Esterification of Carboxylic Acids by Benzyl Chloride Using Quaternary Ammonium Salts

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The nucleophilicity of aliphatic carboxylic acids is enhanced in the presence of quaternary ammonium catalysts; benzyl chloride is esterified directly, *e.g.*, by acetic acid in the absence of a base.

One of the main properties of quaternary ammonium salts (QX) is their ability to function as anion exchangers. Numerous phase transfer catalysed processes are based on this feature.[1] Another important characteristic of these compounds, particularly in apolar media, is their tendency to associate with protic compounds (HY) *via* hydrogen bonding to form adducts of the general structure QX(HY) or $QX(HY)_n$; the strength of the hydrogen bonds in these complexes depends on the nature of Q, X and HY as well as the medium.[2–4] A typical example is the very high affinity of quaternary salts in phase transfer systems towards water molecules which are coextracted into the organic phase along with the reactive nucleophile as adducts with the general structure $QX(H_2O)_n$.[5] The nucleophilicity of the anion X^- is significantly reduced in the hydrated salt as compared with the 'naked anion' in QX.[5] Other protic derivatives like acids or alcohols also impair the nucleophilicity of various anions in a similar fashion.[6] This effect can be utilized for the 'fine tuning' of nucleophilic activity, *e.g.*, in polymerization processes.[7] In addition this phenomenon is the basis for the phase transfer catalysis of uncharged species. Thus, hydrohalogenation of alcohols or ethers, hydrocyanation of oximes and oxidation of various substrates with hydrogen peroxide or hypochloric acid are catalysed by quaternary ammonium salts in two-phase systems.[1,8]

While the nucleophilicity of X^- is reduced in the hydrogen bonded complex QX(HY) one can expect an increased basicity and nucleophilicity for HY in the same complex as compared with the free acid.

$$MeCO_2H + PhCH_2Cl \rightleftarrows MeCO_2CH_2Ph + HCl \qquad (1)$$

We have examined the reversible reaction of acetic acid with benzyl chloride, [reaction (1)], which proceeds effectively from right to left. When a stream of dry HCl is applied on liquid benzyl acetate at 120 °C complete conversion is obtained in less than 30 min. In the opposite direction, however, the reaction is sluggish. At 135 °C equivalent amounts of benzyl chloride and acetic acid yield less than 3 mole% of benzyl acetate after 24 h. The reason for this low result is not thermodynamic but apparently the very poor nucleophilicity of acetic acid[9] combined with the slow transport of hydrogen chloride gas from the liquid to the atmosphere above it. This result is in contrast to the very effective esterification reaction of benzyl chloride by acetate anion (which is a much stronger nucleophile) under phase transfer conditions.[10,11] The nucleophilicity of acetic acid in esterification reactions has been enhanced by hydrogen bonding with an equivalent amount of fluoride or acetate anions.[12,13]

We have now observed that quaternary ammonium chloride or bromide salts are active catalysts in the esterification reaction of simple aliphatic carboxylic acids by benzyl chloride in the absence of a stoichiometric base. Upon the addition of tetraethylammonium bromide (TEAB) (0.1 equiv.) to a mixture of acetic acid (2 equiv.) and benzyl chloride (1 equiv.) at 135 °C, hydrochloric acid is evolved with formation of benzyl acetate. Over 99% conversion to benzyl acetate was measured after 24 h. The reaction follows first-order kinetics until 90% conversion with a rate constant of 0.071 h^{-1}. The activation energy was measured to be 102.4 kJ mol^{-1} indicating that the process is clearly kinetically controlled. Similar results obtained with other quaternary salts are presented in Table 1. Comparing the rates with different catalysts we found that smaller ammonium cations were more effective than the larger ones (with the exception of tetramethylammonium) and that salts with a bromide counter ion were superior to those with chloride. To our surprise no reaction was observed at all when benzyl chloride was substituted in reaction (1) with benzyl bromide. Aliphatic alkyl halides, namely n-octyl chloride or bromide also failed to react.

The esterification rate of simple aliphatic carboxylic acids under the above conditions was found to be essentially the same but the final conversion was lower for the higher acids. Thus, after 24 h formic acid yielded 100% of benzyl formate, acetic acid 95% of benzyl acetate, propionic acid 60% of benzyl propionate and butyric acid 31% of benzyl butyrate.

