REACTIVITY OF o-AMINOMETHYLPHENOLS IN THE MENSHUTKIN REACTION

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The presence of an intramolecular hydrogen bond (IHB) in o-aminomethylphenols (OAMP) governs the specificity of their physicochemical properties [1-4] and their unique behavior in chemical reactions [5-8]. The strong IHB between the phenolic hydroxyl group and the amino group lowers the reactivity of the latter in cases where it acts as a nucleophilic reaction center. Processes of this type include the formation of tetraalkylammonium salts with alkyl halides, i.e., the Menshutkin reaction. This reaction is known for OAMP [9, 10], but its kinetics have not been studied.

We have performed a kinetic investigation of the reaction of alkyl halides with several OAMP and also for comparison, with dimethylbenzylamine (I), which has no IHB, in order to elucidate the role of the latter in the nucleophilic reactivity of the amino group in OAMP. We have obtained data on the reaction rate in various media, which are of interest in that the strength of the IHB in OAMP depends on the nature of the solvent [11].

The results presented in Tables 1 and 2 show the effect of changes in the structure of the OAMP and the alkyl halides on the reaction rate in ethanol. The rate constants for reactions with alkyl iodides are 2-2.5 times higher than those for reactions with alkyl bromides of the same structure. This was to be expected, since the tendency to undergo anionic cleavage increases as the atomic number of the halogen increases [12], probably due to the fact that the C−I bond has a lower energy than the C−Br bond [13, p. 134]. As the number of C atoms (m) in the alkyl radicals increases, the rate constant k first decreases and then becomes almost constant at high m values. A smooth variation in k is observed for n-alkyl-radicals (Fig. 1). Branching of the hydrocarbon chain results in a sharper decrease in rate (see Fig. 1) due to the negative influence of the steric factor on the reaction rate.

Changes in the steric conditions in the nucleophilic reagent are also reflected in the reaction rate. For example, replacement of methyl radicals by Et and Pr on the nitrogen atom causes the log k values for corresponding OAMP (see Table 2) to deviate negatively by 0.34 and 0.58 from the Brönsted equation

$$\lg k = 0.281 \cdot \mathrm{p}K_a - 6.61 \quad (n = 6.\ r = 0.974.\ s = 0.04)$$

This equation also describes the behavior of ring-substituted o-dimethylaminomethylphenols in which the steric conditions at the N atom are unaffected, whereas a positive deviation (Δlog k = 0.35) from this equation is observed for (I) (Table 3) due to the absence of an IHB.

TABLE 1. Rate Constants for Reaction of o-Dimethylaminomethylphenol (II) with Alkyl Halides (RX) in Ethanol at 60°C

RX	$k \cdot 10^5$, liter/mole · sec	RX	$k \cdot 10^5$, liter/mole · sec
MeI	984	n-BuBr	2,47
EtI	26,2	i-BuBr	1,07
EtBr	9,56	n-AmI	4,82
n-PrI	5,81	n-AmBr	2,09
n-PrBr	2,82	n-C_8H_{17}Br	2,43
i-PrI	3,71	n-C_9H_{19}Br	2,25
n-BuI	5,09		

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TABLE 2. Rate Constants for Reaction of Propyl Bromide with Substituted o-Dialkylaminomethylphenols in Ethanol at 60°C

Alkyl	R *	pK_a (EtOH)	$k \cdot 10^5$, liter/mole • sec	Alkyl	R *	pK_a (EtOH)	$k \cdot 10^5$, liter/mole • sec
Me	H	7,30 [11]	2,87	Me	*p*-Me	7,30	2,61
Et	H	7,10 [11]	1,06	Me	*p*-Cl	6,65	1,64
Pr	H	6,74	0,50	Me	*o*-Me	6,05	1,32
Me	*p*-MeO	7,10 [11]	2,58	Me	*m*-Me	7,35	2,82

*Substituent in the benzene ring.

