Long-Range Effects of Through-Bond Orbital Interactions on the Desilylation Rate of Silyl Ethers

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Received May 18, 1995[⊗]

The kinetics of the desilylation reactions of a range of sulfonated and methoxylated norbornyl silyl ethers **1**–**10** were investigated to establish the quantitative correlation between the geometry of the σ-relay and the rate of desilylation. These desilylation rates generally decrease in the order W > sickle-like > U arrangement of the σ-relay. The methoxylated silyl ethers show a decreased reactivity in comparison with the corresponding sulfonated silyl ethers. The orientation of the silyloxy group does not affect the reaction rate. Conformational mobility and alkyl substitution of the σ-relay also are of influence on the rate of desilylation. The observed effects are confirmed by similar behavior in the desilylation reactions of the silyl ethers **11**–**14** derived from *trans*-perhydronaphthalene-1,4-diols.

Introduction

Up to now, our attention was primarily focused on the reaction behavior of 1,4-diol monosulfonate esters under strongly basic conditions in apolar non-nucleophilic solvents.[1] Long-range orbital interactions through the four σ-bonds between the alcoholate anion (electron donor) and the sulfonate ester group (electron acceptor) are considered to be responsible for the intramolecularly induced heterolysis of the sulfonate ester bond. The extent of these through-bond orbital interactions (TBI)[2] depends on the geometry of the σ-relay (the intervening σ-framework). A W arrangement of the σ-relay is the most favorable geometry for transmission of TBI (trans rule).[3] The introduction of a gauche interaction in the σ-relay leads to a sickle-like arrangement and makes transmission of TBI more difficult, thereby reducing the reactivity of the compounds involved. Compounds in which two gauche interactions are present (U arrangement) do not react via TBI-induced heterolysis of the sulfonate ester bond. Although a rough estimate of the relative reaction rates could be obtained from comparison of the quantities of recovered starting material after a limited reaction time, accurate kinetic measurements on these compounds are problematic.[4]

From our recent work,[1e] it was found that the silyl ether bond of tosylate **1** is remarkably unstable. It was assumed that the remote tosylate group facilitates the cleavage of the Si–O bond, probably by a similar TBI-controlled mechanism that induces heterolysis of the sulfonate ester bond. If this assumption is correct, the stability of the Si–O bond should also depend on the geometry of the σ-relay. Therefore, in order to provide more detailed insight into this interaction, we have studied the kinetics of desilylation reactions of a range of structurally different silyl ethers at appropriate temperatures.

The sulfonated norbornyl silyl ethers **1**–**3** were investigated to establish the quantitative correlation between the geometry of the σ-relay and the rate of desilylation. As indicated in Chart 1 by the bold bonds, the silyl ethers **1**, **2**, and **3** have the W, sickle-like, and U arrangement of the σ-relay, respectively. The silyl ethers **4** and **5** were studied to find out whether the orientation of the silyl ether function has any influence on the rate of desilylation. Information about the effect of a primary vs secondary sulfonate ester group on the desilylation rate was obtained from the silyl ethers **5**–**7**. If the rate of desilylation is indeed affected by a remote sulfonate ester group, then this rate will change when the sulfonate ester group is replaced by a less strongly electron-withdrawing group, e.g., a methoxy group. In order to confirm this hypothesis, the silyl ethers **8**–**10** were investigated. Finally, the general occurrence of these TBI-controlled reactions and especially the influence of the geometry of the σ-relay (bold bonds) were checked up on the silyl ethers **11**–**14** derived from *trans*-perhydronaphthalene-1,4-diols (Chart 2).

Results and Discussion

The tosylated silyl ether **1** was obtained upon treatment of the corresponding alcohol[1e] with TBDMSCl in $CHCl_3$ and could only be isolated in pure form after reversed-phase chromatography. The tosylated silyl ethers **2**–**7** and the mesylated silyl ethers **11**–**14** were prepared according to standard procedures (see Experimental Section). The known carboxylic acid **15**[5] was used as starting material for the synthesis of the silylated methyl ether **8** (Scheme 1). For the preparation of **9** and **10**, the corresponding monosilylated 1,4-diols[1e] were treated with *t*-BuOK and MeI in THF at 0 °C.[6]

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

(1) (a)Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; Brunekreef, G. A.; de Groot, A. *J. Org. Chem.* **1990**, *55*, 941. (b) Jenniskens, L. H. D.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1991**, *56*, 6585. (c) Orrū , R. V. A.; Wijnberg, J. B. P. A.; Jenniskens, L. H. D.; de Groot, A. *J. Org. Chem.* **1993**, *58*, 1199. (d) Orrū, R. V. A.; Wijnberg, J. B. P. A.; Bouwman, C. T.; de Groot, A. *J. Org. Chem.* **1994**, *59*, 374. (e) Bastiaansen. P. M. F. M.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1995**, *60*, 4240.

(2) 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 and references cited therein.

