

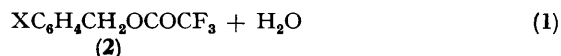
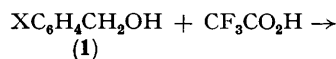
Kinetic Study of the Esterification of Arylmethanols in Trifluoroacetic Acid: Mechanistic Change Consequent upon Aryl Substituent Effects

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Summary Aryl substituent effects upon the rate constants for the esterification of a series of arylmethanols in neat trifluoroacetic acid are in accordance with a reverse $A_{AC}2$ mechanism for those substrates bearing an electron-withdrawing substituent ($\rho = -0.79$), whereas a reverse $A_{AL}1$ mechanism is indicated for those bearing a methyl substituent.

ALTHOUGH the kinetics and mechanisms of acid-promoted ester hydrolysis have been thoroughly investigated, there have been fewer studies of the reverse reaction.¹ We have carried out a kinetic study of such a process, *viz.* the esterification of a series of arylmethanols (**1**) in trifluoroacetic acid [equation (1)].



The rates of the reactions (**1**) \rightarrow (**2**) were conveniently followed using ¹H n.m.r. spectroscopy since, with neat trifluoroacetic acid as solvent, the singlet methylene proton resonances in the spectra of the alcohols and the ester products were well separated from each other ($\Delta\delta$ ca. 0.55 p.p.m.) and from other proton signals. Since a large molar excess of acid over alcohol was used, the observed reactions cleanly followed to completion a pseudo-first-order kinetic expression. Rate constants (Table) were calculated both from the rate of growth of the ester CH₂ singlet and from the rate of disappearance of the corresponding alcohol singlet; good internal agreement was found in all cases and duplicate determinations gave reproducible results.

For the reactions of those alcohols (**1b—g**) bearing an electron-withdrawing substituent in the benzene ring, a Hammett plot of $\log(k_X/k_H)$ values against the appropriate σ_X substituent constants gave a good linear correlation (correlation coefficient = 0.996) with a derived reaction constant $\rho = -0.79$. However, the rates of esterification of the tolylmethanols (**1h, i**) under identical conditions

TABLE. Rate constants for trifluoroacetylation of $\text{XC}_6\text{H}_4\text{-CH}_2\text{OH}$ (**1**).^a

Substrate	X	T/°C	$10^4 k_X/s^{-1b}$	k_X/k_H^c
(1a)	H	-12	0.421	
		0	0.975	
		5	1.39	
		35	7.76 ^d	
(1b)	<i>m</i> -Cl	35	4.24	0.55
(1c)	<i>p</i> -Cl	35	5.00	0.64
(1d)	<i>m</i> -NO ₂	35	2.02	0.26
(1e)	<i>p</i> -NO ₂	35	1.86	0.24
(1f)	<i>m</i> -OH	35	5.73	0.74
(1g)	<i>m</i> -OMe	35	6.17	0.79
(1h)	<i>m</i> -Me	5	3.32	2.39
(1i)	<i>p</i> -Me	-12	16.4	39.0
		0	40.0	41.0

^a In neat $\text{CF}_3\text{CO}_2\text{H}$ in large molar excess; values are considered accurate to $\pm 2\%$. ^b Average values from at least two independent experiments. ^c Rate constants relative to the value for **(1a)** = 1.0 at the same temperature. ^d Value obtained by extrapolation of an Arrhenius plot for data for lower temperatures.

were much faster than those expected from the ρ value and the σ constants for the *m*- and *p*-methyl substituents, clearly indicating a change in mechanism. Unfortunately, we were unable to study the rates of trifluoroacetylation of other benzylic alcohols bearing alternative electron-donating substituents. The (methoxyphenyl)methanols (**1**; X = *o*- and *p*-OMe), for example, do not undergo esterification in trifluoroacetic acid but instead afford methyl trifluoroacetate and (presumably) products derived from liberated quinone methides, which have not yet been investigated.

