column at 130 °C; mass spectrum $M^+ = 144$.

5-Bromo-1-cyclooctene (2). In a 150-mL, three-neck flask, containing 1.0 mL of $SnCl_4$, was added 50 mL (0.4 mol) of 1,5-cyclooctadiene. This mixture was cooled to 0 °C, and then dry HBr (gas) was passed through the mixture for a period of 60 min. The mixture was washed with water (150 mL), extracted with pentane (250 mL), washed with a solution of $NaHCO_3$ (3 × 250 mL), dried over $MgSO_4$, and then concentrated under vacuum. Fractional distillation yielded 18.8 g (24.2% yield) of analytical pure **2**, which exhibited the following: bp 65–66 °C at 0.1 mmHg; ^1H NMR 1.38–2.96 (10 H, m), 4.18–4.62 (1 H, m), 5.58–6.0 (2 H, m); GLC purity 99% on a 30-m capillary DB.1 column at 130 °C; mass spectrum, m/e (relative intensity) $M^+ + 2 = 190$ (1.40), $M^+ = 188$ (1.28). Anal. Calcd: C, 50.81; H, 6.94. Found C, 51.00; H, 7.01.

5-Iodocyclooctene (1). To 150 mL of acetone were added 20 g of NaI and 8.0 g of the crude 1-cyclooctenetosylate. After refluxing for 48 h, the mixture was cooled, diluted with pentane, and subjected to standard workup. Distillation yielded 4.0 g (45% yield) of analytically pure **1**, which exhibited the following: bp 73–74 °C at 0.1 mmHg; 1H NMR 1.38–2.95 (10 H, m), 4.28–4.78 (m, 1 H), 5.58–5.90 (2 H, m); GLC purity 99% on a 30-m capillary DB.1 column at 130 °C; mass spectrum, m/e (relative intensity) $M^+ = 236$ (100) (CI). Anal. Calcd: C, 40.69; H, 5.56. Found: C, 40.89; H, 5.57.

Acknowledgment. We are grateful to the National Science Foundation (Grant No. CHE-8403024) for support of this work.

Registry No. **1** (X = I), 103620-47-9; **2** (X = Br), 17223-82-4; **3** (X = Cl), 1855-55-6; **4** (X = OTs), 7212-64-8; **4** (X = OH), 31598-74-0; **5**, 931-88-4; **5** (free radical), 103620-46-8; **5** (75% deuterated), 97797-83-6; **6**, 1755-05-1; **6** (free radical), 103620-49-1; **6** (25% deuterated), 103620-48-0; **7** (X = I), 92285-04-6; DCPH, 829-84-5; DCPD, 91523-73-8; $LiAlD_4$, 14128-54-2; $LiAlH_4$, 16853-85-3; AlH_3, 7784-21-6; cyclohexadiene, 29797-09-9; 1,5-cyclooctadiene, 111-78-4.

The Predominance and Quantification of Steric Effects in the Solvolysis of Secondary Aliphatic Esters[1]

Hans-Jörg Schneider,* Norman Becker, Günther Schmidt, and Fred Thomas

FR Organische Chemie der Universität des Saarlandes, D-6600 Saarbrücken 11, West Germany

Received December 23, 1985

The solvolysis rates of 35 tosylates in hexafluoroisopropyl alcohol are measured and compared to MM2 calculated strain energies, ΔSI, between weighted sp^3 states and the lowest sp^2 state. For unhindered (pseudo)equatorially substituted cycloalkyl tosylates a linear correlation, free from ambiguities involved, e.g., with the leaving group simulation, is obtained which shows a sensitivity of $m = 1.04 \pm 0.05$, indicating an extremely late transition state or limiting behavior. Based on the corresponding equation, it is shown that alkyl substituents in the γ- and in the β-position do not promote significant rate increases, even when there is an antiperiplanar disposition between the leaving group and a migrating β-methyl substituent. Instead, these substituents can lead to substantial ΔG^* increase (by up to 5 kcal/mol in comparison to the ΔSI prediction), which is related to steric hindrance of solvation and/or hindrance for elimination. 17-(Tosyloxy)androstanes show extremely large epimeric rate ratios of >30 000; these are not due to anchimeric assistance but only to the exceedingly slow reaction of the hindered 17β isomer, whereas the fast reaction of the 17α tosylate (e.g., 200 times higher than cyclopentyl tosylate) is in line with the ΔSI calculation. *endo*-Bicyclo[2.2.1]heptane esters show evidence for steric hindrance; *exo*-norbornyl tosylate has, however, a ΔG^* value lower by 4 kcal/mol than predicted. k_s/k_c values, obtained by rate comparison in 80% ethanol and 97% HFIP, vary between 0.5 and 300, mainly as a result of different steric hindrance to rearside nucleophilic substitution.

In recent years there has been a strong tendency to associate large reactivity differences in solvolytic reactions with a different degree of charge delocalization in the corresponding transition states.[2] Such claims are usually made on the grounds of what is considered to be an abnormally fast reaction, requiring a nonclassical charge dispersion in a bridged transition state. The prevailing arbitrariness, however, in the decision of what is regarded to be a "normal", that is sterically controlled reaction is most vividly illustrated by many reports on the norbornyl cation problem.[3] Other major efforts in recent years have been directed toward the study of carbocations under free ion conditions, which are also amenable to molecular orbital calculation.[3,4] Several studies demonstrated the formation of substantially delocalized bridged structures, even with the aid of "hard" C–H bonds, e.g., in the transannular position of medium rings.[5] It should, however, be borne in mind that the presence of solvolytic media is expected to change the nature of the intermediates by providing effective charge delocalization not only for the leaving group anion but also for the cationic in-

(1) Alicyclic Reaction Mechanisms. 10. Part 9: ref 30.