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

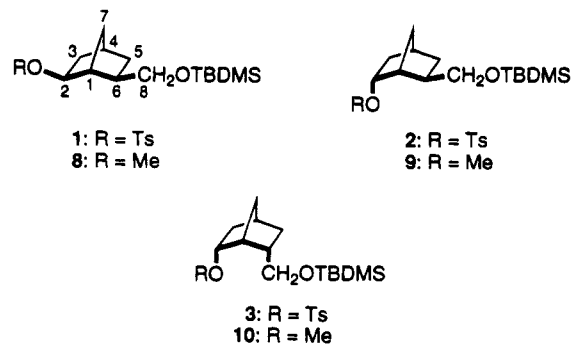
(4) The vigorous conditions (excess of strong base, refluxing benzene) at which the heterolysis of 1,4-diol monosulfonate esters proceeds do not allow for easy kinetic measurements.

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

(6) Green, T. W.; Wuts, P. G. M. In *Protective Groups in Organic Synthesis*; Wiley-Interscience: New York, 1991; p 15.

0022-3263/95/1960-6154$09.00/0

Chart 1



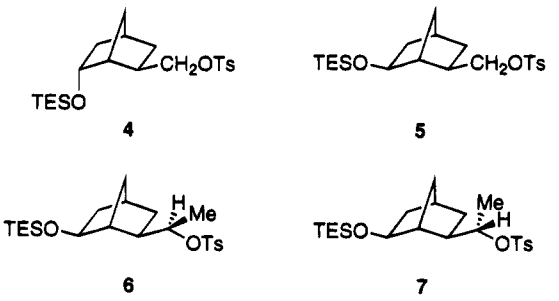
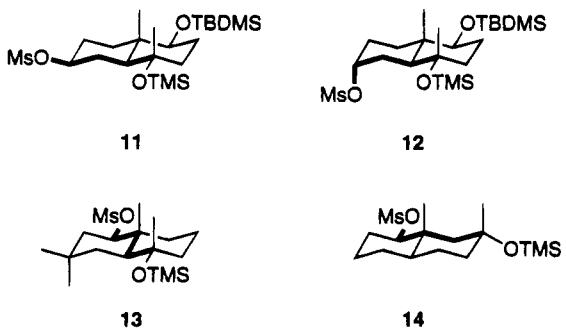
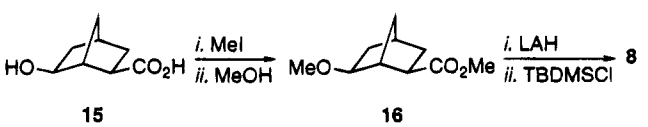


Chart 2



Scheme 1



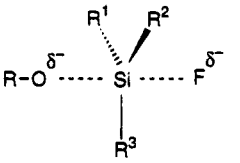
The desilylation reactions were performed under standardized conditions using dry acetonitrile as the solvent and commercial tetrabutylammonium fluoride (TBAF) as desilylating reagent.[7] The reactions were studied under pseudo-first-order conditions and resulted in the generation of the corresponding alcohols.[8] The extent of reaction was followed by HPLC, monitoring the change in concentration of the silyl ether with time.[9] In this way, linear plots were obtained from which the pseudo-first-order rate constants (k_{obs}) could easily be determined. For practical reasons,[10] the use of TBDMS ethers derived from primary alcohols was preferred. In case of secondary and tertiary alcohols the corresponding triethylsilyl (TES)[11] and TMS ethers, respectively, were employed. The kinetic data obtained from these experiments are collected in Tables 1–3.

Table 1. Pseudo-First-Order Rate Constants (k_{obs}) for Desilylation of TBDMS Ethers with TBAF in Acetonitrile at 25 °C[a]

entry	substrate	$k_{obs} \times 10^{-3}$ min^{-1}	r^{b}
1	1	15.4	0.999
2	2	4.3	0.996
3	3	1.3	0.996
4	8	5.6	0.999
5	9	2.3	0.995
6	10	0.4	0.993

[a] The pseudo-first-order rate constants (k_{obs}) were determined in triplicate with an excess of TBAF (10 equiv) and were reproducible to within ±5%. Temperature control was within ± 0.1 °C. [b] Correlation coefficient at worst.

Chart 3



The tosylated silyl ethers **1**, **2**, and **3** show distinct differences in their rate of desilylation (Table 1, entries 1–3). A decrease in k_{obs} is noticed in the order **1** > **2** > **3** which corresponds with a reactivity order W > sickle-like > U arrangement of the σ-relay, respectively. A similar tendency is observed for the methylated silyl ethers **8**, **9**, and **10**, on the understanding that each Me compound reacts more slowly than its tosyl analog upon treatment with TBAF (Table 1, entries 4–6).

