78-83-1; **16c**, 100-49-2; **16d**, 107-18-6; **16e**, 111-70-6; **16f**, 504-61-0; **16g**, 4407-36-7; **16h**, 4325-82-0; **16i**, 18325-75-2; **16k**, 822-67-3; **17**, 124781-46-0; **18**, 124781-47-1; **19**, 124781-48-2; **20**, 1438-14-8; *erythro*-**21**, 65534-62-5; *threo*-**21**, 36471-61-1; *erythro*-**21** (acetonide), 124781-54-0; *threo*-**21** (acetonide), 124781-55-1; **22** (isomer 1), 108647-08-1; **22** (isomer 2), 124916-15-0; **23** (isomer 1), 124781-49-3; **23** (isomer 2), 124916-16-1; **24**, 930-22-3; *anti*-**26**, 122592-64-7; *syn*-**26**, 122592-65-8; *anti*-**26** (acetonide, 124781-56-2; *trans*-**27**, 124781-50-6; *cis*-**27**, 124781-51-7; **30**, 34485-82-0; *anti*-**31**, 124781-52-8; *syn*-**31**, 124781-53-9; **32** (Y = H), 556-52-5; **32** (Y = MOM), 45631-57-0; *anti*-**33** (Y = H), 124781-57-3; *syn*-**33** (Y = H), 124781-58-4; *anti*-**33** (Y = MOM), 124781-59-5; *syn*-**33** (Y = MOM), 124820-65-1; **34**, 7160-77-2; **35**, 81617-08-5; **36a**, 124781-61-9; **36b**, 124781-62-0; **37**, 124781-60-8; DBB, 1625-91-8; LDBB, 61217-61-6; PhSMe, 100-68-5; *p*-$MeOC_6H_4CHO$, 123-11-5; Me_2CHCHO, 78-84-2; *p*-$C_6H_{11}CHO$, 2043-61-0; CH_2=CHCHO, 107-02-8; *n*-$C_6H_{13}CHO$, 111-71-7; (*E*)-MeCH=CHCHO, 123-73-9; (*E*)-PhCH=CHCHO, 14371-10-9; Me_2CH=CHCHO, 107-86-8; $Ti(i\text{-}PrO)_4$, 546-68-9; $CeCl_3$, 7790-86-5; cyclohexanone, 108-94-1; 1-acetylcyclohexene, 932-66-1; 2-cyclohexen-1-one, 930-68-7.

Supplementary Material Available: ^1H NMR spectra for **15i**, **15k**, **15l**, *anti*-**15l**, **15m**, **15n**, **17**, **18**, **19**, **23**, **26**, *anti*-**26**, *syn*-**36**, *anti*-**36**, **33** (Y = MOM), **33** (Y = H), **34**, **36ab**, **36a**, and **37** (20 pages). Ordering information is given on any current masthead page.

Geometrical Dependence of γ-Trimethylsilyl Groups on Norbornyl Solvolyses. Rapid-Injection Kinetic Methods for Solvolyses of Unstable Mesylates

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Solvolytic rate constants in ethanol and aqueous ethanol mixtures are reported for solvolyses of unstable mesylates, prepared in situ from *tert*-butyl alcohol, and the following 6-trimethylsilyl (TMS) substituted 2-*exo*-norbornanols: 6-*exo*- and 6-*endo*-(trimethylsilyl)-substituted and 6,6-bis(trimethylsilyl)-substituted. These kinetic data for ethanol at 25 °C show similar relative rates to those observed for solvolyses of the corresponding *p*-nitrobenzoates in 97% w/w trifluoroethanol/water at 100 °C; there are up to ca. 100-fold larger rate enhancements due to γ-silicon than those previously reported for acyclic and monocyclic systems; e.g. in ethanol 3.3×10^4 for 6-*exo*-(trimethylsilyl)-2-*exo*-norbornyl mesylate; these results support recent experimental and theoretical studies showing that a *W* conformation is preferred. In contrast, for solvolyses of the corresponding 2-*endo*-brosylates in 80% ethanol/water and in 97% trifluoroethanol, the 6-*exo*-TMS substituent shows only a 2-4-fold rate enhancement, and the 6-*endo*-TMS substituent shows rate retardation. Additional rate constants are reported for conventional solvolyses of mesylates of 1-adamantanol, 2-*exo*-norbornanol, and 6-*exo*-(trimethylsilyl)-2-*endo*-norbornanol. These data for 6-*exo*-TMS compounds establish a 2-*exo*-/2-*endo*-norbornyl rate ratio of $>10^6$, the largest observed for an unhindered secondary system.

