. A sample of this TBDMS ether (0.613 g, 1.50 mmol) was desilylated with HF as described for the synthesis of **1**. Workup and flash chromatography (2:1 petroleum ether (bp 40–60 °C)/EtOAc) afforded 0.408 g (92%) of **2**: ^{1}H NMR δ 1.04–1.57 (m, 5 H), 1.89 (m, 1 H), 2.09–2.38 (m, 4 H), 2.43 (s, 3 H), 3.27 (dd, J = 8.3, 10.5 Hz, 1 H), 3.35 (dd, J = 6.9, 10.5 Hz, 1 H), 4.78 (ddd, J = 4.2, 4.2, 10.3 Hz, 1 H), 7.34 (d, J = 8.2 Hz, 2 H), 7.79 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 21.30 (q), 33.54 (t), 33.63 (t), 34.44 (d), 35.68 (t), 35.94 (d), 42.75 (d), 65.22 (t), 82.28 (d), 127.50 (2d), 129.64 (2d), 133.54 (s), 144.60 (s); MS m/z (relative intensity) 296 (M^+, 1.6), 173 (26), 155 (36), 125 (100), 107 (60), 96 (45), 94 (23), 92 (80), 81 (58), 80 (40); HRMS calcd for $C_{15}H_{20}O_4S$ (M^+) 296.1082, found 296.1081.

(2-*exo*,6-*endo*)-6-Hydroxybicyclo[2.2.1]heptane-2-methanol α-(4-Methylbenzenesulfonate) (4). The silyl ether **18** (1.00 g. 3.91 mmol) was desilylated with HF as described for the synthesis of **1**. The crude diol was dissolved in 20 mL of dry pyridine and cooled to 0 °C, and then 0.780 g (4.09 mmol) of TsCl was added. The reaction mixture was stirred at 0 °C for 1 h and was allowed to come to rt, and stirring was continued for 100 h. An additional portion of 0.475 g (3.910 mmol) of TsCl was added, and stirring was continued for 16 h. After concentration under reduced pressure, workup and flash chromatography (3:1 petroleum ether (bp 40–60 °C)/EtOAc) afforded 0.51 g (29%) of (2-*exo*,6-*endo*)-6-[(4-methylbenzenesulfonyl)oxy]bicyclo[2.2.1]heptane-2-methanol 4-methylbenzenesulfonate (**32**) as white crystals: mp 98–99 °C (from hexane); ^{1}H NMR δ 0.92–1.24 (m, 4 H), 1.38 (m, 1 H), 1.82 (m, 1 H), 2.00–2.13 (m, 2 H), 2.22–2.45 (m, 1 H), 2.36 (s, 6 H), 3.60 (d, J = 7.4 Hz, 2 H), 4.65 (ddd, J = 4.0, 4.0, 10.4 Hz, 1 H), 7.26 (d, J = 8.0 Hz, 4 H), 7.60–7.71 (2d, J = 8.0 Hz,

4 H); ^{13}C NMR δ 21.41 (2q), 31.31 (d), 33.23 (t), 33.78 (t), 35.46 (t), 35.93 (d), 42.71 (d), 72.12 (t), 81.20 (d), 127.54 (4d), 129.70 (4d), 132.92 (s), 133.81 (s), 144.61 (2s); MS *m/z* (relative intensity) 450 (M^+, 0.3), 253 (23), 197 (26), 155 (20), 149 (21), 108 (36), 102 (56), 92 (38), 89 (23), 44 (100); HRMS calcd for $C_{22}H_{26}O_6S_2$ (M^+) 450.1170, found 450.1170. Anal. Calcd for $C_{22}H_{26}O_6S_2$: C, 58.64; H, 5.82. Found: C, 58.45; H, 5.75. Further elution afforded 0.650 g (56%) of hydroxy tosylate **4**. The spectroscopic data for **4** were identical with those reported in the literature.[11]

***exo,exo*-2-[(4-Methylbenzenesulfonyl)oxy]bicyclo[2.2.1]-heptane-2-methanol (3).** The tosylate **3** was prepared as described previously.[12] The spectroscopic data for **3** are as follows: ^{1}H NMR δ 0.92 (m, 1 H), 1.10–1.28 (m, 2 H), 1.36–1.67 (m, 4 H), 2.03 (br s, OH), 2.24 (m, 1 H), 2.31 (m, 1 H), 2.42 (s, 3 H), 3.34 (d, *J* = 7.5 Hz, 2 H), 4.43 (m, 1 H), 7.31 (d, *J* = 8.2 Hz, 2 H), 7.75 (d, *J* = 8.2 Hz, 2 H); ^{13}C NMR δ 21.40 (q), 32.00 (t), 32.18 (t), 34.89 (d), 38.96 (t), 39.29 (d), 43.94 (d), 65.32 (t), 84,74 (d), 127.43 (2d), 129.56 (2d), 134.20 (s), 144.28 (s); MS *m/z* (relative intensity) 124 (M^+ − 172, 9.1), 173 (98), 125 (61), 108 (38), 96 (65), 92 (100), 83 (42), 82 (44), 81 (84), 80 (45), 70 (32), 68 (42); HRMS calcd for $C_8H_{12}O$ (M^+ − 172) 124.0888, found 124.0888.

