

Solvent Effects on the Products Formed in Some Alkylations of Tetrabutylammonium Salt

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We have recently demonstrated that some tetrabutylammonium salts are readily alkylated in a chloroform solution. In the isopropylation of acetylacetone,¹ oxygen and carbon alkylation occur to almost the same extent, and in the methylation of methyl cyanoacetate, both mono- and disubstituted C-alkylated products are obtained.² The purpose of the present study is to investigate the influence of the solvent on these reactions.

It has been suggested that the ion pair of an ambident anion can be C-alkylated by a concerted mechanism,³ whereas such a mechanism is usually not possible for the O-alkylation. An increased dissociation of the ion pair should thus disfavour the C-alkylation.

The dissociation of alkali salts of β -dicarbonyl compounds has been the subject of much confusion. Brändström³ has discussed the early literature up to 1953 and a calculation of the dissociation of some different alkali salts of ethyl acetoacetate in alcoholic solutions was performed by the same author in 1958.⁴ The degree of dissociation of salts of this type in the dipolar aprotic solvents has not been measured until recently.⁵ The sodium salt of ethyl α -acetobutyrate is thus dissociated to 40 % in DMSO and to 50 % in HMPA in a 0.05 M solution. The experimental facts available are too few to allow a rigid discussion, but it seems reasonable to expect for example that a 1 M solution of the tetrabutylammonium salt of acetylacetone is far from totally dissociated even in DMSO or HMPA.

It seems possible to predict, however, that a decreasing "polarity" of the solvent will decrease the dissociation and thus increase the C/O alkylation ratio. As a measure of the "polarity" both the dielectric constant ϵ and the solvating properties of the solvent should be taken into consideration. Tafts parameters P has been recommended for this purpose.^{6,7}

In agreement with this, the isopropylation of the tetrabutylammonium salt of acetylacetone seems to give C/O ratios that are increasing with a decrease in the "polarity" of the corresponding solvent (Table 1). Acetone might be an exception to this rule giving a lower C/O ratio than acetonitrile and chloroform which have a slightly higher P value than acetone. The important fact, however, is that toluene gives a very high C/O ratio. It is thus possible to change C/O ratio in this reaction from about unity in the polar solvents DMSO, acetonitrile, acetone and chloroform to more than 10 in toluene.

We have also studied the relative extent of mono- and dimethylation of the tetrabutylammonium salt of methyl cyanoacetate in different solvents. The results are presented in Table 2. As might be expected, no great differences could be found in the mono/disubstitution ratio. 1,2-Dimethoxyethane seems to give a little less disubstitution than the other solvents, however, and should therefore be used when disubstitution is an unwanted side-reaction.

In Table 1 it can be seen that some starting material was recovered in dioxane and toluene. This is probably an effect of an increase in propene formation by elimination of HI from the isopropyl iodide, since the importance of elimination usually increases with a decreasing "polarity" of the solvent.⁸ In Table 2 the amount of disubstitution and recovered starting material in some cases is not identical as stoichiometry demands. In the case when methyl acetate was used as a solvent the reason might be a complicated side-reaction which occurs on heating the tetrabutylammonium salt of methyl cyanoacetate in methyl acetate.

Isopropylation of acetylacetone. In 50 ml of the solvent 0.05 mol of the tetrabutylammonium salt of acetylacetone¹ was dissolved, and 0.10 mol of isopropyl iodide was added. The solution was warmed 30 min on a water bath, whereupon the solvent was evaporated. The crystalline residue of tetrabutylammonium iodide was washed with ether and filtered off. The ether solution was evaporated and the residue analyzed by NMR and VPC. For VPC analysis a 2 m \times 1/8" column packed with Carbowax 20 M (5 %) was used at 100°C.

Methylation of methyl cyanoacetate. To 50 ml of a solution containing 0.05 mol of the tetrabutylammonium salt of methyl cyanoacetate²

Table 1. Isopropylation of tetrabutylammonium acetylacetonate.

Solvent	P	ϵ	per cent C-alkyla- tion	per cent O-alkyla- tion	C/O	per cent starting material
DMSO	2.60	48.9	42	58	0.72	—
Acetone	1.95	20.5	42	58	0.72	—
Acetonitrile	2.30	37.5	48	52	0.92	—
Chloroform	2.30	4.8	51	49	1.04	—
Dioxane	1.25	2.2	63	33	1.91	4
Toluene	0.55	2.4	69	5	13.8	26

Table 2. Methylation of tetrabutylammonium methyl cyanoacetate.

Solvent	P	ϵ	per cent mono- alkylation	per cent di-alkyla- tion	mono/di	per cent starting material
1,2-Dichloroethane	2.20	10.0	42	31	1.38	27
Chlorobenzene	1.50	5.4	46	33	1.38	21
Dioxane	1.25	2.2	48	31	1.50	21
Methyl acetate	—	6.7	51	33	1.56	16
Acetonitrile	2.30	37.5	46	28	1.70	26
Chloroform	2.30	4.8	49	26	1.89	25
1,2-Dimethoxy- ethane	—	7.0	57	25	2.23	18

at 25°C 0.10 mol of methyl iodide was added. The temperature rose to about 45°C. After 10 min the solution was treated as described above and analyzed.

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