The kinetic effects of γ-silicon substituents on solvolyses of 2-*exo*-norbornyl mesylates (methanesulfonates) are much larger than those previously reported for solvolyses of secondary acyclic[1a] and monocyclic substrates,[1b,2] and the bicyclic, trimethylsilyl (TMS) substituted compounds (**1-3**, X = OBs) could not be isolated.[3] Also, despite the importance of solvolyses of *tert*-butyl substrates (**4**),[4] few kinetic data for these sulfonates have previously been obtained because they are too unstable to isolate;[5] a relatively slow elimination reaction of *tert*-butyl tosylate has previously been examined in acetonitrile at 0 °C ($k = 1.8 \times 10^{-4}$ s^{-1}).[5a] We now report a procedure, based on convenient syntheses from alcohols[5b,6] and on rapid-injection, conductimetric methods, for obtaining a wide range of these data. Results will be compared with those for conventional solvolyses of other mesylates (**5**, **6**), with solvolyses of corresponding *p*-nitrobenzoates (**1-3**, **6**, X = *p*-nitrobenzoate), and also with solvolyses of 6-TMS-substituted 2-*endo*-norbornyl brosylates (*p*-bromobenzenesulfonates) (**7-10**).

The norbornyl framework acts as a relatively rigid backbone, providing known relative orientations of the TMS substituents and the leaving groups. The results reveal large variations in the geometrical dependence of the substituent effects of γ-TMS groups, and supplement an on-going project on the relative stabilities of TMS-substituted norbornyl cations.[3]

Results

The mesylates of interest were sufficiently stable (i.e. for several hours) that ca. 1 M solutions could be prepared in dichloromethane at −10 °C.[6] Direct injections of a few microliters of these cold solutions into the rapidly stirred, thermostatted solvolysis medium apparently caused local supersaturation, leading to unreliable kinetic data particularly for the more lipophilic substrates, e.g. even for 1-adamantyl mesylate (**5**), which can be isolated as a crystalline solid[6] and studied by conventional kinetic methods.[7a] Reliable kinetic data for solvolyses of **1-4** in

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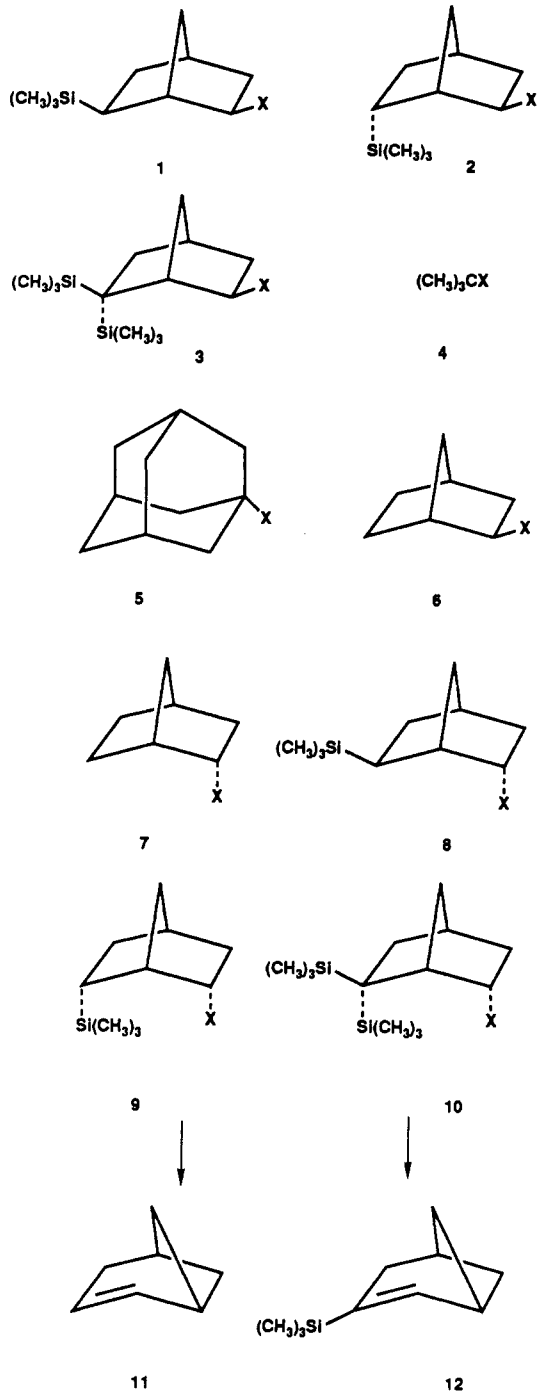