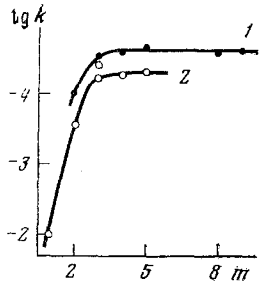

Fig. 1. Plot of log k for reactions of o-dimethylaminomethylphenol (II) with alkyl halides (see Table 1) versus the number of carbon atoms m: 1) in alkyl bromides; 2) in alkyl iodides.

Our data are in accord with the results obtained in [17] for the quaternization of saturated and β- and γ-substituted acetylenic amines with ethyl iodide. We obtained the following correlation between the rate constants obtained in [17] for amines with similar steric conditions at the nitrogen atom ($-E_N \sim 4.5$):

$$\lg k = 0.54 \cdot pK_a - 9.31 \quad (r = 0.98,\ s = 0.06,\ n = 4)$$

Thus, when steric conditions are constant, one of the factors determining the nucleophilic reactivity of amines in quaternization reactions is their basicity.

The difference in the behaviour of benzylamines not having an IHB compared with OAMP shows up clearly when the effects of the medium on the reaction rate are studied. The results obtained by investigating the kinetics of the reaction of (I) and o-dimethylaminoethylphenol (II) with propyl bromide in a number of solvents are given in Table 3. The medium has a greater effect on the reaction rate in the case of (I) than in the case of (II). The reactivity of (I) reaches a maximum in nitromethane, in which (II) has relatively low reactivity. The effect of the medium on the reaction rate of (II) is highly specific, the highest rate constant being obtained in methanol.

Variations in the rate of the Menshutkin reaction in aprotic dipolar solvents are governed by nonspecific solvation of the reactants and the transition state [18]. In solvents capable of forming hydrogen bonds with the reactants, specific solvation becomes important, which explains the low reactivity of the amines when the Menshutkin reaction is conducted in proton-donor media.

The effect of aprotic dipolar solvents on the reaction rate of (I) is analogous to that observed for similar reactions in [18, 19]. Thus, for example, there is a correlation between log k for (I) (Table 3) and log k for the reaction of Me_3N with p-nitrobenzyl bromide [18] in aprotic dipolar solvents

$$\lg k\,(I) = 0.804 \cdot \lg k_{Me_3N} - 3.20 \quad (n = 6,\ r = 0.974,\ s = 0.2)$$

While the rate constant of (I) shows a tendency to increase in media with a high dielectric constant (ε), the dependence of log k on the Kirkwood function [20] is not adhered to in aprotic solvents with different polarities (Fig. 2). The Kirkwood equation is applicable in alcohol media, despite the influence of specific solvation. For the reaction of (I) it may be represented in the form

$$\lg k = 9.82\,(\varepsilon - 1)/(2\varepsilon + 1) - 8.96 \quad (n = 5,\ r = 0.96,\ s = 0.05)$$

TABLE 3. Rate Constants for Reaction of Dimethylbenzylamine (I) and o-Dimethylaminomethylphenol (II) with Propyl Bromide in Various Solvents at 60°C

Solvent	ε, 25°	$k \cdot 10^5$, liter/mole · sec		Solvent	ε, 25°	$k \cdot 10^5$, liter/mole · sec	
		(I)	(II)			(I)	(II)
MeOH	32,6 [13]	6,00	3,32	MeCN	36,2 [13]	21,9	0,76
EtOH	24,3 [13]	3,98	2,82	$MeNO_2$	38,6 [13]	40,8	0,71
PrOH	20,1 [13]	–	2,40	$Ph-NO_2$	34,8 [14]	12,4	0,80
i-PrOH	18,3 [13]	–	2,04	cyclo-$C_6H_{11}OH$	18,3 [14]	7,06	0,76
i-BuOH	17,7 [13]	–	2,39	MeCOPh	17,4 [14]	9,52	0,71
BuOH	17,1 [13]	3,26	2,07	*n*-PrBr	8,09 [16]	–	0,14
AmOH	13,9 [13]	2,94	1,66	$MeCO_2Et$	6,0 [14]	0,88	–
t-BuOH	12,2 [14]	2,42	1,93	C_6H_6	2,3 [14]	0,38	–
n-$C_{10}H_{21}OH$	8,12 [15]	–	1,38	$O(CH_2CH_2)_2O$	2,2 [14]	2,87	0,20

