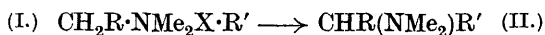


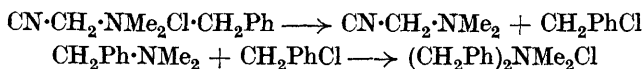
CCLXXI.—*Degradation of Quaternary Ammonium Salts.*
Part III.

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THE quaternary salts whose rearrangement is described in Parts I and II (J., 1928, 3193; preceding paper) all contain a phenacyl radical (I \longrightarrow II; R = COPh). It is now shown that the replacement of the phenacyl group by acetylonyl does not prevent the reaction: thus *acetylonylbenzyl-dimethylammonium chloride* (I; R = COMe, R' = CH₂Ph) yields with alkali α -dimethylamino- α -benzylacetone (II; R = COMe, R' = CH₂Ph). A similar change could not be brought about with *cyanomethyl-* or *carbethoxymethyl-benzyl-dimethylammonium* salts (I; R = CN or CO₂Et, R' = CH₂Ph). The nitrile group of the former compound was rapidly hydrolysed by aqueous alkali, and when sodium ethoxide was employed, complete exclusion of water was rendered difficult by the fact that the only salt which could be obtained crystalline was the *picrate*, which could not be degraded directly, owing to the oxidising action of picric acid in alkaline media. Moreover, the expected product, α -dimethylamino- β -phenylpropionitrile (II, R = CN, R' = CH₂Ph), is readily decomposed to phenylacetaldehyde, but this also did not appear to be formed in any experiment.

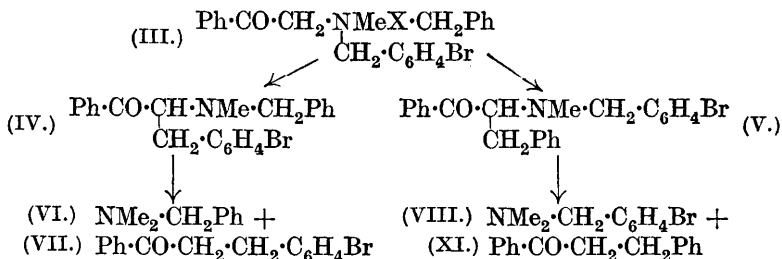


Attempts to prepare cyanomethylbenzyl-dimethylammonium chloride from chloroacetonitrile and benzyl-dimethylamine in *hot* benzene yielded dibenzyl-dimethylammonium chloride, probably owing to a dissociation and combination of the type discovered by Wedekind (*Ber.*, 1902, 35, 767):



Further, *phenacyl-p-bromo-* and *-p-nitro-benzyl*dimethylammonium salts were investigated (I; R = COPh, R' = CH₂·C₆H₄Br or CH₂·C₆H₄·NO₂). The former readily yielded *ω-dimethylamino-ω-p-bromobenzylacetophenone* (II; R = COPh, R' = CH₂·C₆H₄Br), but the latter underwent considerable decomposition, and gave, in addition to *ω-dimethylamino-ω-p-nitrobenzylacetophenone* (II; R = COPh, R' = CH₂·C₆H₄·NO₂), *p*-nitrotoluene and *pp'*-dinitrodibenzyl. The formation of nitrotoluenes by the action of alkalis on simple nitrobenzylammonium salts was noticed by Ing and Robinson (J., 1926, 1667, 1668), and is of interest in connexion with Fenton and Ingold's explanation of the paraffinic decomposition of "onium" salts (J., 1929, 2343).

In order to investigate the relative ease of migration of substituted benzyl groups in this reaction, it was proposed to prepare the salt (III) and to determine the proportion in which the two possible products of its rearrangement are formed, by analysing the mixed product (IV and V) by methylation and reduction, followed by determination of the distribution of bromine between the basic (VI and VIII) and the neutral (VII and IX) products. This salt,



however, could not be prepared, for when phenacylbenzylmethylamine (from benzylmethylamine and *ω*-bromoacetophenone) was treated with *p*-bromobenzyl bromide under a variety of conditions, only gummy materials, insoluble in water, were produced. *Benzyl-p-bromobenzylmethylamine* (from benzylmethylamine and *p*-bromobenzyl bromide) and *ω*-bromoacetophenone behaved similarly. There would therefore appear to be some specific obstacle to the formation of the required salt, irrespective of the order of introduction of the organic radicals. Possibly the formation of such complicated quaternary salts is hindered sterically; tribenzylamine, for example, does not combine with benzyl chloride (Marquardt, *Ber.*, 1886, 19, 1030).