ethanol, 90% ethanol/water, and 80% ethanol/water (Table I) were obtained by first evaporating the cold dichloromethane and then redissolving the mesylates in cold acetonitrile. It was then possible to utilise rapid-injection techniques, which have previously been applied to solution kinetics in conductimetric,[7,8] UV spectroscopic,[9] and NMR procedures.[10] Recent studies include the highly reactive substrate, 1-adamantyl triflate.[8c] The reliability of these methods is illustrated by recent conductimetric studies of temperature dependence, solvent effects, and substituent effects for rapid solvolyses of 2,4,6-trimethylbenzoyl chloride.[7b] Consistent activation parameters were obtained for solvolyses of mesylates **1–4** in ethanol and in ethanol/water mixtures (Table II), including some data for 60% ethanol/water mixtures. Also, relative rates (Table I) are similar to those observed for conventional solvolyses of corresponding *p*-nitrobenzoates (**1–3**, **6**, X = *p*-nitrobenzoate) (Table III), see Table IV. Rates of solvolyses of the 2-*endo*-norbornyl brosylates (**7–10**) are given in Table V and of the mesylate **8** are in Table VI.

Discussion

Solvolyses of 2-*endo*-norbornyl sulfonates (**7**) are weakly sensitive to solvent nucleophilicity (k_s process),[12b,14a] giving mainly 2-*exo*-norbornyl substitution products.[14b,c] In contrast, solvolyses of the 6-*endo*-TMS compounds (**9**, **10**) in trifluoroethanol give norpinene products (**11**, **12**) derived by migration of C_7 from C_1 to C_2 followed by desilylation.[3b] Changes in structure, leading to changes in susceptibility to solvent ionizing power and solvent nucleophilicity, can be measured from rate ratios in 97% trifluoroethanol and 80% ethanol.[12a] This ratio (k_{97T}/k_{80E}) for brosylates varies from 9 for solvolyses of **7** to about 50 for S_N1 solvolyses of more sterically hindered substrates (e.g. 2-adamantyl).[12a] The corresponding value for solvolyses of 2-propyl brosylate, for which solvent nucleophilicity is significant,[12b] is only 0.14.[12a] Hence, variations in k_{97T}/k_{80E} ratios between 9 and 50 are at the higher end of the range of values for solvolyses of secondary substrates and mainly reflect changes in response to solvent ionizing power (m).[12b,15] A 6-*endo*-TMS substituent increases significantly the k_{97T}/k_{80E} ratios (from 9) to 28 for **9** and to 47 for **10** (Table V), strongly suggesting that the m values are high. Products (**11**, **12**) may be consistent with neighboring group participation by silicon (k_Δ process), but as m values are high and rates are not enhanced (see below) anchimeric assistance must be weak.

The main factor influencing the reactivities of **9** and **10** appears to be steric inhibition by the 6-*endo*-TMS substituent to departure and/or solvation of the 2-*endo*-sulfonate group.[16] The preferred orientation in an S_N2 transition state (a linear arrangement of the attacking solvent molecule, C_2, and the departing sulfonate) may not be achieved because of the 6-*endo*-TMS substituent. If so, these solvolyses would be less sensitive to solvent nucleophilicity than solvolyses of **7** and more sensitive to solvent ionizing power, because there is a general tendency for sensitivity to solvent ionizing power (m values) to increase as sensitivity to solvent nucleophilicity decreases.[12b,15] In addition to this argument based on solvent effects on relative rates, the absolute rates are about 50-fold less than for the parent system **7** (depending on the sol-