(2) For recent reviews on solvolysis reactions, see: (a) Kirmse, W. *Top. Curr. Chem.* **1979**, *80*, 125. (b) Bentley, T. W.; Schleyer, P. v. R. *Adv. Phys. Org. Chem.* **1977**, *14*, 1. (c) Harris, J. M. *Progr. Phys. Org. Chem.* **1974**, *11*, 89. (d) Bentley, T. W. *Annu. Rep. Prog. Chem., Sect. B* **1974**, *71*, 111.

(3) (a) Brown, H. C. *The Nonclassical Ion Problem*; Plenum: New York, 1977. (b) Brown, H. C. *Acc. Chem. Res.* **1983** *16*, 432. (c) Olah, G. A.; Prakash, G. K. S.; Saunders, M. *Ibid.* **1983**, *16*, 440. (d) Walling, Ch. *Ibid.* **1983**, *16*, 448. (e) Grob, C. A. *Ibid.* **1983**, *16*, 426. (f) Grob, C. A. *Angew. Chem.*, **1982**, *94*, 87; *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 87. (g) Barkash, V. A. *Top. Curr. Chem.* **1984**, *116/117*, 1. (h) Most recent paper: Brown, H. C.; Rei, M.-H. Chandrasekharan, J.; Somayaji, V. *J. Org. Chem. 1985, 50*, 5578, and earlier references.

(4) For leading references, see: (a) Olah, G. A. *Angew. Chem.* **1973**, *85*, 183; *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 173. (b) Olah, G. A. *Top. Curr. Chem.* **1979**, *80*, 19. (c) Arnett, E. M.; Petro, C. *J. Am. Chem. Soc.* **1978**, *100*, 2563. Arnett, E. M.; Hofelich, T. C. *Ibid.* **1983**, *105*, 1889. (d) Solomon, J. J.; Field, F. H. *J. Am. Chem. Soc.* **1976**, *98*, 1567. (e) Goddard, J. D.; Osamura, Y.; Schaefer, H. *J. Am. Chem. Soc.* **1982**, *104*, 3258. (f) Ragavachari, K.; Haddon, R. C.; Schleyer, P. v. R.; Schaefer, H. *J. Am. Chem. soc.* **1983**, *105*, 5915. (g) Harris, J. M.; Shafer, S. G.; Worley, S. D. *J. Comput. Chem.* **1982** *3*, 208. (h) Morton, Th. M. J. *Tetrahedron* **1982**, *38*, 3195. (i) Yamataka, H.; Ando, T.; Nagase, S.; Hanamura, M.; Morokuma, K. *J. Org. Chem.* **1984**, *49*, 631. (j) Yamabe, S.; Yamabe, E.; Minato, T. *J. Chem. Soc., Perkin Trans 2* **1983**, 1881.

(5) Kirchen, R. P.; Ranganayakulu, K.; Singh, B. P.; Sorensen, T. S. *J. Am. Chem. Soc.* **1981**, *103*, 588. Kirchen, R. P.; Okazawa, N.; Ranganayakulu, K., Rauk, A.; Sorensen, T. S. *Ibid.* **1981**, *103*, 597.

0022-3263/86/1951-3602$01.50/0

termediates.[6] There are large activation energy differences between free ion conditions and solvolytic conditions, although a parallel behavior has been found in several instances.[7] One cannot exclude the possible participation particularly of strained bonds with high p character only under free ion conditions in secondary cations, which do not necessarily need such a stabilization in charge-dispersing solvents.

A better understanding of solvolytic processes obviously needs a more quantitative description of steric contributions, which should be greatly aided by the application of force-field calculations of the molecular mechanics type (MM).[8] The present account not only contains an extension of our earlier MM approach[9] on alkyl-substituted as well as on bicyclic frameworks but was also initiated by the necessity of new measurements in hexafluoroisopropanol (HFIP) and by the discovery of striking reactivity differences in unstrained secondary steroid esters.[1]

The Quantification of Internal Strain Controlled Reactions: Monocyclic Derivatives. A major difficulty in the comparison of different systems, as recognized by Schleyer, Bentley, et al.[10] on the basis of kinetic results, lies in the extremely variable tendency of secondary esters to undergo S_N2-type substitution reactions ($\cong k_s$). Thus, the corresponding quantity k_s/k_c (or k_s/k_Δ)[10] observed in this study varies for secondary tosylates between 0.3 and 300 (measured in 80% ethanol in comparison to HFIP). That even the weak nucleophile trifluorethanol (TFE) can be insufficient to suppress S_N2-type reactions is indicated not only by kinetic results[10b] but evident from the observed inversion in cyclohexyl tosylate trifluorethanolysis[11] as well as by the absence of ionic rearrangements in cyclohexyl systems, which are detectable only in HFIP.[12] Since most of the available kinetic data on secondary sulfonates were obtained in more nucleophilic solvents, which necessarily leads to ill-defined mechanisms, we decided to measure all substrates in HFIP (Table I) in order to secure a firm experimental basis for a strain–reactivity analysis.

The quantitative evaluation of strain changes during a "limiting" solvolysis reaction involves MM energy calculations for the energy weighted sp^3 ground states and for an sp^2-like transition-state model. This approach has been most successfully used by Schleyer and co-workers[13] for the analysis of reactions at tertiary bridgehead systems, which do have the unsurpassed benefit of being protected against S_N2-type rearside attack and which show very large differences due to large strain effects. The application to secondary ester solvolysis, which was first tried by Harris et al.,[14] was hampered not only by the uncertain involvement of k_s-participation and insufficient experimental data

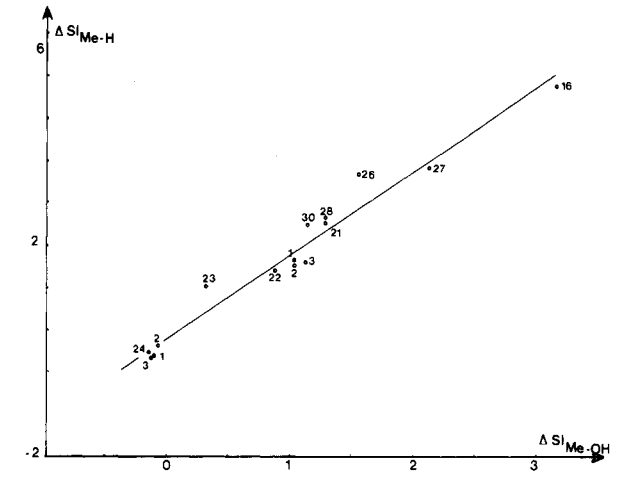


Figure 1. Strain energy differences ΔSI (X = Me, X = H) vs. ΔSI (X = Me, X = OH) for the compounds for which ΔSI_{OH-H} was calculated (see Table S3, supplementary material).

