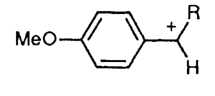
Carbocation Lifetimes that are Independent of Carbocation Stability: the Reaction of α-Substituted 4-Methoxybenzyl Carbocations

Tina L. Amyes and John P. Richard
University of Kentucky, Department of Chemistry, Lexington, Kentucky 40506-0055, USA

The α-methoxy-4-methoxybenzyl carbocation reacts with the solvent trifluoroethanol–water (50 : 50 v/v) with a rate constant $k_s = 3 \times 10^7\ s^{-1}$; 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-CF_3 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(CH_3)$^+$ and 4-MeOArCH(CF_3)$^+$ (Ar = C_6H_4) show the same reactivity towards the solvent trifluoroethanol–water (50:50 v/v) ($k_s = 5 \times 10^7\ s^{-1}$),[1] because the former carbocation is ≈10 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(CF_3)$^+$ towards solvent could



R = OMe, CH_3 or CF_3

4-MeOArCH(R)$^+$

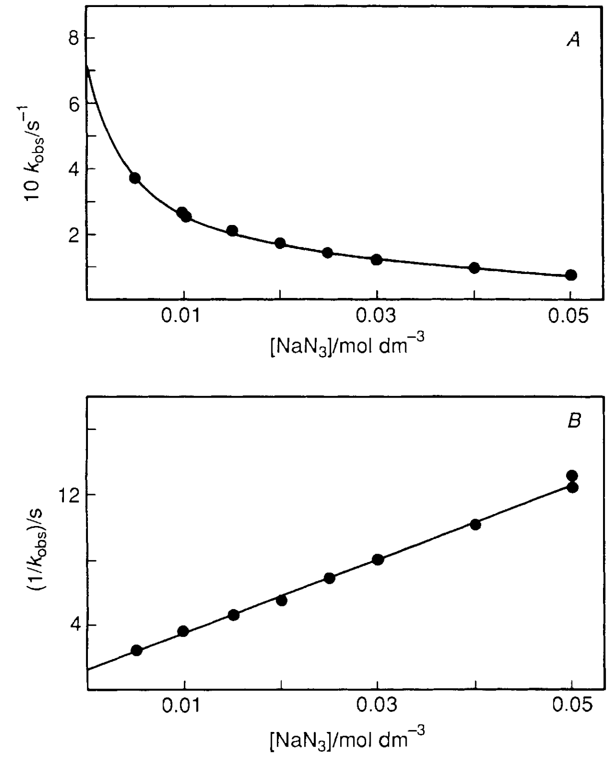


Fig. 1 (*A*) The dependence of k_{obs} on the concentration of added azide ion for the solvolysis of 4-MeOArCH(OMe)N_3 in trifluoroethanol–water (50 : 50 v/v) at 20 °C and ionic strength 0.50 mol dm^{-3} ($NaClO_4$). (*B*) Linear reciprocal plot of the data from (*A*) according to eqn. (1) (r = 0.998). The intercept (1.38 s) and slope (225 s dm^3 mol^{-1}) give values of k_{solv} = 0.72 s^{-1} and k_{az}/k_s = 163 dm^3 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. 1*A* shows that NaN_3 causes strong common ion inhibition of the solvolysis of 4-MeOArCH(OMe)N_3 in trifluoroethanol–water (50 : 50 v/v).[3]† The values of k_{obs} show a good fit to eqn. 1 (Fig. 1*B*), which was derived for stepwise solvolysis (Scheme 1).‡ The intercept of the line in Fig. 1*B*

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_{solv}[b]/s^{-1}	K_{eq}[c] = k_{solv}/k_{az}/ mol dm^{-3}	k_s/s^{-1}
OMe	0.72[d]	1.4×10^{-10}	3×10^7[d]
CH_3	1.1×10^{-7}	2.2×10^{-17}	5×10^7[e]
CF_3	1×10^{-14}	2×10^{-24}	5×10^7[f]

[a] At 25 °C and ionic strength 0.50 mol dm^{-3} ($NaClO_4$), unless otherwise noted. Rate and equilibrium constants are as defined in Scheme 1. [b] Rate constant for solvolysis of 4-MeOArCH(R)N_3, measured or estimated as described in the text. [c] Calculated using a value of k_{az} = 5 × 10^9 dm^3 mol^{-1} s^{-1} (see text). [d] At 20 °C. [e] Ref. 5. [f] Ref. 1.

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

$$\text{4-MeOArCH(OMe)N}_3 \underset{k_{az}[\text{N}_3^-]}{\overset{k_{solv}}{\rightleftharpoons}} \text{4-MeOArCH(OMe)}^+ \xrightarrow{k_s} \text{4-MeOArCH(OMe)OSol} + \text{H}^+$$

Scheme 1

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

The much smaller selectivity of 4-MeOArCH(OMe)$^+$ towards azide ion and solvent (160 dm^3 mol^{-1}), compared with values of ≥ 10^6 dm^3 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_{az} = 5 × 10^9 dm^3 mol^{-1} s^{-1} into the experimental rate constant ratio gives k_s = 3 × 10^7 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(CH_3)N_3 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(CF_3)N_3 was then estimated from the 10^7-fold effect on k_{solv} of an α-CF_3 for α-CH_3 substitution in 4-MeOArCH(CH_3)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(CF_3)$^+$, but that the two carbocations have the expected large difference in equilibrium stability (10^{14}-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

---

† 4-MeOArCH(OMe)N_3 was prepared by the action of Me_3SiN_3 (75 mmol) on 4-methoxybenzaldehyde dimethyl acetal (neat, 75 mmol) under argon for 24 h at room temperature with $SnCl_4$ (150 μl, 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 (≈10%): b.p. 97 °C (1.5 mmHg); IR (liquid film) 2100 cm^{-1} (N_3); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.37 (2H, d, J = 9 Hz, Ar), 6.92 (2H, d, J = 9 Hz, Ar), 5.34 (1H, s, CH), 3.81 (3H, s, ArOMe) and 3.54 (3H, s, OMe); ^{13}C NMR ($CDCl_3$, 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, $C_9H_{11}N_3O_2$ requires 193.0852.

‡ Rate constants for the solvolysis of 4-MeOArCH(OMe)N_3 (≈0.8 mmol dm^{-3}) were determined spectrophotometrically by following the appearance of 4-methoxybenzaldehyde at 305 nm.

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

¶ 4-MeOArCH(CH_3)N_3 was prepared by reaction of 4-MeOArCH(CH_3)(3,5-dinitrobenzoate) (10 mmol dm^{-3}) with NaN_3 (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$(CF_3)^+$ 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.

This work was supported by a grant (GM 39754) from the National Institutes of Health.

Received, 28th August 1990; Com. 0/03863F

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. Louden and C. Berke, *J. Am. Chem. Soc.*, 1974, **96**, 4508.

12 C. F. Bernasconi, *Tetrahedron*, 1985, **41**, 3219.