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Table I. Kinetic Data for Solvolyses of 6-Substituted 2-*exo*-Norbornyl and Tertiary Alkyl Mesylates in Ethanol and Aqueous Ethanol (% v/v) at 25 °C[a]

mesylate (solvent)	rate constants (k/s^{-1}) EtOH	90% EtOH	80% EtOH	m^b
6-*exo*-TMS (1)	0.103	0.85[c,d]	2.2[c,d]	0.61 ± 0.05
6-*endo*-TMS (2)	1.50×10^{-4}	7.68×10^{-4}	2.25×10^{-3}	0.53 ± 0.02
6,6-bis-TMS (3)	7.11×10^{-2}	0.27	0.64[c]	0.43 ± 0.01
tert-butyl (4)	4.06×10^{-2}	0.40	1.71[c]	0.73 ± 0.02
1-adamantyl (5)[e]	2.49×10^{-5}	6.1×10^{-4}	4.17×10^{-3}	1.0[f]
2-*exo*-norb (6)[g]	3.1×10^{-6}	5.08×10^{-5}	2.8×10^{-4}	0.88 ± 0.01

[a] Determined conductimetrically at least in duplicate in buffered solvents, except where stated otherwise; averages shown are typically ±3%. [b] Slope of a plot of logarithms of rate constants vs logarithms of rate constants for solvolyses of 1-adamantyl mesylate (5). [c] Calculated from kinetic data at other temperatures. [d] Rate constants also determined by direct measurements at 25 °C. [e] Kinetic data from ref 7a for 80% EtOH and from ref 8c for EtOH. [f] By definition. [g] Kinetic data for EtOH determined titrimetrically as described in ref 11.

Table II. Activation Parameters for Solvolyses of Unstable Mesylates in Ethanol and Aqueous Ethanol[a]

mesylate	solvent	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal mol^{-1} K^{-1}
6-*exo*-TMS (1)	EtOH[b]	18.2	−2.0
	90% EtOH[c]	18.0	1.6
	80% EtOH[d]	17.0	−0.2
	60% EtOH[e]	(18.1)	(7.5)
6-*endo*-TMS (2)	60% EtOH[f]	18.8	−4.7
6,6-bis-TMS (3)	EtOH[g]	18.0	−3.3
	90% EtOH[h]	17.4	−2.8
	80% EtOH[i]	17.3	−1.4
tert-butyl (4)	EtOH[j]	19.4	0.1
	80% EtOH[k]	15.7	−4.7
	60% EtOH[l]	(17.0)	(4.2)

[a] Kinetic data from Table I and additional values (determined at least in duplicate) in the footnotes given below (T, °C; k, s^{-1}). [b] At 9.9 °C, k = 0.019. [c] At −10.0 °C, k = 0.0132; 10.0 °C, k = 0.162. [d] At −10.0 °C, k = 0.040; 0.0 °C, k = 0.156; 10.0 °C, k = 0.423. [e] At −10.0 °C, k = 0.215; 0.1 °C, k = 0.80; for 25 °C, k(calc) = 14. [f] At 10.1 °C, k = 0.001 82; 25 °C, k = 0.0106; 40.1 °C, k = 0.0489. [g] At 9.9 °C, k = 0.0133. [h] At −10.0 °C, k = 0.004 80; 9.7 °C, k = 0.0519. [i] At −10.0 °C, k = 0.0116; 10.0 °C, k = 0.129. [j] At 10.2 °C, k = 0.006 99. [k] At −10.1 °C, k = 0.0436; 10.0 °C, k = 0.397. [l] At −10.0 °C, k = 0.37; 0.0 °C, k = 1.26; for 25 °C, k(calc) = 19.

Table III. Rate Constants (k) for Solvolyses of 6-(Trimethylsilyl)-2-*exo*-norbornyl *p*-Nitrobenzoates in 97% w/w Trifluoroethanol/Water at 100 °C[a]

substrate	k, s^{-1}	substrate	k, s^{-1}
6-H (6)[b]	$(2.0 \pm 0.2) \times 10^{-8}$	6-*exo* (1)[c]	$(2.9 \pm 0.1) \times 10^{-4}$
6-*endo* (2)[c]	$(1.8 \pm 0.1) \times 10^{-6}$	6,6-bis (3)	$(6.3 \pm 0.2) \times 10^{-4}$

[a] Determined by HPLC from the rate of disappearance of ester and the rate of appearance of acid; solutions contained $<10^{-3}$ M substrate and 3.4×10^{-3} M 2,6-lutidine; similar, but less precise results were obtained in unbuffered solutions. [b] Initial rate over 79 days calculated by including theoretical infinity values; unbuffered solutions gave ca. 8-fold faster rates, probably because of acid catalysis. [c] Additional data determined conductimetrically in duplicate at 70.9 °C gave $k = (2.38 \pm 0.03) \times 10^{-5}$; hence $\Delta H^{\ddagger}$ = 21.2 kcal/mol, $\Delta S^{\ddagger}$ = −18 cal mol^{-1} K^{-1}.

