370. *The Fission of Aryltrimethylammonium Chlorides in Aqueous Solution by Means of Sodium Amalgam.*

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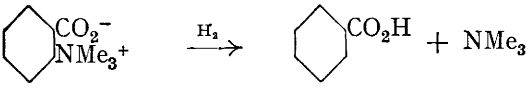
There are relatively few recorded observations of the reductive fission of quaternary salts derived from aromatic amines, although a wide range of structures has been examined in connexion with the development of Emde's useful alternative to exhaustive methylation of cyclic bases (compare a survey by Emde and Küll, *Arch. Pharm.*, 1934, **272**, 469). Willstätter and Khan (*Ber.*, 1904, **37**, 1859) showed that benzbetaines, for example, *o*-benzbetaine, are readily reduced by sodium amalgam in aqueous solution, furnishing benzoic acid and trimethylamine :



Later, Emde (*Arch. Pharm.*, 1909, **247**, 385) found that phenyltrimethylammonium iodide was for the most part unchanged by sodium amalgam in neutral solution ; some dimethylaniline, but no trimethylamine, was formed. Fichter (*Helv. Chim. Acta*, 1933, **17**, 571) obtained similar results with lead amalgam ; Emmert (*Ber.*, 1909, **42**, 1507, 1997) had, however, shown that the quaternary iodide yields benzene and trimethylamine when reduced at a lead cathode.

We have found that the aryltrimethylammonium chlorides can be reduced by means of *clean* sodium amalgam, provided that a sufficient excess of the reagent is employed (we have used 12 times the theoretical amount). Great care has been taken to ensure purity of the salts reduced and the standard method involved carrying the reaction out at 95—100° and estimation of the trimethylamine and primary aromatic amine produced.

One comparison of the different salts employed could be made, approximately, on the basis of the percentage of salt decomposed under standard conditions. A second comparison is concerned with the direction of fission, either to tertiary aromatic amine and methane or to aromatic hydrocarbon (or substituted hydrocarbon) and trimethylamine. The salts studied and the results were the following, calculated on the assumption that the percentage of reacting molecules yielding aromatic tertiary base is 100 minus the figure in the second column :

Salt reduced.	% Salt decomposed.	% Reacting molecules yielding trimethylamine.
Phenyltrimethylammonium chloride	44—46	71·1
o-Tolyl ,, ,,	88—90	62·9
m-Tolyl ,, ,,	61—63	60·1
p-Tolyl ,, ,,	27—30	30·8
o-Anisyl ,, ,,	34—37	88·6
m-Anisyl ,, ,,	62·5—65·5	64
p-Anisyl ,, ,,	65—68	20·2
3-Diphenylyl ,, ,,	89—91	92·5
4-Diphenylyl ,, ,,	93·5—96	85·8
β-Naphthyl ,, ,,	90—91	94·7

The ready fission of the salts derived from diphenyl and from naphthalene and the high yield of trimethylamine obtained in these cases point to the fact that increased unsaturation of the aryl group facilitates the reaction by increasing the rate of fission between the nitrogen atom and the aromatic nucleus.

It is, however, extremely difficult to generalise on the basis of these results, which evidently represent the combined operation of several factors.

EXPERIMENTAL.

Phenyltrimethylammonium Chloride.—Dimethylaniline and methyl sulphate combined in dry benzene solution with evolution of heat and the crude solid methosulphate (yield, 90%) crystallised from acetone in long stout needles, m. p. 126° (Vorländer and Siebert, *Ber.*, 1919, **52**, 284, give m. p. 71—92°, apparently for a crude product). The related *picrate* crystallised from ethyl alcohol in stout yellow needles, m. p. 123—124° (large depression on admixture with picric acid) (Found : C, 49·6; H, 4·4; N, 15·9. $C_{15}H_{16}O_7N_4$ requires C, 49·5; H, 4·4; N, 15·4%). The pure picrate was dissolved in methyl-alcoholic hydrogen chloride, and the *chloride* precipitated by means of ether as a liquid which solidified over phosphoric oxide in a desiccator. Careful repetitions of the process gave crystalline precipitates and ultimately a white crystalline material, m. p. 220° (decomp.), free from picric acid, very hygroscopic, and readily soluble in water and the simple alcohols, was obtained (Found in material dried at 110° in a high vacuum : C, 62·5; H, 8·1; N, 7·9; Cl, 20·4. $C_{19}H_{14}NCl$ requires C, 63·0; H, 8·2; N, 8·2; Cl, 20·7%).