One could argue that a relief in *endo*-crowding[12] might affect the desilylation rate of compounds in which an U arrangement of the σ-relay is present (**3** and **10**). However, this argument is not valid for explaining the differences in reaction rate between **1** and **8** and between **2** and **9**, because in each pair the TBDMS group is free of steric hindrance. We therefore assume that the differences in reaction rate are directly related to the differences in the leaving-group ability of the alcohol function.[13] If the breaking of the Si–O bond occurs by a one-step concerted reaction (S_N2–Si mechanism),[14] partial negative charge will be built up on oxygen in the transition state (Chart 3). Stabilization of this partial negative charge by the remote sulfonate ester group via an electronic coupling through the intervening C–C bonds will lower the energy of the transition state, and consequently, the rate of desilylation will increase. As the k_{obs} values in Table 1 clearly show, the sulfonate ester group is, in this respect, more effective than the less strongly electron-withdrawing methoxy group.

The relatively fast desilylation rate of the compounds **1** and **8** in the tosyl and Me series, respectively, is consistent with the trans rule (Table 1, entries 1 and 4). According to this rule, the W arrangement of the σ-relay in **1** and **8** ensures a proper alignment of the orbitals

(7) TBAF is available commercially as a 1.1 M solution in THF, containing 4.5–5% H_2O. This amount of H_2O can serve as proton donor in the desilylation reactions.

(8) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

(9) Bently, T. W.; Gream, G. E. *J. Org. Chem.* **1985**, *50*, 1776.

(10) When TMS or TES ethers derived from primary alcohols were desilylated at room temperature or 0 °C, the reaction proceeded so fast that accurate kinetic measurements were not possible. Likewise, the TBDMS ethers (too slow) and TMS ethers (too fast) of secondary alcohols were not suitable for these measurements.

(11) The kinetic measurements on TES ethers were performed at 0 °C.

(12) Grob, C. A.; Günther, B.; Hanreich, R. *Helv. Chim. Acta* **1982**, *65*, 2110.

(13) Colvin, E. In *Silicon in Organic Synthesis*; Butterworths: London, 1981; Chapter 15.

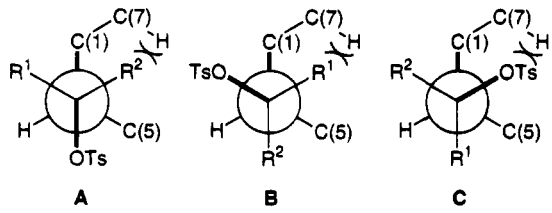
(14) The exact mechanism for Si–O bond breaking is still a point of discussion. For example, see: Dietze, P. E. *J. Org. Chem.* **1993**, *58*, 5653.

Table 2. Pseudo-First-Order Rate Constants (k_{obs}) for Desilylation of TES Ethers with TBAF in Acetonitrile at 0 °C[a]

entry	substrate	$k_{obs} \times 10^{-2}$ min^{-1}	r[b]
1	4	5.1	0.991
2	5	4.6	0.991
3	6	4.8	0.983
4	7	1.9	0.997

[a] The pseudo-first-order rate constants (k_{obs}) were determined in triplicate with an excess of TBAF (10 equiv) and were reproducible to within ±5%. Temperature control was within ±0.1 °C. [b] Correlation coefficient at worst.

Chart 4



5: $R^1 = R^2 = H$
6: $R^1 = Me$; $R^2 = H$
7: $R^1 = H$; $R^2 = Me$

involved through which transmission of TBI is more efficient and, as a result, a relative fast reaction can occur. In the corresponding reactions of compounds in which one (**2** and **9**) or two (**3** and **10**) gauche interactions are present, transmission of TBI will be more difficult, thereby reducing the reactivity of these compounds.

The reactions of the TES ethers **4** and **5** show no significant difference in the rate of desilylation (Table 2, entries 1 and 2). Apparently, the orientation of the silyl ether group has little influence on the transmission of TBI. This phenomenon has also been observed in the base-induced heterolysis of 1,4-diol monosulfonate esters.[1c]

By the interpretation of the k_{obs} values determined for the reactions of **5**–**7** (Table 2, entries 2–4), one has to keep in mind that these compounds will adopt the minimum-energy geometry that is available by rotation about the C(6)–C(8) bond.[15] From the Newman projections of the three staggered ground state conformations of **5**–**7** around the C(6)–C(8) bond, it is clear that the lowest-energy conformations will be **5A** or **5B**, **6A**, and **7B**, respectively (Chart 4). In these conformations only a small steric repulsion between syn H-7 and H-8 will exist. The other staggered conformations are assumed to be higher in energy because of more steric repulsion between syn H-7 and, in these cases, the larger C(8) substituents (Me in **6B** and **7A**; tosylate in **5C**, **6C**, and **7C**). The Newman projections of the lowest-energy conformations of **5**–**7** also point to differences in the σ-relay of these conformations. The anti relationship between the C(1)–C(6) bond and the C(8)–OTs bond in **5A** and **6A** corresponds with a W arrangement of the σ-relay, while in **5B** and **7B** the gauche relationship between these two bonds represents a sickle-like arrangement. In line with this reasoning and with the knowledge that conformations in which a W arrangement of the σ-relay is present are more reactive than those with a sickle-like arrangement,[1e] the differences in k_{obs} found for the reactions of **5**–**7** can be better understood. With

