TABLE II

PICRATES OF ISOMERIC 2-IMINOTOLYL-3-TOLYL-4-*p*-HALOGEN-PHENYL-$\Delta^{4,5}$-THIAZOLINES

	Picrates of Δ^4-thiazoline	Appearance
1	2-Iminophenyl-3-phenyl-4-*p*-chlorophenyl-	Golden shimmering platelets
2	2-Iminophenyl-3-phenyl-4-*p*-bromophenyl-	Golden shimmering platelets
3	2-Imino-*o*-tolyl-3-*o*-tolyl-4-*p*-chlorophenyl-	Yellow cleavage-like crystals
4	2-Imino-*o*-tolyl-3-*o*-tolyl-4-*p*-bromophenyl-	Yellow brilliant aggregates
5	2-Imino-*p*-tolyl-3-*p*-tolyl-4-*p*-chlorophenyl-	Yellow brilliant needles
6	2-Imino-*p*-tolyl-3-*p*-tolyl-4-*p*-bromophenyl-	Yellow lustrous granules

			Analyses, salicyl sulfonic acid method			
	Formula	M. p., °C. (corr.)	Weight, g.	Cc. of 1 *N* HCl consumed	Nitrogen, % Found	Calcd.
1	$C_{27}H_{18}O_7N_5SCl$	206	0.1331	11.0	11.58	11.84
2	$C_{27}H_{18}O_7N_5SBr$	203	.1209	9.4	10.89	11.01
3	$C_{29}H_{22}O_7N_5SCl$	187	.1237	9.7	10.98	11.30
4	$C_{29}H_{22}O_7N_5SBr$	196	.1145	8.5	10.40	10.54
5	$C_{29}H_{22}O_7N_5SCl$	183	.1115	9.0	11.31	11.30
6	$C_{29}H_{22}O_7N_5SBr$	193	.1713	12.6	10.30	10.54

Summary

p-Chloro and *p*-bromo-ω-acetophenones have been condensed with diphenyl, di-*o*-tolyl and di-*p*-tolyl thioureas to yield 2-imino aryl-3-aryl-4-*p*-halogen-phenyl-Δ^4-thiazolines. The corresponding picrates have also been isolated and described.

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The Influence of a Quaternary Ammonium Group on the Hydrogen Atoms of an Adjacent Methylene Group

BY ARNOLD O. JACKSON AND C. S. MARVEL

It is a well-known fact that when two groups, such as carbonyl, cyano, sulfono, nitro and others of this type which are meta-directing in the benzene nucleus, are attached to a methylene group, the methylene group can be alkylated by the action of sodium ethylate and an alkyl halide. The quaternary ammonium salt group $-NR_3^+$ is also a meta-directing group in benzene and it seemed logical to expect that a molecule of the type represented in formula I would be easily alkylated. Such a reaction would be exceedingly useful in the synthesis of complex betaines.

$$[(CH_3)_3NCH_2COOC_2H_5]^+Cl^- \quad \text{I} \qquad [(CH_3)_3NCH_2COOC_2H_5]^+Br^- \quad \text{II}$$

$$[(CH_3)_3NCH_2CONH_2]^+Br^- \quad \text{III} \qquad [(CH_3)_3NCHCNCONH_2]^+Br^- \quad \text{IV}$$

Treatment of carbethoxymethyltrimethylammonium chloride (I) with sodium ethylate and ethyl bromide under the conditions usually used for the alkylation of such molecules as malonic or acetoacetic ester caused only an interchange of halogen with the formation of the bromide (II).

Under the same conditions carbethoxymethyltrimethylammonium bromide (II) could not be alkylated by the action of sodium ethylate and ethyl bromide. The quaternary ammonium salt was recovered unchanged from the reaction mixture. It is thus apparent that one carbonyl and one quaternary ammonium salt group attached to a $-CH_2-$ group will not activate it sufficiently to permit alkylation under the mild conditions used for typical active methylene compounds.

When cyanacetamidotrimethylammonium bromide (IV) was treated with sodium ethylate and an alkyl halide in boiling alcohol, the cyano group was removed and carbamylmethyltrimethylammonium bromide (III) was produced. Sodium ethylate in alcohol produced the same compound from cyanacetamidotrimethylammonium bromide. This removal of the cyano group is analogous to the conversion of tricarbethoxymethane to diethyl ethylmalonate by the action of sodium ethylate and ethyl bromide.[1] It also seems to be related to the cleavage of phenacylpyridinium salts by alkali which has recently been described by Fuson and Babcock.[2] The recovery of carbamylmethyltrimethylammonium bromide (III) in this experiment shows that it does not alkylate in the presence of sodium ethylate and an alkyl halide.