***exo,exo*-2-Carbomethoxy-6-[[(1,1-dimethylethyl)-dimethylsilyl]oxy]bicyclo[2.2.1]heptane (20).** The hydroxy ester **19**[12] (12.64 g, 74.3 mmol) was treated with TBDMSCl for 90 min as described for the silylation of **11**. Workup and flash chromatography (50:1 petroleum ether (bp 40–60 °C)/EtOAc) gave 20.21 g (96%) of **20** as a clear oil: ^{1}H NMR δ 0.00 (s, 3 H), 0.01 (s, 3 H), 0.83 (s, 9 H), 1.22–1.38 (m, 3 H), 1.48–1.78 (m, 3 H), 2.08 (dd, *J* = 5.6, 9.0 Hz, 1 H), 2.25 (m, 1 H), 2.30 (m, 1 H), 3.63 (s, 3 H), 3.68 (m, 1 H); ^{13}C NMR δ −4.97 (q), −4.92 (q), 17.73 (s), 25.56 (3q), 32.59 (t), 33.11 (t), 34.69 (d), 41.64 (d), 42.03 (t), 48.38 (d), 51.44 (q), 74.19 (d), 175,83 (s); MS *m/z* (relative intensity) 284 (M^+, 0.3), 227 (46), 189 (33), 150 (9), 149 (16), 148 (100), 134 (14), 122 (14), 94 (10), 76 (18), 74 (17); HRMS calcd for $C_{15}H_{28}O_3Si$ (M^+) 284.1807, found 284.1807.

***exo,exo*-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-bicyclo[2.2.1]heptane-2-methanol (21).** The ester **20** (20.21 g, 71.2 mmol) was treated with LAH at −78 °C for 4 h as described for the synthesis of alcohol **11**. Workup and flash chromatography (10:1 petroleum ether (bp 40–60 °C)/EtOAc) gave 18.14 g (99%) of **21** as a clear oil: ^{1}H NMR δ 0.02 (s, 6 H), 0.84 (s, 9 H), 0.92 (m, 1 H), 1.05–1.66 (m, 7 H), 2.00 (m, 1 H), 2.20 (m, 1 H), 3.29–3.48 (m, 2 H), 3.66 (m, 1 H); ^{13}C NMR δ −4.82 (2q), 17.81 (s), 25.65 (3q), 31.54 (t), 32.78 (t), 34.83 (d), 39.87 (d), 42.34 (t), 46.30 (d), 66.10 (t), 74.84 (d); MS *m/z* (relative intensity) 256 (M^+, 0.3), 219 (13), 200 (15), 199 (100), 131 (10), 119 (40), 108 (50), 80 (90), 74 (18), 70 (17); HRMS calcd for $C_{15}H_{28}O_2Si$ (M^+) 256.1858, found 256.1858.

***exo,exo*-6-Hydroxybicyclo[2.2.1]heptane-2-methanol α-(4-Methylbenzenesulfonate) (5).** The silyl ether **21** (0.363 g, 1.42 mmol) was treated with TsCl as described for the synthesis of **4**. Workup and flash chromatography (250:1 petroleum ether (bp 40–60 °C)/EtOAc) afforded 0.430 g (75%) of *exo,exo*-6-[[(1,1-dimethylethyl)dimethylsilyl]oxy]bicyclo[2.2.1]-heptane-2-methanol α-(4-methylbenzenesulfonate): ^{1}H NMR δ −0.01 (s, 6 H), 0.80–1.00 (m, 2 H), 0.83 (s, 9 H), 1.11–1.37 (m, 2 H), 1.42–1.67 (m, 3 H), 1.90 (m, 1 H), 2.16 (m, 1 H), 2.43 (s, 3 H), 3.60 (m, 1 H), 3.78 (d, *J* = 7.7 Hz, 2 H), 7.33 (d, *J* = 8.2 Hz, 2 H), 7.77 (d, *J* = 8.2 Hz, 2 H); ^{13}C NMR δ −4.72 (q), −4.66 (q), 17.94 (s), 21.60 (q), 25.80 (3q), 31.69 (t), 32.72 (t), 35.00 (d), 36.48 (d), 42.24 (t), 46.40 (d), 72.88 (t), 74.48 (d), 127.79 (2d), 129.78 (2d), 133.19 (s), 144.61 (s). A sample of this silyl ether (0.394 g, 0.96 mmol) was desilylated with HF as described for the synthesis of **1**. Workup and flash chromatography (2:1 petroleum ether (bp 40–60 °C)/EtOAc) afforded 0.272 g (96%) of **5**: ^{1}H NMR δ 0.84 (m, 1 H), 1.03 (m, 1 H), 1.11–1.35 (m, 2 H), 1.40–1.68 (m, 3 H), 2.02 (m, 1 H), 2.07 (br s, OH), 2.19 (m, 1 H), 2.41 (s, 3 H), 3.65–3.82 (m, 3 H), 7.31 (d, *J* = 8.2 Hz, 2 H), 7.74 (d, *J* = 8.2 Hz, 2 H); ^{13}C NMR δ 21.60 (q), 31.50 (t), 32.27 (t), 35.12 (d), 36.49 (d), 41.11 (t), 46.19 (d), 72.62 (t), 74.06 (d), 127.78 (2d), 129.85 (2d), 132.94 (s), 144.77 (s); MS *m/z* (relative intensity) 124 (M^+ − 172, 63), 106 (20), 95 (16), 91 (35), 81 (28), 80 (100), 79 (17), 67 (13); HRMS calcd for $C_8H_{12}O$ (M^+ − 172) 124.0888, found 124.0887.