Within the mechanistic classification introduced by Ingold^{1a} for acid-catalysed ester hydrolysis, four alternative mechanisms may be considered for acid-promoted esterification, *viz.* reverse A_{AC1} , A_{AL1} , A_{AC2} , and A_{AL2} . The kinetic data for trifluoroacetylation of the less reactive alcohols (**1b–g**) are incompatible with the first two of these, which would involve rate-limiting formation of the cations CF_3CO^+ and $\text{XC}_6\text{H}_4\text{CH}_2^+$, respectively. However, the low negative ρ value for these esterifications is consistent with either of the remaining mechanisms whose rate-determining steps involve alternatively nucleophilic addition of the alcohol to the self-protonated acid (reverse A_{AC2})

† Correlation of $\log(k_X/k_H)$ values for the alcohols (**1h, i**) with methyl σ^+ substituent constants leads to a ρ value of -5.1 , strongly suggestive of a mechanism involving a transition state of pronounced carbocation character (see: J. E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions', Wiley, New York, 1963, pp. 208–209).

¹ (a) C. K. Ingold, 'Structure and Mechanism in Organic Chemistry', Cornell University Press, Ithaca, New York, 1963, ch. XIV; (b) J. March, 'Advanced Organic Chemistry: Reactions, Mechanisms, and Structure', 2nd edn., McGraw-Hill Kogakusha, Tokyo, 1977, ch. 10; (c) *ibid.*, p. 315; (d) A. J. Kirby in 'Comprehensive Chemical Kinetics', eds. C. H. Bamford and C. F. H. Tipper, Elsevier, New York, 1972, vol. 10, ch. 2; (e) *ibid.*, pp. 139–140.

² B. Johnston, A. C. Knipe, and W. E. Watts, unpublished work.

³ T. S. Abram and W. E. Watts, *J.C.S. Perkin I*, 1975, 113.

⁴ See: J. J. Dannenberg, *Angew. Chem. Internat. Edn.*, 1975, **14**, 641.

or nucleophilic displacement by acid of water from the protonated alcohol (reverse A_{AL2}). Of these possibilities, we favour the former. Firstly, no example of an A_{AL2} mechanism of ester hydrolysis has yet been noted.¹ Secondly, we have also found² that the rate constants for esterification of methyl, ethyl, benzyl, and neopentyl alcohols in neat trifluoroacetic acid are remarkably similar in magnitude, a finding inconsistent with an S_N2 -type reaction for which it is well recognised^{1c} that an increase in steric encumbrance of the reaction site produces a large rate retardation.

On the other hand, the exceptionally enhanced reactivity of the tolylmethanols (**1h, i**) is more in accordance with a reverse A_{AL1} process, with an appreciable build-up of positive charge at the benzylic carbon atom in the transition state for rate-determining formation of the intermediate carbocation ($\text{MeC}_6\text{H}_4\text{CH}_2^+$).[†] Such an S_N1 -type mechanism would obviously be disfavoured for those substrates (**1b–g**) incorporating an electron-withdrawing ring substituent. Furthermore, we have found that dissolution of benzhydrol in trifluoroacetic acid results in very fast formation of the ester ($\text{Ph}_2\text{CHOCOCF}_3$), presumably *via* the benzhydryl cation; similar treatment of triphenylmethanol affords the corresponding cation (Ph_3C^+) as the sole detectable (¹H n.m.r. spectroscopy) product.³ The capacity of trifluoroacetic acid to sustain carbocations in solution is well documented.⁴

Further mechanistic information was gained from variable-temperature studies of the rates of trifluoroacetylation of the alcohols (**1a, b**). Calculation of thermodynamic quantities (for 298 K) from Arrhenius plots of $\log(k_{\text{obs}})$ against $1/T$ gave values of ΔH^\ddagger and $-T\Delta S^\ddagger$ of 39.0 and 53.1 kJ mol⁻¹, respectively, for (**1a**), and 48.2 and 45.8 kJ mol⁻¹, respectively, for (**1b**). These very large entropy contributions [$\Delta S^\ddagger = -178$ and -154 J deg⁻¹ mol⁻¹ for (**1a**) and (**1b**), respectively] to the free energies of activation are typical^{1e} of those for esterification of carboxylic acids by the A_{AC2} mechanism, which features a highly structured transition state.

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