TABLE 4. Activation Parameters for Reaction of Propyl Bromide with Compounds (I) and (II) in Various Media

Medium	Compound	T., °C	$k \cdot 10^5$, liter/mole · sec	E, kcal/mole	lg *A*
EtOH	(I)	47	1,64	16,7	6,61
		58	3,78		
		60	3,98		
		69	8,73		
	(II)	45	0,72	18,8	7,78
		54	1,51		
		60	2,82		
		67	4,85		
MeCN	(I)	45	8,23	13,5	5,22
		53	14,8		
		60	21,9		
	(II)	54	0,53	21,1	8,74
		60	0,76		
		68	2,03		
MeCOPh	(I)	60	9,52	12,8	4,38
		71	19,2		
		82	32,6		
		95	60,2		
	(II)	60	0,71	13,6	3,80
		71	1,35		
		85	2,71		
		100	6,40		

Compound (II) is less reactive than (I) in all the solvents investigated, but the ratio $k_{(I)}/k_{(II)}$ is considerably greater in aprotic dipolar solvents than in alcohols. This behavior may be due to the presence of the IHB in (II). The strength of the IHB in OAMP increases on passing from ethanol to media such as nitromethane and acetonitrile [11]. Evidently, the reactivity of (II) in the various media decreases concurrently with the increase in the strength of the IHB. The influence of the IHB probably explains the low slope of the Kirkwood plot for (II) in alcohols

$$\lg k = 5.55\,(\varepsilon - 1)/(2\varepsilon + 1) - 7.19 \quad (n = 9,\ r = 0.92,\ s = 0.05)$$

The presence of the IHB increases the activation energy (E) for (II) compared with (I) (Table 4), the increase being greater in solvents capable of increasing the strength of the IHB [11]. We also observe an increase in E for (I) in ethanol. This indicates that intermolecular and intramolecular hydrogen bonding with amines has a similar effect on the value of E in the Menshutkin reaction. An increase in E for the Menshutkin reaction in MeOH compared with DMF has also been observed in [21].

EXPERIMENTAL

The experiments were performed using o-aminomethylphenols (OAMP) prepared as in [2] and freshly distilled alkyl halides; the solvents were purified by known methods.

TABLE 5. Properties and Analyses of Quaternary Ammonium Salts of o-Dimethylaminomethylphenol with Alkyl Halides

Alkyl	Halide	Yield, %	Found, %			Calculated, %		
			C	H	N	C	H	N
Me	I^-	99	40,22	5,19	4,69	40,96	5,45	4,78
Et	I^-	60	42,96	6,22	4,83	43,00	5,86	4,56
n-Pr	Br^- *	40	52,65	7,39	4,76	52,55	7,30	5,11
n-Pr	I^-	98	45,10	6,10	4,49	44,86	6,23	4,36
n-Bu	I^-	50	46,75	6,54	4,20	46,57	6,57	4,18

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*Found: Br 29.36%. Calculated: Br 29.20%.

The reacion kinetics were studied on the basis of the variation in the OAMP concentration, which was determined by potentiometric titration in samples with 0.1 N HCl in absolute ethanol. The initial concentration of the OAMP in the experiments was 0.02-0.04 mole/liter, and that of the alkyl halides was 0.6-1.0 mole/liter, and that of the alkyl halides was 0.6-1.0 mole/liter. In the presence of excess alkyl halide, the reaction rate was described by a first-order kinetic equation. The bimolecular rate constants were obtained by dividing the first-order rate constants by the alkyl halide concentration. The Arrhenius parameters were determined from the data in Tables 3 and 4. The pK_a values of the OAMP in ethanol were determined as in [11].

