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Acyl Trifluoroacetates. Part II.¹ The Influence of an Alkaline Aqueous Phase on the Reaction of Phenols with Acetyl Trifluoroacetate in Carbon Tetrachloride

By T. G. Bonner and E. G. Gabb

The change in product from phenyl acetate to phenyl trifluoroacetate which occurs when solutions of a phenol and acetyl trifluoroacetate in carbon tetrachloride are brought into contact with saturated aqueous potassium hydrogen carbonate solution appears to be dependent upon the conversion of the phenol into its anion. It can be interpreted as a shift in the relative importance of bond formation and bond fission in the acylation reaction.

PHENOLS react with acetyl trifluoroacetate in carbon tetrachloride to form phenyl acetates almost exclusively.^{1,2} The formation of the trifluoroacetate, however, can supersede completely the acetate reaction if the solution of the reactants is shaken with aqueous saturated potassium hydrogen carbonate.¹ The reaction in the two-phase system is extremely fast and, with

¹ Part I, T. G. Bonner and E. G. Gabb, J. Chem. Soc., 1963, 3291.

acetyl trifluoroacetate in large excess (10:1) over *p*-chlorophenol, immediate treatment with the aqueous solution gives over 90% yield of *p*-chlorophenyl trifluoroacetate. Lower concentrations of the anhydride reduce the yield of trifluoroacetate but without producing any detectable amount of acetate ester. A detailed study has been made of the effect of the pH of the aqueous

² E. J. Bourne, M. Stacey, J. C. Tatlow, and R. Worrall, J. Chem. Soc., 1958, 3268.

phase on the acylation reaction in the two-phase system.

The Influence of the Aqueous Phase on Ester Formation. —The importance of the composition of the aqueous phase on the reaction is shown in Table 1 for acetyl

TABLE 1

Reaction of p-chlorophenol and acetyl trifluoroacetate

		()				
		. ,	Ester product			
⊅-Chloro- phenol (10⁴м)	АТF (10 ⁴ м)	Aqueous phase	Trifluoro- acetate (10 ⁴ M)	Acetate (10 ⁴ м)		
97	860	KHCO ₃ (satd.)	90	0		
93	84		55	0		
87	210	Water	0	0		
,,	,,	$\rm KHCO_3(0.1N)$	5	0		
,,	,,	$K_2CO_3(0.1N)$	79	0		
,,	,,	NaOH(0·1n)	17	0		
,,	,,	$NaOOCCH_3(0.1N)$	0	0		
,,	,,	NaOOCCF ₃ (0·1N)	0	0		

trifluoroacetate and p-chlorophenol. The most effective basic aqueous medium is saturated potassium hydrogen carbonate solution. Similar results were obtained for phenol itself, and subsequent investigations using different aqueous buffered solutions were carried out on this substrate. The results reported in Table 2 show that

TABLE 2

Reaction of phenol and acetyl trifluoroacetate (0.020m)

Phenc	DI (10-M)				Ester	product
	in				tri-	~
in	aqueous	Aqueous	pI	Ŧ	fluoro-	
CCI4	phase	phase			acetate	acetate
(2 ml.)	(5 ml.)	(buffer)	initial	final	(10 ₄ м)	(104м)
94		None	5.7	$2 \cdot 2$	0	0
	42	,,	,,	,,	0	0
94		Borax	6.15	5.05	0	0
	42				0	0
94			7.05	6.5	0	0
	42					
94			8.10	7.40	15	10
	42		,,	.,	15	9
94			9.10	8.85	69	16
	42		,,	,,	69	17
94			10.10	9.80	72	19
	42			.,	74	20
94		Ammonia	9.10	8.75	15	0
	42		,,		11	0
94		Na _s CO _s /	9.10	8.00	19	10
		NaHCO.				
	42		.,		16	13
94		KHCO,	8.70	8.70	50	0
		(satd.)				
	42	,	,,	.,	41	0

the product composition is not greatly influenced by the initial environment of the phenol. Different buffer solutions of the same pH (pH 9) do not, however, give the same yield of esters, and the borax and carbonate-hydrogen carbonate buffer solutions produce some acetate ester while the ammonia buffer solution and saturated potassium hydrogen carbonate do not. The last has a concentration of ca. 2.5M, and the effect of diluting it by stages to 0.05M is shown in Table 3.

