A Study on the Reaction between Phenacyl Bromide and Certain Tertiary Amines in Acetone: Effect of Addition of Water and Phenol(s)

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Rate constants for the reaction between phenacyl bromide and certain tertiary amines have been determined conductometrically using Guggenheim's method under equimolar concentrations at 30°C. The rate is correlated with steric effects of base(s). Effects of addition of water and phenol(s) on the rate of the reaction between phenacyl bromide and triethylamine are discussed. The critical region in aq. acetone mixed solvents for this reaction is reported. Phenol(s) with pka > 7.15 does not affect the rate of quaternization in all concentrations of water in acetone, whereas *p*-nitrophenol retards the rate just by the addition of water.

INTRODUCTION

The reaction between phenacyl bromide and triethylamine readily takes place to give quaternary salt. When carboxylic acid or phenol is introduced, esterification[1,2] or etherification[3] occurs. In these reactins, triethylamine is protonated by acid or phenol which in turn causes for the generation of carboxylate or phenolate ion. Further, it is reported that triethylamine is not able to ionize the phenols with pKa > 7.15 in the polarity of the medium upto the range of 40ε.[3,4] Therefore, it is interesting to study the reaction in more polar medium like aq-acetone mixed solvents with a view to knowing the effect of polarity of mixed media on phenol-triethylamine interaction under equimolar concentration. Further, certain tertiary amines containing more than one nitrogen atom are used to compare their reactivity.

EXPERIMENTAL

N-Methylaniline (NMA), N,N-dimethylaniline (NNDMA), triethylamine (TEA), tetramethylethylenediamine (TMEDA), pyridine, 1,4-diazabicyclo[2,2,2]-octane (DABCO), 1,8-diazabicyclo[5,4,0]-undec-7-ene [DBU] and phenols are AnalaR or E-Merk samples. They are purified by standard methods before use. Phenacyl bromide is prepared by bromination of acetophenone.

The solutions of phenacyl bromide and tertiary amine in acetone (10^{-2} mol dm^{-3}, 25 mL, each) were prepared. The conductivity experiments were carried

out as described elsewhere[4]. Second order rate constant (k_2) was derived from the conductivity data using the equation

$$X_2 - X_1 = k_2Co[t_1X_1 - t_2X_2] - k_2CoX_\infty(t_1 - t_2)$$

where X_1, X_2 and X_∞ are the conductances at times t_1, t_2 and t_∞ respectively. Co is the initial concentration of the reactants. The conductivity experiments were carried out using Elico MHO's pH-meter Model PE-133.

The thermostated ($\pm 0.1°C$) solution of phenacyl bromide (25 mL, 0.1 mol dm^{-3}) and a solution of triethylamine (25 mL, 0.1 mol dm^{-3}) in acetone-water (v/v) mixed solvents were mixed. The course of the reaction was followed by Volhard's method. Second order rate constant (k_2) was derived from the equation

$$k_2 = \frac{1}{t} \frac{X}{a(a-x)} \ dm^3 \ mol^{-1} \ min^{-1}$$

by applying the method of least squares analysis with the correlation coefficient $r = 0.999$. A similar experimental procedure was followed for the reaction between phenacyl bromide and Et_3N-phenol(s).

Product Analysis: Equal volumes of equimolar solutions of phenacyl bromide and triethylamine (25 mL, 0.025 mol dm^{-3}) were mixed under kinetic conditions and kept overnight at room temperature. The solid thrown out was filtered off; yield 70% and m.p. (66–67°C) was found comparable to the reported value[5].

Equal volumes of equimolar solutions of phenacyl bromide and Et_3N-p-NO_2—C_6H_4OH in 80% acetone-water (v/v) were mixed under kinetic conditions and kept overnight at room temperature. The pale yellow coloured solids thrown out were filtered off and recrystallized from 50% chloroform-petroleum ether (60–80%) (v/v); yield 85%, m.p. 147–48°C. It was identified as phenacyl p-nitrophenyl ether from IR and ^1H NMR spectral data. IR (KBr): 1690 ($v(C=O)$), 1470 and 1320 $v(N=O)$ ($ArNO_2$), 1220 ($v(C—O—C)$) cm^{-1}; ^1H NMR (Acetone-d_6); δ 8.21 (m, —CO—Ar), 7.6–7.18 (m, —O—Ar), 5.78 (s, —CO—CH_2).

Similar method is followed for Et_3N—X—C_6H_4—OH (X = p-H, p-Cl, p-Me and p-OMe) in 80% acetone-water (v/v). The reaction mixture was tested by TLC using 20% acetone-water (v/v) as eluent and found two spots. The spots were identified as phenacyl triethylammonium bromide and added phenol by running co-chromatogram.

RESULTS AND DISCUSSION

Second order rate constants (k_2) of the reactions between phenacyl bromide and certain tertiary amines such as NMA, NNDMA TEA, pyridine, TMEDA, DABCO and DBU have been determined by conductometric method in acetone at 30°C. The results are presented in Table-1.