***exo,exo*-6-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-bicyclo[2.2.1]heptane-2-carboxaldehyde (22).** To a suspension of 6.76 g (31.4 mmol) of PCC and 1.19 g (14.5 mmol) of NaOAc in 50 mL of dry CH_2Cl_2 was added a solution of 5.13 g (20.0 mmol) of alcohol **21** in 50 mL of dry CH_2Cl_2 at rt. The suspension was stirred at rt for 210 min and, after dilution with 100 mL of ether, filtered through Celite. The filter cake was washed with three 100 mL portions of ether, and the combined filtrates were concentrated to 100 mL. The concentrate was washed with 25 mL of saturated aqueous $NaHCO_3$ and 50 mL of brine. After drying and evaporation, flash chromatography (50:1 petroleum ether (bp 40–60 °C)/EtOAc) gave 3.82 g (75%) of pure aldehyde **22** as a colorless oil: ^{1}H NMR δ 0.02 (s, 3 H), 0.03 (s, 3 H), 0.85 (s, 9 H), 1.01 (m, 1 H), 1.16 (ddd, *J* = 2.7, 9.2, 9.2 Hz, 1 H), 1.33 (m, 1 H), 1.52–1.84 (m, 3 H), 2.10 (m, 1 H), 2.30 (m, 1 H), 2.35 (m, 1 H), 3.76 (m, 1 H), 9.62 (d, *J* = 1.6 Hz, 1 H); ^{13}C NMR δ −4.94 (2q), 17.74 (s), 25.56 (3q), 29.18 (t), 32.32 (t), 34.81 (d), 42.58 (t), 45.70 (d), 50.01 (d), 74.41 (d), 202.10 (d); MS *m/z* (relative intensity) 254 (M^+, 1.1), 200 (5), 198 (15), 197 (100), 169 (12), 132 (19), 106 (11), 80 (9), 76 (46), 74 (16); HRMS calcd for $C_{14}H_{26}O_2Si$ (M^+) 254.1702, found 254.1706.

(α*R*,exo,exo)- and (α*S*,exo,exo)-α-Methyl-6-[[(1,1-dimethylethyl)dimethylsilyl]oxy]bicyclo[2.2.1]heptane-2-methanol (23 and 24). To 50 mL of 0.9 M MeMgI in dry ether was added dropwise a solution of 3.82 g (15.0 mmol) of aldehyde **22** in 50 mL of dry ether at 0 °C. The reaction mixture was stirred at 0 °C for 30 min, after which time the excess of MeMgI was cautiously destroyed with saturated aqueous NH_4Cl. After dilution with H_2O, the two-phase mixture was separated, and the aqueous layer was extracted with four 150 mL portions of ether. The combined organic layers were washed with 100 mL of brine, dried, and evaporated. The remaining mixture of diastereoisomers was chromatographed (20:1 petroleum ether (bp 40–60 °C)/EtOAc) to give 1.92 g (47%) of **24** as a white solid: mp 78–79 °C (from hexane); ^{1}H NMR δ 0.02 (s, 3 H), 0.03 (s, 3 H), 0.86 (s, 9 H), 0.90 (m, 1 H), 1.02–1.64 (m, 7 H), 1.10 (d, *J* = 6.2 Hz, 3 H), 2.13–2.24 (m, 2 H), 3.38 (m, 1 H), 3.67 (m, 1 H); ^{13}C NMR δ −4.89 (q), −4.80 (q), 17.78 (s), 20.82 (q), 25.64 (3q), 31.68 (t), 33.35 (t), 35.23 (d), 41.99 (t), 45.92 (2d), 70.26 (d), 75.07 (d); MS *m/z* (relative intensity) 255 (M^+ − 15, 3.2), 214 (16), 213 (100), 122 (49), 96 (11), 94 (49), 80 (35), 76 (74), 74 (27), 45 (15); HRMS calcd for $C_{14}H_{27}O_2Si$ (M^+ − 15) 255.1780, found 255.1781. Anal. Calcd for $C_{15}H_{30}O_2Si$: C, 66.63; H, 11.18. Found: C, 66.95; H, 11.46. Further elution provided 1.95 g (48%) of **23** as an oil: ^{1}H NMR δ −0.01 (s, 6 H), 0.83 (s, 9 H), 1.00–1.36 (m, 5 H), 1.17 (d, *J* = 6.1 Hz, 3 H), 1.42–1.59 (m, 2 H), 1.77–1.89 (m, 2 H), 2.21 (m, 1 H), 3.46 (m, 1 H), 3.62 (m, 1 H); ^{13}C NMR δ −4.95 (q), −4.84 (q), 17.80 (s), 22.27 (q), 25.64 (3q), 32.35 (t), 33.07 (t), 35.20 (d), 41.88 (t), 45.63 (d), 47.48 (d), 70.88 (d), 75.23 (d); MS *m/z* (relative intensity) 255 (M^+ − 15, 3.6), 214 (18), 213 (100), 122 (75), 96 (17), 94 (57), 80 (38), 76 (92), 74 (37), 68 (9); HRMS calcd for $C_{14}H_{27}O_2Si$ (M^+ − 15) 255.1780, found 255.1776. Anal. Calcd for $C_{15}H_{30}O_2Si$: C, 66.63; H, 11.18. Found: C, 66.73; H, 11.31.

