

Studies in Solvolysis. Part IV.¹ Substituent and Solvent Isotope Effects in the Solvolysis of a Series of Benzyl Trifluoroacetates

JUNE G. WINTER AND J. M. W. SCOTT

Chemistry Department, Memorial University, St. John's, Newfoundland

Received December 17, 1971

The rates of neutral hydrolysis of a series of 4-substituted benzyl trifluoroacetates 4-X-C₆H₄CH₂OCOCF₃, X = NO₂, Cl, H, CH₃, and OCH₃ have been studied in water and deuterium oxide, both solvents containing 0.012 mol fraction of acetone. The alteration of the rates with the nature of the 4-substituent and the kinetic solvent isotope effect ($k(\text{H}_2\text{O})/k(\text{D}_2\text{O})$) are consistent with the proposal that the esters with X = NO₂, Cl, H, and CH₃ all react by an acyl-oxygen B_{Ac}2 mechanism. On the other hand, the same mechanistic criteria indicate that the 4-methoxybenzyl ester reacts by both the B_{Ac}2 and the S_N1 alkyl-oxygen fission paths in equal amounts.

Les vitesses de l'hydrolyse neutre d'une série de trifluoroacétates de benzyle substitués en 4-(X-C₆H₄CH₂-OCOCF₃ avec X = NO₂, Cl, H, CH₃, et OCH₃) ont été étudiées dans l'eau et dans l'eau lourde contenant toutes deux 0.012 fraction molaire d'acétone. La modification des vitesses avec la nature du substituant en 4 et l'effet isotopique du solvant sur la cinétique ($k(\text{H}_2\text{O})/k(\text{D}_2\text{O})$) sont compatibles avec le mécanisme B_{Ac}2 proposé selon lequel les esters avec X = NO₂, Cl, H, et CH₃ réagissent tous par l'oxygène de l'acyle. De plus, ce même mécanisme montre que l'ester méthoxy-4 benzyle réagit à la fois par le schéma B_{Ac}2 et par le schéma S_N1 correspondant à la rupture de la liaison alkyl-oxygène, dans le même rapport.

Canadian Journal of Chemistry, 50, 1886 (1972)

Introduction

Using ¹⁸O tracer studies Bunton and Hadwick (2) have deduced that the neutral hydrolysis of methyl trifluoroacetate takes place by a B_{Ac}2 acyl-oxygen fission reaction. On the other hand Moffat and Hunt (3) cite the extent of olefin formation in the solvolysis of *t*-butyl trifluoroacetate and conclude that the neutral hydrolysis of this substrate is mechanistically similar to *t*-butyl chloride, *i.e.*, the tertiary carboxylic ester is considered to react via an S_N1 carbonium ion mechanism involving alkyl-oxygen fission.

These views have been amply confirmed in more extended studies (4, 5) of the α -methylated series CF₃COOR (R = Me, Et, *i*-Pr, and *t*-Bu) using the kinetic solvent isotope effect (*k.s.i.e.* $k(\text{H}_2\text{O})/k(\text{D}_2\text{O})$), the thermodynamic parameters $\Delta H^\ddagger$, $\Delta S^\ddagger$, and $\Delta C_p^\ddagger$ and secondary C—H/C—D isotope effects as mechanistic criteria. The summarized data from these studies are reported in Table 1 and the mechanistic conclusions to be derived from it are clear cut; the primary and secondary esters react by the B_{Ac}2 path and the tertiary ester reacts by an S_N1 route. A comparison of *t*-butyl chloride param-

eters with those for the corresponding trifluoroacetate is again useful (*c.f.* ref. 3).

The reasons for the change in mechanism B_{Ac}2 $\rightarrow$ S_N1 in the α -methylated series must be energetic but even a qualitative analysis of the contributing factors is difficult. These factors are presumably a blend of electronic, steric, and solvation effects which alter as the structure of the alkyl group is varied. In the alkyl-oxygen fission reaction the alkyl group is the reaction seat and hence the S_N1 path must display greater sensitivity to the structure of the alkyl group than the competitive B_{Ac}2 process in which the same structural alterations are relatively remote from the reaction center. A combination of two reaction paths (B_{Ac}2 and S_N1) of widely disparate sensitivity to structural alterations is an ideal situation for mechanistic changes but in the α -methylated series does not provide the possibility of assessing the relative importance of the contributing factors mentioned above. On the other hand a sequence of 4-substituted benzyl trifluoroacetates provides a more tractable series of reactants in which solvation and steric factors remain constant to a first approximation, leaving the residual electronic factors as paramount in the emergence of the S_N1 process. The facility of heterolytic fission in the gas phase as measured by the enthalpy change

¹Reference 1 is to be considered as Part III of the present series.