The rates of the reactions of phenacyl bromide with different amines are compared. Steric factor appears to be more significant over electrical factors. The rate of quaternization of amines such as NMA, NNDMA and TEA is found to be 2.5 times slower than that of pyridine (Table-1). This may be due to the steric

hindrance caused by alkyl substituents on the donation of lone pair of electron to the electrophile. However, the rate of the reaction with TMEDA is about 112 times faster than that of NNDMA. Conjugation effect by phenyl group and steric effect by methyl group in the latter may be the reasons for its low reactivity.

TABLE-1

SECOND ORDER RATE CONSTANTS OF THE REACTION OF
PHENACYL BROMIDE TERTIARY AMINES(S) IN ACETONE AT 30°C

$[PhCOCH_2Br] = [Tertiary amine] = 2.5 \times 10^{-3}$ mol dm^{-3}

Amine	k_2, dm^{3}mol^{-1}min^{-1}
N-Methylaniline	0.202
N, N-Dimethylaniline	0.101
Pyridine	0.270
Triethylamine	0.108
Tetramethylethylenediamine	11.360
DABCO	68.200
DBU	213.000

TABLE-2

SECOND ORDER RATE CONSTANTS OF $PhCOCH_2Br + NEt_3$ AND
$PhCOCH_2Br + Et_3N—XC_6H_4OH$ REACTIONS IN ACETONE-WATER
MIXED SOLVENTS AT 30°C

$[PhCOCH_2Br] = [NEt_3] = [X—C_6H_4—OH] = 0.05$ mol dm^{-3}

Percentage of acetone (v/v)	k_2, dm^3 mol^{-1} min^{-1}						
	NEt$_3$	Et$_3$N—X—C$_6$H$_4$—OH					
		X = p-H	X = p-OCH$_3$	X = p-CH$_3$	X = p-Cl	X = p-Br	X = p-NO$_2$
100	0.108	0.107	0.100	0.106	0.112	0.113	0.112
99	0.109	0.104	—	—	—	—	0.173
97	0.107	0.104	0.100	—	—	—	0.152
95	0.105	0.102	0.100	0.108	0.112	0.110	0.147
93	—	—	—	—	—	—	0.149
90	0.103	0.102	0.099	0.107	0.113	0.113	0.147
85	0.120	0.120	0.120	—	—	—	–0.150
80	0.134	0.134	0.134	0.136	0.138	—	0.147
75	0.154	0.150	0.150	—	0.150	—	—

Amines such as TMEDA, DABCO and DBU have two active nitrogens which are identical. The electrophile can interact with either one of the nitrogen atoms in the molecule. Control experiment was carried out by taking two equivalents of phenacyl bromide and one equivalent of amine. The rate of this reaction was

too fast to measure. The reactivity of these amines with phenacyl bromide is found to be in the order: TMEDA < DABCO << DBU. This may be due to the free exposure of lone pair of electrons of nitrogen in DABCO and DBU to the electrophile rather than in TMEDA.

Second order rate constants of the reactions of phenacyl bromide with equimolar mixture of TEA and p-X—C_6H_4—OH, (X=H, CH_3, OMe, Cl and NO_2) have been determined in acetone and acetone-water mixed solvents (v/v) at 30°C. The results are presented in Table-2. Control experiment showed that solvolysis of phenacyl bromide did not take place during the completion of reaction in acetone-water mixed solvents at all concentration ranges of water. The plot of the value of k_2 against solvent composition is shown in Fig. 1. Addition of these phenols except p-nitrophenol did not alter the value of rate constant of the $PhCOCH_2Br/TEA$ reaction in these mixed media. Thus, TEA was free to act as a nucleophile even in the presence of phenol(s). The rates of the reactions in the presence of phenol(s) remained constant up to 10% addition of water to acetone and thereafter increased linearly with increase in percentage of water (Fig. 1). The change in the value of rate constant occurs in aq. organic mixed
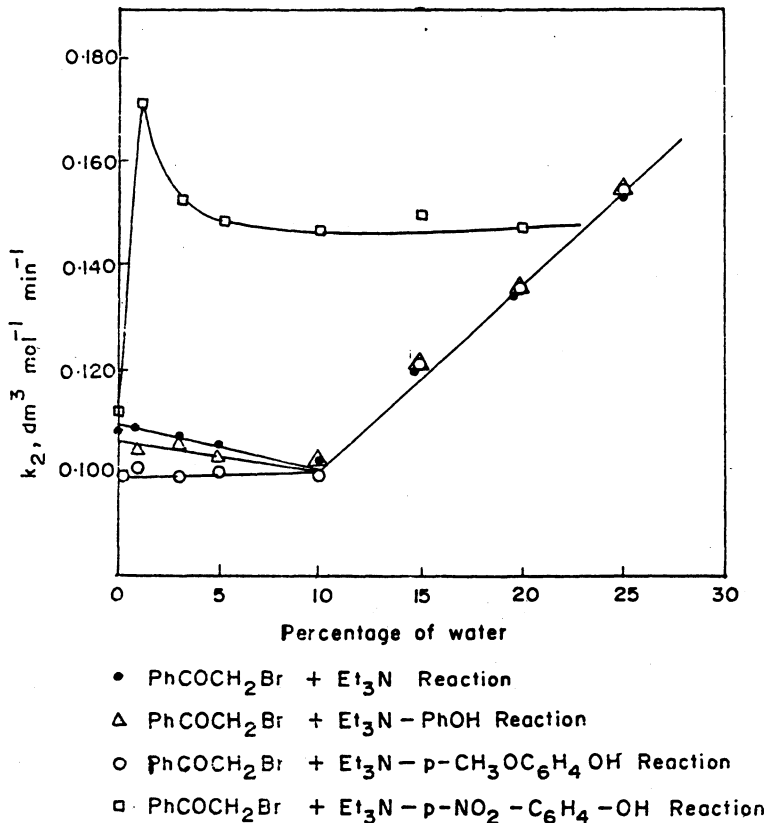