EXPERIMENTAL.

*Acetylbenzyl*dimethylammonium Chloride.—This salt, prepared from chloroacetone and benzyl dimethylamine in benzene solution,

was obtained as an oil which crystallised very reluctantly. It formed stout plates from alcohol-ether, m. p. 75—77°, containing 1 mol. of water of crystallisation (Found: Cl, 14.4. $C_{12}H_{18}ONCl \cdot H_2O$ requires Cl, 14.5%). The *picrate* crystallised from methyl alcohol in irregular dark yellow prisms, m. p. 141—143° (Found: $C_6H_2O_7N_3'$, 54.0. $C_{18}H_{20}O_8N_4$ requires $C_6H_2O_7N_3'$, 54.3%).

α -Dimethylamino- α -benzylacetone.—The above quaternary chloride was heated on the water-bath with *N*-sodium hydroxide solution. Some tar was produced, and the aminoketone distilled in steam as an unpleasant-smelling oil, which was taken up in acetic acid and treated with aqueous picric acid. *α -Dimethylamino- α -benzylacetone picrate* formed stout yellow needles from alcohol, m. p. 140—144° (Found: C, 51.2; H, 5.0. $C_{12}H_{17}ON, C_6H_3O_7N_3$ requires C, 51.4; H, 4.8%). To confirm the structure assigned to the base, the methosulphate, prepared in benzene, was reduced with zinc dust and dilute sulphuric acid, and the resulting benzylacetone identified as the semicarbazone (m. p. and mixed m. p. 142°).

Carboxymethylbenzyltrimethylammonium Chloride.—The combination of ethyl chloroacetate and benzyltrimethylamine in benzene or in acetone-ether gave hard, colourless nodules, which were hygroscopic, and melted at 176° (decomp.) (Found: Cl, 13.8. $C_{13}H_{20}O_2NCl$ requires Cl, 13.8%). The *picrate* formed a micro-crystalline powder, m. p. 126—128°. When the *chloride* was heated with sodium hydroxide solution, no oily base was produced, and the only product isolable on neutralisation and treatment with picric acid was identical with that obtained from the original quaternary salt by acid hydrolysis; it was therefore *carboxymethylbenzyltrimethylammonium picrate*. This salt separated most readily from solutions containing a trace of mineral acid, and crystallised from aqueous methyl alcohol in bright yellow needles, m. p. 146—148° [Found by titration: *M*, 429. $C_{17}H_{18}O_9N_4$ (monobasic) requires *M*, 422]. In another experiment, the quaternary chloride was heated with a solution of sodium in anhydrous alcohol, but after hydrolysis the greater part of the material was recovered as the *picrate* just mentioned, and no other product could be detected.

Cyanomethylbenzyltrimethylammonium Salts.—When chloroacetonitrile and benzyltrimethylamine were refluxed in benzene solution, an oily salt was obtained which yielded a *picrate*, m. p. 144—146°, identical with dibenzyltrimethylammonium *picrate*, prepared from benzyltrimethylamine and benzyl chloride (compare Baker and Ingold, J., 1926, 2462). On the other hand, when the components were allowed to react in cold, anhydrous ether, a colourless, viscous gum separated, which could not be induced to

crystallise. The corresponding *picrate* formed stout, bright yellow needles, m. p. 140—143° (Found : $C_6H_2O_7N_3'$, 56·2. $C_{17}H_{17}O_7N_5$ requires $C_6H_2O_7N_3'$, 56·6%). The chloride was rapidly hydrolysed by 0·25% sodium hydroxide solution, yielding carboxymethylbenzyl-dimethylammonium hydroxide, isolated as *picrate*. Even when the reaction was carried out in a current of steam, neither α -dimethylamino- β -phenylacetonitrile nor phenylacetaldehyde could be detected in the distillate. To avoid this hydrolysis, the *picrate* was dissolved in absolute alcohol, the *picrate* radical precipitated by nitron sulphate, and the filtrate heated with sodium ethoxide, but no evidence of rearrangement was obtained.

