

Carbocation Lifetimes that are Independent of Carbocation Stability: the Reaction of α -Substituted 4-Methoxybenzyl Carbocations

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The α -methoxy-4-methoxybenzyl carbocation reacts with the solvent trifluoroethanol–water (50 : 50 v/v) with a rate constant $k_s = 3 \times 10^7 \text{ s}^{-1}$; k_s increases by less than twofold when the carbocation is destabilised by replacement of the strongly electron donating α -OMe substituent by the strongly electron withdrawing α -CF₃ substituent.

It is axiomatic in organic chemistry that intermediates which are highly unstable in a thermodynamic sense are highly reactive in a kinetic sense. We were therefore surprised to observe that the α -substituted 4-methoxybenzyl carbocations 4-MeOArCH(CH₃)⁺ and 4-MeOArCH(CF₃)⁺ (Ar = C₆H₄)

show the same reactivity towards the solvent trifluoroethanol–water (50 : 50 v/v) ($k_s = 5 \times 10^7 \text{ s}^{-1}$),¹ because the former carbocation is $\approx 10 \text{ kcal mol}^{-1}$ (1 cal = 4.184 J) more stable than the latter, relative to the neutral chloride adducts.² The low reactivity of 4-MeOArCH(CF₃)⁺ towards solvent could

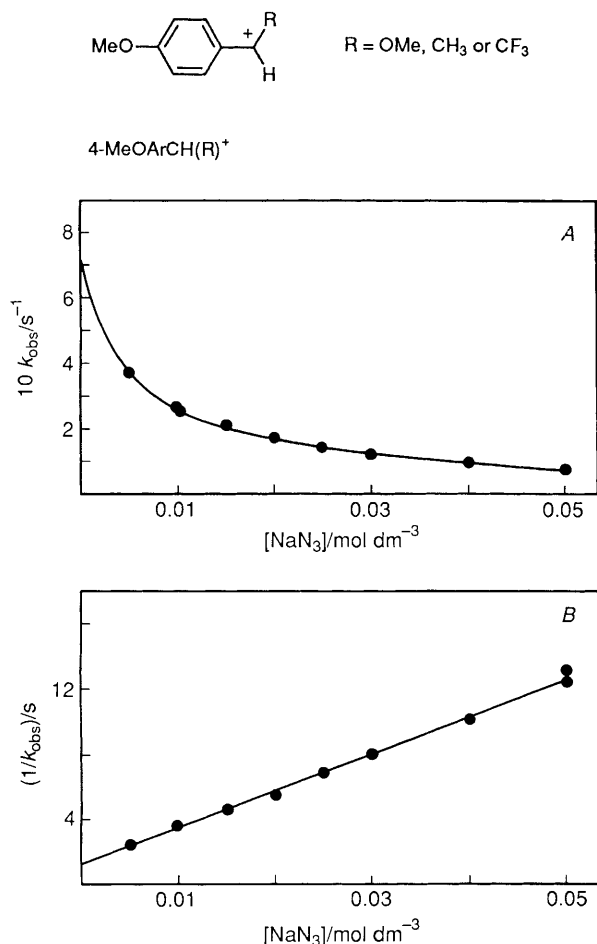


Fig. 1 (A) The dependence of k_{obs} on the concentration of added azide ion for the solvolysis of 4-MeOArCH(OMe)N₃ in trifluoroethanol–water (50 : 50 v/v) at 20 °C and ionic strength 0.50 mol dm⁻³ (NaClO₄). (B) Linear reciprocal plot of the data from (A) according to eqn. (1) ($r = 0.998$). The intercept (1.38 s) and slope (225 s dm³ mol⁻¹) give values of $k_{\text{solv}} = 0.72 \text{ s}^{-1}$ and $k_{\text{az}}/k_{\text{s}} = 163 \text{ dm}^3 \text{ mol}^{-1}$.

represent an unexpected inhibition of the addition of solvent by the β -fluorine substituents; or it could represent a general insensitivity of the chemical reactivity of 4-methoxybenzyl carbocations to α -substituents. In order to distinguish between these possibilities, we have now investigated the effect of the strongly electron donating α -OMe group on the reactivity of the 4-methoxybenzyl carbocation.

