226. Polar Substituent Effects in the Solvolysis of Primary and Tertiary Alkyl Halides. Polar Effect IX

by **Cyril A. Grob** and **Adrian Waldner**[1])

Institute of Organic Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel

(24.IX.80)

Summary

When the *Hammett-Taft* equation $\log(k/k_o) = \rho^q \cdot \sigma_I^q$ is applied to the solvolysis of the 3-substituted propyl bromides **6a–6i** in ethanol/water 4:1 *(v/v)* log k correlates linearly with σ_I^q except in cases where R exerts an anchimeric effect. The reaction constant ρ^q for **6** is -0.12 and is typical for a nucleophilic solvent-assisted k_s process at a primary C-atom. The tertiary halides **1** and **3**, however, which react with little or no nucleophilic solvent assistance, *i.e.* by k_c processes, lead to larger ρ^q values of -0.71 and -1.14, respectively. The reaction constant ρ^q is therefore a sensitive gauge for charge development in the transition state for solvolysis of saturated compounds.

Introduction. - As recently reported [1] the solvolysis rates of the tertiary chlorides **1** in ethanol/water 4:1 *(v/v)* fit the *Hammett-Taft* equation (1) only if R in **1** is a neutral

$$\log(k/k_o) = \rho^q \cdot \sigma_I^q \qquad (1)$$

or electron withdrawing substituent, such as H, CH_3, $(CH_3)_2NCH_2$, $ClCH_2$, Cl, CN or NO_2. The value of σ_I^q in equation (1) is the inductive substituent constant of R derived from the pK_a of 4-R-substituted quinuclidinium perchlorates **2** [2]. The linear relationship between log k for **1** and σ_I^q shows that the substituents control the rates of these tertiary chlorides by their inductive effect only[2]). The reaction constant ρ^q, a measure of the sensitivity of the rate to the nature of R, was -0.71. Consequently, a ρ value of this magnitude was considered to be characteristic for the solvolysis of acyclic tertiary halides, which were hitherto thought to ionize without nucleophilic solvent assistance and were therefore classified as k_c processes [5] [6].

Recently, however, *Bentley et al.* [7] have adduced evidence for significant assistance by the more nucleophilic solvents in the solvolysis of t-butyl bromide,

---

[1]) With the collaboration of Mr. *Rolf Bielmann.*

[2]) When R was a n-electron donor, such as $(CH_3)_2N$, OH or CH_3O, or an electrofugal σ-electron donor, such as $(CH_3)_3Sn$, equation (1) was no longer obeyed and higher rates were observed. These exalted effects of R confirm our earlier results [3] and support our contention that substituent 'constants' are not independent of the reaction type [4].

0018-019X/80/8/2152-07$01.00/0

which therefore shows some k_s[3] character [5] [6][4]. On the other hand, solvolyses of 1-bromoadamantanes (**3**, R=H), in which rearside attack by solvent is excluded, must be considered true k_c processes.

A gradual increase in nucleophilic solvent participation in going from a k_c- to a k_s-process should be reflected in a decrease in the size of the reaction constant ρ^q (equation 1) because the amount of positive charge developed at C(a) in the transition state diminishes. Thus, in the transition state **4** for the ionization of **3** the positive charge is transferred to the incipient adamantyl cation, whereas in the transition state for **1** part of the charge is transferred to the solvent SOH, as illustrated in **5**. This is borne out by the observed ρ^q values for **3** and **1**, which are -1.14 [3] and -0.71 [1], respectively.

It was therefore of interest to determine the ρ^q value for primary halides, such as the 3-substituted propyl bromides **6a-i**, since they should react by solvent displacement, *i.e.* by a true S_N2 or k_s-process [6] [9] with little or no positive charge development at the primary C-atom in the transition state **7**. Hence, electrostatic interaction with the substituent R is expected to be minimal and a low ρ value should result.

