28. *The Amino-derivatives of Pentaerythritol. Part II. The Thermal Decomposition of the Tetrahydrochlorides of Tetrakismethylaminomethylmethane and of Tetrakisdimethylaminomethylmethane.*

By GEOFFREY M. GIBSON, JOHN HARLEY-MASON, ALAN LITHERLAND, and FREDERICK G. MANN.

Thermal decomposition of the tetrahydrochloride of the methylamino-base gives the dihydrochloride of $\alpha\gamma$-bismethylaminopropane (I) by simple fission of the molecule. That of the tetrahydrochloride of the dimethylamino-base is entirely different and yields the hydrochloride of an amine $C_8H_{18}N_2$, which has been shown to have the structure (III), and thus to be constitutionally analogous to β-methylglutaconic acid. This base has many interesting properties, in particular, the low reactivity of its double bond, its ready hydrogenation to *iso*butane, and the abnormal behaviour of its quaternary salts with silver oxide. An attempted synthesis of the dimethiodide of this base gave a product which proved to be the second geometric isomeride. The properties of these various amino-derivatives have been studied in detail.

In Part I (Litherland and Mann, J., 1938, 1588) the synthesis of tetrakisaminomethylmethane, $\mathrm{C(CH_2{\cdot}NH_2)_4}$, and its subsequent methylation to the octamethyl derivative $\mathrm{C(CH_2{\cdot}NMe_2)_4}$ were described, and it was shown that the reaction of the latter compound with methyl iodide was abnormal, since under the usual conditions of quaternary salt formation only a dimethiodide, $\mathrm{C(CH_2{\cdot}NMe_2)_2(CH_2{\cdot}NMe_3I)_2}$, was formed. This, however, underwent thermal decomposition just above its m. p., with formation of the quadri-quaternary iodide, $\mathrm{C(CH_2{\cdot}NMe_3I)_4}$.

The latter reaction is also so abnormal that an investigation of the thermal decomposition of several other quaternary alkyl halide derivatives of the octamethyl base has been undertaken (see Part III, following paper). A necessary preliminary investigation, however, was that of the thermal decomposition of the tetrahydrochloride of the octamethyl base, now to be described, together with the results of a simpler investigation.

When the tetrahydrochloride of tetrakismethylaminomethylmethane, $\mathrm{C(CH_2{\cdot}NHMe,HCl)_4}$, prepared by van Alphen's method (*Rec. Trav. chim.*, 1938, **57**, 265), was heated just above its m. p., decomposition occurred with formation of the *dihydrochloride* of *αγ-bismethylaminopropane* (I), the identity of which has been confirmed by direct synthesis. It is clear that this reaction is essentially merely the fission of two of the side chains from the original molecule :

$$\mathrm{(HCl,NHMe{\cdot}CH_2)_2}\vdots\mathrm{C(CH_2{\cdot}NHMe,HCl)_2} \longrightarrow \mathrm{CH_2(CH_2{\cdot}NHMe,HCl)_2} \quad \text{(I.)}$$

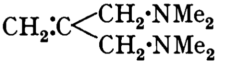
It should be emphasised that this is a reaction only of the salt, the free tetramethyl base being volatile without decomposition.

When, however, the hydrated tetrahydrochloride of the octamethyl base, $\mathrm{C(CH_2{\cdot}NMe_2,HCl)_4, 3H_2O}$, was heated at 232—233°, *i.e.*, just above its m. p., a brisk evolution of formaldehyde occurred, and the residual syrup was found to contain the hydrochlorides of mono-, di-, and tri-methylamine and of an *amine* of molecular formula $\mathrm{C_8H_{18}N_2}$. The mode of decomposition of the tetrahydrochloride of the octamethyl base is thus entirely different from that of the corresponding tetramethyl base. The amine $\mathrm{C_8H_{18}N_2}$, which will be referred to as the " pyro "-base, has considerable stability and can be distilled unchanged at atmospheric pressure; its dihydrochloride can be sublimed unchanged.

The constitution of the " pyro "-base rests on the following evidence :

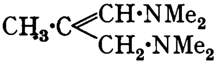
(1) It is a di-tertiary amine, and readily formed a *dimethiodide*, etc.