p-Bromobenzyl-dimethylamine.—*p*-Bromobenzyl bromide was conveniently prepared by brominating *p*-bromotoluene with undiluted bromine; the reaction, which set in spontaneously, was completed by heating under reflux, and the product isolated by distillation in a vacuum and recrystallisation from alcohol. Conversion into the tertiary base by the hexamine method (Sommelet and Guioth, *Compt. rend.*, 1922, 174, 687) gave only a moderate yield, together with a considerable quantity of *p*-bromobenzaldehyde (m. p. and mixed m. p. 57°). Better results were obtained by treating *p*-bromobenzyl bromide with dimethylamine (2—3 mols.) in alcoholic solution. After remaining for 12 hours, the mixture was heated for 2 hours on the water-bath, concentrated, diluted with water, and extracted with benzene. On treatment with picric acid, the benzene layer yielded *p*-bromobenzyl-dimethylamine *picrate* (minute, bright yellow prisms, m. p. 133—135°, from benzene), together with a little of the *picrate* of the quaternary base, most of which remained in the aqueous layer. *p*-Bromobenzyl-dimethylamine hydrochloride forms white microcrystals from alcohol-ether, m. p. 219—220° (Found : Cl, 14·1. $C_9H_{13}NClBr$ requires Cl, 14·2%). *Di-p*-bromobenzyl-dimethylammonium *picrate* forms stout, deep yellow prisms, m. p. 165—167°, which are scarcely soluble in benzene (Found : Br, 26·2. $C_{22}H_{20}O_7N_4Br_2$ requires Br, 26·1%).

Phenacyl-p-bromobenzyl-dimethylammonium bromide, prepared from *p*-bromobenzyl-dimethylamine and ω -bromoacetophenone in hot benzene solution, crystallised from alcohol-ether in minute laminae, m. p. 193° (Found : ionisable Br, 19·5. $C_{17}H_{19}ONBr\cdot Br$ requires Br, 19·4%).

ω -Dimethylamino- ω -*p*-bromobenzylacetophenone.—The foregoing bromide was heated on the water-bath for an hour with excess of 2*N*-sodium hydroxide solution, and the product recrystallised from methyl alcohol, giving colourless needles, m. p. 61°, which slowly resinified on keeping (Found : Br, 24·0. $C_{17}H_{18}ONBr$ requires Br, 24·1%). The *picrate* formed dark yellow nodules from methyl

alcohol, m. p. 149—150°. When the methosulphate, prepared in benzene solution, was boiled with dilute alkali, phenyl *p*-bromostyryl ketone was produced, and this separated from alcohol in colourless needles or plates, m. p. 124°, which did not depress the m. p. of a specimen prepared from *p*-bromobenzaldehyde and acetophenone. Weygand (*Annalen*, 1927, 459, 118) describes the substance as forming yellowish crystals, m. p. 123·5°.

Phenacyl-p-nitrobenzyltrimethylammonium bromide, prepared from *p*-nitrobenzyltrimethylamine (Goss and Ingold, J., 1926, 2459) and ω -bromoacetophenone in hot benzene, forms cubes, m. p. 169—171°, from alcohol-ether, and is rather sparingly soluble in cold water (Found: Br, 20·7. $C_{17}H_{19}O_3N_2Br$ requires Br, 21·1%).

ω -Dimethylamino- ω -p-nitrobenzylacetophenone.—The above salt was heated on the water-bath for 7 minutes with an excess of *N*-sodium hydroxide solution. A dark red gum rapidly separated, alkaline vapours were evolved, and the odour of *p*-nitrotoluene was readily perceptible. The cooled mixture was extracted with ether, which dissolved almost all the gum, and the basic products were extracted from the ether by very dilute hydrochloric acid (A). On concentration, the ethereal solution deposited yellow needles of *pp'*-dinitrodibenzyl, m. p. 181°, not depressed by admixture with a specimen prepared by the method of Green, Davies, and Horsfall (J., 1907, 91, 2079). By evaporation of the ethereal mother-liquors, and distillation of the residue in steam, *p*-nitrotoluene was isolated, m. p. and mixed m. p. 52—54°. The possibility that the dinitrodibenzyl might be a secondary product resulting from atmospheric oxidation of *p*-nitrotoluene under the influence of the alkaline medium was excluded by heating that substance with *N*-sodium hydroxide solution for 2 hours in an open vessel on the water-bath, no dinitrodibenzyl being produced.