The yields of esters obtained in the presence of saturated potassium hydrogen carbonate solution are much less when the carbon tetrachloride solution (0.01M in

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phenol and 0.1M in anhydride) contains either trifluoroacetic anhydride (30% yield of ester) or acetic anhydride (50% yield of ester) in place of acetyl trifluoroacetate (90% yield of phenyl trifluoroacetate).

The Distribution of Reactants in the Two-phase System. —From infrared (i.r.) absorption spectra examination, it appears that when acetyl trifluoroacetate $(0 \cdot 1M)$ in carbon tetrachloride is shaken with saturated aqueous potassium hydrogen carbonate solution, it is almost completely hydrolysed in *ca.* 15 secs. Reaction may be even more rapid than indicated, since it has been reported that acetyl trifluoroacetate is hydrolysed almost immediately when exposed to moist air.³ No appreciable accumulation of acetic and trifluoroacetic acids occurs in the organic phase. Phenols in general are rapidly

TABLE 3

The effect of different aqueous KHCO_3 solutions on the reaction of phenol (0.0094m) and acetyl trifluoroacetate (0.020m)

			Ester product		
Volumes of water added to 1 vol. satd. KHCO ₃	pH of aqueous KHCO3 phase initial final		trifluoro- acetate (10 ⁴ м)	acetate (10 ⁴ M)	
0	8.70	8.70	50	0	
1	,,	,,	44	0	
5	.,	,,	37	Trace	
10	,,	8.55	21	10	
25	,,	8.15	Trace	Trace	
50		7.60	0	0	

distributed (ca. 10 sec.) between the carbon tetrachloride and the aqueous phase on vigorous shaking. No esters are produced from phenol when acetyl trifluoroacetate is replaced with the acids which are its hydrolytic products, nor when the system is saturated with carbon dioxide.

Any esters formed arise by reaction with acetyl trifluoroacetate either in the carbon tetrachloride or at its interface with the basic aqueous phase. A phenol must be partially converted to the phenate ion in the aqueous medium, the extent of ionisation depending on the pK_a value of the phenol and the pH of the aqueous solution. Since saturated aqueous potassium hydrogen carbonate has a pH of 8.7, phenol would be ca. 5% converted to phenate ion. The failure to obtain any appreciable trifluoroacetylation in the presence of water alone is evidently due to the development of acidity in the aqueous solution, and suggests that the production of phenate ion is necessary for reaction. The pH falls from 5.7 to 3.2 when 10% of the anhydride has hydrolysed and to $2 \cdot 2$ when hydrolysis is complete (in *ca*. 15 sec.). The degree of ionisation of a given phenol in saturated aqueous potassium hydrogen carbonate is therefore about 3×10^5 times greater than in water which has hydrolysed 10% of the anhydride.

Since the un-ionised phenol gives only the acetate ester with acetyl trifluoroacetate in carbon tetrachloride, the production of the trifluoroacetate ester in contact

³ A. F. Ferris and W. D. Emmons, J. Amer. Chem. Soc., 1953, 75, 232.

with saturated aqueous potassium hydrogen carbonate suggests that the reaction is with phenoxide ions, and that in the short time available before the acetyl trifluoroacetate is wholly hydrolysed it occurs either in the organic phase or more probably at its interface with the aqueous phase. The conditions for trifluoroacetate ester formation are clearly critical. The aqueous solutions must be well buffered to maintain alkalinity, but the pH must not be so high that alkaline hydrolysis of the ester could occur.

In order to confirm that the provision of phenoxide ions is a pre-requisite for trifluoroacetate ester formation, tetrabutylammonium phenate was prepared. This salt could only be obtained as its diphenolate, *i.e.*, $\operatorname{Bu_4NOC_6H_5} \cdot 2C_6H_5OH.$ It was soluble in carbon tetrachloride. The i.r. absorption spectrum did not show the characteristic phenolic OH stretching frequencies observed with phenol itself at a similar concentration, but only strongly hydrogen-bonded OH absorption, indicating that association of the phenate ion and phenol molecules is unusually marked.⁴

The product of reaction of the salt (0.003M) with acetyl trifluoroacetate (0.04m) in carbon tetrachloride (at 25°), formed in less than one minute of mixing the reactant solutions, is phenyl trifluoroacetate in 85%yield based on the total phenol present, *i.e.*, phenoxide and phenol. (It appeared that the yield of this product increased slowly over 24 hours to a maximum of 95%). No phenyl acetate was detected. Since phenol under these conditions slowly forms only phenyl acetate, the trifluoroacetate reaction appears to require the more strongly nucleophilic form of phenol which is provided by both the phenate ion and by strongly hydrogenbonded phenol.