Fig. 1A shows that NaN₃ causes strong common ion inhibition of the solvolysis of 4-MeOArCH(OMe)N₃ in trifluoroethanol–water (50 : 50 v/v).^{3†} The values of k_{obs} show a good fit to eqn. 1 (Fig. 1B), which was derived for stepwise solvolysis (Scheme 1).[‡] The intercept of the line in Fig. 1B

[†] 4-MeOArCH(OMe)N₃ was prepared by the action of Me₃SiN₃ (75 mmol) on 4-methoxybenzaldehyde dimethyl acetal (neat, 75 mmol) under argon for 24 h at room temperature with SnCl₄ (150 μ l, added at -60 °C) as a catalyst.^{3,4} Purification, by passage down a short column of basic alumina and fractional distillation, gave the azide (46%) as an oil, contaminated with the starting acetal ($\approx 10\%$): b.p. 97 °C (1.5 mmHg); IR (liquid film) 2100 cm⁻¹ (N₃); ¹H NMR (CDCl₃, 200 MHz) δ 7.37 (2H, d, $J = 9 \text{ Hz}$, Ar), 6.92 (2H, d, $J = 9 \text{ Hz}$, Ar), 5.34 (1H, s, CH), 3.81 (3H, s, ArOMe) and 3.54 (3H, s, OMe); ¹³C NMR (CDCl₃, 50 MHz) δ 160.3, 129.2, 127.5, 114.0 (Ar), 93.7 (CH), 56.1 (ArOMe) and 55.2 (OMe); MS: found $M^+ m/z$ 193.0851, C₉H₁₁N₃O₂ requires 193.0852.

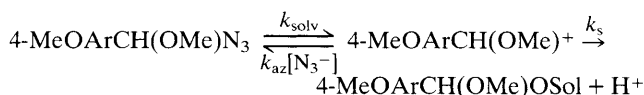
[‡] Rate constants for the solvolysis of 4-MeOArCH(OMe)N₃ ($\approx 0.8 \text{ mmol dm}^{-3}$) were determined spectrophotometrically by following the appearance of 4-methoxybenzaldehyde at 305 nm.

Table 1 Rate and equilibrium constants for the formation and reaction of 4-MeOArCH(R)⁺ in trifluoroethanol–water (50 : 50 v/v)^a

R	$k_{\text{solv}}/\text{s}^{-1}$	$K_{\text{eq}}^c = k_{\text{solv}}/k_{\text{az}}/\text{mol dm}^{-3}$	$k_{\text{s}}/\text{s}^{-1}$
OMe	0.72 ^d	1.4×10^{-10}	3×10^{17d}
CH ₃	1.1×10^{-7}	2.2×10^{-17}	5×10^{17e}
CF ₃	1×10^{-14}	2×10^{-24}	5×10^{17f}

^a At 25 °C and ionic strength 0.50 mol dm⁻³ (NaClO₄), unless otherwise noted. Rate and equilibrium constants are as defined in Scheme 1. ^b Rate constant for solvolysis of 4-MeOArCH(R)N₃, measured or estimated as described in the text. ^c Calculated using a value of $k_{\text{az}} = 5 \times 10^9 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ (see text). ^d At 20 °C. ^e Ref. 5. ^f Ref. 1.

gives $k_{\text{solv}} = 0.72 \text{ s}^{-1}$ and the ratio of the slope and the intercept gives $k_{\text{az}}/k_{\text{s}} = 163 \text{ dm}^3 \text{ mol}^{-1}$, for partitioning of the carbocation between capture by azide ion and solvent.



Scheme 1

$$1/k_{\text{obs}} = 1/k_{\text{solv}} + (k_{\text{az}}/k_{\text{s}}k_{\text{solv}})[\text{N}_3^-] \quad (1)$$

The much smaller selectivity of 4-MeOArCH(OMe)⁺ towards azide ion and solvent (160 dm³ mol⁻¹), compared with values of $\geq 10^6 \text{ dm}^3 \text{ mol}^{-1}$ that are observed for the reactions of more stable carbocations, is sufficient evidence to demonstrate that the reaction of 4-MeOArCH(OMe)⁺ with azide ion is diffusion limited.^{1-3,5-7} The diffusion-limited reaction serves as a 'clock' for the reaction of solvent; substitution of $k_{\text{az}} = 5 \times 10^9 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ into the experimental rate constant ratio gives $k_{\text{s}} = 3 \times 10^7 \text{ s}^{-1}$ for the capture of 4-MeOArCH(OMe)⁺ by trifluoroethanol–water (50 : 50 v/v).[§]

Rate and equilibrium constants for the formation and reaction of 4-MeOArCH(R)⁺ are given in Table 1. The rate constant for the solvolysis of 4-MeOArCH(CH₃)N₃ in trifluoroethanol–water (50 : 50 v/v) was determined from the initial velocity of the reaction, which was followed by HPLC.[¶] The rate constant for solvolysis of 4-MeOArCH(CF₃)N₃ was then estimated from the 10⁷-fold effect on k_{solv} of an α -CF₃ for α -CH₃ substitution in 4-MeOArCH(CH₃)Cl.²