These trends were in fact anticipated by *Streitwieser* [10] who applied equation (1) and *Taft*'s σ^* polar substituent constants to literature data on the solvolysis of primary, secondary and tertiary halides and sulfonates. However, in view of the paucity of data and the contradictory statements of *Pritzkow & Schöppler* [11][5] a more detailed study of polar substituent effects in the solvolysis of primary halides seemed desirable. The bromides **6a-i** were chosen in order to permit a comparison with their tertiary counterparts **1**.

As also pointed out by *Streitwieser* [10] neighboring nucleophilic substituents R participate in the ionization and thus cause deviations from the expected linear correlation of log k with σ_I^q, which provide a reliable measure of *Winstein*'s anchimeric effect[6]. However, R-participation was not anticipated in the case of **6a-e**, but did present a likely reaction pathway for **6g**, **6h** and **6i**.

Results. - The rate constants for the bromides **6a-i** *(Table 1)*, which were measured conductometrically in ethanol/water 4:1 *(v/v)* obeyed the pseudo first order or first order rate law. Inclusion of a base, such as triethylamine, to neutralize the HBr generated in the reaction, is necessary because the acid tends to react with ethanol above 100°, causing a decrease in conductivity. However, addition of 1 to 3 mol-equiv. of triethylamine did not affect the rate constants at low concentrations of the bromides **6**, *i.e.* 0.001 M.

Preparative solvolyses of the bromides **6a-i** were carried out in acetone/water 7:3 *(v/v)*, because ethanol interfered with the quantitative determination of volatile products and their identification by gas chromatography. Solutions of **6** of higher

---

[3] Nucleophilically solvent-assisted processes are designated k_s [5] [6].

[4] Earlier work in this laboratory has demonstrated intramolecular nucleophilic attack on tertiary chlorides [8].

[5] These authors claimed that the acetolysis rates of primary p-toluenesulfonates do not fit the *Hammett-Taft* equation (1).

[6] For a recent review of neighboring group effects see [12].

Table 1. *First order rate constants* k *for* 10^{-3}M *3-substituted propyl bromides* **6** *in ethanol/water 4:1* (v/v) ($3 \cdot 10^{-3}$M in NEt_3)

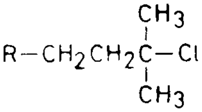
Nr.	R	T [°]	$k \cdot 10^4$ [s^{-1}]	$H^{\ddagger}$ kcal/mol	$S^{\ddagger}$ cal/mol · degree
6a	H	119.95	1.76	18.71	−28.68
		124.38	2.31		
		129.98	3.27		
		130.00	3.27[a])		
6b	CH_3	119.26	1.57	18.73	−28.76
		124.38	2.18[b])		
		130.52	3.16		
		130.00	3.07[a])		
6c	C_6H_5	125.00	1.82	19.10	−28.24
		130.00	2.52		
		135.00	3.37		
6d	Cl	125.00	0.965	21.60	−23.24
		130.00	1.37		
		135.18	1.95		
6e	CN	125.10	1.11	20.42	−25.93
		130.12	1.54		
		135.15	2.15		
		130.00	1.53[a])		
6f	OCH_3	124.75	1.66	19.23	−28.08
		129.90	2.30		
		135.02	3.16		
		130.00	2.31[a])		
6g	OH	124.92	2.24	20.27	−24.89
		129.91	3.14		
		134.96	4.29		
		130.00	3.14[a])		
6h	$COOC_2H_5$	120.13	5.13	22.51	−16.91
		125.00	7.34		
		130.20	10.80		
		130.00	10.62[a])		
6i	$N(CH_3)_2$	30.00	2.10	21.85	−3.31
		40.00	6.92		
		50.00	21.17		
		130.00	$2.26 \cdot 10^4$		

[a]) Extrapolated.

[b]) With 1 mol-equiv. NEt_3: $k = 2.13 \cdot 10^{-4}$.