In the presence of water the reaction rate was dramatically lower, thus a tenfold decrease in rate was observed when the above mixture contained 3% w/w of water. We believe that the esterification reaction (1) proceeds *via* the formation of a hydrogen bonded salt between the carboxylic acid and the ammonium salt [eqn. (2)].

$$RCO_2H + Q^+X^- \rightleftarrows RCO_2H\cdots X^-\ Q^+ \qquad (2)$$

The hydrogen bond in the above complex results in a charge redistribution with formation of partial negative charge on the carboxylic oxygen resulting in increased nucleophilicity. The latter complex attacks the electrophilic benzyl chloride to yield benzyl acetate and an ammonium hydrogen halide complex [eqn. (3)].

$$RCO_2H\cdots X^-\ Q^+ + PhCH_2Cl \rightleftarrows RCO_2CH_2Ph + QX\cdots HCl \qquad (3)$$

The ammonium hydrogen halide complex decomposes under the reaction conditions to free hydrogen chloride and the original ammonium catalyst. It is quite reasonable to assume that the complex $QX(HCl)_2$ might also play a role in

Table 1 First-order rate constants for various ammonium salt catalysts in reaction (1)[a]

Ammonium salt catalyst	Rate constant/h^{-1}
Tetramethylammonium chloride	0.029
Tetraethylammonium bromide	0.071
Tetrapropylammonium bromide	0.065
Tetrabutylammonium bromide	0.059
Tetrahexylammonium bromide	0.041
Tetrahexylammonium chloride	0.015
Didecyldimethylammonium bromide	0.011
Aliquat 336	0.009

[a] *Reaction conditions*: 0.1 mol benzyl chloride, 0.2 mol acetic acid and 0.01 mol catalyst at 135 °C.

the mechanism. Since the esterification reaction takes place even at room temperature when a stoichiometric amount of ammonium salt is present we tend to believe that this decomposition is the rate determining step of the catalytic process. The relative stability of the QX–HCl and QX–$(HCl)_2$ complexes formed in the course of the reaction determines the effectiveness of the catalysis. Thus, the smaller (and harder) cations Q^+ are then the more effective as they are more tightly bound to X^-; larger (softer) anions X^- are then more efficient as they are less associated to HCl in $Q^+X^-\cdots\cdot HCl$ complexes. There is also evidently a difference in the stability of $Q^+Br^-\cdots\cdot HBr$ as compared with $Q^+Br^-\cdots\cdot HCl$ with the latter being less stable. This is probably the reason for the relative inertness of benzyl bromide in the esterification process. These preliminary results clearly indicate that quaternary ammonium salts can function as an *in situ* regenerable base in esterification reactions. A similar catalytic role for quaternary salts was reported in dehydrohalogenation reactions of alkyl halides in the absence of a base.[1]

Received, 2nd April 1991; Com. 1/01511G

References

1 E. V. Dehmlow and S. S. Dehmlow, *Phase Transfer Catalysis*, Verlag Chemie, Weinheim, 2nd edn., 1983.
2 F. Kaufler and E. Kunz, *Berichte*, 1909, **42**, 385, 2482.
3 K. M. Harmon, S. D. Alderman, K. E. Benker, D. J. Diestler and P. A. Gebauer, *J. Am. Chem. Soc.*, 1965, **87**, 1700.
4 J. Emsley, *Chem. Soc. Rev.*, 1980, **9**, 91.
5 D. Landini, A. M. Maia and F. Montanari, *J. Am. Chem. Soc.*, 1978, **100**, 2796.
6 H. A. Zahalka and Y. Sasson, *J. Chem. Soc. Chem. Commun.*, 1984, 1581.
7 I. B. Dicker, G. M. Cohen, W. B. Farnham, W. R. Hertler, E. D. Laganis and D. Y. Sogah, *Macromolecules*, 1990, **23**, 4034.
8 E. V. Dehmlow, in *Organic Synthesis*, 6th IUPAC Symp., ed. O. Chizhov, Blackwell Scientific, Oxford, 1987, 179.
9 P. E. Peterson and F. J. Waller, *J. Am. Chem. Soc.*, 1972, **94**, 991.
10 C. L. Liotta, H. P. Harris, M. McDermott, T. Gonzalez and K. Smith, *Tetrahedron Lett.*, 1974, 2417.
11 J. Barry, G. Bram, G. Decodts, A. Loupy, P. Pigeon and J. Sansoulet, *Tetrahedron*, 1983, **39**, 2673.
12 J. H. Clark, *Chem. Rev.*, 1980, **80**, 429.
13 J. Emsley, O. P. A. Hoyte and R. E. Overill, *J. Am. Chem. Soc.*, 1978, **100**, 3303.