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

Table 3. Pseudo-First-Order Rate Constants (k_{obs}) for Desilylation of TMS Ethers with TBAF in Acetonitrile at Ambient Temperature[a]

entry	substrate	$k_{obs} \times 10^{-2}$ min^{-1}	r[b]
1	11	17.3	0.999
2	12	4.2	0.997
3	13	>35[c]	
4	14	6.1	0.998

[a] Reactions were performed at ambient temperature (21–24 °C). The pseudo-first-order rate constants (k_{obs}) were determined in triplicate with an excess of TBAF (6.7 equiv) and were reproducible to within ± 5%. [b] Correlation coefficient at worst. [c] Under these circumstances the desilylation of **13** proceeded so fast that k_{obs} could not be determined accurately.

the use of the Winstein–Holness (W–H) principle,[16] it follows that **6** will react more rapidly than **7** (Table 2, entries 3 and 4) and that the reaction rate of **5** and **6** will be broadly the same (Table 2, entries 2 and 3), assuming that the contribution of conformation **5B** to the overall rate constant of **5** is only modest.[17] The approximately equal k_{obs} values determined for **5** and **6** also suggest that the nature of the sulfonate ester group (primary or secondary) has little influence on the desilylation rate. In this respect, it should be mentioned that in the base-induced reactions of the corresponding 1,4-diol monosulfonate esters large differences in reactivity between primary and secondary compounds are observed.[1e]

The compounds **11**–**14** of the *trans*-perhydronaphthalene series show a similar relationship between reactivity and geometry of the σ-relay as has been found for the compounds of the norbornane series. The TMS ether **11** reacts more rapidly than the corresponding TMS ether **12**. This finding corresponds with a reactivity order W > sickle-like arrangement of the σ-relay (Table 3, entries 1 and 2).[18] The same tendency is observed for the TMS ethers **13** and **14** (Table 3, entries 3 and 4). The data in Table 3 also show that the compounds **11** and **13** react with different rates (k_{obs} (**11**) ≈ 0.5 k_{obs} (**13**)). The compounds **12** and **14** show a similar but less explicit behavior (k_{obs} (**12**) ≈ 0.7 k_{obs} (**14**)). Because the operating σ-relay in each pair is identical (W- or sickle-shaped), one might expect broadly the same k_{obs} values for **11** and **13** and for **12** and **14**. This is not the case, and apparently, next to the geometry of the σ-relay, other factors contribute to the rate of desilylation of these compounds. One of these factors might be the degree of alkyl substitution of the σ-relay. As their structures show, the σ-relay of **13** has two alkyl substituents more than that of **11** and the σ-relay of **14** has one alkyl substituent more than that of **12**. These differences in degree of substitution of the σ-relay might explain the differences in k_{obs} found for these compounds. Similar alkyl substituent effects have

(16) According to the W–H principle, the overall rate constant (k_{obs}) is the average of the specific rate constants of the individual conformers weighted by their mole fractions: Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83.

(17) It might be possible that the conformational equilibrium position of ground state conformations is affected by TBI. This possibility 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. *J. Am. Chem. Soc.* **1989**, *111*, 4433.

(18) During the kinetic measurements on **11** and **12** no cleavage of the Si–O bond of the TBDMS ether function was observed.

(19) Orrū, R. V. A.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **1995**, *60*, 4233.

(20) Bastiaansen. P. M. F. M.; Wijnberg, J. B. P. A.; de Groot, A. Manuscript in preparation.

been observed in the heterolysis reactions of 1,4-[19] and 1,5-diol monosulfonate esters.[20]

Concluding Remarks

These kinetic experiments clearly show that the rate of desilylation of the compounds studied is directly related to the geometry of the σ-relay and generally decreases in the order W > sickle-like > U arrangement. These findings confirm, once again, the validity of the trans rule in TBI-controlled processes. Replacing of the sulfonate ester group by the less electron-accepting methoxy group leads to a decrease of reactivity.[21] The orientation of the silyloxy group does not affect the rate of desilylation. The differences in k_{obs} found for the conformationally mobile silyl ethers are easily understood with the W−H principle. The degree of alkyl substitution of the σ-relay may also be of influence on the reaction rate.

Similar effects on the reactivity has been found for 1,4-diol monosulfonate esters in the base-induced heterolysis reactions.[1d,e,19] From this similarity, one may conclude that in the desilylation reaction as well as in the heterolysis reaction the same through-bond orbital interactions are involved.

In conclusion, it appears that long-range through-bond orbital interactions do affect the rate of desilylation in a predictable manner and that the desilylation reaction offers a simple method for exploring the extent of such interactions. The results of this study may also be helpful for explaining unexpected features of polyfunctional systems, as for example the remarkable instability of the Si−O bond of compound **1**.