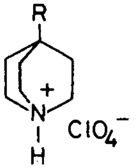
concentration (0.05M) were reacted at 130° in the presence of 0.055M diisopropylamine, since triethylamine tended to react with **6** under these conditions. Reaction times (*ca.* 10 half lives) and products are listed in *Table 2.*

The bromides **6a–f** underwent hydrolysis to the corresponding primary alcohols, accompanied in some cases by small amounts of olefins. The bromoalcohols **6g** yielded 25% of oxetane **8** beside 1,3-propanediol. Hydrolysis of the bromoester **6h** yielded mostly ethyl 4-hydroxybutyrate **9** beside γ-butyrolactone **10**, which appears

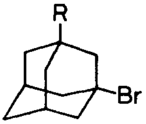


$R{-}CH_2CH_2C(CH_3)_2{-}Cl$

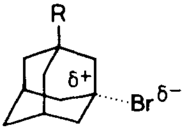
1



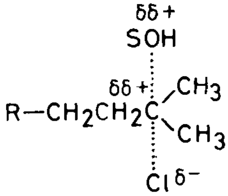
2



3



4



$R{-}CH_2CH_2\overset{\delta\delta+}{C}(CH_3)_2 \cdots \overset{\delta\delta+}{SOH}\ \cdots\ Cl^{\delta-}$

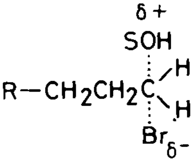
5

$R{-}CH_2CH_2CH_2Br$

6

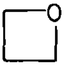
R =

a) H
b) CH_3
c) C_6H_5
d) Cl
e) CN
f) OCH_3
g) OH
h) $COOC_2H_5$
i) $N(CH_3)_2$



$R{-}CH_2CH_2CH_2 \cdots \overset{\delta+}{SOH}\ \cdots\ Br_{\delta-}$

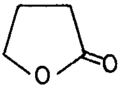
7



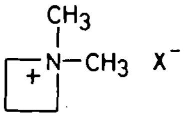
8

$HO(CH_2)_3COOC_2H_5$

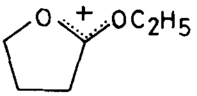
9



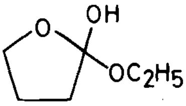
10



11



12



13

to be a secondary product, since its yield increased to 100% after a longer reaction time *(Table 2)*. Compound **6i** afforded only *N,N*-dimethylazetidinium bromide **11** (X = Br), which was isolated in quantitative yield as the Reineckate **11** ($X = Cr(NH_3)_2(SCN)_4$).

Discussion. - In the *Figure* log *k* values for the bromides **6a**-**i** are plotted against the corresponding σ_I^q values listed in *Table 3*. The points for **6a**-**f** fit the regression line, whereas the points for R = OH (**6g**), $COOC_2H_5$ (**6h**) and $N(CH_3)_2$ (**6i**) deviate significantly. These deviations correspond to rate accelerations of 1.6, 5.2 and $9.4 \cdot 10^3$, respectively, and must be attributed partly or wholly to neighboring group participation[7]. In support of this kinetic evidence **6g** yields 25% of oxetane by partic-

---

[7] This is also reflected in less negative $S^{\neq}$ values *(Table 1)*.

Table 2. *Reaction products from $R-CH_2CH_2CH_2Br$ (6) in acetone/water 7:3* (v/v) *at 130°*

Nr.	R	Reaction time (h)	Products (in %)
6a	H	6.66	86 $CH_3CH_2CH_2OH$a)
6b	CH_3	6.0	85 $CH_3(CH_2)_3OH$a)
6c	C_6H_5	8.58	99 $C_6H_5(CH_2)_3OH$ 1 $C_6H_5CH_2CH=CH_2$
6d	Cl	14.58	100 $Cl(CH_2)_3OH$
6e	CN	13.83	100 $NC(CH_2)_3OH$
6f	OCH_3	8.83	100 $CH_3O(CH_2)_3OH$
6g	OH	6.66	75 $HO(CH_2)_3OH$ 25 oxetane (**8**)
6h	$COOC_2H_5$	2.27	84 $HO(CH_2)_3COOC_2H_5$ (**9**) 16 lactone (**10**)b)
6i	$N(CH_3)_2$	1.0	100 azetidiniumc) bromide **11** (X = Br)

a) Beside not identified olefin.
b) After 87 h the yield of lactone **10** was 100%.
c) Reaction temperature 50°.