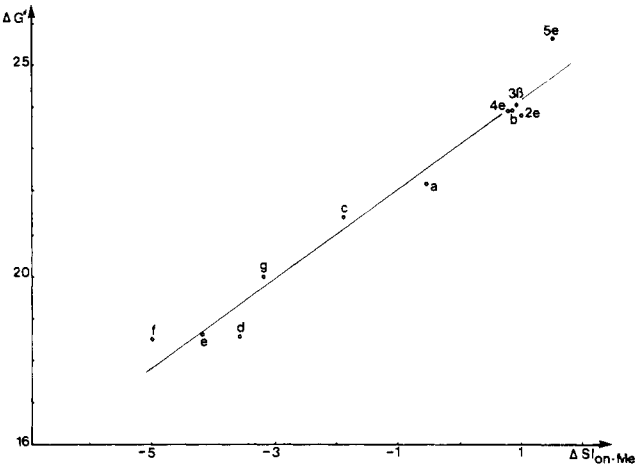
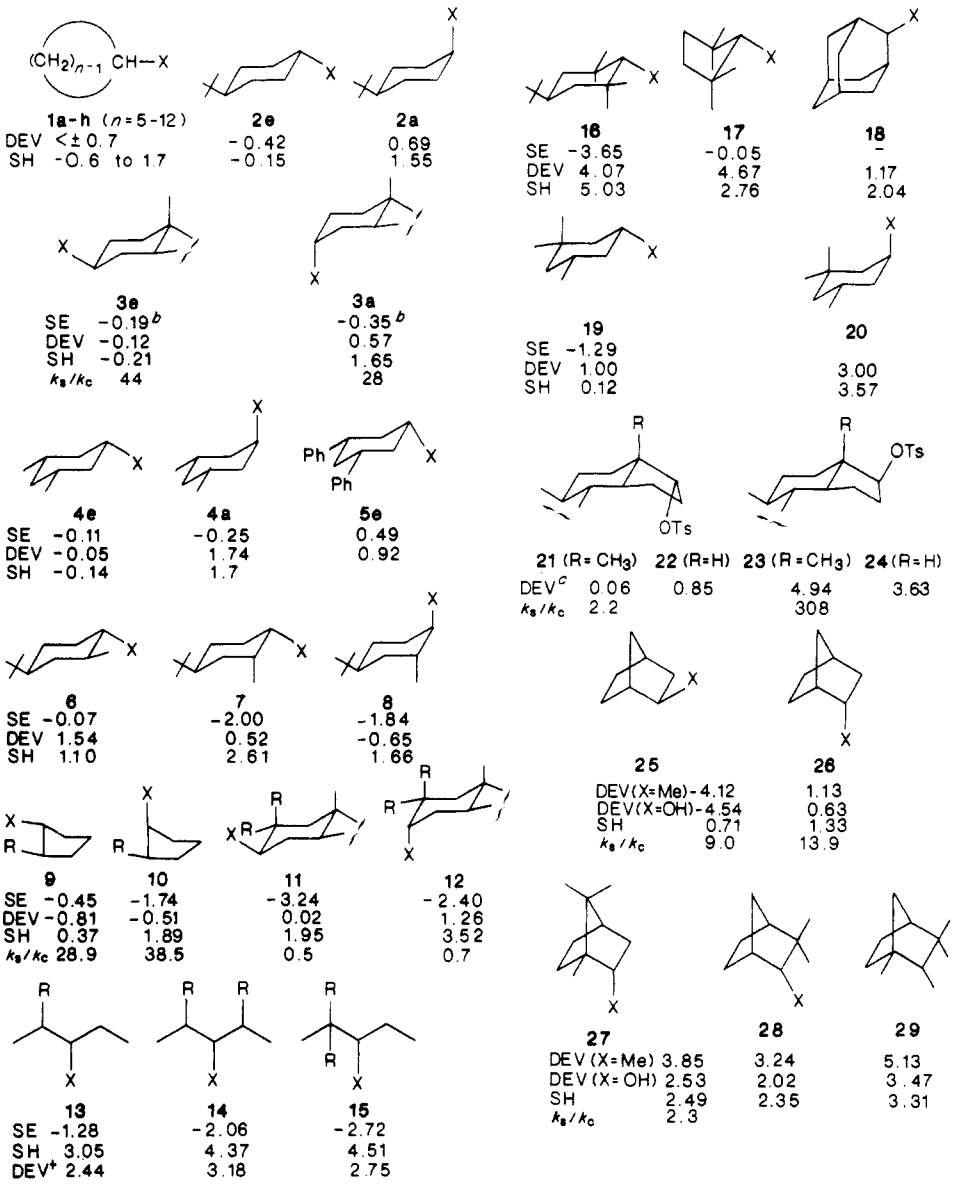


Figure 2. Solvolysis in HFIP: ΔG^* vs. $\Delta SI_{sp^3/sp^2}$ for unhindered secondary tosylates; compounds **a–g**: **1a–1g** [n = 5–11; **1h** (n = 12) omitted, see ref 9 and earlier references]; **2e–5e** (see Scheme I); 3β: 3β-(tosyloxy)-5α-androstane.

