GENERATION AND DETERMINATION OF THE LIFETIME OF AN α -CARBONYL SUBSTITUTED CARBOCATION¹

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Summary: The α -carboxyethyl-4-methoxybenzyl carbocation reacts with a solvent of 50:50 (v:v) trifluoroethanol/water with a rate constant $k_s = 1.4 \times 10^7 \text{ s}^{-1}$, which is 14-fold *slower* than the capture of the unsubstituted 4-methoxybenzyl carbocation.

There is indirect evidence for the formation of α -carbonyl substituted carbocations as intermediates of solvolysis reactions;² but there have been no measurements of the lifetimes of these unstable species. We report the first determination of the lifetime of an α -carbonyl substituted carbocation, **1**. The lifetime of **1** in 50:50 (v:v) trifluoroethanol/water is 14-fold *longer* than that for the unsubstituted carbocation 4-MeOArCH₂⁺.³ This provides another example of a strongly electron-withdrawing α -substituent that *stabilizes* the 4-methoxybenzyl carbocation toward capture by trifluoroethanol/water.⁴



The solvolysis of the pentafluorobenzoate ester 2 was followed by HPLC.^{5,6} The observed pseudofirst-order rate constant for solvolysis of 2 in 50:50 (v:v) trifluoroethanol/water containing 0.50 M NaClO₄ at 25 °C is $k_{solv} = 5.5 \times 10^{-7} \text{ s}^{-1.8}$ There is no change (±10%) in k_{obsd} as the concentration of azide ion is increased from zero to 0.01 M at constant ionic strength of 0.50 (NaClO₄). The yield of the azide adduct to 1 from these reactions, determined by HPLC analysis, increases to 75% as [NaN₃] is increased to 0.01 M.⁶ These results show that 2 reacts with azide ion by a stepwise $S_N 1$ ($D_N + A_N$)⁹ mechanism through the liberated α -CO₂Et-substituted carbocation intermediate 1 (Scheme). The partitioning ratio for the reaction of 1 with azide ion and solvent, determined from the ratio of the yields of the azide and solvent adducts, is $k_{az}/k_s \approx 10^6 \cdot 10^8 \text{ M}^{-1}$ for stable carbocations¹¹ is good evidence that the reaction of 1 with azide ion is diffusion limited.^{3,4,7} The rate constant ratio $k_{az}/k_s = 350 \text{ M}^{-1}$ can be combined with an estimated value of



 $k_{az} = 5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ for the diffusion-limited reaction of azide ion,⁷ to obtain a rate constant $k_s = 1.4 \times 10^7 \text{ s}^{-1}$ for the reaction of 1 with solvent.¹² The rate constant for the breakdown of the carbocationpentafluorobenzoate ion pair intermediate to free ions ($k_{-d} \approx 1.6 \times 10^{10} \text{ s}^{-1}$),¹⁴ is 1000-fold larger than k_s for the capture of 1 by solvent.¹⁵ Therefore, this ion pair will separate to give free ions before significant reaction with solvent can occur, and the solvolysis products will be derived from the free carbocation, rather than an ion pair intermediate. The Table compares the effects of the electron-donating α -CH₃ and the

Carbocation	$k_{\rm solv} (\rm s^{-1})^{b}$	k _s (s ⁻¹) ^c
4-MeOArCH(CH ₃) ⁺	8 x 10 ^{-3 d}	5 x 10 ⁷ e
4-MeOArCH ₂ ^{+ f}	2.3 x 10 ⁻⁵	2 x 10 ⁸
4-MeOArCH(CO ₂ Et) ⁺ ^g	5.5 x 10 ⁻⁷	1.4×10^7

Table. Rate Constants k_{solv} for Formation of α -Substituted-4-Methoxybenzyl Carbocations in Solvolysis of Pentafluorobenzoate Esters and k_s for Carbocation Capture by 50:50 (v:v) Trifluoroethanol/Water (Scheme)^a

^a At 25 °C and I = 0.50 (NaClO₄). ^b Rate constant for formation of the carbocation in the S_N1 reaction of the pentafluorobenzoate ester (Scheme). ^c Rate constant for carbocation capture by solvent (Scheme). ^d Calculated from $k_{solv} = 4.6 \times 10^{-4} s^{-1}$ for solvolysis of 1-(4-methoxyphenyl)ethyl 3,5-dinitrobenzoate, ¹⁶ and the ratio of the values of k_{solv} of 17 for 4-methoxybenzyl pentafluorobenzoate and 3,5-dinitrobenzoate. ³ ° Ref. 7. ^f Ref. 3. ^g This work. See ref. 8.