Table IV. Relative Rates of Solvolyses of 6-Trimethylsilyl (TMS) Substituted 2-*exo*-Norbornyl Derivatives

substrates	6-*exo*-H (6)	6-*exo*-TMS (1)	6-*endo*-TMS (2)	6,6-bis-TMS (3)
mesylates[a]	1	3.3×10^4	48	2.3×10^4
p-nitrobenzoates[b]	1	1.5×10^4	90	3.2×10^4

[a] In ethanol at 25 °C; kinetic data from Table I. [b] In 97% trifluoroethanol at 100 °C; kinetic data from Table III.

vent, Table V). Similar results (ca. 20-fold rate retardation) were obtained for acetolysis of 6,6-dimethyl-2-*endo*-norbornyl tosylate, presumably because of the presence of a 6-*endo*-methyl group.[17] Rate retardations

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Table V. Rate Constants (k) for Solvolyses of 6-Trimethylsilyl (TMS) Substituted 2-*endo*-Norbornyl Brosylates in 80% v/v Ethanol/Water and in 97% w/w Trifluoroethanol/Water[a]

substrate	temp, °C	k, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal mol^{-1} K^{-1}
		80% Ethanol/Water		
6-H (7)	25.0[b]	1.6×10^{-6}		
6-*exo* (8)	75.0	$(1.22 \pm 0.03) \times 10^{-3}$		
	50.0	$(8.45 \pm 0.30) \times 10^{-5}$	23.2	−5.6
	25.0[c]	3.8×10^{-6}		
6-*endo* (9)	95.0	$(1.16 \pm 0.02) \times 10^{-4}$		
	75.0	$(1.42 \pm 0.03) \times 10^{-5}$	27.0	−3.6
	50.0[d]	$(6.0 \pm 0.2) \times 10^{-7}$		
	25.0[c]	1.7×10^{-8}		
6,6-bis (10)	95.0	$(1.40 \pm 0.06) \times 10^{-3}$		
	75.0	$(1.97 \pm 0.05) \times 10^{-4}$	25.0	−4.1
	50.0	$(1.06 \pm 0.07) \times 10^{-5}$		
	25.0[c]	3.8×10^{-7}		
		97% Trifluoroethanol/Water		
6-H (7)	25.0[b]	1.4×10^{-5}		
6-*exo* (8)	50.0	$(9.84 \pm 0.18) \times 10^{-4}$		
	25.0	$(5.58 \pm 0.08) \times 10^{-5}$	21.4	−6.4
6-*endo* (9)	75.0	$(1.60 \pm 0.02) \times 10^{-4}$		
	50.0	$(1.08 \pm 0.03) \times 10^{-5}$	23.4	−8.9
	25.0[c]	4.7×10^{-7}		
6,6-bis (10)	75.0	$(3.41 \pm 0.04) \times 10^{-3}$		
	50.0	$(2.99 \pm 0.03) \times 10^{-4}$	21.1	−9.5
	25.0[c]	1.8×10^{-5}		

[a] Determined conductimetrically in duplicate except where noted otherwise; errors shown are average deviations. [b] Reference 12a. [c] Calculated from kinetic data at higher temperatures. [d] Determined by HPLC from the rate of disappearance of ester and the rate of appearance of acid.

Table VI. Rate Constants (k) for Solvolyses of 6-Trimethylsilyl (TMS) Substituted Norbornyl Mesylates and 2-*exo*/2-*endo* Rate Ratios at 25 °C

substrate	solvent	rate constants 2-*exo*	2-*endo*	*exo*/*endo*
6-*exo* (1, 8)	EtOH	0.103[a]	5.0×10^{-8}[b]	2.1×10^6
	80% EtOH	2.2[a]	4.4×10^{-7}[c]	5.0×10^6
2-norb (6, 7)	EtOH	4.46×10^{-6}[d]	1.5×10^{-8}[d]	3.0×10^2
	80% EtOH	2.31×10^{-4}[e]	3.2×10^{-7}[f]	7.2×10^2