Experimental Section[22]

Materials. All reagents were purchased from Aldrich or Janssen and were used without further purification. The monotosylated 1,4-diols[1e] used in the synthesis of **1** and **4**−**7**, the monomesylated 1,4-diols[1c] used in the synthesis of **13** and **14**, and the monosilylated 1,4-diols[1e] used in the synthesis of **9** and **10** were prepared following previously described procedures. Compounds **2**,[1e] **3**,[1e] **11**,[1c] and **12**[1c] have been synthesized and fully characterized before. The carboxylic acid **15** was prepared as described previously.[5]

***exo,exo*-6-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]bicyclo[2.2.1]heptan-2-ol 4-Methylbenzenesulfonate (1).** This compound was prepared upon treatment of a solution of 0.203 g (0.68 mmol) of the corresponding monotosylated 1,4-diol in 10 mL of dry $CHCl_3$ with 0.077 g (1.13 mmol) of imidazole and 0.143 g (0.95 mmol) of TBDMSCl. The solution was stirred at rt for 7 h, after which time another portion of TBDMSCl (0.070 g, 0.47 mmol) was added. Stirring was continued for 16 h, and then five drops of MeOH were added. The solution was stirred for an additional 15 min and poured into 25 mL of ether. The organic layer was washed with H_2O and brine, dried, and evaporated. The remaining oil was chromatographed on a SPE column filled with reversed-phase C_{18} partical size 40 μm (3:1 H_2O/CH_3CN to CH_3CN) to give 0.102 g (37%) of **1**: ^1H NMR δ −0.02 (s, 6 H), 0.82 (s, 9 H), 0.89 (m, 1 H), 1.06−1.27 (m, 2 H), 1.30−1.51 (m, 2 H), 1.55−1.64 (m, 2 H), 2.22 (m, 1 H), 2.26 (br s, 1 H), 2.41 (s, 3 H), 3.19−3.40 (m, 2 H), 4.41 (m, 1 H), 7.30 (d, J = 8.2 Hz, 2 H), 7.75 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ −5.40 (2 q), 18.20 (s), 21.58 (q), 25.85 (3 q), 32.06 (2 t), 35.12 (d), 39.31 (t), 39.39 (d), 44.09 (d), 65.50 (t), 85.33 (d), 127.59 (2 d), 129.73 (2 d), 134.62 (s), 144.28 (s); MS m/z (relative intensity) 353 (M^+ − 57, 5), 230 (14), 229 (100), 149 (4), 107 (20), 91 (8), 79 (7), 75 (5), 73 (7); HRMS calcd for $C_{17}H_{25}O_4SSi$ (M^+ − 57) 353.1243, found 353.1249.

General Procedure for the Preparation of TES Ethers 4−7. To a solution (0.074−0.104 M) of the corresponding monotosylated 1,4-diol in dry DMF were added imidazole (ca. 2 equiv) and TESCl (ca. 1.5 equiv). The reaction mixture was stirred at rt, and the reaction progress was monitored by TLC. At completion, the mixture was poured into 25 mL of H_2O and extracted with four 10 mL portions of ether. The combined organic layers were washed with brine, dried, and evaporated. The resulting product was purified by flash chromatography (50:1 petroleum ether (bp 40−60 °C)/EtOAc).

(2-*exo*,6-*endo*)-6-[(Triethylsilyl)oxy]bicyclo[2.2.1]heptane-2-methanol α-(4-methylbenzenesulfonate) (4): yield 99%; ^1H NMR δ 0.44 (q, J = 7.8 Hz, 2 H), 0.45 (q, J = 7.8 Hz, 4 H), 0.67−1.10 (m, 4 H), 0.94 (t, J = 7.8 Hz, 9 H), 1.39 (m, 1 H), 1.77 (m, 1 H), 1.94 (m, 1 H), 2.05 (m, 1 H), 2.37 (s, 3 H), 2.53 (m, 1 H), 3.68−3.84 (m, 2 H), 4.02 (m, 1 H), 7.26 (d, J = 8.2 Hz, 2 H), 7.71 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 4.72 (3 t), 6.76 (3 q), 21.60 (q), 31.00 (d), 34.10 (t), 34.26 (t), 37.03 (d), 39.02 (t), 45.10 (d), 72.09 (d), 73.52 (t), 127.83 (2 d), 129.74 (2 d), 133.53 (s), 144.51 (s); MS m/z (relative intensity) 381 (M^+ − 29, 0.8), 257 (100), 107 (42), 79 (18), 71 (18), 69 (21), 57 (26), 55 (19), 43 (19); HRMS calcd for $C_{19}H_{29}O_4SSi$ (M^+ − 29) 381.1556, found 381.1550.

