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STERIC EFFECTS ON REACTION RATES — V. AN UPDATED VERSION OF THE FOOTE-SCHLEYER CORRELATION BASED ON MOLECULAR MECHANICS

Paul Müller* and Jiri Mareda,
Département de Chimie Organique, Université de Genève,
1211 Genève 4, Switzerland

Abstract: The strain changes occurring during solvolysis of secondary tosylates are calculated by a molecular mechanics programme (MM2) using an empirical force-field for carbenium ions. The rate constants for acetolysis of k_C-substrates correlate with these strain changes, defining a straight line representative for k_C behaviour.

The rates of solvolysis of tertiary substrates correlate well with the strain difference between the parent hydrocarbon and the corresponding carbenium ion, as calculated by molecular mechanics (1). For secondary substrates the Foote-Schleyer correlation has been widely used to rationalize steric effects on reactivity of k_c substrates and to estimate the magnitude of anchimeric assistance (2). Several attempts were made towards interpretation of this correlation with molecular mechanics; in all these approaches only limited rate ranges were covered (3). This communication deals with a general approach for rationalization of steric effects for k_c substrates. Strain in tosylates was approximated by that of the corresponding alcohols, as calculated by MM2 (4); for transition state strain we have developed a carbenium ion force-field analogous to that in Schleyer's BIGSTRAIN programme (5), but compatible with MM2. Table 2 summarizes the parameters used. The equations are those of Allinger (4). The performance of the parametrization was extensively tested by comparison of geometries and steric energies with those of BIGSTRAIN. Consistent results were obtained in all cases. For the time being, we have not developed increments in order to transform the steric energies of the carbenium ions into enthalpies of formation and strain energies; therefore only the difference in steric energies between alcohol and the ion are given (Table 2). Calculations were carried out for 28 secondary tosylates reacting without significant anchimeric assistance and without leaving group hindrance. The rates of solvolysis are expressed in units of energies, relative to cyclohexyl tosylate. Rate constants measured in acetic acid are used because most data in this solvent are available from the literature. The 28 structures define a straight line with a slope of 0.67 and an intercept of -0.20. The correlation coefficient is 0.96 and standard deviation on $\Delta G^{\dagger}$ 0.93. The fit is certainly not perfect, and there is room for improvement. However, it should be appreciated in the light of the following observations:

a) No allowance was made for polar effects owing to different substitution patterns at Cβ.
b) Rate constants are extrapolated from different temperatures, without consideration for differential $\Delta S^{\dagger}$ contributions.
c) Some of the substrates may be subject to weak anchimeric assistance or leaving group hindrance.

Table 1. Carbenium Ion Force-Field Parameters (a)

Stretching vibration	r_0 (b)(c)	k (b)(c)	Torsion	V_1 (f)	V_2	V_3
C^+-C	1.480	7.40	$C^+-C-C-H$	0.00	0.00	0.30
C^+-H	1.0857	7.40	$C^+-C-C-C$	0.15	0.15	0.08 (1.40)
			$C-C^+-C-H$	0.05	0.00	0.32
Angle bending	θ_0 (e)	k (d)	$C-C^+-C-C$	0.25	0.05	0.40 (0.60)
$C-C^+-C$	120.0	2.00 (1.30)	$C-C-C^+-H$	0.00	0.00	0.25
$C-C-C^+$	109.5	0.52 (0.32)	$H-C-C^+-H$	0.05	0.00	0.22
C^+-C-H	109.5	0.52				
$C-C^+-H$	120.0	2.00	Out of plane bending	k (c)		
				0.80		

(a) Values in parentheses are for 4-membered ring when different from the general force-field.
(b) Taken from BIGSTRAIN (ref. 5). (c) Distance in Å. (d) In mdyn/Å. (e) In deg. (f) In kcal/mol.

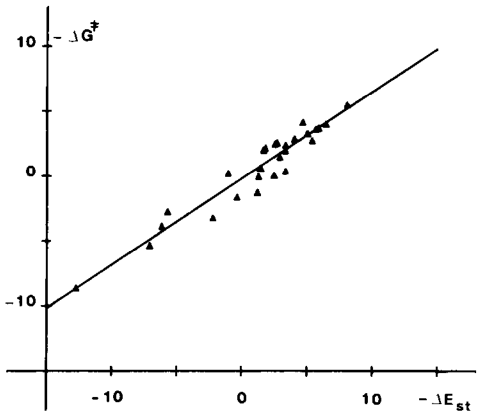

Figure: Plot of rates of tosylate acetolysis ($\Delta G^{\ddagger}$) against ΔE_{st} (ROH - R⊕). Slope: 0.668, intercept -0.20, r = 0.958, standard deviation in $\Delta G^{\ddagger}$ 0.93