(α*R*,exo,exo)-α-Methyl-6-[[(1,1-dimethylethyl)dimethylsilyl]oxy]bicyclo[2.2.1]heptane-2-methanol α-(4-Methylbenzenesulfonate) (25). The method of Kabalka et al.[44] was employed. To a stirred solution of 1.903 g (7.05 mmol) of alcohol **23** in 10 mL of $CHCl_3$ was added 1.10 g (13.90 mmol) of dry pyridine, followed by 1.99 g (10.42 mmol) of TsCl in small portions at 0 °C. The reaction mixture was stirred at rt for 24 h and then concentrated under reduced pressure. The resulting residue was taken up in 100 mL of EtOAc and washed successively with two 10 mL portions of saturated aqueous $NaHCO_3$ and one 10 mL portion of brine. The organic layer was dried and evaporated, and the remaining oil was flash chromatographed (50:1 petroleum ether (bp 40–60 °C)/EtOAc) to afford 2.618 g (88%) of **25** as white crystals: mp 56–57 °C (from hexane); ^{1}H NMR δ −0.02 (s, 6 H), 0.83 (s, 9 H), 1.05–1.56 (m, 7 H), 1.26 (d, *J* = 6.2 Hz, 3 H), 1.70 (m, 1

(44) Kabalka, G. W.; Varma, M.; Varma, R. S. *J. Org. Chem.* **1986**, *51*, 2386.

H), 2.16 (m, 1 H), 2.42 (s, 3 H), 3.57 (m, 1 H), 4.46 (m, 1 H), 7.31 (d, J = 8.2 Hz, 2 H), 7.77 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ −4.90 (2q), 17.77 (s), 19.84 (q), 21.38 (q), 25.59 (3q), 32.32 (t), 32.70 (t), 34.88 (d), 41.68 (t), 43.32 (d), 47.18 (d), 74.92 (d), 83.34 (d), 127.45 (2d), 129.43 (2d), 134.36 (s), 144.17 (s); MS m/z (relative intensity) (M^+ − 57, 2.3), 231 (9), 230 (15), 229 (100), 195 (6), 121 (46), 93 (10), 91 (13), 79 (8), 75 (18), 73 (13); HRMS calcd for $C_{18}H_{27}O_4SSi$ (M^+ − 57) 367.1399, found 367.1398. Anal. Calcd for $C_{22}H_{36}O_4SSi$: C, 62.23; H, 8.55. Found: C, 61.98; H, 8.54.

(α*S*,*exo*,*exo*)-α-Methyl-6-[[(1,1-dimethylethyl)dimethylsilyl]oxy]bicyclo[2.2.1]heptane-2-methanol α-(4-Methylbenzenesulfonate) (26). The alcohol **24** (1.863 g, 6.90 mmol) was treated with TsCl as described for the tosylation of **23**. Workup and flash chromatography (50:1 petroleum ether (bp 40−60 °C)/EtOAc) gave 2.742 g (94%) of tosylate **26** as white crystals: mp 75−77 °C (from hexane); ^{1}H NMR δ −0.04 (s, 6 H), 0.82 (s, 9 H), 0.88 (m, 1 H), 1.09−1.54 (m, 6 H), 1.23 (d, J = 6.1 Hz, 3 H), 1.79 (m, 1 H), 2.14 (m, 1 H), 2.42 (s, 3 H), 3.52 (m, 1 H), 4.25 (m, 1 H), 7.31 (d, J = 8.3 Hz, 2 H), 7.78 (d, J = 8.3 Hz, 2 H); ^{13}C NMR δ −5.03 (q), −4.90 (q), 17.73 (s), 18.83 (q), 21.33 (q), 25.58 (3q), 31.51 (t), 33.18 (t), 35.12 (d), 41.66 (t), 43.35 (d), 46.03 (d), 74.44 (d), 82.08 (d), 127.45 (2d), 129.46 (2d), 134.28 (s), 144.17 (s); MS m/z (relative intensity) (M^+ − 57, 1.4), 231 (10), 230 (16), 229 (100), 195 (32), 121 (34), 93 (9), 91 (15), 75 (29), 73 (14); HRMS calcd for $C_{18}H_{27}O_4SSi$ (M^+ − 57) 367.1399, found 367.1396. Anal. Calcd for $C_{22}H_{36}O_4SSi$: C, 62.23; H, 8.55. Found: C, 62.27; H, 8.72.

(α*R*,*exo*,*exo*)-α-Methyl-6-hydroxybicyclo[2.2.1]heptane-2-methanol α-(4-Methylbenzenesulfonate) (6). The silyl ether **25** (2.41 g, 5.68 mmol) was desilylated with HF as described for the synthesis of **1**. Workup and flash chromatography (2:1 petroleum ether (bp 40−60 °C)/EtOAc) afforded 1.73 g (98%) of **6**: ^{1}H NMR δ 1.10−1.63 (m, 7 H), 1.20 (d, J = 6.1 Hz, 3 H), 1.87 (m, 1 H), 1.97 (br s, OH), 2.18 (m, 1 H), 2.40 (s, 3 H), 3.67 (m, 1 H), 4.44 (m, 1 H), 7.29 (d, J = 8.2 Hz, 2 H), 7.73 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 19.93 (q), 21.57 (q), 32.39 (t), 32.70 (t), 35.21 (d), 41.02 (t), 43.50 (d), 47.00 (d), 74.65 (d), 83.57 (d), 127.57 (2d), 129.70 (2d), 134.46 (s), 144.53 (s); MS m/z (relative intensity) (M^+ − 155, 24), 138 (60), 109 (11), 95 (20), 94 (100), 93 (10), 91 (29), 79 (19), 67 (13); HRMS calcd for $C_9H_{15}O_2$ (M^+ − 155) 155.1072, found 155.1086.