[a] Kinetic data from Table I. [b] Calculated from the following kinetic data, determined titrimetrically in duplicate as described in ref 11: at 75.2 °C, $k = (2.5 \pm 0.1) \times 10^{-5}$, and at 50.0 °C, k = (1.4 ± 0.1) × 10^{-6}; $\Delta H^{\ddagger}$ = 24.9 kcal/mol, $\Delta S^{\ddagger}$ = −8.4 cal mol^{-1} K^{-1}. [c] Calculated from the following kinetic data, determined conductimetrically in duplicate: at 75.4 °C, $k = (2.38 \pm 0.03) \times 10^{-4}$, and at 50.0 °C, $k = (1.27 \pm 0.02) \times 10^{-5}$; $\Delta H^{\ddagger}$ = 25.2 kcal/mol, $\Delta S^{\ddagger}$ = −3.3 cal mol^{-1} K^{-1}. [d] Data for the tosylate from ref 13a. [e] Data for the tosylate from ref 13b. [f] Data calculated in ref 12b from tosylate data in ref 13b.

of similar magnitude for methyl and TMS groups may occur because the greater bond length for C–Si (compared with C–C)[18a] takes the bulkier TMS group farther away

from the reaction site. Despite the steric effect proposed for 6-*endo* compounds (**9**, **10**), $\Delta S^{\ddagger}$ values are very similar to those for **7** and **8**. Also surprisingly, solvolysis of 6-*endo*-*tert*-butyl-2-*endo*-norbornyl tosylate in 80% ethanol/water at 70 °C is only 4-fold less than for the parent compound (**7**),[14c] so the rate retardation for the *tert*-butyl group is 12-fold less than for TMS.

The electronic effect of a γ-TMS group appears to be small for solvolyses of 2-*endo* substrates, because the unhindered 6-*exo*-TMS derivative (**8**) reacts only 2–4 times faster than **7** (Table V), as expected from normal inductive effects ($\rho = -1.0$[19a] in 80% ethanol/water and σ_I^q is −0.16 for the TMS substituent[20a]). There is only a small increase in the k_{97T}/k_{80E} ratio (from 9) to 15. In trifluoroethanol, **8** gives mainly 1,3-elimination of 6-H and 6-TMS, and only 13% of 2-*exo* ether is formed.[3b]

The results for solvolyses of the 2-*exo*-compounds (**1–3**, **6**) contrast markedly with those for the 2-*endo* substrates (**7–10**). A 6-*exo*-TMS substituent increases the reactivity of 2-*exo* compounds (**1**, **3**), e.g. for **1** by 3.3×10^4 for solvolyses of mesylates in ethanol and by 1.5×10^4 for *p*-nitrobenzoates in 97% trifluoroethanol (Table IV). Normal inductive effects of substituents at C_6 are much too small to explain the TMS results ($\rho = -2.0$;[19a] this does account for the 2-fold kinetic effect of a 6-*exo*-*tert*-butyl substituent[19b] for which $\sigma_I^q = -0.20$[20b]). Also, whereas TMS substitution increased m values for solvolyses of the 2-*endo* substrates, *m* values for solvolyses of the 2-*exo* substrates are low (Table I). This effect is most marked for solvolyses of the bis-TMS compound (**3**), which shows an *m* value half that of the parent compound (**6**). Because of the large variations in *m* values, relative rates are solvent dependent; although **3** is slightly less reactive than **1** in ethanol and aqueous ethanol (Table I), during the preparative stages of this work **3** was found to be the least stable of the mesylates in dichloromethane (a less ionizing solvent) at −10 °C.

The main products from solvolyses of the 2-*exo*-*p*-nitrobenzoates (**1**, **2**) in trifluoroethanol at 75–120 °C are from 1,3-elimination (mainly of 6-H).[3b] A detailed study of the deuterium-labeled *p*-nitrobenzoate (**3**) revealed that a novel 6,2-silyl shift occurred prior to desilylation or deprotonation and established that (despite the large rate enhancement) concerted ionization and desilylation were insignificant.[3a] Hence, the low *m* values for solvolyses of **3** cannot be due to neighboring group participation by silicon, and other mechanisms of charge delocalization and rate enhancement are necessary to explain these results. It was suggested recently that the role of a substituent at the 6-position is to donate (or withdraw) electrons to the C_1–C_6 bond by a simple "through bond" inductive effect.[21] The presence of a 6-TMS substituent would greatly increase the electron density in the C_1–C_6 bond;[18b,22] this would increase the nonclassical stabilization in the 2-norbornyl cation,[21] and so rates would increase.