***exo,exo*-6-[(Triethylsilyl)oxy]bicyclo[2.2.1]heptane-2-methanol α-(4-methylbenzenesulfonate) (5):** yield 93%; ^1H NMR δ 0.52 (q, J = 7.8 Hz, 2 H), 0.53 (q, J = 7.8 Hz, 4 H), 0.78−1.03 (m, 2 H), 0.91 (t, J = 7.8 Hz, 9 H), 1.10−1.37 (m, 2 H), 1.43−1.68 (m, 3 H), 1.92 (m, 1 H), 2.17 (m, 1 H), 2.43 (s, 3 H), 3.61 (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 4.79 (3 t), 6.77 (3 q), 21.58 (q), 31.75 (t), 32.69 (t), 35.00 (d), 36.59 (d), 42.30 (t), 46.48 (d), 72.80 (t), 74.34 (d), 127.78 (2 d), 129.76 (2 d), 133.21 (s), 144.61 (s); MS m/z (relative intensity) 381 (M^+ − 29, 1.0), 259 (10), 258 (18), 257 (100), 107 (23), 79 (8), 69 (6), 57 (8); HRMS calcd for $C_{19}H_{29}O_4SSi$ (M^+ − 29) 381.1556, found 381.1555.

(αR,*exo*,*exo*)-α-Methyl-6-[(triethylsilyl)oxy]bicyclo[2.2.1]heptane-2-methanol α-(4-methylbenzenesulfonate) (6): yield 91%; ^1H NMR δ 0.51 (q, J = 7.8 Hz, 2 H), 0.52 (q, J = 7.8 Hz, 4 H), 0.90 (t, J = 7.8 Hz, 9 H), 1.05−1.36 (m, 8 H), 1.42−1.56 (m, 2 H), 1.74 (m, 1 H), 2.16 (m, 1 H), 2.42 (s, 3 H), 3.58 (m, 1 H), 4.45 (m, 1 H), 7.31 (d, J = 8.2 Hz, 2 H), 7.76 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 4.77 (3 t), 6.74 (3 q), 20.05 (q), 21.56 (q), 32.58 (t), 33.00 (t), 35.10 (d), 41.98 (t), 43.67 (d), 47.43 (d), 74.97 (d), 83.57 (d), 127.64 (2 d), 129.63 (2 d), 134.60 (s), 144.37 (s); MS m/z (relative intensity) 395 (M^+ − 29, 2.4), 258 (18), 257 (100), 121 (39), 99 (22), 57 (20), 55 (16); HRMS calcd for $C_{20}H_{31}O_4SSi$ (M^+ − 29) 395.1712, found 395.1710.

(αS,*exo*,*exo*)-α-Methyl-6-[(triethylsilyl)oxy]bicyclo[2.2.1]heptane-2-methanol α-(4-methylbenzenesulfonate) (7): yield 88%; ^1H NMR δ 0.50 (q, J = 7.8 Hz, 2 H), 0.51 (q, J = 7.8 Hz, 4 H), 0.89 (t, J = 7.8 Hz, 9 H), 0.77−0.98 (m, 2 H), 1.09−1.57 (m, 8 H), 1.87 (m, 1 H), 2.15 (m, 1 H), 2.42 (s, 3 H), 3.53 (m, 1 H), 4.27 (m, 1 H), 7.30 (d, J = 8.2 Hz, 2 H), 7.78 (d, J = 8.2 Hz, 2 H); ^{13}C NMR δ 4.77 (3 t), 6.77 (3 q), 18.99 (q), 21.54 (q), 31.80 (t), 33.37 (t), 35.32 (d), 41.98 (t), 43.71 (d), 46.32 (d), 74.51 (d), 82.18 (d), 127.66 (2 d), 129.64 (2 d), 134.50 (s), 144.37 (s); MS m/z (relative intensity) 395 (M^+ − 29, 1.2), 258 (17), 257 (100), 121 (55), 93 (16), 91 (17), 87 (12), 75 (11); HRMS calcd for $C_{20}H_{31}O_4SSi$ (M^+ − 29) 395.1712, found 395.1710.

***exo,exo*-2-Carbomethoxy-6-methoxybicyclo[2.2.1]heptane (16).** To a stirred solution of 0.202 g (1.29 mmol) of carboxylic acid **15** in 10 mL of dry DMF were added successively 10 mL of MeI and 0.150 g (6.25 mmol) of NaH. The reaction mixture was refluxed for 7 h and, after being cooled to rt, quenched with a small amount of saturated aqueous NH_4Cl. After addition of 20 mL of H_2O, the aqueous solution was extracted with five 25 mL portions of EtOAc. The combined organic layers were washed with brine, dried, and evaporated. The resulting oil was dissolved in 50 mL of dry MeOH, and 1 mL (7.88 mmol) of TMSCl was added. The solution was stirred at rt for 3 h and then carefully neutralized by the addition of

(21) Modifications in the electron donor−acceptor system can affect the extent of TBI. See ref 17: Krijnen et al.

(22) For a general description of the experimental procedures employed in this research, see ref 1b.