Table 2. Difference of Steric Energies of Carbenium Ions and Alcohols and Acetolysis Rates of Secondary Alkyl Tosylates (a)

No	Tosylate	E_{st} (ROH)	E_{st} (R+)	$-\Delta E_{st}$ (b)	$-\Delta G^{\ddagger}_{(AcOH)}$ (c)
1	Cyclopentyl	12.63	10.95	1.68	2.05
2	Cyclohexyl	8.22	6.92	1.30	0.00
3	Cycloheptyl	15.56	12.20	3.36	2.42
4	2-*endo*-Norbornyl	24.89	25.91	-1.02	0.24
5	7-Norbornyl	25.40	38.14	-12.74	-8.65
6	Cyclooctyl	20.67	14.79	5.88	3.75
7	2-Bicyclo[2.2.2]octyl	20.99	18.44	2.55	2.51
8	2-*ax*-Bicyclo[3.2.1]octyl	20.89	19.08	1.81	2.19
9	2-*eq*-Bicyclo[3.2.1]octyl	20.56	19.08	1.48	0.64
10	3-*endo*-Bicyclo[3.2.1]octyl	22.09	18.06	4.03	2.90
11	3-*exo*-Bicyclo[3.2.1]octyl	20.98	18.06	2.92	1.51
12	2-*endo*-Norbrendyl	45.82	51.51	-5.69	-2.73
13	Cyclononyl	24.56	18.90	5.66	3.67
14	2-*endo*-Bicyclo[3.3.1]nonyl	19.59	17.10	2.49	0.10 (d)
15	2-*exo*-Bicyclo[3.3.1]nonyl	19.81	17.10	2.71	2.62 (d)
16	3-*endo*-Bicyclo[3.3.1]nonyl	22.78	14.71	8.07	5.53
17	3-*exo*-Bicyclo[3.3.1]nonyl	19.37	14.71	4.66	4.18
18	9-Bicyclo[3.3.1]nonyl	20.22	18.79	1.43	0.65
19	2-*ax*-Noradamantyl	31.05	33.24	-2.19	-3.19
20	2-*endo*-Brendyl	34.11	34.45	-0.34	-1.62
21	Cyclodecyl	25.65	19.20	6.45	4.04
22	2-Adamantyl	18.96	17.74	1.22	-1.24
23	Cycloundecyl	27.21	21.82	5.39	2.78
24	2-*endo*-Homoadamantyl	29.60	26.24	3.36	0.40 (d)
25	2-*exo*-Homoadamantyl	29.58	26.24	3.34	2.00 (d)
26	4-Homoadamantyl	29.24	24.22	5.02	3.32
27	*endo*-*exo*-Tetracyclo[6.1.1.^{3,6}0.^{2,7}]-dodecyl-11-*syn*	55.39	62.46	-7.07	-5.34
28	*exo*-*exo*-Tetracyclo 6.2.1.1[^{3,6}0.^{2,7}]-dodecyl-11-*anti*	54.32	60.46	-6.14	-3.86

(a) Energies in kcal/mol. (b) Steric energy (ROH) - Steric energy (R+). (c) Relative to cyclohexyl. Data from refs 2 and 3 and refs cited therein. (d) Extrapolated from aq. EtOH (ref. 6).

d) Acetic acid is probably not the solvent of choice, since k_s pathways are not entirely negligible (4c).

e) The choice of OH as a steric surrogate for OTs may be questioned (7) and will require further investigation.

For all these reasons it is unwise to discuss deviations from the k_c line of less than 1 kcal/mol. Nevertheless, we believe that the k_c line itself is now well defined. Comparison with that of Harris (3a) (based on 6 compounds) shows that both approaches are consistent (slope 0.60, intercept -1.0, rel. to cyclohexyl) if identical units are used. With the definition of the k_c line the magnitude of anchimeric assistance and of leaving group hindrance of particular substrates may be estimated from deviations in the plot, unless compensating factors complicate the situation.

The slope of our k_c line indicates that 67% of the strain changes occurring are reflected in the reactivities of the compounds. This confirms qualitatively the hypothesis that the transition state resembles the carbenium ion. However, since the force-field is empirical and tailored to rationalize data for solvolysis, the significance of the results with respect to free carbenium ions is yet to be established.

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