(α*S*,*exo*,*exo*)-α-Methyl-6-hydroxybicyclo[2.2.1]heptane-2-methanol α-(4-Methylbenzenesulfonate) (7). The silyl ether **26** (2.54 g, 5.99 mmol) was desilylated with HF as described for the synthesis of **1**. Workup and flash chromatography (2:1 petroleum ether (bp 40−60 °C)/EtOAc) afforded 1.84 g (99%) of **7**: ^{1}H NMR δ 0.77−1.02 (m, 2 H), 1.11−1.86 (m, 6 H), 1.15 (d, J = 6.1 Hz, 3 H), 2.06 (m, 1 H), 2.20 (m, 1 H), 2.42 (s, 3 H), 3.68 (m, 1 H), 4.24 (m, 1 H), 7.32 (d, J = 8.2 Hz, 2 H), 7.78 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 18.50 (q), 21.37 (q), 31.40 (t), 32.87 (t), 35.27 (d), 40.60 (t), 43.48 (d), 46.02 (d), 74.13 (d), 81.91 (d), 127.50 (2d), 129.52 (2d), 134.13 (s), 144.34 (s); MS m/z (relative intensity) (M^+, 0.1), 155 (18), 138 (54), 109 (13), 95 (23), 94 (100), 93 (10), 91 (30), 79 (19), 67 (14); HRMS calcd for $C_{16}H_{22}O_4S$ (M^+) 310.1239, found 310.1234.

***exo*-6-Ethylidenebicyclo[2.2.1]heptan-2-ol (27).** A solution of 0.116 g (0.273 mmol) of tosylate **25** and 0.056 g (0.68 mmol) of NaOAc in 2 mL of dry DMSO was stirred at 50 °C for 24 h and at 70 °C for an additional 30 h. The reaction mixture was allowed to come to rt and poured into 50 mL of H_2O. The aqueous layer was extracted with five 25 mL portions of ether. The combined organic layers were washed with 25 mL of brine, dried, and evaporated. The remaining residue was flash chromatographed (250:1 pentane/ether) to give 0.036 g (52%) of a 19:1 mixture of **27** and the TBDMS ether of **43**,[45] respectively. The spectroscopic data of **27** and the TBDMS ether of **43** are shown below.

27: ^{1}H NMR δ 0.02 (s, 3 H), 0.04 (s, 3 H), 0.88 (s, 9 H), 1.15−1.78 (m, 8 H), 1.97 (m, 1 H), 2.37 (m, 1 H), 2.48 (m, 1 H), 3.72 (m, 1 H), 5.36 (m, 1 H); ^{13}C NMR δ −4.72 (q), −4.58 (q), 14.13 (q), 18.25 (s), 25.93 (3q), 34.92 (t), 35.41 (t), 35.72 (d), 42.44 (t), 53.93 (d), 74.79 (d), 114.43 (d), 142.38 (s); MS m/z (relative intensity) 252 (M^+, <0.1), 196 (16), 195 (100), 122 (12), 121 (19), 120 (11), 106 (7), 94 (8), 76 (34), 74 (15); HRMS calcd for $C_{15}H_{28}OSi$ (M^+) 252.1909, found 252.1910.

TBDMS ether of 43: ^{1}H NMR δ 0.02 (s, 6 H), 0.86 (s, 9 H), 1.10−1.38 (m, 4 H), 1.47−1.73 (m, 2 H), 1.81−1.76 (m, 2 H), 2.23 (m, 1 H), 3.70 (m, 1 H), 4.81−4.98 (m, 2 H), 5.69 (m, 1 H); ^{13}C NMR δ −4.83 (2q), 18.93 (s), 25.65 (3q), 31.90 (t), 35.33 (d), 36.07 (t), 40.81 (d), 42.40 (t), 50.18 (d), 74.77 (d), 111.63 (t), 143.07 (d); MS m/z (relative intensity) 252 (M^+, 0.8), 197 (5), 196 (17), 195 (100), 120 (6), 92 (5), 80 (4), 78 (5), 77 (6), 76 (72), 74 (14); HRMS calcd for $C_{15}H_{28}OSi$ (M^+) 252.1909, found 252.1905.

***exo*,*exo*-2-(Methoxymethyl)-6-[[(1,1-dimethylethyl)dimethylsilyl]oxy]bicyclo[2.2.1]heptane (34).** To a solution of 0.304 g (1.19 mmol) of **21** in a mixture of 10 mL of MeI and 10 mL of dry DMF was added 0.150 g (6.25 mmol) of NaH. The reaction mixture was refluxed for 2 h, allowed to come to rt, and then carefully quenched by the addition of an excess of saturated aqueous NH_4Cl, followed by 20 mL of H_2O. The aqueous mixture was extracted with three 25 mL portions of EtOAc. The combined organic layers were washed with 10 mL of brine, dried, and evaporated. The resulting oil was flash chromatographed (100:1 petroleum ether (bp 40−60 °C)/EtOAc) to afford 0.253 g (79%) of **34**: ^{1}H NMR δ 0.00 (s, 3 H), 0.01 (s, 3 H), 0.84 (s, 9 H), 0.86 (m, 1 H), 1.03−1.37 (m, 3 H), 1.41−1.60 (m, 3 H), 1.98 (m, 1 H), 2.17 (m, 1 H), 3.03−3.23 (m, 2 H), 3.29 (s, 3 H), 3.66 (m, 1 H); ^{13}C NMR δ −4.90 (2q), 17.75 (s), 25.62 (3q), 31.58 (t), 33.14 (t), 34.83 (d), 36.88 (d), 42.32 (t), 46.62 (d), 58.35 (q), 74.79 (d), 76,12 (t); MS m/z (relative intensity) 213 (M^+ − 57, 100), 214 (19), 140 (35), 108 (65), 92 (8), 90 (27), 82 (6), 80 (46), 76 (44), 74 (23); HRMS calcd for $C_{11}H_{21}O_2Si$ (M^+ − 57) 213.1311, found 213.1308.