However, it is also necessary to explain why the rate-enhancing effect (Table IV) of a 6-*endo*-TMS substituent is only 10–100-fold, whereas that of the 6-*exo*-TMS substituent is >10^4-fold ($\rho = -1.75$ for the 6-*endo* series;[19a] i.e. only slightly less than for the 6-*exo* series). TMS substituents in both 6-*exo* and 6-*endo* orientations help stabilize the developing positive charge by charge delocalization (*m* values are very similar, Table I), but the 6-*exo*-TMS substituent has a much more favorable geometry for rate enhancements. These results support recent experimental[1] and theoretical evidence favoring a *W* conformation,[18b,23] and involving direct bonding between C_6 and C_2[21,23] or a "through-three bond" electron delocalization mechanism.[24] A further possibility is that the 6-*endo*-TMS substituent may also show a steric effect, leading to reduced rates analogous to observed rate retardations of 20-fold for acetolysis of 6,6-dimethyl-2-*exo*-norbornyl tosylate.[17] However, these effects appear to be smaller in aqueous media, because solvolysis of 6-*endo*-*tert*-butyl-2-*exo*-norbornyl tosylate in 80% ethanol/water occurs at the same rate as that of **6**.[25]

The results for brosylates (Table V) implied high 2-*exo*/2-*endo* rate ratios in solvolyses of 6-*exo* substrates. Additional studies of mesylates confirmed these expectations, showing the highest firmly-established 2-*exo*/2-*endo* rate ratio (>10^6, see Table VI) for unhindered secondary substrates (**1**, **8**). Typical 2-*exo*/2-*endo* rate ratios in the parent system (**6**/**7**) are <10^3 (Table VI). Substituent effects for trialkyltin are known to be even larger than those for TMS.[24,26] In related work, rate enhancements of 6×10^5 have been calculated indirectly for a solvolysis of 2-*exo*-norbornyl having a CH_2SnMe_3 substituent at C_1; a 2-*exo*/2-*endo* rate ratio of 10^9 has been claimed[26a] without experimental data for the appropriate 2-*endo* compound (we estimate 10^7).

The *m* value of 0.73 for solvolyses of *tert*-butyl mesylate (**4**) (Table I) is almost the same as the value of 0.75 for *tert*-butyl chloride (vs Y_{Cl}).[4] Also, despite the 10^5 greater reactivity of mesylates than chlorides, the **4**/**5** rate ratio in 80% ethanol/water of 4.1×10^2 for mesylates is similar to the value of 1.0×10^3 for chlorides.[4] These results appear to be determined more by structural features of *tert*-butyl (e.g. sensitivity to nucleophilic solvent assistance,[4] and/or cation lifetime[27]) than by the leaving group. Larger differences in rate ratios were expected from recent studies of heptafluorobutyrates (only slightly less reactive than chlorides), showing that the **4**/**5** rate ratio in 80% ethanol/water is reduced 5-fold to 2.1×10^2.[28]

Conclusions

γ-Silicon substituents have a marked effect on both rate- and product-determining steps of solvolyses of 2-norbornyl substrates. Solvolyses of 6-*endo*-(trimethylsilyl)-2-*endo*-norbornyl sulfonates (**9** and **10**) lead to rearranged products (**11**, **12**), increased *m* values, and rate retardations (i.e. these solvolyses are weak k_Δ processes, whereas **7** reacts by a weak k_s process); in contrast for 2-*exo*-norbornyl sulfonates, *m* values decrease and rates increase, ca. 10^4 for the 6-*exo*-TMS substituent (see **1** and **3**). Neighboring

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group participation by silicon is not involved, at least for the 6,6-bis-TMS derivative (3).[3] The results are consistent with a specially favorable electronic effect for the 6-*exo*-TMS substituent in a *W* conformation, although an additional steric effect reducing the reactivity of the 6-*endo*-TMS compound (2) cannot be excluded. A wider range of solvolytic reactivity is now accessible by convenient syntheses from alcohols of very reactive mesylates. Kinetic data obtained by rapid-injection kinetic methods provide an alternative to conventional kinetic studies of substrates having less reactive leaving groups (e.g. trifluoroacetates[2,22,28] and *p*-nitrobenzoates[3]).