Table 1 shows that the rate constant k_{s} for capture of the relatively stable oxocarbenium ion 4-MeOArCH(OMe)⁺ is virtually the same (less than twofold smaller) as that for capture of the highly destabilised carbocation 4-MeOArCH(CF₃)⁺, but that the two carbocations have the expected large difference in equilibrium stability (10¹⁴-fold), relative to the neutral azide adducts. This result stands in sharp contrast to a large body of data which show that the reactivity of carbocations increases with decreasing equilibrium stability.⁹

The data in Table 1 may be explained by considering the effect of the α -substituent on the resonance interactions

[§] Diffusion-limited rate constants of $(4-7) \times 10^9 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ for the reaction of azide ion with unstable carbocations in water or predominately aqueous solutions have been measured directly.⁸

[¶] 4-MeOArCH(CH₃)N₃ was prepared by reaction of 4-MeOArCH(CH₃)(3,5-dinitrobenzoate) (10 mmol dm⁻³) with NaN₃ (20 mmol dm⁻³) in trifluoroethanol–water (95 : 5) containing 10 mmol dm⁻³ NaOAc, at room temp. for 20 h (monitored by HPLC). The resulting solution was used directly for the kinetic studies by making a 100-fold dilution into the solvolysis mixture. HPLC analyses were performed with peak detection at 278 nm.⁵

between C- α and the 4-methoxybenzyl ring. Resonance electron delocalisation of the 4-methoxybenzyl ring at 4-MeOArCH(CF₃)⁺ is so great that amines show similar reactivities towards C- α and the C-4 ring position,¹⁰ and electron delocalisation from the ring will decrease as the substituent at C- α is made progressively more electron donating.¹¹ We propose that this decrease in resonance electron delocalisation from the aromatic ring is accompanied by a decrease in the intrinsic kinetic barrier which offsets the increase in the barrier to the reaction associated with the change in the thermodynamic driving force. The situation is similar to that for the protonation of carbanions, where the intrinsic kinetic barriers to the reaction increase with increasing carbanion stabilisation by resonance.¹² The effects of resonance on intrinsic barriers are a manifestation of the principle of nonperfect synchronization.¹²

In conclusion, for carbocation capture, the substituent effects on k_s can be understood only by considering the substituent effect on both the thermodynamic driving force and on the intrinsic kinetic barrier for the reaction. Groups such as α -phenyl substituents or electron-donating aromatic ring substituents cause the thermodynamic driving force to carbocation capture to decrease, and the intrinsic barrier to increase. Both of these changes cause a decrease in k_s , so that carbocation reactivity decreases with increasing thermodynamic stability. The substituent effects reported here appear unusual because the effect on k_s of the change in equilibrium stability of the carbocation is equal, but opposite, to the effect on k_s of the change in the intrinsic barrier to the reaction. The

overall effect is therefore such that k_s is virtually independent of the thermodynamic driving force for the reaction.

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References

- 1 J. P. Richard, *J. Am. Chem. Soc.*, 1989, **111**, 1455.
- 2 J. P. Richard, T. L. Amyes, L. Bei and V. S. Stubblefield, *J. Am. Chem. Soc.*, 1990, **112**, 9513.
- 3 T. L. Amyes and W. P. Jencks, *J. Am. Chem. Soc.*, 1989, **111**, 7888.
- 4 S. Kirchmeyer, A. Mertens and G. A. Olah, *Synthesis*, 1983, 500.
- 5 J. P. Richard and W. P. Jencks, *J. Am. Chem. Soc.*, 1984, **106**, 1361.
- 6 R. Ta-Shma and Z. Rappoport, *J. Am. Chem. Soc.*, 1983, **105**, 6082.
- 7 W. P. Jencks, *Acc. Chem. Res.*, 1980, **13**, 161.
- 8 R. A. McClelland, V. M. Kanagasabapathy and S. Steenken, *J. Am. Chem. Soc.*, 1988, **110**, 6913.
- 9 R. A. Diffenbach, K. Sano and R. W. Taft, *J. Am. Chem. Soc.*, 1966, **88**, 4747; C. D. Ritchie, *Can. J. Chem.*, 1986, **64**, 2239; R. A. McClelland, V. M. Kanagasabapathy, N. S. Banait and S. Steenken, *J. Am. Chem. Soc.*, 1989, **111**, 3966.
- 10 J. P. Richard, *J. Am. Chem. Soc.*, 1989, **111**, 6735.
- 11 S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, *J. Am. Chem. Soc.*, 1952, **74**, 1113-1120; P. G. Gassman and A. F. Fentiman, *J. Am. Chem. Soc.*, 1969, **91**, 1545; G. M. Loudon and C. Berke, *J. Am. Chem. Soc.*, 1974, **96**, 4508.
- 12 C. F. Bernasconi, *Tetrahedron*, 1985, **41**, 3219.