***exo*,*exo*-6-(Methoxymethyl)bicyclo[2.2.1]heptan-2-ol 4-Methylbenzenesulfonate (35).** The silyl ether **34** (0.220 g, 0.81 mmol) was desilylated with HF as described for the synthesis of **1**. Workup afforded 0.121 g of a clear oil. This crude oil was treated with TsCl for 8 h as described for the tosylation of **14**. Workup and flash chromatography (10:1 petroleum ether (bp 40−60 °C)/EtOAc) afforded 0.180 g (71%) of pure **35** as an oil: ^{1}H NMR δ 0.93 (m, 1 H), 1.10−1.29 (m, 2 H), 1.41−1.63 (m, 4 H), 2.16−2.28 (m, 2 H), 2.41 (s, 3 H), 2.99−3.18 (m, 2 H), 3.24 (s, 3 H), 4.42 (m, 1 H), 7.30 (d, J = 8.2 Hz, 2 H), 7.74 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 21.35 (q), 32.07 (t), 32.45 (t), 34.91 (d), 36.46 (d), 38.98 (t), 44.23 (d), 58.37 (q), 75.34 (t), 84.75 (d), 127.42 (2d), 129.51 (2d), 134.29 (s), 144.16 (s); MS m/z (relative intensity) 139 (M^+ − 171, 64), 155 (48), 139 (64), 138 (36), 109 (46), 108 (44), 92 (100), 80 (58), 67 (43), 46 (37); HRMS calcd for $C_9H_{15}O$ (M^+ − 171) 139.1126, found 139.1126.

Reactions of Tosylates 1−7 and 35 with Sodium *tert*-Amylate. Procedure A. All reactions were carried out at a concentration of ca. 0.1 M tosylate in dry benzene. The solutions were degassed and refluxed under an Ar atmosphere. Circa 5 equiv of sodium *tert*-amylate (3.2 M in toluene) was added at once, via syringe, to the refluxing solution of the tosylate. The reaction mixture was heated at reflux temperature for 1 or 10 min, quenched with precooled saturated aqueous NH_4Cl, and then quickly cooled to 0 °C. The mixture was vigorously stirred for 20 min, followed by extraction with five 10 mL portions of ether. The combined organic layers were dried and carefully evaporated under reduced pressure to afford the crude reaction products. Product ratios, yields, and pure compounds were obtained by chromatographical techniques.

Procedure B. Procedure A was employed by using a mixture of the tosylate and 1.0 equiv of an internal standard (ethylbenzene). After workup, qunatitative GC analyses of the combined organic layers (prior to evaporation) were performed with the use of authentic compounds and the internal standard. A response factor was used for analysis in a standard way. Mass spectra, for the identification of products, were measured with GCMS. Evaporation and flash chromatography afforded the nonvolatile products.

a. Procedure A was employed by using 0.199 g (0.67 mmol) of **1**. The reaction time was 10 min. Workup and flash chromatography (pentane to ether) afforded, in order of elution, 0.065 g (22%) of the ditosylated compound **29**, 0.011 g (12%) of lactol **30**, 0.030 g (15%) of unreacted **1**, and 0.021 g

(45) Treatment of **25** with sodium *tert*-amylate (procedure A, reaction time 10 min) gave this compound as the sole product in a slow reaction.

(22%) of diol **28**. The spectroscopic data of **28–30** are shown below.

***endo,endo*-6-Hydroxybicyclo[2.2.1]heptane-2-methanol (28)**: ^{1}H NMR δ 0.87 (ddd, J = 3.1, 4.7, 12.7 Hz, 1 H), 1.14–1.40 (m, 3 H), 1.63 (m, 1 H), 1.93 (m, 1 H), 2.03–2.23 (m, 3 H), 3.58–3.79 (m, 2 H), 4.13 (m, 1 H), 5.60 (br s, 2 OH); ^{13}C NMR δ 31.34 (t), 36.92 (d), 38.20 (t), 38.60 (t), 41.33 (d), 45.90 (d), 62.16 (t), 73.38 (d); MS m/z (relative intensity) 124 (M^+ – 18, 14), 106 (16), 96 (15), 95 (15), 82 (27), 81 (100), 80 (33), 68 (35), 67 (18), 56 (15), 42 (17); HRMS calcd for $C_8H_{12}O$ (M^+ – 18) 124.0888, found 124.0891.

***endo,endo*-6-[(4-Methylbenzenesulfonyl)oxy]bicyclo-[2.2.1]heptane-2-methanol 4-methylbenzenesulfonate (29)**: ^{1}H NMR δ 0.89–1.48 (m, 4 H), 1.81–2.07 (m, 2 H), 2.16–2.47 (m, 3 H), 2.44 (s, 6 H), 4.22 (d, J = 7.3 Hz, 2 H), 4.78 (m, 1 H), 7.27–7.40 (2d, 4 H), 7.68–7.80 (2d, 4 H); ^{13}C NMR δ 21.42 (2q), 34.35 (t), 36.23 (d), 36.47 (t), 37.65 (t), 39.26 (d), 43.33 (d), 73.88 (t), 82.51 (d), 127.50 (2d), 127.67 (2d), 129.59 (4d), 132.89 (s), 133.64 (s), 144.32 (s), 144.57 (s); MS m/z (relative intensity) 450 (M^+, 0.2), 172 (29), 155 (61), 124 (34), 108 (68), 107 (23), 96 (17), 92 (100), 81 (21), 80 (39); HRMS calcd for $C_{22}H_{26}O_6S_2$ (M^+) 450.1171, found 450.1170.