Experimental Section

Syntheses of starting materials and product studies are reported in detail elsewhere.[3] The unstable mesylates were prepared from the corresponding alcohols (ca. 10 mg), dissolved in dry dichloromethane (200–400 μL) at −10 °C; triethylamine (2.5 equiv) was then injected, followed by portionwise addition of methanesulfonyl chloride (0.9 equiv) with magnetic stirring.[6] (In a parallel experiment the reaction leading to 1 was shown by NMR to be rapid in $CDCl_3$ at −10 °C.) After 10 min, aliquots (50 μL) of solvent were evaporated under reduced pressure at −10 °C, and the remaining solid was partially dissolved in cold acetonitrile (50 μL). Most of this solution was transferred to a cold syringe (using a glass wool plug to avoid the transfer of solid materials), and rapid injection kinetic studies could then be performed as described previously.[7] Other conductimetric kinetic studies were carried out by standard methods.[12] Kinetic studies by HPLC (in sealed 1-mL ampoules) required no internal standard or additional calculations,[29] because of the highly reproducible (±1%) injection volumes possible with an autosampler (Perkin Elmer ISS 101).

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Registry No. 1 (X = mesylate), 124717-77-7; 1 (X = *p*-nitrobenzoate), 124816-93-9; 2 (X = mesylate), 124816-92-8; 2 (X = *p*-nitrobenzoate), 124717-79-9; 3 (X = mesylate), 124717-78-8; 3 (X = *p*-nitrobenzoate), 120852-95-1; 4 (X = mesylate), 16427-41-1; 5 (X = mesylate), 25236-60-6; 6 (X = mesylate), 28627-77-2; 6 (X = *p*-nitrobenzoate), 10472-43-2; 7 (X = mesylate), 28627-78-3; 7 (X = brosylate), 840-89-1; 8 (X = mesylate), 124816-94-0; 8 (X = brosylate), 124098-88-0; 9 (X = brosylate), 124152-00-7; 10 (X = brosylate), 124098-91-5.

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Synthesis of Polypropionate Subunits by S_N2' Addition of Cuprates to Nonracemic Acyclic Vinyloxiranes

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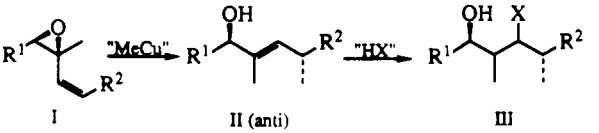
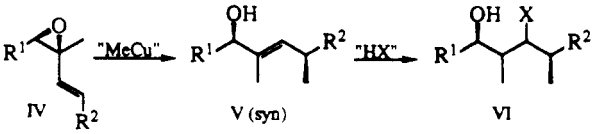
Synthetic sequences have been devised for conversion of the chiral pool ester 1 to differentially protected polypropionate subunit polyols 11, 13, 18, and 20. The following stereochemically significant steps were employed: (1) reagent directed Sharpless epoxidation of allylic alcohol 4 (75:25); (2) substrate directed anti S_N2' addition of MeCu(CN)Li to vinyloxirane 8 (>95:5); (3) substrate directed homogeneous hydrogenation of homoallylic alcohol 10 (94:6); (4) substrate directed hydroboration of allylic alcohol 14 (88:12). The stereochemistry of alcohol 13 was confirmed through conversion to lactone 27 an intermediate in Suzuki's synthesis of protomycinolide.

Within the past decade considerable effort has been devoted to the development of methodology for the synthesis of carbon chains with alternating methyl and hydroxyl substituents.[1] The driving force for these activities comes from the vast array of biologically and medicinally important polypropionate or polyketide natural products such as macrolides and polyether antibiotics.[2] In recent years we have been developing a new approach to such compounds employing highly stereoselective S_N2' additions of methyl cuprates to nonracemic vinyloxiranes such as I and IV to afford 1,4-anti and syn intermediates such as II and V (eq 1 and 2).[3]



I II (anti) III (1)



IV V (syn) VI (2)

These allylic alcohol intermediates should be transformable to a variety of potential polypropionate subunits III and VI (X = H or OH) by precedented contemporary methodology. The present report describes the successful application of this strategy to differentially protected 1,4-anti arrays such as III. One important aspect of these applications is the ability to prepare α,ω-diols protected at either terminus, thereby permitting a high degree of flexibility in subsequent chain elongation protocols.

The starting material for these studies, ester 1, was prepared from (*S*)-(+)-methyl 3-hydroxy-2-methylpropionate.[4] The derived aldehyde 2, upon condensation with Still's trifluoroethyl phosphonopropionate Horner–Emmons reagent, afforded the *Z* conjugated ester 3[5]

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