TABLE 1. Thermodynamic parameters, solvent isotope effects, and secondary isotope effects for the solvolysis of a series of alkyl trifluoroacetates and *t*-butyl chloride*

Mechanism	Ester or chloride	$\Delta H^*(H_2O)$ (kcal/mol)	$\Delta S^*(H_2O)$ (e.u.)	$k(H_2O)^\dagger$	$k(H)^\S$
				$k(D_2O)$	$k(D)$
$B_{Ac}2$	CF_3COOCH_3	10.60	-32.3	3.54	1.050 (d_3)
	$CF_3COOCH_2CH_3$	10.53	-35.1	3.67	1.036 (d_5)
	$CF_3COOCH(CH_3)_2$	10.51	-37.1	3.83	1.026 (d_6)
S_N1	$CF_3COOC(CH_3)_3$	25.44	13.7	1.24	2.175 (d_9)
	$(CH_3)_3CCl$	23.79¶	14.41¶	1.38**	2.45†† (d_9)

Except where stated otherwise the figures are from ref. 4. The errors in the values of ΔH^ are considered slightly less than ± 0.1 kcal/mol and the errors in ΔS^* about ± 0.5 e.u. on average.

†Average values at 4.98°C except for *t*-butyl chloride which is at 4.00°C.

§From ref. 5. Average values at 10°C except for *t*-butyl chloride and trifluoroacetate which are at 25°C.

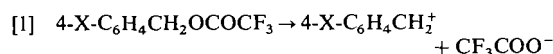
||Deuteration on methyl groups, *i.e.*, $-CH(CD_3)_2$.

¶From ref. 6.

**From ref. 7.

††From ref. 8.

(ΔH_g^i) associated with the reaction



should provide a useful guide as to which structures are likely to react by the S_N1 path. Unfortunately such data are not available for the trifluoroacetates. However, the values for the related series of benzyl chlorides in which the enthalpies of ionization are expected to parallel those of the related trifluoroacetates can be calculated from available thermochemical information. The data for the chlorides are recorded in Table 2 and the relatively low values for the 4-MeO and 4-CH₃ compounds suggest that the related trifluoroacetates would be likely candidates for the S_N1 reaction.

We proposed to detect such a change in mechanism via the k.s.i.e. (see Table 1) and also using the Hammett equation on the assumption that deviations from a linear free energy plot ($\log k$ vs. σ) would characterize any shift in mechanism $B_{Ac}2 \rightarrow S_N1$. The results of such experiments are reported below.

Experimental

General

Nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer using carbon tetrachloride as solvent and tetramethylsilane as internal standard. Infrared

TABLE 2. Estimated gas phase enthalpies of ionization (ΔH_g^i) for a series of 4-substituted benzyl chlorides

X (4-X-C ₆ H ₄ CH ₂ Cl)	Ionization potential (kcal/mol)	ΔH_g^{i*} (kcal/mol)
NO ₂	201	179
Cl	183	161
H	179	157
CH ₃	172	150
OCH ₃	157	135

*The gas phase enthalpies of ionization (ΔH_g^i) for the series of benzyl chlorides were calculated using the relationship $\Delta H_g^i = D(R-Cl) + I_p(R^\cdot) + E_e(Cl^\cdot)$ where D is the dissociation energy of the $R-Cl$ bond, I_p is the ionization potential of $R^\cdot$ and E_e is the electron affinity of $Cl^\cdot$. Bond dissociation energies for the chlorides were calculated from those for the bromides (9) with reference to the heats of formation (ΔH_f°).

$$D(R-Cl) = \Delta H_f^\circ(R^\cdot) + \Delta H_f^\circ(Cl^\cdot) - \Delta H_f^\circ(RCl)$$

$$D(R-Br) = \Delta H_f^\circ(R^\cdot) + \Delta H_f^\circ(Br^\cdot) - \Delta H_f^\circ(RBr)$$

which gives on subtraction,

$$D(R-Cl) - D(R-Br) = \Delta H_f^\circ(Cl^\cdot) - \Delta H_f^\circ(Br^\cdot) - \Delta H_f^\circ(RCl) + \Delta H_f^\circ(RBr)$$

Reported heats of formation for several chlorides and bromides (10) lead to the average value of $D(R-Cl) - D(R-Br) = 13 \pm 2$ kcal/mol. Values of $D(R-Cl)$ that were calculated for the above series were constant to within the error reported below and an average value of 62 ± 2 kcal/mol was employed. The electron affinity for $Cl^\cdot$ was taken as 84 kcal/mol (11). The most significant contribution to changes in ΔH_g^i is the ionization potential of the $R^\cdot$ group. The values of ionization potentials quoted above are from the work of Lossing and co-workers (12), the value for the 4-nitrobenzyl radical being extrapolated from a least squares calculation of ionization potential vs. the Brown σ^+ parameter for a series of twelve 3- and 4-substituted benzyl radicals. The gas phase enthalpies of ionization are considered accurate to ± 4 kcal/mol.