to separate the sterically controlled reactions from nonclassical systems but also by uncertainties regarding the choice of a proper force-field representation of the sp^3 and sp^2 states.[9,15] These problems are also apparent in related work by Müller et al.[15] and have already been discussed elsewhere.[9,15] The present approach is according to the Curtin–Hammett principle based on the use of weighted methylcycloalkane conformers as a model for the sp^3 state and of the lowest energy cycloalkanone conformation for the sp^2 state. As shown previously[9] and qualitatively advanced already in Brown's I-strain concept,[16] the strain changes in cycloalkane reactions reside mostly in torsional (Pitzer) energy changes, which with medium rings are partially relieved in the trigonal state. The major problem in the force-field application, however, lies not so much in the sp^2 model but in the appropriate model for the leaving group in the sp^3 ground states. We have shown[9] that indiscriminate use of, e.g., methyl as a model for the reacting substituent can lead to a description of steric hindrance around the substituent site instead of the desired description of the sp^3/sp^2 strain change. The choice of OH instead of CH_3 as a substituent model leads, for

(6) Schmid, R.; Sapunov, V. N., *Non-Formal Kinetics*; Verlag Chemie: Weinheim, West Germany 1982; p 144 ff.
(7) (a) Arnett, E. M.; Petro, C.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1979**, *101*, 522. (b) Arnett, E. M.; Pienta, N. J. *Ibid.* **1980**, *102*, 3329.
(8) (a) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, DC, 1982. (b) Osawa, E.; Musso, M. *Angew. Chem.* **1983**, *95*, 1; *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 1; *Top. Stereochem.* **1982**, *13*, 117.
(9) Schneider, H.-J.; Schmidt, G.; Thomas, F. *J. Am. Chem. Soc.* **1983**, *105*, 3556.
(10) (a) Bentley, T. W.; Bowen, C. T.; Morton, D. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5466 and references cited therein. (b) Schadt, F. L.; Bentley, W. T.; Schleyer, P. v. R. *Ibid.* **1976**, *98*, 7667. (c) For a recent report on solvent-independent rates, see: Kevill, D. N.; Anderson, S. W. *Ibid.* **1986**, *108*, 1579.
(11) Schneider, H.-J.; Schmidt, G. *Chem. Ber.* **1986**, *119*, 65.
(12) Schneider, H.-J.; Busch, R. *J. Org. Chem.* **1982**, *47*, 1766.
(13) Schleyer, P. v. R.; Bingham, R. C. *J. Am. Chem. Soc.* **1971**, *93*, 3189. Schleyer, P. v. R.; Chandrasekhar, J. *J. Org. Chem.* **1981**, *46*, 225. See also: Bentley, T. W.; Roberts, K. *J. Org. Chem.* **1985**, *50*, 5852 and references cited therein.
(14) Smith, M. H.; Harris, J. M. *J. Org. Chem.* **1978**, *43*, 3588.
(15) Müller, P.; Blanc, J.; Perlberger, J. C. *Helv. Chim. Acta* **1982**, *65*, 1418. Müller, P.; Mareda, J. *Tetrahedron Lett.* **1984** 1703; *Helv. Chim. Acta* **1985**, *68*, 119. We thank Professor Müller for preprints.
(16) Brown, H. C. *J. Chem. Soc.* **1956**, 1248.

Scheme I[a]



[a] DEV, SE, and SH are free energy differences in kcal/mol at 298 K; SE: substituent effect, SE = ΔG^* (substituted compound) – ΔG^* (unsubstituted compound), if applicable; ΔG^* values for ROTs reaction in HFIP. DEV: deivation between ΔG^* (observed) – ΔG^* (calculated with eq 1); SH: steric hindrance model for backside approach; evaluated as strain energy difference (MM2 calculation) between RX (X = CH_3) and RH. k_s/k_c: kinetic parameter for solvent assistance,[10] obtained by rate comparison in 97% HFIP and 80% EtOH/H_2O. [b] By comparison to **2e** or **2a**. [c] DEV values obtained with X = OH instead X = CH_3: **21**, 2.36; **22**, -1.79; **23**, 4.60; **24**, 3.73.

sterically hindered positions, to a smaller strain energy difference ΔSI sp^3/sp^2. Consequently, the differences between the CH_3 and OH model itself ($\Delta\Delta SIsp^3/sp^2 = \Delta SI_{X=Me} - \Delta SI_{X=OH}$) is, as to be expected, a function of the steric hindrance around the substituent, if we describe this hindrance by the strain difference $\Delta SI_{Me/H}$ between methylcycloalkane and cycloalkane (Figure 1). Monocylic compounds without additional substituents are found to be the *only* systems that are free from the obvious ambiguity involved with the substituent modeling;[9] only a few other compounds such as **2e**, **3e**, **4e**, **5e**, etc. show $\Delta SI_{Me/OH}$ differences small enought to warrant inclusion in a strain–reactivity plot (Scheme I).

The construction of a strain–reactivity scale without inclusion of arbitrarily chosen force-field models and of reactions with significant differences in the mechanism—such as S_N2 participation or steric hindrance of solvation, etc.—is an essential prerequisite for the quantitative evaluation of steric effects in solvolysis reactions. It is gratifying that comparison of ΔG^* for cycloalkyl tosylates in HFIP with the $\Delta SI_{sp^3/sp^2}$ values yields a linear relation ($r = 0.9819$) with a sensitivity or slope of $m = 1.0$ (Figure 2, eq 1). The sensitivity of $m = 1.0$ compared to $m = 0.8$

$$\Delta G^*_{25°C,HFIP} = (1.04 \pm 0.03)\Delta SI_{sp^3/sp^2} + (23.00 \pm 0.07) \quad (1)$$

in TFE[9] indicates that the hexafluorisopropanolysis of the secondary tosylates is limiting in the sense that the transition state is extremely late[9] and shows trigonal hybridization. The remaining scatter in Figure 2 is not unexpected in view of, e.g., differential torsional angles X–Cα–Cβ–H in the different X-substituted cycloalkanes[17] which is of relevance for the velocity[11,18] of the predominating but variable elimination in the products. Also, a differential degree of ion pair return[19] prior to the con-

(17) For examples, see supplementary material to ref 9.
(18) Gschwendtner, W.; Hoppen, V.; Schneider, H.-J. *J. Chem. Res., Synop.* **1981**, 96; *J. Chem. Res., Miniprint* **1981**, 1201.
(19) See, e.g.; Chang, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1984**, *106*, 810 and references cited therein.