For some of the OAMP the quaternization products were prepared and characterized (Table 5). The products were isolated as follows: an equimolar mixture of the reactants was boiled in absolute ethanol for 2 h and the product was precipitated with ether, dissolved in acetone and reprecipitated twice with ether.

CONCLUSIONS

1. The kinetics of the reaction of o-aminomethylphenols and dimethylbenzylamine with alkyl halides have been studied. The rate of quaternization of the amino group depends on the steric conditions in the nucleophilic and electrophilic reagents, the basicity of the nucleophile, the length and degree of branching of the hydrocarbon chains in the alkyl halides, and on the presence of an intramolecular hydrogen bond (IHB) between the amino nitrogen atom and the phenolic hydroxyl group.

2. The sharp decrease in the reactivity of the o-aminomethylphenols compared with the benzylamine in protonic dipolar solvents is due to an increase in the strength of the IHB in these media.

3. Compared with aprotic dipolar solvents, the reactivity of o-dimethylaminomethylphenol in alcohols is increased due to weakening of the IHB. Dimethylbenzylamine has low reactivity in alcohols due to its specific solvation by alcohols.

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POLYENE COMPOUNDS AS FREE-RADICAL ACCEPTORS

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In chain reactions involving oxidation with molecular oxygen, organic compounds are consumed mainly as a result of reaction with free radicals in the chain propagation step. The overall reaction rate depends to a considerable extent on the rate of this elementary step. The object of the present work has been to determine the kinetic parameters and rate constants for the reaction of β-carotene (A_1) and retinyl acetate (A_2) with various types of free radicals and to compare the reactivities of isolated and conjugated unsaturated bonds; this is a necessary step in the search for antioxidants which will stabilize these valuable and easily oxidized substances.

EXPERIMENTAL

The β-carotene (A_1) and retinyl acetate (A_2) were commercial products from Hoffmann La Roche (Basle) and Serva (Heidelberg). The concentration of the polyenes was determined from the optical density of the solutions at the long-wave absorption maxima. The experiments were carried out as described in [1]. The free-radical sources were azobisisobutyronitrile (AIBN) and dicyclohexyl peroxydicarbonate (PC). The rate of radical formation by thermal decomposition of the initiators (w_i) was calculated using the formulas

$$w_i^{\mathrm{AIBN}} = 1.2 \cdot 1.58 \cdot 10^{15} \exp(-30\,800/RT) \cdot [\mathrm{AIBN}]\ \text{mole/liter} \cdot \text{sec}\ [2]$$

$$w_i^{\mathrm{PC}} = e \cdot 10^{14\ 94} \exp(-28\,700/RT)\ [\mathrm{PC}]\ \text{mole/liter} \cdot \text{sec}\ [3]$$

where e = 0.9 in benzene [4], 1.35 in m-xylene, and 1.4 in ethylbenzene [3].

DISCUSSION OF RESULTS

We obtained kinetic curves for consumption of the polyenes in various solvents over a wide range of initial concentrations ($10^{-6}-10^{-3}$ mole/liter) and free-radical initiation rates ($10^{-8}-10^{-6}$ mole/liter · sec). Analysis of the kinetic equations for the consumption of the hydrocarbon during initiated oxidation, taking into account the elementary reactions of the primary initiator radicals ($I^\cdot$) and the hydrocarbon being oxidized in the steps of chain initiation, propagation, and termination [1], showed that the most suitable equations for determining the rate constants for reaction of the free radicals with the hydrocarbon are Eqs. (I) and (II), which are obeyed when $W_A \ll w_i$ and $W_A > w_i$ respectively

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