TABLE 3. Physical properties of some esters derived from trifluoroacetic acid

Ester (X-C ₆ H ₄ -CH ₂ OCOCF ₃)	Nuclear magnetic resonance (τ)	Infrared ν (C=O) (cm ⁻¹)	Saponification* value	B.p.† (°C)
NO ₂	1.49, 2.4, 4.50	1790	240 (249)	134–136 m.p. 47–48 Lit. 47 (13)
Cl	2.72, 4.74	1784	240 (238)	33–36
H	2.69, 4.75	1790	202 (204)	63–64
CH ₃	2.87, 4.80, 7.00	1780	217 (218)	30
OCH ₃	2.74, 3.14, 4.77, 6.26	1780	234 (234)	39–41
CF ₃ COOCH ₃	6.05	1790	133 (128)	42–42.5 at 760 mm Lit. 43 (14)

*Theoretical value in brackets.

†Boiling point values quoted for vacuum of 0.05–0.1 mm unless stated otherwise.

spectra were recorded on a Perkin–Elmer model 237B grating spectrophotometer using a liquid cell technique with carbon tetrachloride as solvent. Mass spectra were recorded on a Hitachi Perkin–Elmer RMU6E spectrometer at 50 °C using an ionizing potential of 70 V with no appreciable difference between initial and final total ion current.

Materials

Esters were prepared by the usual method, either from trifluoroacetic anhydride/alcohol or silver trifluoroacetate/bromide and were distilled under vacuum. 4-Nitrobenzyl trifluoroacetate was recrystallized several times from petroleum ether (40–60 °C). All the esters were stored at 0 °C in a desiccator. The 4-methoxybenzyl trifluoroacetate was very unstable and tended to polymerize to a deep red tar if left at room temperature for more than 2–3 h before distillation and, consequently, this material was vacuum distilled immediately after preparation.

All kinetic measurements were made soon after purification. Purity was established by saponification, mass spectra, n.m.r., and infrared measurements. The excellent first order plots also vindicated the purity of the esters. The analytical and spectral data are recorded in Table 3.

Deuterium oxide was obtained from Atomic Energy of Canada and was used several times without appreciable loss of purity. The solvent was recovered after each kinetic run and was distilled, any acid present having been neutralized before hand with dried sodium carbonate. The first fraction containing acetone was discarded. The concentration of deuterium oxide was never less than 97%, determined by using n.m.r. spectrometry with purified acetonitrile as an internal standard.

Acetone was purified by treatment with small amounts of potassium permanganate until the pink color persisted. After drying with anhydrous potassium carbonate the material was distilled at 55.5–56 °C.

Kinetics

Rates were determined conductimetrically using appa-

ratus described elsewhere (5). The concentration of ester in the kinetic determinations was *ca.* 10⁻⁴ M and the solvent systems used were water/acetone or deuterium oxide/acetone mixtures containing 0.012 mol fraction of acetone to facilitate dissolution of the ester. All rates were measured at 5.05 °C. A stock solution of the ester in acetone was prepared (*ca.* 0.002 M) and cooled to 5.05°. An aliquot (2 ml, 1.65 ± 0.02 g) of this solution was added, using a 2 ml syringe, to a measured volume of backing electrolyte (41 ml, 40.72 ± 0.06 g) at 5.05° in a stirred cell. The backing electrolyte was prepared by allowing a suitable amount of the appropriate ester to react with distilled water so as to reduce the initial resistance of the solution to a convenient value. The two weights quoted above, 1.65 ± 0.02 and 40.72 ± 0.06 g, are both averages of eight weight determinations. The backing electrolyte was introduced into the cell at room temperature using a 50 ml burette, the cell having been rinsed three times with backing electrolyte and then cleared of as much liquid as possible before refilling. The residual liquid on the sides of the cell weighed 0.2 g and did not vary from run to run. The amount of residual liquid is included in the weight of backing electrolyte quoted above.

For kinetic runs with deuterium oxide as the solvent, the volume of backing electrolyte used was adjusted so that the final reaction mixture contained 0.012 mol fraction of acetone.

Resistance readings were taken over approximately three half-lives and when the reaction was complete the infinity resistance was measured. At least four rate determinations were made for each ester and solvent combination.

