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TETRAMETHYLETHYLENEDIAMINE AS A PHASE TRANSFER CATALYST: A REEXAMINATION

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It was recently reported that the reaction of potassium acetate with benzyl chloride in acetonitrile solution to give benzyl acetate is catalyzed by the presence of certain phosphoramidates and a dozen di- and polyamines[1] (see equation 1). This discovery was, in fact, hailed as a milestone.[2]

$$C_6H_5CH_2Cl \quad + \quad KOAc \xrightarrow{\text{amine}} C_6H_5CH_2OCOCH_3 \quad + \quad KCl \qquad (1)$$

It has been known for over sixty years that the reaction shown in equation 1 is assisted by the presence of tertiary amines[3] and the fact that quaternary ammonium salts formed in situ from amine and alkyl halide actually catalyze this reaction was demonstrated by Hennis and coworkers over a decade ago.[4] We inferred from the assertion in reference 1 "...that quaternary ammonium salts corresponding to the diamines do not activate anions under the experimental conditions used..." that this was not a case of quaternary ammonium salt catalysis.

Inasmuch as the most effective quaternary ammonium salt catalysts used in phase transfer reactions are those which are highly substituted about nitrogen,[5] it was not difficult to accept the observation that the quaternary ammonium salts which might be presumed to be present were not effective in this reaction. It was more difficult for us to understand, however, just what is the mode of catalysis in light of the information currently available.[6]

The complexation of the lithium ion by tetramethylethylenediamine (TMEDA)[7] is a well-established phenomenon, but the complexation by TMEDA of a much larger and softer cation such as potassium seems much less likely. Solvation in analogy to crown ether solvation would require a large loss of entropy and also seems unlikely.[8] Moreover, recent studies involving polyethylene oxides indicate that effective phase transfer catalysis is realized only when there are multiple heteroatom binding sites in the chain.[9] In addition, where nitrogen has been substituted for oxygen in crown ethers, the binding constants have generally been lower, not higher.[10]

We have investigated the reaction corresponding to equation 1 using a variety of substances as catalysts. In particular, we have focussed attention on tetramethylethylenediamine as a representative polyamine.[1] We have independently prepared both the monobenzyl ($C_6H_5CH_2N^+Me_2CH_2CH_2NMe_2\ Cl^-$, 1)[11] and dibenzyl [$(C_6H_5CH_2N^+Me_2CH_2)_2\ Cl_2^=$, 2][12] derivatives of TMEDA. In figure 1 are plotted the experimentally determined rates for reaction 1 at 30.0°C.

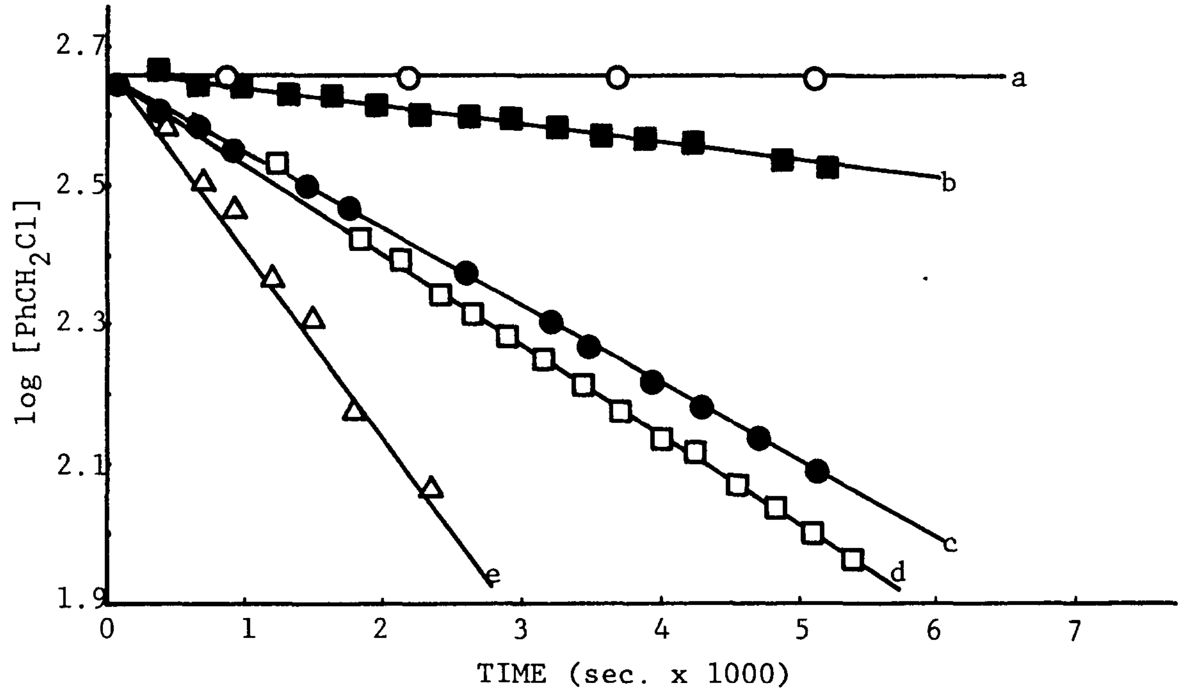
In the absence of any catalyst, the concentration of benzyl chloride remains essentially constant for over two hours (open circles). The bis-quaternary ammonium compound (diquat, compound 2) catalyzes reaction 1 (closed squares) but poorly. The reaction rates for the cases involving TMEDA (closed circles) and the corresponding monoquat (compound 1, open squares) are the same within experimental error suggesting that 1 is probably the catalytically active species.