Table I. Kinetic Parameters for the Tosylate Solvolysis in HFIP[a]

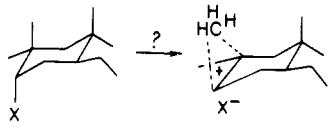
	10^5k_{298}	ΔG^*_{298}	ΔH^*	ΔS^*	ΔSI
1a	35.4	22.15	15.15	−23.5	−0.02
1b	17.8[b]	23.87	19.0	−15.7	0.99
1c	144	21.32	15.72	−18.8	−1.82
1d	17300	18.48	15.33	−10.6	−3.52
1e	12800	18.66	15.85	−9.5	−4.16
1f	15600	18.54	16.66	−6.3	−4.99
1g	1320	20.00	16.51	−11.7	−3.12
1h	33	22.19	20.16	−6.8	−2.99
2e	2.38	23.75	18.12	−18.0	1.13
2a	7.25	23.09	20.11	−10.0	−0.57
3α	16.6[c]	22.61	21.6	−3.2	−0.92
3β	2.0[c]	23.85	18.8	−17.1	0.94
4e	1.5[e]	24.00	*d*	*d*	1.02
4a	2.87	23.64	18.98	−15.6	−0.82
5e	0.1[e]	25.60	*d*	*d*	1.62
6	268	23.68	20.07	−12.1	−0.81
7	212	21.09	15.16	−19.9	−0.31
8	161	21.25	16.59	−15.6	
9	75.2	21.71	17.8	−13.1	−0.46
10	666[c]	20.41	13.8	−22.0	−1.98
11	502[c]	20.6	16.5	−13.5	−2.31
12	966[c]	20.2	18.6	−5.3	−3.88
13	57.0	21.88	13.8	−27.0	−3.40
14	614	20.44	14.8	−18.7	−5.08
15	209	21.10	15.7	−18.2	−4.86
16	180	21.18			−6.67
17	36.7[c]	22.13	17.7	−15.0	−5.33
18	8.6[b]	22.98			−1.13
19	20.9	22.46	19.8	−8.8	0.44
20	23.9	22.38	21.5	−3.1	−3.45
21	6270[c]	19.09	14.1	−16.8	−2.43
22	2435[c]	19.6	16.0	−12.2	−2.43
23	0.2[c]	25.16	21.1	−13.5	−2.62
24	0.1[c]	25.6	17.3	−27.7	−0.98
25	9410	18.84	13.8	−16.9	−0.37
26	7.23	23.09	17.9	−17.5	−0.99
27	35.8	22.14	19.2	−9.7	−4.52
28	3.22	23.57	23.8	1	−2.55
29	9.77	22.91	19.5	−11.4	−4.99

[a] Measurements in HFIP (97% wt, 3% wt H_2O; ±1%); k_{298}, ΔH^*, and ΔS^* from regression analysis of three to five measurements of three to five temperatures (see Table S1, supplementary material); k in s^{-1}, ±1%; ΔH in kcal/mol, ±0.5; ΔS in cal/(deg mol), ±3 (average error). ΔSI: strain energy difference. (MM2 calculation) between sp^2 (ketone) and sp^3 (methyl compound), see text. [b] Calculated from the literature[10a] data. [c] Data from: Becker, N., Dissertation, Universität des Saarlandes, Saarbrücken, 1985. [d] Too slow reaction for accurate ΔH^* and ΔS evaluation. [e] k_{298} calculated by using ΔH and ΔS data from **2e** and single value for **5e** at higher temperature (Table S1, supplementary material).

ductometrically measured tosylate liberation can contribute to deviations from linearity. Correlation with ΔH^* instead of ΔG^* values showed considerable scatter. This is attributed to both statistical errors in the small ΔH^* differences and to an eventual nonlinearity of the Eyring plots due to temperature-dependent reaction fields, which would have a pronounced effect on the very polar reaction in HFIP.

Alkyl Substituent Effects. Before one can hope to apply strain–reactivity correlations successfully to polycyclic and eventually also to strained frameworks, the reactivity variations generated by simple alkyl groups in the vicinity of the reaction centers must be understood or at least be empirically estimated within the limit given by the desired comparison between steric and nonclassical control. Again, we were forced to measure suitable tosylates in HFIP, since available data in conventional solvents were obscured by quite variable k_s contributions. Thus, k_s/k_c ratios[10] (calculated from rates in 80% ethanol and in HFIP, Table I) drop from 191 for cyclopentyl tosylate (**1**, $n = 5$), to 1.7 upon introduction of four vicinal methyl

Scheme II. Bridged Structure



groups (**17**[20]). Not only vicinal but also diaxial C–C bonds in the γ-position lead to increased steric hindrance for nucleophilic attack and subsequently lower the k_s participation even in nucleophilic solvents. Thus, compounds such as **11**, **12**, and **16–19** as well as the 17α-steroids **21** and **22** discussed below will show S_N1-type reaction even in aqueous solution. In order to quantify the decrease in the solvent assisted reaction ($\cong k_s$) one must evaluate the steric hindrance for rearside approach of the nucleophilic solvent. Such a description of steric hindrances still poses major problems.[21] Since several observations indicated that the strain energy difference between methyl compound RX (X = Me) and the parent hydrocarbon RX (X = H) increases with steric hindrance around X[9,22] (see above), we have included SH = SI_{RMe}–SI_{RH} in Scheme I. The available data indicate SH ≥ 2 kcal/mol for the rearside of the leaving group X for the compounds **11**, **12**, and **16–19**, which show $k_s/k_c < 2.5$, as far as measured (SH was obtained by MM2 strain calculation for the epimeric methylalkane), whereas all systems having larger k_s/k_c values are characterized by lower SH (Scheme I). It should be stressed, that the easily obtained SH values reflect only very approximately steric hindrance.[22] In the case of classical S_N2 reactions the transition state is better defined, and more consistent data as well as MM treatments are available.[23]