2-Oxatricyclo[4.2.1.0^{4,8}]nonan-3-ol (30): ^{1}H NMR δ 1.14–1.93 (m, 6 H), 2.15–2.42 (m, 2 H), 2.80–3.05 (m, 2 H), 4.52 (m, 1 H), 5.25 (m, 1 H); ^{13}C NMR δ 32.88 (t), 34.58 (d), 37.47 (t), 40.67 (t), 43.83 (d), 45.39 (d), 79.95 (d), 102.47 (d); MS m/z (relative intensity) 123 (M^+ – 17, 43), 119 (100), 117 (98), 97 (35), 95 (42), 85 (18), 83 (17), 80 (32), 67 (22), 28 (65); HRMS calcd for $C_8H_{11}O$ (M^+ – 17) 123.0810, found 123.0812.

b. Procedure B was employed by using 0.120 g (0.40 mmol) of **2**. The reaction time was 10 min. According to GC(MS) analysis, 0.007 g (19%) of **31**[15] was formed. Further workup and flash chromatography (pentane to ether) afforded, in order of elution, 0.008 g (4%) of **32** and 0.021 g (21%) of unreacted **2**.

c. Procedure B was employed by using 0.076 g (0.26 mmol) of **3**, except that the reaction was stirred at rt for 10 min. According to GC(MS) analysis, 0.013 g (55%) of **31** and 0.002 g (6%) of **33**[16] were formed.

d. Procedure B was employed by using 0.050 g (0.17 mmol) of **3**, except that the solution of **3** was added to the refluxing solution of sodium *tert*-amylate. The reaction time was 1 min. According to GC(MS) analysis, 78% of **31** and 3% of **33** were formed.[46]

e. Procedure B was employed by using 0.532 g (1.80 mmol) of **4**. The reaction time was 10 min. According to GC(MS) analysis, 0.062 g (28%) of **36**[11] was formed. Further workup and flash chromatography (pentane to ether) afforded 0.021 g (4%) of unreacted **4**.

f. Procedure A was employed by using 0.164 g (0.55 mmol) of **5**. The reaction time was 10 min. After workup, a complex mixture was obtained from which only unreacted **5** (48%) could be isolated.

g. This procedure is the same as above, except that the reaction mixture was heated at reflux for 1 min. With 0.250 g (0.85 mmol) of **5** as starting material, workup and flash chromatography (pentane to ether) afforded, in order of elution, 0.012 g (5%) of **37**, 0.180 g (72%) of unreacted **5**, 0.006 g (5%) of **16**, and 0.004 g (3%) of **38**. The spectroscopic data of **37** and **38** are shown below.

***exo*-6-[(4-Methylbenzenesulfonyl)oxy]bicyclo[2.2.1]-heptan-2-one (37)**: ^{1}H NMR δ 1.37 (m, 1 H), 1.55–1.73 (m, 3 H), 1.83 (m, 1 H), 1.97–2.20 (m, 2 H), 2.44 (s, 3 H), 2.47 (m, 1 H), 2.67 (m, 1 H), 3.90 (d, J = 7.4 Hz, 2 H), 7.34 (d, J = 8.2 Hz, 2 H), 7.77 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 21.68 (q), 31.76 (t), 34.50 (t), 35.29 (d), 35.62 (d), 44.44 (t), 51.76 (d), 71.15 (t), 127.89 (2d), 129.95 (2d), 133.12 (s), 145.02 (s), 215.52 (s); MS m/z (relative intensity) 294 (M^+, 27), 122 (100), 94 (49), 93 (33), 91 (80), 81 (37), 80 (60), 79 (88), 78 (94); HRMS calcd for $C_{15}H_{18}O_4S$ (M^+) 294.0926, found 294.0926.

***exo,exo*-6-Hydroxybicyclo[2.2.1]heptane-2-methanol (38)**: ^{1}H NMR δ 0.86 (m, 1 H), 1.07–1.70 (m, 6 H), 2.14 (m, 1 H), 2.23 (m, 1 H), 2.70 (br s, 2 OH), 3.24–3.48 (m, 2 H), 3.76 (m, 1 H); ^{13}C NMR δ 31.46 (t), 32.43 (t), 35.12 (d), 39.97 (d), 41.41 (t), 46.20 (d), 65.77 (t), 74.60 (d); MS m/z (relative intensity) 124 (M^+ – 18, 11), 106 (53), 93 (36), 91 (35), 81 (31), 80 (100), 79 (41), 67 (72), 55 (22), 41 (25); HRMS calcd for $C_8H_{12}O$ (M^+ – 18) 124.0888, found 124.0881.

