# Solvolysis of Cubyl Trifluoromethanesulphonate: Solvent and Remote Substituent Effects

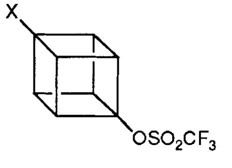
**Dennis N. Kevill,*[a] Malcolm J. D'Souza,[a] Robert M. Moriarty,*[b] Sudersan M. Tuladhar,[b] Raju Penmasta,[b] and Alok K. Awasthi[b]**

[a] *Department of Chemistry, Northern Illinois University, DeKalb, Illinois 60115, USA*
[b] *Department of Chemistry, University of Illinois at Chicago, Box 4348, Chicago, Illinois 60680, USA*

Cubyl trifluoromethanesulphonate solvolyses at a convenient rate and with a high sensitivity to solvent ionizing power; substituents on C-4 retard the solvolysis, modestly for methyl and enormously for methoxycarbonyl or halogen.

Due to the unfavourable geometric constraints involved in forming a carbocation at the corner of a cube, the solvolysis of cubyl derivatives *via* an $S_N1$ mechanism was long thought to be highly unlikely. The present manuscript provides a detailed quantitative study of the remarkably high reactivity of cubyl trifluoromethanesulphonate.[1] Both solvent effects (establishing an $S_N1$ reaction) and substituent effects (strongly favouring a powerful through bond and/or space effect, with little charge relayed to C-4 by skeletal adjustments) have been studied.

Specific rates of acid production in the solvolysis, without rearrangement,[1] of cubyl trifluoromethanesulphonate and a series of 4-substituted derivatives, (**1**) (X = H, Me, $CO_2Me$, Cl, Br, I), have been determined in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) (Tables 1 and 2). For (**1**) (X = H, Me), the effect of solvent variation was studied and for (**1**) (X = H) analysed in terms of the Grunwald–Winstein equation,[2] using $Y_{OTf}$ (Tf = trifluoromethylsulphonyl) values determined from the solvolysis of 2-admantyl trifluoromethanesulphonate[3,4] (Table 1).



(**1**)

**Table 1.** Specific rates of solvolysis ($k$/s$^{-1}$) of cubyl trifluoromethanesulphonate in solvents of widely varying ionizing power.

| Solvent[a] | $T$/°C | $10^6k$[b,c] | | log $(k/k_0)$[d] | $Y_{OTf}$[e] |
|---|---|---|---|---|---|
| HFIP | 0.0 | 589 | ± 19 | | |
| | 10.9 | 2 240 | ± 50 | | |
| | 25.0[f] | 10 760 | | 2.73 | 2.51[g] |
| TFE | 25.0 | 131 | ± 5 | 0.81 | 0.96[g] |
| 80% EtOH | 25.0 | 20.2 | ± 0.5 | 0.00 | 0.00 |
| 60T–40E[h] | 25.0 | 5.93 | ± 0.16 | −0.53 | −0.31[i] |
| 40T–60E[h] | 25.0 | 1.42 | ± 0.06 | −1.15 | −1.02[i] |
| MeOH | 25.0 | 1.01 | ± 0.03 | −1.30 | −0.79 |
| EtOH | 25.0[f] | 0.224 | | −1.96 | −1.66 |
| | 42.4 | 3.04 | ± 0.04 | | |
| | 62.6 | 44.1 | ± 0.4 | | |

[a] Substrate concentration *ca.* 0.0025 M; mixed solvents on volume-volume basis. [b] With associated standard deviation. [c] For 4-methylcubyl trifluoromethanesulphonate values of: $398(\pm10) \times 10^{-6}\,s^{-1}$ at 0.0 °C and $1670(\pm50) \times 10^{-6}\,s^{-1}$ at 10.9 °C in HFIP, $110(\pm2) \times 10^{-6}\,s^{-1}$ at 25.0 °C in TFE, and $10.3(\pm0.5) \times 10^{-6}\,s^{-1}$ at 25.0 °C in 80% EtOH. The extrapolated value for solvolysis in HFIP at 25.0 °C is $9050 \times 10^{-6}\,s^{-1}$. [d] Specific rate in 80% ethanol designated as $k_0$. [e] Unless otherwise stated, values are at 25.0 °C (ref. 4). [f] Extrapolated value, using the Arrhenius equation. [g] Determined for a solvent containing 3% (by weight) water. [h] TFE(T)–ethanol(E) mixtures. [i] Values determined at −20 °C (ref. 3).