Alkyl substituents in the vicinity of the leaving group can, by steric hindrance,[3a,b,24] *hinder* nucleophilic substitution and also, due to electron donation, enhance rates. In fact, quite often one can see fairly linear dependencies of log k on polar substituent parameters of alkyl groups,[2,25] In view of the still disputed justification of such σ^* effects for alkyl groups[26] and their necessary dependence on orientation toward the developing cationic center,[27] we refrained from attempts to correct our data for polar alkyl substituent effects. A further possibility for enhanced rates of secondary esters with β-alkyl substituents[28] lies in their ability to form carbon-bridged transition states or inter-

(20) Cf.: Krapcho, A. P.; Horn, D. E. *Tetrahedron Lett.* **1966**, 6107.
(21) (a) Wipke, W. T.; Gund, P. *J. Am. Chem. Soc.* **1976**, *98*, 8107. One of the disadvantages of this approach is an arbitrary dissection in more or less hindered ketones. A more promising MM evaluation of steric hindrance in nucleophilic addition is described by Perlberger et al. [(b) Perlberger, J. C.; Müller, P. *J. Am. Chem. Soc.* **1977**, *99*, 6316], which, however, still involves large errors in epimeric ratio prediction.
(22) Schneider, H.-J.; Buchheit, U., unpublished results.
(23) See, e.g.: (a) Brown, H. C.; Cahn, A. *J. Am. Chem. Soc.* **1955**, *77*, 1715. (b) DeTar, D. F.; McMullen, D. F.; Luthra, N. P. *Ibid.* **1978**, *100*, 2484. (c) For recent reports on steric β-substituent effects in solvolysis reactions, see, e.g.: Kaftory, M.; Apeloig, Y.; Rapoport, Z. *J. Chem. Soc., Perkin Trans. 2* **1985**, 29.
(24) Tidwell, T. T. *J. Org. Chem.* **1974**, *39*, 3533.
(25) Bentley, T. W.; Liggero, S. H.; Imhoff, M. A.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1974**, *96*, 1970.
(26) DeTar, D. J. *J. Org. Chem.* **1980**, *45*, 5166. Charton, M. *J. Am. Chem. Soc.* **1975**, *97*, 3691 and references cited therein. Hanson, P. *J. Chem. Soc.* **1984**, 101 and references cited therein.
(27) Harris, J. M.; Moffatt, J. R.; Case, M. G.; Clarke, F. W.; Polley, J. S.; Morgon, Th. K.; Ford, Th. M.; Murray, R. K. *J. Org. Chem.* **1982**, *47*, 2740.
(28) For other examples, see, e.g.: (a) Liggero, S. H.; Harper, J. J.; Schleyer, p. v. R.; Krapcho, A. P.; Horn, D. E. *J. Am. Chem. Soc.* **1970**, *92*, 3789. (b) Shiner, V. J.; Fisher, R. D.; Dowd, W. *Ibid.* **1969**, *91*, 7748. (c) Yamataka, H.; Tamura, S.; Hanafusa, T.; Ando, T. *J. Chem. Soc., Chem. Commun.* **1984**, 362. (d) Shiner, V. J.; Imhoff, M. A. *J. Am. Chem. Soc.* **1985**, *107*, 2121 and references cited therein.

mediates with delocalized charges[2,3,28a,29] (Scheme II). In fact, compounds such as **8**, **12**, **14**, **15**, and **21** do have already the ideal antiperiplanar orientation of leaving group X and a vicinal methyl substituent R; in **12**, **15**, and **21**—after conformational change also in **17**—an additional stabilization could be expected from the possible transformation from a secondary to a tertiary cationic center. Noticeably, however, *none* of the systems shows kinetic deviations by DEV > 0.8 kcal/mol (Scheme I) from the strain controlled rates predicted by eq 1. Within the limits of the strain–reactivity analysis there is no evidence either for a significant contribution of polar alkyl substituent effects nor for bridging. The open chain compounds **13–15** show ΔG^* values consistently lower by DEV = 2.8 ± 0.35 kcal/mol. If one includes the 3-pentyl tosylate (**13**, R = H) in a separate ΔG^* vs. SI plot, the four compounds again show a linear correlation with a normal sensitivity of m = 0.92 ± 0.06 (r = 0.975). This behavior would be consistent with a constant additional entropy contribution in comparison to the cyclic systems of $\Delta S^* \simeq -10$ eu.

Bicyclic Systems. This class of compounds is renowned for many examples of unusual reactivity, in terms of absolute rates as well as epimeric ratios.[2,3] We recently found[30] that the solvolysis of the 17-(tosyloxy)androstanes **21–24** show epimeric rate ratios of $>10^4$, larer than other systems already reported to be unusual.[31] The 17α-epimer **21** reacts 400× faster than a parent axially substituted cyclohexyl system (**2a**, **3a**) and still 200× faster than cyclopentyl tosylate (**9**, R = H). This, of course, is reminiscent of earlier arguments by H. C. Brown[3a,b] in favor of normal rates in the 2-norbornyl systems, where, in fact, the epimeric rate ratio is only $\sim 10^3$. Although the higher reactivity of the 17α-isomer **21** and its aptitude to undergo 1,2-methyl migration in conventional solvents had earlier been attributed to the antiperiplanar setup of the Me–C13–C17–X arrangement,[32] our analysis of parent cyclic systems (**8**, **12**, **15**, **17**, **22** see above) clearly indicates that this is not the responsible factor. Furthermore, the norsteroid **22** displays a similar reactivity compared to the epimer **24**; the less likely possibility here of a 1,2-hdyrogen shift (or bridge) as a source for the reactivity is ruled out by comparison to **10**, **13**, and **14**. That it is only the tendency of the 17β-isomer to undergo S_N2-type displacement at the unprotected rearside (see the high k_s/k_c value, Scheme I), which is responsible for the smaller reactivity difference and the nonexistence of 1,2-methyl migration for the 17β-reaction in conventional solvents, is demonstrated by the *same* degree of rearrangement (>90%) from *both* epimers **21** and **23** in HFIP.[30] The strain–reactivity analysis finally shows that the fast reaction of the 17α-isomers **21** and **22** is, in fact, predicted by strain relief (eq 1), whereas the 17β-epimers **23** and **24** are slower by 4–5 kcal/mol, presumably because of steric hindrance to solvation.