h. Procedure A was employed by using 0.396 g (1.28 mmol) of **6**. The reaction time was 1 min. Workup and flash chromatography (pentane to 2:1 pentane/ether) afforded 0.098 g (51%) of [(1′α,3′α,5′α,6′α)-6′-methylbicyclo[3.1.0]hexan-3′-yl]-acetaldehyde (**39**) as the sole product: ^{1}H NMR δ 0.58 (m, 1 H), 0.82–0.98 (m, 2 H), 0.89 (d, J = 5.9 Hz, 3 H), 1.20–1.42 (m, 2 H), 1.80–2.07 (m, 3 H), 2.31–2.43 (m, 2 H), 9.66 (t, J = 2.1 Hz, 1 H); ^{13}C NMR δ 14.01 (d, J = 158.6 Hz), 17.32 (q), 25.14 (2d, J = 165.0 Hz), 29.88 (d), 34.36 (2t), 49.45 (t), 202.23 (d); MS m/z (relative intensity) 138 (M^+, 0.8), 95 (25), 94 (100), 93 (13), 79 (63), 77 (11), 67 (16), 55 (27), 41 (14); HRMS calcd for $C_9H_{14}O$ (M^+) 138.1045, found 138.1046.

i. Procedure A was employed by using 0.215 g (0.69 mmol) of **7**. The reaction time was 1 min. Workup and flash chromatography (pentane to ether) afforded, in order of elution, 0.040 g (42%) of an inseparable 15:4:1 mixture of **40**, **41**, and **42**, respectively, 0.006 g (6%) of **43**, and 0.051 g (24%) of unreacted **7**. Analytical samples of the aldehydes **40–42** were obtained by preparative GC. The spectroscopic data of **40–43** are shown below.

[(1′α,3′α,5′α,6′β)-6′-Methylbicyclo[3.1.0]hexan-3′-yl]-acetaldehyde (40): ^{1}H NMR δ 0.76 (m, 1 H), 0.92 (d, J = 6.2 Hz, 3 H), 1.19–1.32 (m, 2 H), 1.40–1.56 (m, 2 H), 1.87 (dd, J = 8.2, 13.2 Hz, 2 H), 2.11 (m, 1 H), 2.42 (dd, J = 2.1, 7.0 Hz, 2 H), 9.68 (t, J = 2.1 Hz, 1 H); ^{13}C NMR δ 7.91 (q), 13.93 (d, J = 151.8 Hz), 21.20 (2d, J = 165.4 Hz), 31.88 (2t), 34.80 (d), 51.95 (t), 202.35 (d); MS m/z (relative intensity) 138 (M^+, 56), 109 (23), 95 (32), 94 (100), 91 (36), 79 (26), 71 (30), 57 (43), 55 (31); HRMS calcd for $C_9H_{14}O$ (M^+) 138.1045, found 138.1043.

[(3′α,5′α)-3′-Methylcyclohexen-5′-yl]acetaldehyde (41): ^{1}H NMR δ 0.96 (d, J = 7.1 Hz, 3 H), 1.50–1.85 (m, 3 H), 2.02–2.43 (m, 5 H), 5.45–5.66 (m, 2 H), 9.78 (t, J = 2.2 Hz, 1 H); MS m/z (relative intensity) 138 (M^+, 49), 121 (32), 95 (15), 94 (100), 93 (14), 91 (36), 79 (26), 75 (14), 67 (12); HRMS calcd for $C_9H_{14}O$ (M^+) 138.1045, found 138.1043.

(1′-Ethylcyclopenten-4′-yl)acetaldehyde (42): ^{1}H NMR δ 1.02 (dd, J = 7.4, 7.4 Hz, 3H), 1.84–2.13 (m, 4 H), 2.43–2.82 (m, 5 H), 5.25 (m, 1 H), 9.75 (t, J = 1.9 Hz, 1 H); MS m/z (relative intensity) 138 (M^+, 49) 97 (17), 95 (22), 94 (100), 91 (36), 79 (29), 57 (30), 43 (24), 41 (19); HRMS calcd for $C_9H_{14}O$ (M^+) 138.1045, found 138.1043.

(2-*exo*,6-*exo*)-2-Hydroxy-6-ethenylbicyclo[2.2.1]-heptane (43): ^{1}H NMR δ 1.14–1.74 (m, 7 H), 1.87–2.08 (m, 2 H), 2.28 (m, 1 H), 3.82 (m, 1 H), 4.83–4.99 (m, 2 H), 5.74 (ddd, J = 7.4, 10.0, 17.1 Hz, 1 H); ^{13}C NMR δ 31.78 (t), 35.47 (d), 35.59 (t), 40.76 (d), 41.52 (t), 50.06 (d), 74.49 (d), 112.02 (t), 142.62 (d); MS m/z (relative intensity) 138 (M^+, 11), 120 (83), 105 (57), 95 (90), 94 (60), 93 (96), 92 (46), 84 (42), 80 (100), 78 (41); HRMS calcd for $C_9H_{14}O$ (M^+) 138.1045, found 138.1045.

j. This procedure is the same as above, except that, in addition to sodium *tert*-amylate, 1 equiv of 15-crown-5 was used. After workup, flash chromatography (pentane to ether) gave, in order of elution, 0.042 g (53%) of **40**, 0.009 g (11%) of **43**, and 0.021 g (12%) of unreacted **8**.

k. Procedure A was employed by using 0.105 g (0.34 mmol) of **35**. The reaction time was 10 min. After workup, 87% of unreacted **35** was recovered. No reaction products could be isolated.

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Supplementary Material Available: ^{1}H NMR spectra for compounds **2**, **3**, **5–7**, **13**, **14**, **16–18**, **20–22**, **27–30**, **34**, **35**, and **37–43** (30 pages). This material is contained in libraries on microfiche, immediately 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.

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(46) This reaction is another example of the highly selective formation of nortricyclene in norbornyl reactions: Shine, H. J.; Yueh, W. *J. Org. Chem.* **1994**, *59*, 3553.