electron-withdrawing α -CO₂Et substituents on the rate constant k_{solv} for formation of the 4-methoxybenzyl carbocation from the corresponding pentafluorobenzoate ester, and on the rate constant k_s for capture of the carbocation by 50:50 (v:v) trifluoroethanol/water. The α -CH₃ substituent causes the expected increase (350-fold) and the α -CO₂Et substituent causes the expected decrease (42-fold) in k_{solv} . Surprisingly, *both* substituents cause the reactivity of the carbocation toward solvent to *decrease*; the effect of the α -CO₂Et

substituent (14-fold) is larger than that of the α -CH₃ substituent (4-fold).

Other strongly electron-donating (α -OMe; $k_s = 3 \times 10^7 \text{ s}^{-1}$ for 4-MeOArCH(OMe)⁺)¹⁷ and strongly electron-withdrawing (α, α -di-CF₃; $k_s = 5 \times 10^6 \text{ s}^{-1}$ for 4-MeOArC(CF₃)₂⁺)^{4c} α -substituents also cause only small changes in k_s for the reaction of 4-MeOArCH₂⁺. For all of these examples, the expected change in the reactivity of the carbocation toward solvent due to the inductive and/or resonance substituent effect is masked by additional substituent effect(s) which cause a *decrease* in k_s . We have proposed that this kinetic stabilization arises, in part, from the tendency of strongly electron-withdrawing α -substituents to increase resonance electron donation from the 4-methoxybenzyl ring to the α -carbon.⁴ Additional resonance stabilization of 1 may also be provided by the π -electrons of the carbonyl group (see 3).^{2,18}



3

For the strongly electron-withdrawing α -carbonyl substituent the added resonance stabilization only partly offsets the destabilizing inductive substituent effect, and the equilibrium constant for the formation of 1 from the corresponding neutral azide adduct is ~40-fold smaller than that for the formation of the 4-methoxybenzyl carbocation from 4-methoxybenzyl azide.¹⁹ However, the resonance and inductive substituent effects on k_s may cancel if capture of the carbocation by solvent proceeds through an unbalanced transition state in which loss of the (relatively small) resonance interactions of the 4-methoxybenzyl ring with C- α has progressed significantly further than has the change in the (relatively large) inductive dipole interactions between the α -substituent and the cationic center.⁴ There is evidence for imbalances in the change in resonance and inductive interactions at the transition states for the capture of several carbocations by solvent.^{7,20}

The principal (or rule) of nonperfect synchronization provides an alternative formulation of the above explanation for the α -substituent effects. This rule states that a reactant stabilizing factor (e.g., resonance) will increase the intrinsic barrier for a reaction (e.g., capture of a carbocation by solvent), if the stabilizing factor is largely lost on moving from the reactant to the transition state.²¹ Thus, the addition of the α -CO₂Et substituent to 4-MeOArCH₂⁺ increases resonance electron donation which leads to an increased intrinsic barrier for the addition of solvent to 1. The overall observed effect of the α -carbonyl substituent suggests that the increase in this intrinsic barrier results in a decrease in k_s that arises from the increase in the thermodynamic driving force for the reaction.

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- (6) Separation of 2 and of the reaction products by HPLC, with UV detection at 273 nm, and determination of the product yields was carried out as described previously.^{3,4,7}
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- (12) Diffusion-limited rate constants of $(4 7) \ge 10^9 \text{ M}^{-1} \text{ s}^{-1}$ for reaction of substituted trityl and benzhydryl carbocations with N₃⁻ in largely aqueous solvents have been determined directly. The results show that the values of k_s calculated from the product rate constant ratio k_{az}/k_s and $k_{az} = 5 \ge 10^9 \text{ M}^{-1} \text{ s}^{-1}$ are accurate to within a factor of 2.¹³
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- (19) Calculated from $K_{eq} = k_{solv}/k_{az}$ (M) for formation of 4-methoxybenzyl carbocations from the neutral azide adducts. Values of k_{solv} for 4-MeOArCH₂N₃ and 4-MeOArCH(CO₂Et)N₃ were estimated from data in the Table and the estimated 4 x 10³-fold decrease in k_{solv} on changing from a pentafluorobenzoate to an azide ion leaving group.¹⁶ The rate constant $k_{az} = 5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ was used for the diffusion-limited capture of the two carbocations by azide ion.¹²
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