1 N aqueous NaOH. The solution was concentrated under reduced pressure, and the remaining residue was taken up into 20 mL of EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried, and evaporated. The resulting oil was flash chromatographed (10:1 petroleum ether (bp 40–60 °C)/EtOAc) to give 0.158 g (66%) of **16** as a clear oil: ^{1}H NMR δ 1.24–1.60 (m, 5 H), 1.73 (m, 1 H), 2.09 (m, 1 H), 2.26 (m, 1 H), 2.58 (m, 1 H), 3.19–3.28 (m, 4 H), 3.63 (s, 3 H); ^{13}C NMR δ 33.01 (t), 33.38 (t), 34.81 (d), 38.64 (t), 42.03 (d), 43.98 (d), 51.76 (q), 56.16 (q), 83.37 (d), 175.94 (s); MS *m/z* (relative intensity) 184 (M^+, 7), 153 (24), 152 (100), 125 (21), 124 (38), 120 (18), 93 (74), 92 (25), 67 (22); HRMS calcd for $C_{10}H_{16}O_3$ (M^+) 184.1099, found 184.1099.

***exo,exo*-6-Methoxy-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]bicyclo[2.2.1]heptane (8).** To a solution of 0.136 g (0.74 mmol) of **16** in 15 mL of dry THF was added 0.028 g (0.74 mmol) of LAH at 0 °C. The reaction mixture was stirred at this temperature for 1 h and the excess of LAH was destroyed by careful addition of a small amount of saturated aqueous Na_2SO_4. After addition of 20 mL of EtOAc, the mixture was dried and evaporated. The resulting oil was dissolved in 5 mL of dry DMF and imidazole (0.070 g, 1.03 mmol) and TBDMSCl (0.110 g, 0.83 mmol) were added. The solution was stirred at rt for 16 h and then diluted with 15 mL of H_2O. After extraction with three 10 mL portions of EtOAc, the combined organic layers were washed with brine, dried, and evaporated. The resulting oil was flash chromatographed (50:1 petroleum ether (bp 40–60 °C)/EtOAc) to give 0.120 g (76%) of **8** as a clear oil: ^{1}H NMR δ 0.02 (s, 6 H), 0.81–0.98 (m, 1 H), 0.88 (s, 9 H), 1.08–1.60 (m, 6 H), 2.20 (m, 1 H), 2.33 (m, 1 H), 3.20–3.45 (m, 6 H); ^{13}C NMR δ −5.30 (2 q), 18.30 (s), 25.90 (3 q), 31.70 (t), 32.70 (t), 34.97 (d), 38.85 (t), 40.11 (d), 41.83 (d), 55.81 (q), 66.14 (t), 84.15 (d); MS *m/z* (relative intensity) 213 (M^+ − 57, 65), 119 (30), 107 (100), 89 (66), 79 (63), 75 (39), 73 (21), 91 (16); HRMS calcd for $C_{11}H_{21}O_2Si$ (M^+ − 57) 213.1311, found 213.1313.

Preparation of the Silylated Methyl Ethers 9 and 10. A stirred solution (0.015–0.020 M) of the corresponding monosilylated 1,4-diol in dry THF was cooled to 0 °C, and then *t*-BuOK (ca. 10 equiv) was added, immediately followed by addition of MeI (ca. 40 equiv). The reaction mixture was stirred at 0 °C for 30 min and then diluted with 25 mL of ether. The organic layer was washed with brine, dried, and evaporated. The resulting residue was flash chromatographed (30:1 petroleum ether (bp 40–60 °C)/EtOAc) to give the pure product.

(2-*endo*,6-*exo*)-6-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-2-methoxybicyclo[2.2.1]heptane (9): yield 85%; ^{1}H NMR δ 0.03 (s, 6 H), 0.80–1.47 (m, 5 H), 0.88 (s, 9 H), 1.88 (m, 1 H), 2.09–2.27 (m, 2 H), 2.41 (m, 1 H), 3.24 (s, 3 H), 3.27–3.46 (m, 2 H), 3.71 (m, 1 H); ^{13}C NMR δ −5.33 (2 q), 18.40 (s), 25.89 (3 q), 33.75 (2 t), 33.94 (d), 36.45 (d), 36.55 (t), 40.76 (d), 56.35 (q), 66.16 (t), 81.43 (d); MS *m/z* (relative intensity) 213 (M^+ − 57, 26), 133 (13), 107 (70), 91 (13), 89 (100), 79 (79), 75 (28), 73 (24), 59 (13); HRMS calcd for $C_{11}H_{21}O_2Si$ (M^+ − 57) 213.1311, found 213.1314.

***endo,endo*-6-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-2-methoxybicyclo[2.2.1]heptane (10)**: yield 87%; ^{1}H NMR δ 0.03 (s, 6 H), 0.83–1.01 (m, 2 H), 0.88 (s, 9 H), 1.30–1.36 (m, 2 H), 1.78–2.25 (m, 4 H), 2.46 (m, 1 H), 3.28 (s, 3 H), 3.70–3.99 (m, 3 H); ^{13}C NMR δ −5.23 (2 q), 18.30 (s), 25.96 (3 q), 35.12 (t), 36.68 (d), 37.33 (t), 38.41 (t), 41.06 (d), 44.06 (d), 57.23 (q), 65.93 (t), 84.54 (d); MS *m/z* (rel intensity) 213 (M^+ − 57, 76), 107 (77), 91 (14), 89 (100), 79 (80), 75 (24), 73 (27), 59 (14); HRMS calcd for $C_{11}H_{21}O_2Si$ (M^+ − 57) 213.1311, found 213.1308.