Reduction of Phenyltrimethylammonium Chloride.—The reductions were carried out in a distilling flask, heated on the steam-bath, and in a current of carbon dioxide (the reaction of the solution was usually on the alkaline side); the side tube of the flask was inclined upwards and water-jacketed to act as a reflux condenser and the gases were then passed through known volumes of standard hydrochloric acid contained in two flasks connected in series : the trimethylamine collected by the acid and the dimethylaniline remaining in the flask were estimated.

In this case the dried salt (3 g.) was dissolved in water (60 c.c.) and reduced by the gradual addition of sodium amalgam (450 g. of 1%) (compare "Organic Syntheses," VIII, 89) through a tap funnel during 4·5—5 hours. The reduction was continued for 6 hours after the amalgam had been introduced.

The base remaining in the flask was identified as dimethylaniline (picrate, m. p. 163°; platinichloride, m. p. 171—172°) and it was free from monomethylaniline as shown by attempted fractionation of the platinichloride, which proved to be homogeneous (compare Emde, *Arch. Pharm.*, 1909, **247**, 77). The volatile base collected in the hydrochloric acid (100 c.c. of *N*/10) was proved to be pure trimethylamine (hydrochloride, m. p. 274°; picrate, m. p. 216°; platinichloride, m. p. 240—245°, all with decomp.). The trimethylamine was estimated by titration

(Found : yield of NMe_3, based, as in all figures quoted in the experimental section, on the percentage of the theoretical yield from the amount of quaternary salt employed, *not* from the salt undergoing change, 33·3, 32·6, 30·3, 30·9, 29·5%).

The liquid remaining in the flask was acidified with hydrochloric acid, the solution evaporated to dryness, the *dry* residue extracted with *absolute* alcohol, and the solvent removed. The content of dimethylaniline in this residue was determined by titration with a solution of *p*-nitrobenzenediazonium chloride prepared as described by Bucherer (*Z. angew. Chem.*, 1907, **20**, 877) and standardised by means of a solution of pure dimethylaniline (1·62 g. in 100 c.c.) in dilute hydrochloric acid (Found : yield of $NPhMe_2$, 12·8, 12·2, 14·0%). It should be noted that the variations in the yields affect chiefly the value for the percentage of salt decomposed; the ratio of fission in the two possible directions was found to be much more constant. In some of the examples mentioned below, the aromatic *tert.*-base and the neutral product were together isolated by means of ether and the base was separated by washing the ethereal solution with dilute hydrochloric acid.

In some cases the unchanged quaternary salt was recovered and the total products accounted for by actual isolation amounted to 94% of the theoretical, sometimes more, and never less than 90%.

o-*Tolyltrimethylammonium Chloride.*—*o*-Toluidine was methylated by vigorously stirring a mixture with methyl sulphate and aqueous sodium hydroxide on the steam-bath, with addition of the reagents when necessary, until a test portion gave no separation of a base on the addition of an excess of sodium hydroxide. The precipitation of the picrate from this solution (which succeeds in many similar cases) is not very satisfactory owing to the difficulty of methylation of *o*-toluidine and the necessary accumulation of sodium salts causing sodium picrate to separate.

Eventually *o*-toluidine (1 mol.) was heated with methyl sulphate (1·75 mols.) at 135—140° for 4 hours and the *N*-dimethyl-*o*-toluidine, b. p. 183—184°, isolated (yield, 35—45%). This base was combined with methyl sulphate, and the product methylated as first described : in this way full methylation is possible without addition of too large an excess of sodium hydroxide.

The picrate precipitated from the acidified solution crystallised from alcohol in needles, m. p. 112·5—113° (compare Vorländer, *Ber.*, 1919, **52**, 598) (Found : C, 50·6; H, 4·8; N, 15·0. Calc. for $C_{16}H_{18}O_7N_4$: C, 50·8; H, 4·8; N, 14·8%). The picrate was not found to be a suitable salt from which to obtain the *chloride* and it was necessary to prepare the pure iodide (von Braun, *Ber.*, 1916, **49**, 1107) and treat this in aqueous solution with silver chloride. The filtered solution was evaporated to dryness; the viscous residue crystallised in a desiccator and then separated in long needles on careful addition of dry ether to a solution in absolute methyl alcohol (Found in anhydrous material : C, 64·9; H, 8·7; N, 7·6. $C_{10}H_{16}NCl$ requires C, 64·7; H, 8·6; N, 7·6%). This salt is hygroscopic and readily soluble in water and the simple alcohols.