The $m$ value of slightly greater than unity (1.12 ± 0.05 at 25.0 °C, $r$ 0.996, $n$ 7) suggests a transition state slightly later than that for the 2-adamantyl trifluoromethanesulphonate solvolysis. At 25.0 °C, the cubyl ester reacts 840 times slower in 80% ethanol than the 2-adamantyl ester,[4] and therefore[5] about $10^8$ times slower than the bridgehead substituted 1-adamantyl ester. Indeed, cubyl derivatives would be good substrates for establishing $Y$ scales for excellent leaving groups. Another factor which could lead to an $m$ value above unity would be an increase in ion-pair return relative to the standard compound.[6] Indeed, it has been suggested that the rate determining step in the solvolysis of adamantyl derivatives involves the solvent separation of the contact ion-pair,[7] and, further, it has been suggested that ion-pair return might be unusually important in the unimolecular solvolysis of trifluoromethanesulphonate esters.[4]

Correlation against $Y_{OTs}$ values[8,9] ($m$ 0.87 ± 0.07 at 25.0 °C, $r$ 0.984, $n$ 7) shows curvature with deviation of the 80% ethanol point and the success of the $Y_{OTf}$ correlation supports the use of separate ionizing power scales for each leaving group.[10]

Very small retardations are observed on introduction of a methyl group at C-4; at 25.0 °C, in both HFIP and 2,2,2-trifluoroethanol (TFE), retardation by a factor of 1.2 is observed and in 80% ethanol this ratio increases to 2.0. That care must be taken in interpreting such small ratios is

**Table 2.** Specific rates of solvolysis[a] ($k$) of 4-substituted cubyl trifluoromethanesulphonates in HPIP at various temperatures.

| 4-Substituent | $10^6\,k$/s$^{-1}$ | | | |
|---|---|---|---|---|
| | 62.6 °C | 75.0 °C | 83.7 °C | $\sigma_I$[b] |
| $CO_2Me$[c] | 4.15 | 12.5 | 31.3[d] | 0.34 |
| I[e,f] | 6.47 | 18.8 | 32.3 | 0.39 |
| Br | 1.10 | 2.97 | 6.15 | 0.45 |
| Cl | 0.53 | 1.29 | 2.61 | 0.47 |

[a] Sealed tube technique with *ca.* 0.0035 M substrate; unless otherwise indicated, standard deviations within 4% of reported values. [b] Charton's inductive constants (ref. 12). [c] Also, a value of $6.98 \pm (0.20) \times 10^{-7}\,s^{-1}$ at 50.2 °C. [d] Standard deviation of $\pm 2.0 \times 10^{-6}\,s^{-1}$. [e] Also, values of $2.44 \pm (0.06) \times 10^{-6}\,s^{-1}$ at 50.2 °C and $11.1\,(\pm0.5) \times 10^{-6}\,s^{-1}$ at 68.0 °C. [f] For the five temperatures studied, $\Delta H^\ddagger$ and $\Delta S^\ddagger$ values at 75.0 °C (with standard errors) of $72.2 \pm 2.3\,kJ\,mol^{-1}$ and $-129 \pm 7\,J\,K^{-1}\,mol^{-1}$ can be calculated, leading to an extrapolated specific rate at 10.9 °C of $5.2 \times 10^{-8}\,s^{-1}$.

emphasized by the calculation that for solvolyses in HFIP the ratio would fall to below unity above 48 °C. Similar small retardations of the solvolysis of bridgehead derivatives by remote methyl groups have been observed previously.[11]

Introduction of a series of four electron-withdrawing substituents at C-4 causes an enormous deceleration, leading to specific rates which are remarkably insensitive to the identity of the substituent (Table 2). Extrapolating the data in HFIP for (**1**) (X = I) to 10.9 °C shows that it reacts 43 000 times slower than (**1**) (X = H). The question arises as to whether 'non-classical' character leads to relay of the developing charge to the 4-position.[1b,c] The Charton inductive constants[12] (Table 2) would suggest similar retardations for the four electron-withdrawing substituents and a modest effect of a methyl group ($\sigma_I$ −0.05), as is observed. If appreciable positive charge was being relayed to C-4 then one would expect Brown's $\sigma_p{}^+$ constants[13] to apply, at least semi-quantitatively. On this basis, a relatively large acceleration for introduction of methyl, a more modest retardation for a halogen, and a severe retardation for a methoxycarbonyl substituent would be predicted, contrary to observation. We believe the evidence to be firmly in favour of an essentially classical incipient cubyl cation.

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