Table 3. *Relative first order rate constants for the bromides* **6** *at 130°, inductive substituent constants* σ_I^q *and accelerations based on the deviations from the inductive regression line*

Compound	R	k(rel)	σ_I^q [2b]	Acceleration
6a	H	1	0	
6b	CH_3	0.94	0.11	
6c	C_6H_5	0.77	0.87	
6d	Cl	0.42	2.51	
6e	CN	0.47	3.06	
6f	OCH_3	0.76	1.89	
6g	OH	0.96	1.76	1.60
6h	COOEt	3.25	1.70	5.2
6i	$N(CH_3)_2$	6914	1.12	$9.4 \cdot 10^3$

ipation of the O-atom at C(3), whereas the ester **6h** evidently reacts by participation of the O-atom at C(4) to furnish the intermediate **12**, which adds water to the cyclic ortho-diester **13**, the precursor of the hydroxyester **9** and the γ-lactone **10**. Prolonged heating converts the former quantitatively to the lactone **10** *(Table 2)*. The dimethylamino group in **6i** exerts the largest anchimeric acceleration of *ca.* 10^4, which is in good agreement with our earlier findings for the corresponding chloride (**6i**, Cl for Br) [13].

The reaction constant ρ^q derived from the slope of the regression line *(Fig.)* for the primary bromides **6a-f** is -0.12. This value is *ca.* six times and ten times, respectively, smaller than the ρ^q values observed for the tertiary chlorides **1** and the adamantyl bromides **3** and confirms the small effect of polar substituents on the solvolysis rates of primary reactants. These variations of ρ values substantiate their usefulness as a tool for gauging charge development at the reaction site in the transition state. However, as shown elsewhere [14] other factors beside nucleophilic

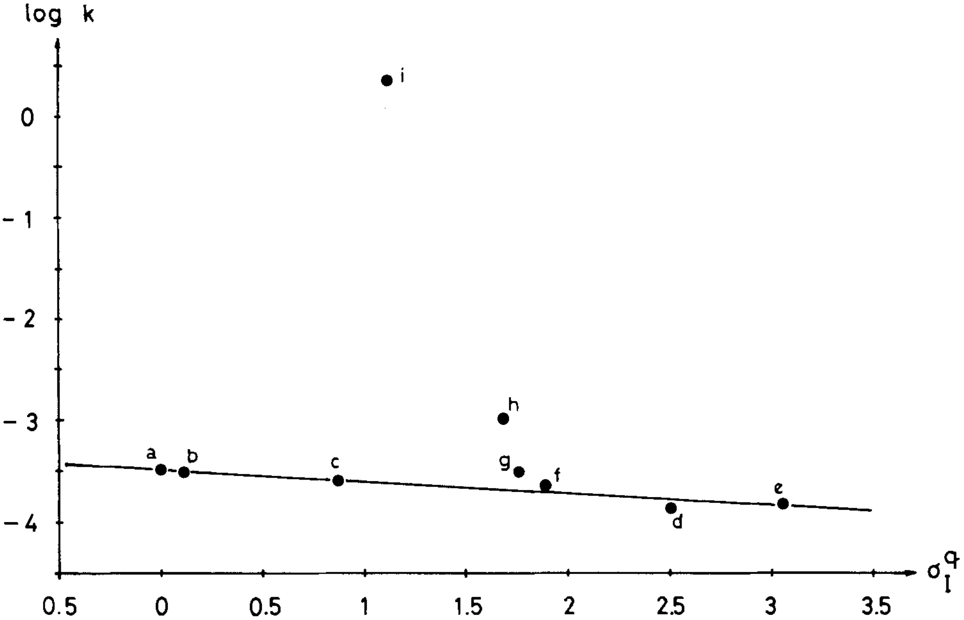


Fig. *Plot of log* k *for* **6a–i** *in ethanol/water 4:1* (v/v) vs. *inductive substituent constants for R*