The hydrochloric acid extract (A) yielded, on basification with ammonia, about 60% of the theoretical quantity of *ω -dimethylamino- ω -p-nitrobenzylacetophenone*, which crystallised from methyl alcohol in light yellow prisms, m. p. 79—82° (Found: C, 68·0; H, 6·2. $C_{17}H_{18}O_3N_2$ requires C, 68·4; H, 6·0%). When stronger alkali or more prolonged heating was used in the degradation, the yield of base was diminished, and phenyl *p*-nitrostyryl ketone (m. p. 165°; semicarbazone, m. p. 178—179°) was produced in quantity. The dimethylamino-picrate separated from methyl alcohol in clusters of yellow prisms, m. p. 144—145°. The methosulphate, prepared in warm benzene, appeared to be fairly stable in the absence of alkali; addition of potassium hydroxide solution caused immediate decomposition and production of phenyl *p*-nitrostyryl ketone (m. p. and mixed m. p. 164°). It may be recalled that

Hanhart and Ingold obtained *p*-nitrostyrene, but no quaternary salt, by the action of β -phenylethyl chloride on β -*p*-nitrophenylethyldimethylamine (J., 1927, 1008).

In order to establish the constitutions of dimethylamino-*p*-nitro- and -*p*-bromo-benzylacetophenones, attempts were made to prepare them from dimethylaminobenzylacetophenone of known constitution (Part I, p. 3194) by nitration and bromination respectively, but in each case the initial material was either recovered unchanged, or, under more drastic conditions, completely destroyed. On careful reduction with stannous chloride, or with zinc and acetic acid, the nitro-compound yielded a diazotisable amine. This substance was difficult to obtain pure in reasonable quantity, and the replacement of the amino-group by bromine or hydrogen could not be effected.

Benzylmethylamine.—The following method (compare Zauschirm, *Annalen*, 1888, 245, 282; Fischer, *Ber.*, 1886, 19, 748) gave an over-all yield of above 40%. A slight excess of benzaldehyde was added to methyl-alcoholic methylamine (8%, from the hydrochloride and sodium methoxide). After 12 hours, the solvent was distilled off through a column, the residue diluted with water, and the product extracted with ether, dried, and distilled (b. p. 178—182°). The crude material, in 25 parts of absolute ethyl alcohol, was stirred and reduced in the cold with twice the theoretical quantity of sodium amalgam. Most of the alcohol was then distilled (column), the residue acidified, extracted with ether to remove neutral products, made strongly alkaline, and the base isolated in the usual manner.

Phenacylbenzylmethylamine.— ω -Bromoacetophenone (1 mol.), dissolved in ether, was added to benzylmethylamine (2 mols.) in the same solvent; the reaction proceeded rapidly, and after 12 hours the separated benzylmethylamine hydrobromide was collected, and the tertiary base extracted from the ethereal solution by acid. It is an oil, b. p. 195—205°/15 mm.; the *picrate* formed yellow crystals from alcohol, m. p. 137—138° (Found: C, 56.2; H, 4.5. $C_{16}H_{17}ON, C_6H_3O_7N_3$ requires C, 56.4; H, 4.3%). The methobromide, prepared *via* the methosulphate, is identical (mixed m. p.) with benzyldimethylamine phenacylobromide (Part I, p. 3196).

Many attempts were made to combine the base with *p*-bromobenzyl bromide, in various solvents, at different temperatures, and for various periods of heating. An oil which separated showed no tendency to form a *picrate* under a variety of conditions.

Benzyl-p-bromobenzylmethylamine.—This *base*, prepared in the same way as phenacylbenzylmethylamine, was obtained as an oil, b. p. 194—196°/20 mm. (Found: Br, 27.9. $C_{15}H_{16}NBr$ requires

Br, 27.6%). The picrate and hydrochloride showed no tendency to crystallise, and the phenacylbromide could not be prepared.

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