Experimental

Bromocyanacetamide.—To a solution of 21 g. of cyanacetamide in 500 cc. of glacial acetic acid, 40 g. of bromine was added dropwise. The solution was stirred during the bromination. The first half of the bromine was added at room temperature. Then the reaction mixture was placed in a water-bath and warmed slightly so that when all of the bromine had been added the temperature was about 40°. When the color due to bromine had disappeared, the solvent was removed under reduced pressure and the residue was recrystallized from water. The yield was 25 g. (61% of the theoretical amount) of a product of m. p. 176–177°.

Anal. Calcd. for $C_3H_3ON_2Br$: Br, 49.08. Found: Br, 48.86.

TABLE I

TRIMETHYLAMMONIUM HALIDE DERIVATIVES

Compound prepared	Halogen derivative used	Solvent for crystallization	Yield, %	M. p., °C.	Analyses, % Calcd.	Found
$[(CH_3)_3NCH_2COOC_2H_5]Cl$	$ClCH_2COOC_2H_5$	Alcohol and ether	72	166–167[a]	Cl, 19.56	19.31 19.63
$[(CH_3)_3NCH_2COOC_2H_5]Br$	$BrCH_2COOC_2H_5$	....	67	158–159	[b]	
$[(CH_3)_3NCH_2CONH_2]Br$	$BrCH_2CONH_2$	Abs. alcohol	86	203–204	C, 30.46	30.47
					H, 6.5	6.50
					N, 14.2	13.4
					Br, 40.61	40.9
$[(CH_3)_3NCH(CN)-CONH_2]Br$	$BrCH(CN)-CONH_2$	Abs. alcohol	77	199–200	Br, 36.03	36.04

[a] Koeppen, *Ber.*, **38,** 167 (1905), reports the product as melting at 143–144°.

[b] Characterized previously by Hunt and Renshaw, *J. Pharmacol.*, **25,** 319 (1925).

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(1) Michael, *Am. Chem. J.*, **14**, 500 (1892).

(2) Babcock and Fuson, THIS JOURNAL, **55**, 2946 (1933).

Quaternary Ammonium Salt.—The quaternary ammonium salts were prepared in the usual fashion from the halogen derivatives and alcoholic trimethylamine solution. The properties are recorded in Table I.

Alkylation Experiments.—To a solution of 0.45 g. of sodium in 75 cc. of absolute alcohol was added 3.6 g. of carbethoxymethyltrimethylammonium chloride in 50 cc. of alcohol and 2.5 cc. of ethyl bromide. The reaction mixture was boiled under a reflux condenser for about ten hours. The reaction mixture was cooled to room temperature and filtered to remove inorganic salts. The solution was concentrated to about 40 cc. under reduced pressure and on cooling a small amount of a compound melting at 294–295° was obtained. This compound (A) was not the desired ethylated derivative and it contained bromine. The analysis did not give a clue to its identity.

Anal. Found: Br, 23.62, 23.53; N, 8.38.

The mother liquors from compound (A) were diluted with dry ether. In this manner a second bromine-containing compound, m. p. 158–160°, was obtained. This material was shown to be carbethoxymethyltrimethylammonium bromide by analysis and by taking a mixed melting point with an authentic specimen of this bromide.

In a similar manner carbethoxymethyltrimethylammonium bromide was treated with sodium ethylate and ethyl bromide. A small amount of the compound melting at 294–295° was obtained but most of the starting material was recovered unchanged.

To a solution of 0.4 g. of sodium in 150 cc. of absolute alcohol was added 4 g. of cyanacetamidotrimethylammonium bromide. This solution was refluxed with ethyl bromide and then worked up as described in the preceding alkylation experiments. The product obtained melted at 204–205° and by analysis and mixed melting point determinations it was identified as carbamylmethyltrimethylammonium bromide. The same product was obtained in 90% yield by treating cyanacetamidotrimethylammonium bromide with alcoholic sodium ethylate.

Summary

Treatment of the compounds $[(CH_3)_3NCH_2COOC_2H_5]^+Cl^-$ and $[(CH_3)_3NCH_2COOC_2H_5]^+Br^-$ with sodium alcoholate and ethyl bromide did not effect alkylation of the $—CH_2—$ group. Cyanacetamidotrimethylammonium bromide was converted to carbamylmethyltrimethylammonium bromide by the action of hot alcoholic sodium ethylate.

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