Preparation of the TMS Ethers 13 and 14. To a solution (0.015–0.032 M) of the corresponding monomesylated 1,4-diol in dry pyridine were added TMSCl (ca. 7.5 equiv) and hexamethyldisilazane (HMDS) (ca. 10 equiv). The reaction mixture was stirred at rt, and the reaction progress was monitored by TLC. At completion, the mixture was concentrated at reduced pressure and the remaining residue was directly submitted to flash chromatography (3:1 petroleum ether (bp 40–60 °C)/EtOAc) to give the pure product.

(2α,4aα,8β,8aβ)-Decahydro-2,8a-dimethyl-2-[(trimethylsilyl)oxy]-8-naphthalenol methanesulfonate (13): yield 92%; ^{1}H NMR (C_6D_6) δ 0.14 (s, 9 H), 0.58–1.83 (m, 12 H), 0.62 (s, 3 H), 1.17 (s, 3 H), 2.00 (d, J = 13.5 Hz, 1 H), 2.21 (s, 3 H), 4.17 (dd, J = 6.7, 12.7 Hz, 1 H); ^{13}C NMR (C_6D_6) δ 2.83 (3 q), 12.83 (q), 23.75 (t), 26.28 (t), 26.38 (t), 27.75 (t), 29.87 (q), 37.92 (q), 39.03 (s), 42.03 (t), 44.16 (d), 52.79 (t), 74.01 (s), 89.91 (d); MS *m/z* (relative intensity) 348 (M^+, 20), 269 (44), 163 (38), 143 (100), 110 (31), 75 (30); HRMS calcd for $C_{16}H_{32}O_4SSi$ (M^+) 348.1790, found 348.1786.

(1α,4aβ,5β,8aα)-Decahydro-1,4a,7,7-tetramethyl-1-[(trimethylsilyl)oxy]-5-naphthalenol methanesulfonate (14): yield 81%; ^{1}H NMR (C_6D_6) δ 0.00 (s, 9 H), 0.74 (s, 3 H), 0.77 (s, 3 H), 0.82 (s, 3 H), 0.84–1.85 (m, 11 H), 1.00 (s, 3 H), 2.19 (s, 3 H), 4.32 (dd, J = 6.3, 11.4 Hz, 1 H); ^{13}C NMR (C_6D_6) δ 2.52 (3 q), 12.14 (q), 17.85 (t), 26.66 (q), 29.94 (q), 31.15 (s), 33.10 (q), 33.97 (t), 37.63 (t), 38.30 (q), 39.41 (s), 41.31 (2 t), 47.97 (d), 74.79 (s), 87.88 (d); MS *m/z* (relative intensity) 376 (M^+, 10), 361 (16), 297 (39), 191 (27), 183 (43), 143 (100), 133 (92), 117 (27), 73 (55); HRMS calcd for $C_{18}H_{36}O_4SSi$ (M^+) 376.2104, found 376.2102.

Kinetic Studies on the Silyl Ethers 1–10. The reactions were studied under pseudo-first-order conditions at which [TBAF] >> [silyl ether]. The disappearance of the silyl ether was monitored by HPLC. The following procedure was adopted: 70 μL of 1.1 M TBAF in THF was added at once, via syringe, to 1.0 mL of 0.0075 M silyl ether in dry acetonitrile in a sealed ampule. The solution was stirred continuously, and the extent of reaction was followed at the indicated temperature until at least 60% of the silyl ether was disappeared.

Kinetic Studies on the Silyl Ethers 11–14. The same as above except that 50 μL of 1.1 M TBAF in THF was added at once, via syringe, to 1.5 mL of 0.0055 M silyl ether in dry acetonitrile. The solution was mixed thoroughly, and the extent of reaction was followed at ambient temperatures (21–24 °C) until at least 80% of the silyl ether was disappeared.

High Performance Liquid Chromatography. The HPLC equipment was a high precision pump and a refractive index and UV (262 nm) detector assembled with a 10 μL loop injection valve. The chromatography column (25 × 1/4 m) was packed with 10 μm SPHERISORB ODS 2. Results were obtained by eluting with acetonitrile/H_2O (isocratic, 80 or 95% v/v) at a column temperature of 26 °C. The solvent mixture was degassed prior to elution (flow rate = 1 mL/min).

Acknowledgment. This investigation was supported, in part, by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for Scientific Research (NWO). We thank A. van Veldhuizen for recording ^{1}H NMR and ^{13}C NMR spectra and C. J. Teunis and H. Jongejan for mass spectral data.

Supporting Information Available: ^{1}H NMR spectra for compounds **1**, **4–10**, **13**, **14**, and **16** (11 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

JO950920D