Reduction. The chloride was reduced as described for the lower homologue and the *tert.*-base produced was identified as dimethyl-*o*-toluidine (picrate, m. p. 124—125°). The trimethylamine was estimated as before (yield of NMe_3, 56·1, 56·0, 57·7%), but the aromatic *tert.*-base could not be estimated by coupling with a diazonium salt and recourse was had to a bromination method. This was carried out in dilute hydrochloric acid solution at 0° and the potassium bromate solution employed was standardised by means of the pure dimethyl-*o*-toluidine (Found : bromine used by 1 g.-mol. of the base, 165, 164, 169 g. Theory, 160 g.) (Found : yield of $C_6H_4Me{\cdot}NMe_2$, 32·6, 34·7, 33·0%).

m-*Tolyltrimethylammonium Chloride.*—*m*-Toluidine, prepared from aceto-*p*-toluidide by nitration and the known series of reactions, was readily methylated by the methyl sulphate–aqueous sodium hydroxide method. The *picrate* precipitated after acidification crystallised from alcohol in light yellow needles or short rods, m. p. 108° (Found : C, 50·8; H, 4·8; N, 14·8%). The *chloride* was obtained by repeated precipitation from a solution in methyl-alcoholic hydrogen chloride by ether, at first as an oil and later as a solid. It is somewhat less hygroscopic than the isomeric salts and the slender needles have m. p. 180—185° (decomp.) (Found : C, 64·7; H, 8·5; N, 7·6%).

Reduction. This was carried out as usual, and the aromatic *tert.*-base produced identified as *N*-dimethyl-*m*-toluidine (picrate, m. p. 130°, alone or mixed with an authentic specimen); the hydrocarbon product was toluene (the formation of hydrocarbons, benzene, toluene, etc., and also anisole in the appropriate cases was always observed but is not recorded in each example). The trimethylamine was estimated as usual, and the aromatic *tert.*-base by the diazo-coupling method (Found : yield of NMe_3, 37·5, 37·1, 36·5% ; yield of $C_6H_4Me{\cdot}NMe_2$, 25·0, 24·8, 24·9%).

p-*Tolyltrimethylammonium Chloride.*—Methyl sulphate and sodium hydroxide were used to trimethylate *p*-toluidine and the *picrate* was precipitated in 69% yield. The derivative crystallised from ethyl alcohol in yellow needles, m. p. 193—198° (Found : C, 50·9; H, 4·9; N, 14·8%). The *chloride*, obtained as usual, is very hygroscopic (Found : C, 64·2; H, 8·5; N, 7·8%).

Reduction. The process was not varied; the aromatic *tert.*-base produced was *N*-dimethyl-*p*-toluidine [picrate, m. p. 130°; platinichloride, m. p. 168—174° (decomp.); methiodide, characteristic plates, m. p. 218—220° (subl.)]. This base was estimated by bromination (we consider that the yields given in the literature for the formation of the dimethyltoluidines by the direct action of methyl sulphate on the primary bases are overstated; in spite of careful work we achieved consistently only about one-half of the amount claimed) (Found : yield of NMe_3, 8·8, 8·5, 8·8, 9·3%; yield of $C_6H_4Me{\cdot}NMe_2$, 20·1, 21·0, 18·5%). Large amounts of unchanged quaternary chloride were recoverable.

o-*Methoxyphenyltrimethylammonium Chloride.*—Although *o*-anisidine is an *o*-substituted aniline, it could be fully methylated by means of methyl sulphate and aqueous sodium hydroxide at 100°. The *picrate* was precipitated from the acidified resulting solution in 78% yield; the light yellow flakes that separated from alcoholic solution had m. p. 125° (Found : C, 48·6; H, 4·7; N, 14·2. $C_{16}H_{18}O_8N_4$ requires C, 48·7; H, 4·5; N, 14·2%). The *chloride* separated in well-formed needles when a solution of the picrate in methyl-alcoholic hydrogen chloride was mixed with ether; it was recrystallised in the same way, m. p. 140° (decomp.) (Found in anhydrous material: C, 59·5; H, 8·0; N, 6·7. $C_{10}H_{16}ONCl$ requires C, 59·5; H, 8·0; N, 7·0%).

Reduction. The standard method was employed, and the aromatic *tert.*-base determined by diazo-coupling (Found : yield of NMe_3, 31·6, 30·2, 31·0%; yield of $MeO{\cdot}C_6H_4{\cdot}NMe_2$, 3—5%). The method in this case was rather unsatisfactory and bromination was still less reliable; however, it is certain that the amount of dimethyl-*o*-anisidine formed is very small.

m-*Methoxyphenyltrimethylammonium Chloride.*—*m*-Anisidine was readily methylated by means of methyl sulphate and aqueous sodium hydroxide, and the *picrate* was precipitated from the resulting solution as a paste which changed into large needles (yield, 94%). It crystallised from alcohol in light yellow needles, m. p. 132·5—133·5° (Found : C, 49·1; H, 4·7; N, 14·0%). The readily soluble and hygroscopic *chloride* crystallised from ether–alcoholic hydrogen chloride in needles, which began to melt and decompose at 195° (Found in anhydrous material : C, 59·6; H, 7·9; N, 6·9%).