(2) Catalytic reduction at room temperature of the amine *dihydrochloride* in aqueous or alcoholic solution readily occurred with absorption of 3 mols. of hydrogen and the production of *iso*butane and dimethylamine : the dimethiodide similarly gave *iso*butane and trimethylamine. It follows therefore that the " pyro "-base must have the constitution (II), (III), or (IV).



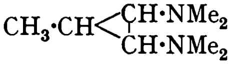
$$\mathrm{CH_2{:}C{<}}\begin{matrix}\mathrm{CH_2{\cdot}NMe_2}\\ \mathrm{CH_2{\cdot}NMe_2}\end{matrix}$$

(II.)



$$\mathrm{CH_3{\cdot}C{\lessgtr}}\begin{matrix}\mathrm{CH{\cdot}NMe_2}\\ \mathrm{CH_2{\cdot}NMe_2}\end{matrix}$$

(III.)



$$\mathrm{CH_3{\cdot}CH{<}}\begin{matrix}\mathrm{CH{\cdot}NMe_2}\\ |\\ \mathrm{CH{\cdot}NMe_2}\end{matrix}$$

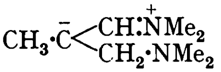
(IV.)

Attempts to arrest the hydrogenation when only 1 or 2 mols. of hydrogen had been absorbed gave unchanged material and the above reduction products, and the intermediate reduction products, whose nature would have furnished valuable evidence for the structure of the " pyro "-base, could not be isolated. The " pyro "-base did not undergo this ready hydrogenation, and was also unaffected by other reducing agents, *e.g.*, sodium and alcohol.

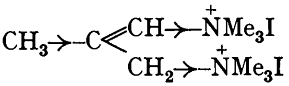
(3) Of the above three possibilities for the " pyro "-base, the compound (II) could clearly be produced most simply from the octamethyl hydrochloride. The following evidence shows almost conclusively that the structure (II) is incorrect.

(*a*) The " pyro "-base and its salts are very stable compounds and lack many of the properties of unsaturated compounds; *e.g.*, the quaternary salts of the base were unaffected by bromine or iodine in aqueous or alcoholic solution, and the dihydrochloride in aqueous solution was unaffected by small quantities of bromine and gave solely an orange perbromide with excess of bromine. The free base is rather more reactive than its derivatives, and in chloroform solution it reacted with bromine, with the production, however, of the *dihydrobromide* of the unchanged base, no other crystalline derivative being isolated. [This result recalls Thorpe's inability (J., 1919, **115**, 680) to obtain any definite product from the action of bromine on the " normal " form of β-methylglutaconic acid of m. p. 149°, which apart from the terminal groups has the same structure as the base (III).] Furthermore, the *dimethochloride* in aqueous or acetic acid solution did not undergo ozonolysis. This lack of reactivity of the double bond would be expected in (III), but certainly not in (II). The free base of conventional formula (III) would actually exist as a resonance hybrid between (III) and (III A), and would therefore have greater stability and less reactivity than formula (III) implies. The simple and quaternary salts cannot show this resonance. In these compounds, however, the positive poles on the nitrogen atoms must act as vigorous electron-attractors : this attraction by the upper nitrogen atom (III B), which is further reinforced by the inductive effect of the methyl group, will cause a neutralisation of the polarity of the adjacent double bond, and thus render this bond only feebly active to cationoid reagents such as bromine. These factors in the quaternary salts are presumably more potent than the resonance factor in the free base.

(IIIA.)



$$\mathrm{CH_3{\cdot}\bar{C}}\Big<\begin{matrix}\mathrm{CH{:}\overset{+}{N}Me_2}\\ \mathrm{CH_2{\cdot}NMe_2}\end{matrix}$$



$$\mathrm{CH_3{\rightarrow}{-}C}\Big\lessdot\begin{matrix}\mathrm{CH{\rightarrow}{-}\overset{+}{N}Me_3I}\\ \mathrm{CH_2{\rightarrow}{-}\overset{+}{N}Me_3I}\end{matrix}$$

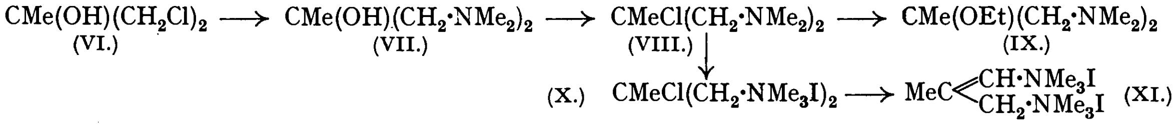
(IIIB.)