solvent participation contribute to the magnitude of ρ in solvolytic reactions of compounds of the type R–C–C–C–X.

It is instructive to compare ρ values based on σ^q_I constants with those based on *Taft*'s σ_I constants [15]. A plot of log k for **6a–f** against the latter constants leads to a ρ value of -0.60, which is numerically five times as large as our ρ^q value of -0.12. This difference is due to the different models from which the substituent constants σ_I *(Taft)* and σ^q_I are derived [2a][8]). In fact they are related by the equation $\sigma_I = 0.200 \cdot \sigma^q_I - 0.07$.

This work was supported by the *'Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung'*, grant Nr. 2.819.0.77.

Experimental Part

Melting points (m.p.) were determined on a *Kofler*-Block and are corrected (± 1°). If not stated otherwise, IR.- and ^{1}H-NMR.-spectra were in agreement with the indicated structures.

Syntheses. Most of the compounds **6** and their hydrolysis products are commercially available. The rest were prepared as follows:

Preparation of 3-bromo-1-dimethylaminopropane (**6i**) *hydrobromide.* A mixture of 51.5 g (0.5 mol) 3-dimethylamino-1-propanol with 220 ml of 48% aqueous HBr-solution was prepared by cooling and then boiled under reflux. After each further hour 57, 22, 18, 9, 7 and 4 ml of solvent were distilled off and after 3 further hours another 72 ml. The yellowish solution was cooled to 70°, 300 ml of acetone

---

[8]) It should also be recalled that *Taft* employs two scales or substituent constants, *i.e.* σ_I and σ^* and that $\sigma_I = 0.45 \cdot \sigma^*$ [16].

were added and the mixture was cooled to 0°. The hygroscopic crystals, which were deposited after 12 h, were filtered off under argon and dried over P_2O_5. Yield 97.6 g (79%) of **6i** · HBr, m.p. 107-109°.

$C_5H_{13}Br_2N$ (246.98) Calc. C 24.31 H 5.30 N 5.67% Found C 24.14 H 5.45 N 5.85%

Preparation of 3-bromo-1-methoxypropane (**6f**). A suspension of 6.0 g (0.043 mol) 3-bromo-1-propanol and 8.43 g (0.057 mol) trimethyloxonium tetrafluoroborate in 60 ml CH_2Cl_2 was heated under reflux. Then 20 ml water and solid K_2CO_3 were added carefully until the solution reacted alkaline. The organic layer was separated, washed once with sat. aqueous NaCl-solution and dried over Na_2SO_4. Distillation through a *Vigreux*-column yielded 3.8 g (58%) of colorless oil, b.p. 130-131° (Lit. [17]: b.p. 129°).

Preparation of 3-methoxy-1-propanol. To 20.0 g (0.144 mol) of 3-bromo-1-propanol in 20 ml of abs. methanol a solution of 6.62 g (0.288 mol) sodium in 70 ml of abs. methanol was added with stirring at 20° within 1 h. After 1 h of refluxing the solution was neutralized with 2N HCl and extracted twice with ether. The combined extracts were dried over Na_2SO_4 and evaporated to dryness through a column. The oily residue was distilled *in vacuo* yielding 2.58 g (20%), b.p. 53°/14 Torr (Lit. [18]: 149-150°/760 Torr).

3-Hydroxybutyronitril was prepared according to [19].