Reduction. Under the standard conditions, anisole, *N*-dimethyl-*m*-anisidine, and trimethylamine were recognised as products of the reaction (Found : yield of NMe_3, 41·3, 40·1, 42·8, 41·8%; yield of $MeO{\cdot}C_6H_4{\cdot}NMe_2$ by diazo-coupling, 24·1, 22·3, 23·0%).

p-*Methoxyphenyltrimethylammonium Chloride.*—The *picrate* was obtained like the *m*-isomeride (yield, 80%), orange needles, m. p. 176—177° (Found : C, 48·7; H, 4·6; N, 14·3%). The *chloride* is freely soluble in water and the simple alcohols; it crystallises from ether–methyl-alcoholic hydrogen chloride in colourless needles which begin to melt and decompose above 200° (Found in anhydrous material : C, 59·2; H, 7·9; N, 7·0%).

Reduction. Anisole, trimethylamine, and *N*-dimethyl-*p*-anisidine, m. p. 49°, were recognised products of the standard process (Found : yield of NMe_3, 12·7, 14·0, 13·4, 12·9%; yield of $MeO{\cdot}C_6H_4{\cdot}NMe_2$ by diazo-coupling with *p*-nitrobenzenediazonium chloride with the use of salt and an end-point compared with that obtained with the pure synthetic base, 54·1, 52·3, 53·1%).

3-*Diphenylyltrimethylammonium Chloride.*—3-Aminodiphenyl was prepared by Fichter's method (*Ber.*, 1904, **37**, 883) and methylated by means of an excess of methyl sulphate and aqueous sodium hydroxide on the steam-bath. The *picrate* (yield, 74%) crystallised from hot water or alcohol in yellow leaflets, m. p. 166—167° (Found : C, 57·4; H, 4·9; N, 12·8. $C_{21}H_{20}O_7N_4$ requires C, 57·3; H, 4·5; N, 12·7%). The *chloride*, obtained in the usual way, crystallised in colourless plates, m. p. above 200° (decomp.) and although readily soluble in water and alcohol it was not markedly hygroscopic (Found in anhydrous material : C, 73·0; H, 7·3; N, 5·4. $C_{15}H_{18}NCl$ requires C, 72·7; H, 7·4; N, 5·6%).

Reduction. As the reduction proceeded very readily, the sodium amalgam employed was 75% of that used in the preceding cases. Actually, one-half of that amount suffices to bring about a completed reaction. It should also be noted that in this and the other cases the quaternary salt employed was proved to be stable towards hot dilute sodium hydroxide solution (3 g., heated at 100° with 50 c.c. of 8% solution, remained unchanged after 8 hours).

Diphenyl was proved to be the main product of the reaction, and the small amount of aromatic *tert.*-base formed had the properties of 3-dimethylaminodiphenyl (see below) (Found : yield of NMe_3, 82·9, 83·4, 83·9%; yield of $Ph{\cdot}C_6H_4{\cdot}NMe_2$ by diazo-coupling, 6·5, 7·5, 6·3%).

3-*Dimethylaminodiphenyl.*—(A) A vigorously stirred aqueous suspension of 3-aminodiphenyl (1 mol.) and methyl sulphate (2 mols.) was heated on the steam-bath for 1 hour, and the *base* isolated, b. p. 171—173°/12 mm. (Found : C, 85·5; H, 7·5; N, 7·2. $C_{14}H_{15}N$ requires C, 85·3; H, 7·6; N, 7·1%). The pale yellow, viscous oil exhibits a violet fluorescence; it is a weak base and its hydrochloride is partly decomposed on dilution of the aqueous solution. The methiodide crystallises from water in elongated plates, m. p. 182—183°, and affords the above-described quaternary picrate, m. p. 167°, on treatment with aqueous picric acid.

(B) The quaternary chloride, or the iodide, m. p. 182° (prepared in 90% yield by addition of potassium iodide to the methylation product of 3-aminodiphenyl), was boiled with *iso*amyl alcohol containing sodium hydroxide; the *tert.*-base can then be isolated in good yield (10 g. of the chloride gave 6·5 g.), b. p. 171—173°/12 mm.