(*b*) Since the reactivity of the double bond in (II) cannot be markedly affected by the nitrogen atoms, the first stage in catalytic reduction would be saturation of this bond with the formation of *αγ-bisdimethylamino-β-methylpropane*, $\mathrm{CH_3{\cdot}CH(CH_2{\cdot}NMe_2)_2}$. This compound has now been synthesised by the action of dimethylamine on αγ-dibromo-β-methylpropane, and its *dimethiodide* could not be catalytically reduced under the previous conditions. It follows that this dimethiodide cannot be an intermediate in the catalytic reduction of the dimethiodide of the " pyro "-base. Reduction of the compound (III), however, would probably remove first the lower $\mathrm{NMe_2}$ group, and then, since the stability of the double bond would thus be (if anything) enhanced, would next remove the upper $\mathrm{NMe_2}$ group before final reduction to *iso*butane. Some evidence for the priority of the first of these stages is provided by Mannich, Handke, and Roth (*Ber.*, 1936, **69**, 2116), who showed that αγ-bisdimethylamino-Δ^{α}-butene, $\mathrm{NMe_2{\cdot}CH{:}CH{\cdot}CHMe{\cdot}NMe_2}$, on catalytic reduction at 40° gave a mixture of α-dimethylamino- and αγ-bisdimethylamino-butane and dimethylamine.

(*c*) Even if the compound (II) were initially formed, at the high temperature of the reaction it would probably undergo rapid conversion into (III), since during the formation of olefins at high temperatures the double bond usually adopts that position which gives the most highly substituted ethylene.

(4) Oxidation of the " pyro "-base quaternary salts by alkaline permanganate gave formaldehyde and oxalic acid. The formaldehyde was undoubtedly obtained from the $-\overset{+}{\mathrm{N}}\mathrm{Me_3}$ groups, several similar examples being known. The production of oxalic acid does not differentiate between (II) and (III). The amine (II), on oxidative fission of the double bond, should give mesoxalic acid and hence finally oxalic acid. The amine (III), on similar fission, should give pyruvic acid. Now the latter is known to yield oxalic acid on oxidation with nitric acid (Böttinger, *Annalen*, 1877, **188**, 299; Œschsner de Coninck, *Bull. Acad. roy. Belg.*, 1905, 524) : we find that pyruvic acid on treatment with alkaline permanganate under the above conditions gives oxalic acid in 90% yield, the pyruvic acid therefore reacting presumably in the enolic form, $\mathrm{CH_2{:}C(OH){\cdot}CO_2H}$.

(5) The possibility that the " pyro "-base is 2 : 3-bisdimethylamino-1-methyl*cyclo*propane (IV) could not be excluded, as the *cyclo*propane ring is known sometimes to be formed from the pentaerythritol skeleton (Litherland and Mann, *loc. cit.*). This structure is exceedingly unlikely, as the production of *iso*butane would involve fission of the ring between carbon atoms 2 and 3, and that of oxalic acid would involve a double fission between carbon atoms 1 and 2, and 1 and 3. Furthermore, the high-temperature formation of the " pyro "-base would almost certainly have given the most stable form of the base, which in (IV) would probably have the dimethylamino-groups in the *trans*-position and thus enable the molecule to show optical activity. Attempts to resolve the amine or its quaternary salts failed, however.



$$\begin{tikzcd}[column sep=small] \underset{\text{(VI.)}}{\mathrm{CMe(OH)(CH_2Cl)_2}} \arrow[r] & \underset{\text{(VII.)}}{\mathrm{CMe(OH)(CH_2{\cdot}NMe_2)_2}} \arrow[r] & \underset{\text{(VIII.)}}{\mathrm{CMeCl(CH_2{\cdot}NMe_2)_2}} \arrow[r] \arrow[d] & \underset{\text{(IX.)}}{\mathrm{CMe(OEt)(CH_2{\cdot}NMe_2)_2}} \\ & \text{(X.)} & \mathrm{CMeCl(CH_2{\cdot}NMe_3I)_2} \arrow[r] & \mathrm{MeC}\Big\lessdot\begin{matrix}\mathrm{CH{\cdot}NMe_3I}\\ \mathrm{CH_2{\cdot}NMe_3I}\end{matrix}\ \text{(XI.)} \end{tikzcd}$$