The Mechanisms of Acetylation and Trifluoroacetylation of Phenol with Acetyl Trifluoroacetate.-The two most important factors which determine the ester product appear to be the nucleophilic character of the phenol substrate and the nature of the leaving group.^{5,6} The reaction can be represented as shown.



Ester formation requires bond formation represented by a and bond fission shown at b. If attack on the carbonyl group is by a relatively weak nucleophile such as phenol then reaction will be greatly assisted by the bond-breaking step involving a good leaving group, *i.e.*, the trifluoroacetate anion; the product will then be the acetate ester. In contrast, if the attack is by powerful nucleophile such as the phenate ion, then the bondbreaking step is less important, and the product is

⁴ D. Hadzi, A. Novak, and J. E. Gordon, J. Phys. Chem., 1963, 67, 1118.

⁶ J. M. Briody and D. P. N. Satchell, Proc. Chem. Soc., 1964, 268.

governed by whichever carbonyl carbon atom provides the more effective bond-forming site; this will be the trifluoroacetyl group, giving rise to the trifluoroacetyl ester.

Substrates of nucleophilic strength intermediate between that of phenol and the phenate ion might be expected on the basis of the mechanism proposed to form both esters in carbon tetrachloride alone. Alcohols are in this category, and these in general are found to form both acetate and trifluoroacetate esters with acetyl trifluoroacetate in the homogeneous system.²

EXPERIMENTAL

Materials.—All reactants other than those described below were obtained as described previously.¹ Phenyl trifluoroacetate was obtained by heating phenol and trifluoroacetic anhydride under reflux in the presence of sodium trifluoroacetate and separating by fractional distillation; b. p. 147-148°.

Tetra-n-butylammonium phenoxide diphenolate was obtained by converting tetra-n-butylammonium iodide (9.2 g.) in methanol solution into the hydroxide with freshly precipitated silver hydroxide, adding phenol (7 g.) to the filtrate, and evaporating the solution to a syrup. On addition of a small amount of ether a white solid separated; this gave white crystals from ether, m. p. 65-67° (Found: C, 76.9; H, 10.1; N, 2.8. C₃₄H₅₃NO₃ requires C, 78.0; H, 10.2; N, 2.7%). The total phenol present (i.e., phenol and phenoxide ion), determined by bromination, addition of iodine solution, and back titration with thiosulphate, was 0.121n-phenol for a solution which was made up to contain 0.116N total phenol.7 A similar determination on a solution of 0.121N AnalaR phenol gave 0.117Nphenol. During titration, carbon tetrachloride was used to dissolve the brominated phenol, and prolonged shaking was necessary near the end point.

Buffer solutions of pH 6, 7, 8, 9, and 10 were made up by mixing suitable volumes of borax (0.05M) and potassium hydrogen phthalate (0.1M).8 An ammonium hydroxideammonium chloride buffer of pH 9 was made up from м-ammonium hydroxide and м-hydrochloric acid, and a sodium carbonate-hydrogen carbonate buffer also of pH 9 from M-sodium hydrogen carbonate and M-sodium hydroxide. The final pH of each solution was measured on an Electronic Instrument Direct Reading pH meter, model 23A.

Isolation and Determination of Reaction Products.—The carbon tetrachloride solutions (2 ml.) and aqueous solutions (5 ml.) of the reactants were shaken together vigorously (for 10-20 sec.) immediately on mixing. The products were retained in the carbon tetrachloride, which was separated and dried $(MgSO_4)$. The esters were determined to an accuracy of ca. 5% by means of calibration curves based on measurement of the optical densities of their carbonyl absorption bands with a Perkin-Elmer Infracord instrument as described previously.1

ROYAL HOLLOWAY COLLEGE, UNIVERSITY OF LONDON, Englefield Green,

EGHAM, SURREY. [6/232 Received, February 23rd, 1966]

7 F. Wild, "Estimation of Organic Compounds," Oxford University Press, 1953, p. 86. ⁸ H. T. S. Britton, "Hydrogen Ions," Chapman & Hall,

London, 1955, vol. I, pp. 359, 363.

⁵ D. P. N. Satchell, Quart. Rev., 1963, 17, 160.