The pseudo first order rate constants and *k*.s.i.e.'s are quoted in Table 4 for the 4-substituted benzyl esters along with those values for the methyl trifluoroacetate in the same solvent system for comparison. The *k*.s.i.e. of 3.4 for hydrolysis of this last ester in 0.012 mol fraction of acetone in water is in close agreement with the *k*.s.i.e. of 3.5 measured (4) in pure water. Therefore comparisons between the two solvent systems are considered legitimate.

TABLE 4. Rates of solvolysis of a series of trifluoroacetates in 0.012 mol fraction acetone in water and deuterium oxide at 5.05 °C

Ester (CF ₃ COOR)	$k_{\text{H}_2\text{O}}$ ($\times 10^3 \text{ s}^{-1}$)*	$k_{\text{D}_2\text{O}}$ ($\times 10^3 \text{ s}^{-1}$)*	$k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}}$
4-Nitrobenzyl	7.996(7) ± 0.065	2.030(4) ± 0.029	3.9
4-Chlorobenzyl	3.305(9) ± 0.065	0.8731(4) ± 0.0112	3.8
Benzyl	2.448(10) ± 0.035	0.6563(4) ± 0.0109	3.7
4-Methylbenzyl	1.939(5) ± 0.028	0.5356(4) ± 0.0058	3.6
4-Methoxybenzyl	3.212(8) ± 0.038	1.794(4) ± 0.013	1.8
Methyl	1.934(4) ± 0.026	0.5644(4) ± 0.0024	3.4

*Number of rate determinations in parentheses.

Discussion

We propose a useful rule which states that if the members of a series of substrates can each conceivably react by two distinct paths, A and B, and if both paths can be correlated by a linear free energy relationship using a common substituent scale, then deviations from the separate correlations, caused by a change in mechanism from A to B or vice versa, must be positive. This rule follows from the principle that if two reaction paths exist the path of minimum free energy will be the most important. The above rule is in accord with experience in the present study since the rate of solvolysis for the 4-methoxybenzyl trifluoroacetate deviates positively from a Hammett plot for which the remaining points are satisfactorily linear (see Fig. 1). From the sign of the ρ parameter we assume that this line corresponds to the $\text{B}_{\text{Ac}}2$ mechanism which is in agreement with the k.s.i.e.'s for the $4\text{-CH}_3 \rightarrow 4\text{-NO}_2$ compounds (see Table 4) and consistent with the fact that the sign of ρ for $\text{S}_{\text{N}}1$ reactions is always negative.

The deviation of the 4-OCH₃ compound from the $\text{B}_{\text{Ac}}2$ linear free energy correlation and the magnitude of the k.s.i.e. for this substance indicate that it reacts by a route different from that followed by the other structures but the relatively high value of the k.s.i.e. (1.8) is greater than those usually observed for $\text{S}_{\text{N}}1$ processes extensively studied by Laughton and Robertson

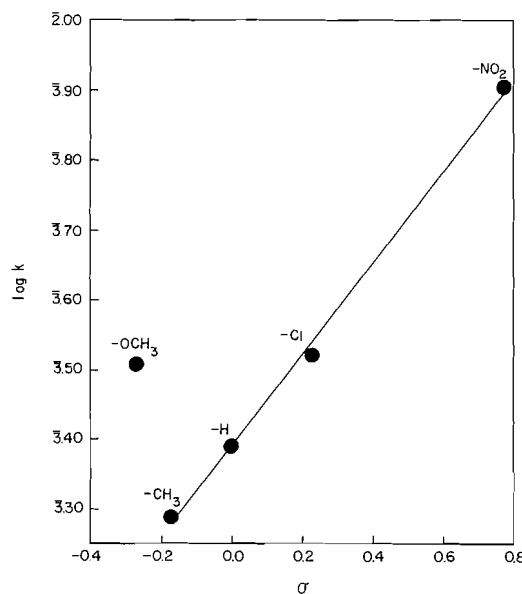


FIG. 1. Correlation of the rates of hydrolysis at 5.05 °C of 4-substituted benzyl trifluoroacetates with the Hammett σ parameter.

(15). This possibly indicates "mixed kinetics", i.e., the observed rate is the sum of $\text{B}_{\text{Ac}}2$ and $\text{S}_{\text{N}}1$ components. Indeed the results for the k.s.i.e. and the Hammett plot provide methods of calculating the relative contributions of the $\text{B}_{\text{Ac}}2$ and $\text{S}_{\text{N}}1$ processes to the observed rate for the 4-methoxybenzyl ester.