N,N-*Dimethylazetidinium-reineckate* (**11**, $X = Cr(NH_3)_2(NCS)_4$) was obtained by reaction of **6i** ethanol/water 4:1 *(v/v)* and precipitation with ammonium reineckate according to an earlier procedure [20]. Violet platelets from acetone/water, m.p. 210° (dec.); yield 100%.

$C_9H_{18}CrN_7S_4$ (404.55) Calc. C 26.72 H 4.48 N 24.23% Found C 26.57 H 4.39 N 24.24%

Preparative solvolyses were carried out in acetone/water 7:3 *(v/v)* at the temperatures and for the periods of time indicated in *Table 2*. Samples of the reaction solutions were injected directly into the gas chromatography apparatus (*Perkin-Elmer* Model 3920) equipped with a 10% *FFAP* on *chromosorb* W-column. Retention times and relative yields were determined by calibration with authentic samples and with the aid of a *Varian* integrator CDS 111.

Rate measurements were carried out in ethanol/water 4:1 *(v/v)* with the conductance apparatus described previously [21].

REFERENCES

[1] *C.A. Grob & A. Waldner,* Helv. *62,* 1736 (1979).

[2] a) *C.A. Grob & M.G. Schlageter,* Helv. *59,* 264 (1976);
b) *C.A. Grob, B. Schaub & M.G. Schlageter,* ibid. *63,* 57 (1980).

[3] *W. Fischer & C.A. Grob,* Helv. *61,* 1588 (1978).

[4] *C.A. Grob,* Angew. Chemie *88,* 621 (1976); Angew. Chem. Int. Ed. *15,* 569 (1976).

[5] *S. Winstein, E. Alfred, R. Heck & R. Glick,* Tetrahedron *3,* 1 (1958).

[6] *F.L. Schadt, T.W. Bentley & P.v.R. Schleyer,* J. Am. Chem. Soc. *98,* 7667 (1976).

[7] *T.W. Bentley, C.T. Bowen, W. Parker & C.I.F. Watt,* J. Am. Chem. Soc. *101,* 2486 (1979).

[8] *C.A. Grob, K. Seckinger, S.W. Tam & R. Traber,* Tetrahedron Lett. *1973,* 3051.

[9] *T.W. Bentley & P.v.R. Schleyer,* J. Am. Chem. Soc. *98,* 7658 (1976).

[10] *A. Streitwieser,* J. Am. Chem. Soc. *78,* 4935 (1956).

[11] *W. Pritzkow & K.H. Schöppler,* Chem. Ber. *95,* 834 (1962).

[12] *B. Capon & S.P. McManus,* 'Neighboring Group Participation', Vol. 1, *Plenum Press,* New York 1976.

[13] *C.A. Grob & F.A. Jenny,* Tetrahedron Lett. *1960,* 25.

[14] *W. Fischer, C.A. Grob & G. von Sprecher,* Tetrahedron Lett. *1979,* 473; *W. Fischer, C.A. Grob, G. von Sprecher & A. Waldner,* ibid. *1979,* 1901, 1905.

[15] *S. Ehrenson, R.T.C. Brownlee & R.W. Taft* in 'Progress of physical organic Chemistry', Vol. *10,* 1 (1973).

[16] *R.W. Taft,* J. Am. Chem. Soc. *79,* 1045 (1957).

[17] *P.M. Laughton & R.E. Robertson,* Can. J. Chem. *39,* 2155 (1961).

[18] *A.B. Foster, A.H. Haines & M. Stacey,* Tetrahedron *16,* 177 (1961).

[19] *F.F. Blicke & B.A. Brown,* J. Org. Chem. *26,* 3685 (1961).

[20] *C.A. Grob, F. Ostermayer & W. Raudenbusch,* Helv. *45,* 1672 (1962).

[21] *C.A. Grob, F.M. Unger, E.D. Weiler & A. Weiss,* Helv. *55,* 501 (1972).