6-*Nitroso*-3-*dimethylaminodiphenyl.*—A solution of sodium nitrite (5·5 g.) was added to one of 3-dimethylaminodiphenyl (14 g.) in concentrated hydrochloric acid (23 c.c.) and water (100 c.c.) cooled in a freezing mixture and well stirred. After about 30 minutes the hydrochloride of the nitroso-compound, which filled the liquid, was collected (14 g.); it crystallised from water in slender yellow needles, m. p. 218—220° (decomp.). The free *nitroso-base* was obtained as a green precipitate and collected by means of chloroform; it crystallised from aqueous acetone (1 : 1) in clusters of flat pointed needles, m. p. 121—122° (Found : C, 74·1; H, 6·4; N, 12·4. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2; N, 12·4%). The substance dissolves in ether and other neutral solvents to deep green solutions, and on evaporation of an ethereal solution it separates as green cubes. It is readily soluble in alcohol and may be crystallised from this solvent; it is sparingly soluble in light petroleum. The solution in sulphuric acid has a bright red colour, but no evidence of anticipated ring-closure to a carbazole derivative was obtained. Several typical oxazines, indamines and indophenols were derived from this nitroso-base, following well-known analogies; the pigments were all more sparingly soluble than the corresponding substances from *p*-nitrosodimethylaniline; no very characteristic properties of these dyes were noted.

4-*Diphenylyltrimethylammonium Chloride.*—The *picrate* of the fully methylated primary base was prepared as usual; it crystallised from alcohol, in which it was sparingly soluble, in large plates, occasionally pointed, m. p. 153° (Found : C, 57·1; H, 4·4; N, 13·0%). The m. p. was unchanged by many crystallisations and the derivative was also obtained from the bromide, m. p. 222°, described by Vorländer *et alios* (*Ber.*, 1925, **58**, 1909); consequently the picrate, m. p. 310°, mentioned by these authors is erroneously described. The *chloride*, obtained in the usual way, is not very hygroscopic; it begins to melt and decompose at 205—208° (Found in anhydrous material : C, 72·4; H, 7·4; N, 5·8%). This salt was found by direct experiment to be completely stable in alkaline solution under more drastic conditions than those employed in the reduction process, and for a longer time.

Reduction. This occurs readily under the standard conditions and the amount of sodium amalgam used can be reduced to 150 g. without affecting the results. Diphenyl and 4-dimethylaminodiphenyl were isolated and recognised products of the reduction.

The 4-dimethylaminodiphenyl formed could not be estimated by coupling with *p*-nitrobenzenediazonium salts, and bromination again proved a suitable alternative, giving results that compared reasonably well with those obtained by direct isolation and weighing, which is feasible in this case. The bromination was carried out at 0° in dilute hydrochloric acid solution by means of an excess of potassium bromate (iodometric back-titration) standardised by means of pure 4-dimethylaminodiphenyl (Found : yield of NMe_3, 81·4, 82·0, 81·0%; yield of $Ph\cdot C_6H_4\cdot NMe_2$ by isolation, 12·6, 14·2, and by bromination, 13·8, 15·0%).

2-*Naphthyltrimethylammonium Chloride.*—β-Naphthylamine was methylated under the usual conditions and the quaternary iodide separated in plates on the eventual addition of potassium iodide; this derivative was recrystallised several times from water, forming well-shaped tablets, m. p. 190°. The *chloride* was obtained by means of silver chloride in aqueous suspension and, after evaporation of its solution to dryness, the salt was crystallised from methyl alcohol–ether; m. p. 173—174° (Found in anhydrous material: C, 70·2; H, 7·4. $C_{13}H_{16}NCl$ requires C, 70·4; H, 7·2%).

Reduction. The standard method was used (amalgam, 350 g., however), but the amount of sodium amalgam used could be greatly diminished (180 g. in some experiments), as the reduction is a particularly facile one. Naphthalene and trimethylamine were definitely identified products, but the 2-dimethylaminonaphthalene was obtained in small yield and was recognised by its reactions and by the preparation of a not quite pure picrate, m. p. 187°, not depressed by admixture with the pure derivative, m. p. 188—189°.

The 2-dimethylaminonaphthalene used for the standardisation of the diazo-solution was prepared by decomposition of the quaternary hydroxide; it had m. p. 46·5° after three crystallisations from aqueous alcohol (compare Bamberger and Müller, *Ber.*, 1899, **22**, 1306). The stability of the quaternary salt under the conditions of the experiment was proved; no decomposition occurred in 7 hours when a 4% solution of the salt in 10% aqueous sodium hydroxide was heated on the steam-bath (Found: yield of NMe_3, 85·5, 86·2%; yield of $C_{10}H_7{\cdot}NMe_2$ by diazo-coupling, 4·0, 4·4, 5·2%).

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