In principle, at low enough temperature, the appearance of benzyl acetate product should occur more slowly at the beginning of the reaction (during quat formation) and then its rate of formation should be equal to the rate of disappearance of benzyl chloride. This phenomenon has been observed for at least one case of which we are aware,[13] but we were unable to demonstrate this unequivocall in our system. This failure is due, we feel, to the heterogeneous nature of the reaction and to the large rate constant for the Menschutkin reaction.[14] We have, however, observed that benzyl acetate is formed faster at the very beginning of the reaction when monoquat (1) rather than TMEDA is used.

In control experiments we have found that doubling the concentration of catalyst in the reaction doubles the rate and that if twice as much solid potassium acetate is used, the rate is unchanged within experimental error. In addition, it should be noted that this heterogeneous reaction is subject to variation in stirring rate. When the reaction is stirred vigorously with a paddle at 500 rpm (± 10%) the rates are as reported in this paper. When the stirring rate is increased to ca. 1700 rpm, the rate constants increase approximately 10%. We found that by maintaining a consistently vigorous stirring rate, the kinetics were satisfactorily reproducible.

It is interesting to note (see fig. 1) that benzyltriethylammonium chloride (BTEAC, triangles), the catalyst used previously in this reaction[3,4] is the best catalyst of those studied. That monoamines can also be effective catalysts for this reaction is suggested by data in reference 1. Of the six phosphoramidates shown in scheme A (of ref. 1), only three of them (compounds 2, 3 and 5) have a nitrogen atom which is not adjacent to phosphorus. Only these three compounds should alkylate readily to form a quaternary ammonium salt and only those three compounds exhibited significant catalytic activity in reaction 1.

FIGURE 1
The Reaction of Benzyl Chloride with Potassium Acetate[15]



NOTES: a. Reaction 1 in the absence of any catalyst. b. Diquat (2), k = 0.53 ± 0.04 x 10^{-4} sec^{-1}. c. TMEDA, k = 2.62 ± 0.30 x 10^{-4} sec^{-1}. d. Monoquat (1), k = 2.76 ± 0.02 x 10^{-4} sec^{-1}. e. BTEAC, k = 5.71 ± 0.23 x 10^{-4} sec^{-1}.

While we have not examined all of the amines presented in reference 1, it seems clear that for the TMEDA case at least, the catalytically active species is the corresponding monoquat (1). We anticipate that in situ quaternary ammonium salt formation[3,4] likely accounts for the catalytic activity of the other amines as well (except perhaps polyamines 10, 11 and 12 in reference 1). The diquat corresponding to TMEDA (2) is a poor catalyst for reaction 1 and it seems likely that the authors of reference 1 precluded quaternary ammonium salt catalysis on the basis of diquat, rather than monoquat, control experiments. This error is even more understandable if a more poorly soluble diquat than 2 was studied.

NOTES AND REFERENCES

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11. The monobenzyl derivative of TMEDA (1), was prepared by adding (syringe) tetramethylethylenediamine (4.53 ml, 0.03 mol) and benzyl chloride (1.30 ml, 0.011 mol) to acetonitrile (10 ml) in a sealed Erlenmeyer flask. The solution was swirled and allowed to stand for 2-3 h. The solution was then condensed *in vacuo*. The remaining oily white residue was triturated with dry hexane. The resulting white powder was filtered under nitrogen and dried *in vacuo*. Yield: 2.62 g (96%), mp: 116-123°C. Anal. Calc'd for $C_{13}H_{23}ClN_2$: C, 64.34%; H, 9.49%; N, 11.55%. Found: C, 64.31%, H, 9.82%; N: 11.37%. ^{1}H-nmr ($CDCl_3$, ppm δ): 2.24 (6H,s) Me_2N; 2.78 (2H,m) $Me_2NC\underline{H}_2$; 3.32 (6H,s) Me_2N^+; 3.88 (2H,m) $C\underline{H}_2N^+$; 5.1 (2H,s) $C\underline{H}_2C_6H_5$; 7.35, 7.65 (5H,m,m aromatic protons.

12. Compound 2 was prepared by adding TMEDA (1.51 ml, 0.01 mol) and benzyl chloride (2.30 ml, 0.02 mol) to acetonitrile (10 ml) in a sealed Erlenmeyer flask (syringe). The solution was swirled and allowed to stand for *ca*. 24 h. The white crystals which formed were filtered under a dry nitrogen atmosphere, washed with dry hexane and then dried under high vacuum. Yield: 3.30 g, (89%), mp: 211-213°C. ^{1}H-nmr (D_2O, ppm δ): 3.22 (12H,s) Me_2N^+; 4.05 (4H,s) $C\underline{H}_2C_6H_5$; 8.09 (10H,s) aromatic protons.

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15. Reactions were conducted in a 25-ml 3-necked flask equipped with mechanical (overhead) stirrer, gas inlet and rubber septum. All equipment was oven dried, cooled under nitrogen and the reactions conducted under nitrogen. All reagents were purified and dried by standard procedures. A typical procedure follows: Potassium acetate (0.90 g, 0.0092 mol) was weighed into a dry 25-ml flask. The catalyst (0.00087 mol) was added either as a solid or, if liquid, by syringe. The reaction vessel was immersed in a constant temperature bath maintained at 30.0 ± 0.2°C and charged with acetonitrile (10 ml). After stirring the heterogeneous mixture for 0.5 h, benzyl chlorid (1.0 ml, 0.0087 mol, preequilibrated at 30.0°C) was added and the timer started. The reaction was monitored using a Varian Aerograph 2720 or 920 gas chromatograph equipped with a 5' x 0.25" 10% SE-30 on 60/80 Chromosorb P column at 170°C and 60 ml/min He flow. Note that data are corrected for the known initial concentration.