On the basis that the k.s.i.e. for $\text{S}_{\text{N}}1$ reactions is *ca.* 1.2 and for $\text{B}_{\text{Ac}}2$ reactions *ca.* 3.6 such a calculation can be made in the following way. Let k_{S} be the rate of the $\text{S}_{\text{N}}1$ reaction and k_{B} the rate of the $\text{B}_{\text{Ac}}2$ reaction; then if k_{o} is the observed rate we have,

$$[2] \quad k_{\text{o}} = k_{\text{S}} + k_{\text{B}}$$

and hence for 4-methoxybenzyl trifluoroacetate

$$[3] \quad \frac{k_{\text{o}}(\text{H}_2\text{O})}{k_{\text{o}}(\text{D}_2\text{O})} = \frac{k_{\text{S}}(\text{H}_2\text{O}) + k_{\text{B}}(\text{H}_2\text{O})}{k_{\text{S}}(\text{D}_2\text{O}) + k_{\text{B}}(\text{D}_2\text{O})} = 1.8$$

But

$$[4] \quad \frac{k_{\text{S}}(\text{H}_2\text{O})}{k_{\text{S}}(\text{D}_2\text{O})} = 1.2 \text{ (average value)}$$

and

$$[5] \quad \frac{k_{\text{B}}(\text{H}_2\text{O})}{k_{\text{B}}(\text{D}_2\text{O})} = 3.6 \text{ (average value)}$$

which, on combining eqs. 3, 4, and 5 gives

$$[6] \quad k_S(\text{H}_2\text{O}) = k_B(\text{H}_2\text{O})$$

i.e., the two paths are of equal importance for the 4-OCH₃ ester.

From the linear free energy relationship (Fig. 1) the extrapolated B_{Ac}2 rate for the 4-OCH₃ compound is $1.64 \times 10^{-3} \text{ s}^{-1}$ whereas the observed rate is $3.21 \times 10^{-3} \text{ s}^{-1}$ giving k_S equal to $1.57 \times 10^{-3} \text{ s}^{-1}$. Thus both methods of calculation lead to the same conclusion, *i.e.*, $k_S(\text{H}_2\text{O}) = k_B(\text{H}_2\text{O})$ for 4-methoxybenzyl trifluoroacetate.

Thanks are due to the Technical Services Department at Memorial University of Newfoundland for their continued care of the apparatus used in this work. We are grateful to Miss Marion Baggs and Mr. Earl Benson for measuring mass and n.m.r. spectra and to our colleagues for many useful discussions. We also express our thanks to the N.R.C.C. for their support of this work.

1. J. M. W. SCOTT and R. E. ROBERTSON. *Can. J. Chem.* **50**, 167 (1972).
2. C. A. BUNTON and T. HADWICK. *J. Chem. Soc.* 3248 (1958).

3. A. MOFFAT and H. HUNT. *J. Am. Chem. Soc.* **80**, 2985 (1958).
4. J. G. WINTER and J. M. W. SCOTT. *Can. J. Chem.* **46**, 2887 (1968).
5. S. LOBO. M.Sc. Thesis. Memorial University of Newfoundland, St. John's, Newfoundland. 1970.
6. E. A. MOELWYN-HUGHES, R. E. ROBERTSON, and S. SUGAMORI. *J. Am. Chem. Soc.* **87**, 2097 (1965).
7. P. M. LAUGHTON and R. E. ROBERTSON. *Can. J. Chem.* **34**, 1714 (1957).
8. L. HAKKA, A. QUEEN, and R. E. ROBERTSON. *J. Am. Chem. Soc.* **87**, 161 (1965).
9. M. SZWARC, C. H. LEIGH, and A. H. SEHON. *J. Chem. Phys.* **19**, 658 (1951).
10. H. A. SKINNER. *Modern aspects of thermochemistry*. The Royal Institute of Chemistry, Lectures, Monographs and Reports. No. 3, 1958. p. 24.
11. R. S. BERRY, C. W. REIMANN, and G. N. SPOKES. *J. Chem. Phys.* **37**, 2278 (1962).
12. A. G. HARRISON, P. KABARLE, and F. P. LOSSING. *J. Am. Chem. Soc.* **83**, 777 (1961).
13. E. J. BOURNE, C. E. M. TATLOW, and J. C. TATLOW. *J. Chem. Soc.* 1367 (1950).
14. A. MOFFAT and H. HUNT. *J. Am. Chem. Soc.* **79**, 54 (1957).
15. P. M. LAUGHTON and R. E. ROBERTSON. *In Solute-solvent interactions*. Edited by J. F. Coetzee and Calvin D. Ritchie. Marcel Dekker, New York. 1969. p. 400.