- ● $PhCOCH_2Br$ + Et_3N Reaction
- △ $PhCOCH_2Br$ + Et_3N – PhOH Reaction
- ○ $PhCOCH_2Br$ + Et_3N – p-$CH_3OC_6H_4$ OH Reaction
- □ $PhCOCH_2Br$ + Et_3N – p-NO_2 –C_6H_4 –OH Reaction

Fig. 1   Plot of k_2 vs solvent composition

medium containing 10% water (v/v). Acetone-water 90/10 (v/v) may be a critical region for this reaction[6].

The rate constant of the reaction between phenacyl bromide and equimolar mixture of Et_3N-p-nitrophenol was found to be 0.173 dm^3 mol^{-1} min^{-1} in 99% acetone-water (v/v) mixed solvents against 0.112 dm^3 mol^{-1} min^{-1} in acetone. Addition of 3% water (v/v) to acetone reduced the value of k_2 to 0.150 dm^3 mol^{-1} min^{-1}. Further addition of water did not affect the rate of the reaction (Table-1).

The product analysis of the reaction in 99% acetone-water (v/v) mixed solvents was done and the isolated product was identified as phenacyl p-nitrophenyl ether (I) from IR (KBr) and ^1H NMR (acetone-d_6) data.

$$\text{C}_6\text{H}_5 - \text{CO} - \text{CH}_2 - \text{O} - \text{C}_6\text{H}_4 - \text{NO}_2$$
$$(I)$$
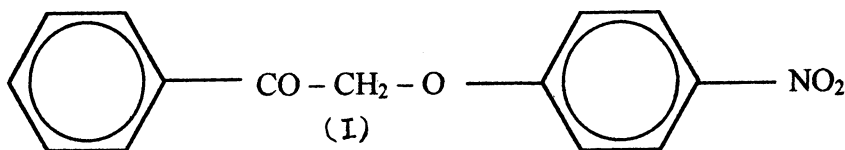
Addition of just 1% water (v/v) caused the ionization of p-nitrophenol which in turn protonated the base. The corresponding phenolate ion would be the active nucleophile which led to the formation of ether (I). The phenolate ion may be in the form of proton transferred H–bonded complex (II) as indicated by spectroscopic studies[7, 8]

$$O_2N - C_6H_4 - O^- - - - - - - HN^+Et_3$$
$$(II)$$
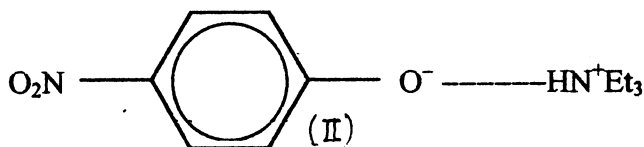
The magnitude of change in second order rate constant for the reaction of phenacyl bromide with equimolar mixture of Et_3N-p-nitrophenol was nearly 14% when the reaction medium was changed from acetone to 3% aqueous acetone (v/v) (k_2 = 0.173 to 0.150 dm^3 mol^{-1} min^{-1}). Further, decrease in the value of rate constants of these reactions with increasing water content in acetone was similar to the trend observed in the reactions of phenacyl bromide with sodium benzoates[9] and triethylammonium benzoates[1, 2] in acetone-water mixed solvents. The considerable decrease in rate may be due to the decomposition of the proton transferred H-bonded complex (a reactive species) to a solvent separated ion-pair or hydrated phenoxylate ion (less active) and triethylammonium ion. Further decrease in rate constant with increasing ionsizing power of the solvent (by adding more water) can be readily accountable on the basis of Hughes-Ingold theory.

Conclusion

The variations in rates of the reactions of phenacyl bromide with certain amines are explained on the basis of steric hindrance. Presence of phenol(s) with pka > 7.15 does not affect the rate of quaternization of TEA by phenacyl bromide in

acetone. The trend of the reaction is found to be same when the medium is moved from acetone to aq. acetone. However, the behaviour of the reaction is changed when water content exceeds 10% (v/v) which is considered as the critical region for this quaternization. *p*-Nitrophenol is able to protonate the TEA just after the addition of water into acetone. This is proved from the product analysis.

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