This corresponds exactly to the explanation given by H. C. Brown[3a,b] for the reactivity differences in the 2-norbornyl systems **25** and **26**. Several examples in Scheme I show that steric hindrance—and/or hindrance to β-proton elimination—indeed can slow down S_N1-type reactions considerably (**16**, **17**, **20**, **23**, **24**), in line with Brown's explanation for the low reactivity of *endo*-norbornyl systems **26**.[3a,b] While **26** is off line by only ~1 kcal/mol, the other *endo*-compounds **27–29** show a large ΔG^* increase (compared to SI) with the number of vicinal methyl substituents. The *exo*-norbornyl compound **25**, however, is the only system in our scheme so far, which reacts distinctively *faster* than expected by the strain–reactivity analysis.[33] Charge delocalization as the reason for the higher reactivity of norbornyl compounds has been discussed in numerous papers and reviews,[3] which allows us to refrain from a repetition of the corresponding arguments. We want, however, to discuss briefly the numerical arguments presented by H. C. Brown[3a,d] in favor of "normal" exo reactivity, since indeed they so far seem not to have been considered seriously by his opponents. The numerical evidence presented by H. C. Brown essentially rests on the observation that introduction of α-methyl or α-phenyl groups R in the 2-position of norbornyl esters leads to nearly the same ΔG^* decrease ($\cong \Delta\Delta G$) in (a) 2-propyl (b) cyclopentyl, and (c) *exo*-2-norbornyl compounds, although formation of a nonclassical stabilized cation from c would require a smaller $\Delta\Delta G$ gain.[3a,b,d] However, the presence of R = CH_3 or R = C_6H_5 in c (with R in the crowded endo position) *leads necessarily to a larger strain relief* ΔSI ($sp^3 \rightarrow sp^2$) *for c, if there would be not other factors stabilizing the c transition state.* If one adds, e.g., the MM2-calculated strain energy difference ΔSI(Me–H) = 1.35 kcal/mol between *endo*-2-methylnorbornane and methylcyclopentane to the $\Delta\Delta G^*$ value of 1.8 kcal, which results for the corresponding rates in HFIP from H. C. Brown's analysis, one ends up with a discrepancy of ~3 kcal/mol, which is not far from our value (DEV = 4.1 kcal/mol). The phenyl substituent as a probe is even less suited in view of the orientational requirements for the corresponding benzyl cations, which may lead to additional strain differences. It should be noted, that the nonclassical contribution observed in our analysis (DEV = 4.1 kcal/mol) is smaller than the epimeric ΔG^* difference (6.0 kcal/mol) obtained from Goering–Schewene diagrams.[3a,b] The DEV value we obtain for the *endo*-norbornyl compound also shows that indeed both steric and nonclassical factors contribute to the differences between the norbornyl epimers.

Conclusions. Many solvolysis reactions of secondary esters are expected to display larger differences in the kinetics and smaller in the products, if carried out in solvents, which for the first time can largely suppress the S_N2-type solvent assisted pathway from a less hindered side. The use of more nucleophilic media until now prevented the discovery of even more extreme reactivity differences, also in the absence of anchimeric assistance, in cases which lack protection against k_s processes. Norbornyl compounds became exceptionally disputed for high epimeric rate ratios, which now in fact look only moderate, because steric hindrance in *both* epimers provide for a S_N1-type process even in conventional solvents. The observation of ionic rearrangements in systems similar to **4e**,[12] **21**, and **23**[30] without a kinetically visible anchimeric assistance, the low k_s/k_c values in some systems and the successful rate prediction on the basis of a $sp^3 \rightarrow sp^2$ strain analysis speak against the assumption[28c] that S_N1-type processes of secondary esters without neighbor group

(29) The observation of solvolysis products pointing to bridged or rapidly equilibrating intermediates (see, e.g.: Dannenberg, J. J.; Goldberg, B. J.; Barton, J. K.; Dill, K.; Weinwurzel, D. H.; Longas, M. O. *J. Am. Chem. Soc.* **1981**, *103*, 7764) does not necessarily imply a similar transition state for the slow step. (See discussion and references in: Shubin, V. G. *Top. Curr. Chem.* **1984**, *116/117*, 283.)

(30) Schneider, H.-J.; Becker, N. *Chem. Ber.* **1986**, *119*, 74.

(31) Paquette, L. A.; DeLucca, G.; Karp, J. D.; Bernal, I.; Swartzendruber, J. K.; Jones, N. D. *J. Am. Chem. Soc.* **1984**, *106*, 1122.

(32) Cf.: Kirk, D. N.; Hartshorn, M. P. *Steroid Reaction Mechanisms*; Elsevier: Amsterdam, 1968; p 270 and references cited therein.

(33) The observed k_s/k_c (or k_s/k_Δ) values (Scheme I) imply that solvent assisted S_N2-type contributions in norbornyl systems in conventional solvents may have been underestimated; for leading references, see ref 10a and: Banert, K.; Kirmse, W. *J. Am. Chem. Soc.* **1982**, *104*, 3766. Roberts, D. D. *J. Org. Chem.* **1984**, *49*, 2521.

participation must remain elusive. The MM approach allows to quantify rate enhancements and to predict in most cases (Scheme I) rate reductions, which obviously can be due to steric hindrance of solvation and/or hindrance of elimination. As elimination dominates in the weakly nucleophilic solvents and as there is evidence of very stringent E_2-type steric requirements for the abstraction of the β-proton[11,34] a detailed study of solvolysis products and particularly of kinetic isotope effects is of obvious need.

(34) The available evidence points toward E_2-type and to a lesser degree to E_1-type mechanism even in weakly nucleophilic solvents; cf. ref 11 and 18 and: Shiner, V. J.; Jewett, J. G. *J. Am. Chem. Soc.* **1965**, *87*, 1383. Saunders, W. H.; Finley, K. T. *Ibid.* **1965**, *87*, 1384. See also the discussion of a large β-deuterium isotope effect in ref 10a.

(35) For a related recent publication, see: Bentley, T. W., Roberts, K. *J. Org. Chem.* **1985**, *50*, 5852.

Experimental and computational details are described in earlier papers;[1,9,30] for reaction conditions see Table I.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Professor Kenny Lipkowitz is thanked for help with the manuscript preparation. The completion of the manuscript was aided by the award of an Akademie–Stipendium of the Stiftung Volkswagenwerk to H.-J.S.

Supplementary Material Available: Rate constants at different temperatures in HFIP and in part in trifluoroethanol (TFE), k_s/k_c ratios and steric hindrance model numbers SH, and strain energies with different functional groups X for **1a–29** (7 pages). Ordering information is given on any current masthead page.

Direct Addition of Elemental Fluorine to Double Bonds

Shlomo Rozen* and Michael Brand

School of Chemistry, Raymond and Beverly Sackler Faculty of Exact Sciences, Tel-Aviv University, Tel-Aviv 69978, Israel

Received March 6, 1986

The addition of elemental fluorine to the carbon–carbon double bond in a variety of olefinic substrates proceeds in a stereoselective syn manner. The addition of a proton donor to the conventional $CHCl_3$–$CFCl_3$ solvent system suppresses radical processes usually resulting in tar formation so the slower ionic type of addition of F_2 to the double bond takes place. Rapid collapse of the ion pair involving the α-fluoro carbocation ion is believed to account for the stereospecificity. This ion is also an intermediate in the formation of the 1,1,2-trifluoroalkanes which are also formed in the fluorination of terminal alkenes. Fluorination of enones which are generally deactivated also proceeds without complications. In such cases dehydrofluorination is an easy optional process resulting in α-fluoro enones.

Addition of most of the halogens to double bonds is a standard procedure since the beginning of modern organic chemistry. It is therefore of note that the first member of the halogen family—F_2—does not share the same popularity when reactions with alkenes are considered. It seems that the major obstacle for generalizing this reaction is the fact that the F–F bond is weak and can be readily cleaved to the very reactive and indiscriminating fluorine radicals. In fact a number of indirect methods have been developed for constructing vicinal difluoro compounds in order to circumvent the direct use of the element itself.[1] Some early success in adding F_2 to unsaturated centers was achieved by using perfluoroalkenes, resulting in formation of the corresponding perfluoroalkanes. In many cases, however, the dominant products are dimers which obviously originate from radical reactions.[2] This has been used very successfully by Scherer for preparing some of the most stable radicals known to organic chemistry.[3]

Working with unfluorinated alkenes, however, is another matter. The expected highly exothermic nature of the reaction of F_2 with olefins discouraged many from experimenting with this halogen. The pioneering work of Merritt[4] showed that it is not impossible to add fluorine to centain simple olefins. His technique was, however, quite unusual and rather inconvenient. As a result, 15 years passed before an additional paper dealing with this subject appeared.[5] We present here a general way for preparing the uncommon 1,2-difluoro compounds directly from F_2 and alkenes.

During our work with elemental fluorine in a direct[6] or indirect[7] mode, we have noticed that low temperature and especially polar solvents can suppress fluorine radical formation and encourage polar processes. We found that the latter are much more gentle and able to perform surprisingly selective reactions.[8] Thus working with a very dilute stream of fluorine in nitrogen in the presence of the highly polar ethanol which also serves as an acceptor for

(1) See, for example: Bornstein, J.; Borden, M. R.; Nunes, F.; Tarlin, H. I., *J. Am. Chem. Soc.* **1963**, *85*, 1609. Sket, B.; Zupan, M. *J. Chem. Soc., Perkin Trans. 1*, **1977**, 2169. Shellhamer, D. F.; Conner, R. J.; Richardson, R. E.; Heasley, V. L. *J. Org. Chem.* **1984**, *49*, 5015.

(2) Miller, W. T.; Staffer, J. O.; Fuller, J.; Currie, A. C. *J. Am. Chem. Soc.* **1964**, *86*, 51.

(3) Scherer, K. V., Jr.; Ono, T.; Yamanouchi, K.; Fernandez, R.; Henderson, P. *J. Am. Chem. Soc.* **1985**, *107*, 718.

(4) (a) Merritt, R. F.; Johnson, F. A. *J. Org. Chem.* **1966**, *31*, 1859. (b) Merritt, R. F.; Steven, T. E. *J. Am. Chem. Soc.* **1966**, *88*, 1822. (c) Merritt, R. F. *J. Org. Chem.* **1966**, *31*, 3871. (d) Merritt, R. F. *J. Am. Chem. Soc.* **1967**, *89*, 609.

(5) Barton, D. H. R.; James, J. L.; Hesse, R. H.; Pechet, M. M.; Rozen, S. *J. Chem. Soc., Perkin Trans. 1*, **1982**, 1105.

(6) See, for example: Gal, C.; Rozen, S. *Tetrahedron Lett.* **1985**, *26*, 2793.

(7) (a) Rozen, S.; Lerman, O.; Kol, M.; Hebel, D. *J. Org. Chem.* **1985**, *50*, 4753. (b) Rozen, S.; Brand, M. *Ibid.* **1985**, *50*, 3342.

(8) See, for example: Gal, C.; Rozen, S. *Tetrahedron Lett.* **1985**, *26*, 2793. Rozen, S.; Gal, C.; Faust, Y. *J. Am. Chem. Soc.* **1980**, *102*, 6861.

0022-3263/86/1951-3607$01.50/0