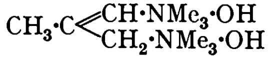
(6) The synthesis of a compound of structure (III) was therefore attempted. *s*-Dichloroacetone was converted by methylmagnesium bromide into *αγ-dichloro-β-methyl*iso*propyl alcohol* (VI), which, heated with dimethylamine gave *αγ-bisdimethylamino-β-methyl*iso*propyl alcohol* (VII), but all attempts to dehydrate (VII) and so obtain the required compound (III) failed. The amine (VII) was therefore converted by thionyl chloride into *β-chloro-αγ-bisdimethylamino-β-methylpropane* (VIII), from which, however, hydrogen chloride could not be eliminated, alcoholic potash in particular giving the *β-ethoxy*-compound (IX). The chloro-compound (VIII) was therefore converted into its *dimethiodide* (X), which when treated with 1 equiv. of potassium hydroxide readily gave *αγ-bistrimethylammonium-β-methylpropenylene di-iodide* (XI), *i.e.*, the dimethiodide of (III). The elimination of hydrogen chloride would

almost certainly proceed as indicated, and would not have involved the methyl group to give the highly reactive $CH_2{:}C{=}$ grouping : this is confirmed further by the fact that this elimination is controlled by the positive charge on the nitrogen atom, which would obviously influence a neighbouring rather than a distant hydrogen atom. These synthetic results are in close harmony with those of Ingold and Rothstein (J., 1931, 1666), who were unable to dehydrate the compound $CH(OH)(CH_2{\cdot}NEt_2)_2$ or to eliminate hydrogen chloride from $CHCl(CH_2{\cdot}NEt_2)_2$, but found that the dimethiodide of the latter was smoothly converted by alcoholic potash into $[NEt_2Me{\cdot}CH{:}CH{\cdot}CH_2{\cdot}NEt_2Me]I_2$.*

It was found, however, that the synthetic methiodide (XI) had m. p. 203—204°, and the " pyro "-base methiodide m. p. 216—217°, whereas a mixture had m. p. 206—210°; furthermore, the *dimethopicrate* obtained from (XI) had m. p. 245—246°, that from the " pyro "-base m. p. 257—257·5°, and a mixture m. p. 250—253°. *X*-Ray powder photographs of the two methiodides, kindly taken by Mr. H. S. Peiser, showed conclusively that the two compounds were not identical. The closeness of each of the above pairs of m. p.'s, and the intermediate value of each mixed m. p., indicate, however, that the two compounds in each pair must be chemically closely allied. Evidence that the difference between the two methiodides is in fact stereochemical and not structural, *i.e.*, that they are geometric isomerides, is provided by the following reactions :

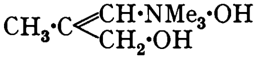
(*a*) The synthetic dimethiodide (XI) also underwent smooth catalytic reduction at room temperature with absorption of 3 mols. of hydrogen to give *iso*butane and 2 mols. of trimethylammonium iodide. On oxidation with alkaline permanganate it also gave oxalic acid.

(*b*) Both dimethiodides when boiled with alcoholic potash underwent decomposition with liberation of all their nitrogen as trimethylamine. When, however, they were boiled in aqueous solution with an excess of silver oxide, only 1 mol. of trimethylamine was liberated, and the solution then contained the ion $[C_{14}H_{30}N_2O]^{++}$ (XIV); this was isolated as the *dipicrate, dichloroaurate,* and *chloroplatinate,* the same dipicrate being obtained from both dimethiodides. The mechanism of this reaction is uncertain. The first product of the action of the silver oxide, *viz.*, the dihydroxide (XII), cannot undergo normal quaternary ammonium hydroxide decomposition at either pole, since this would involve loss of trimethylamine and the removal of a β-hydrogen atom as a molecule of water by the hydroxyl ion. In such circumstances, formation of the alcohol (XIII) would be expected; actually, the corresponding ether (XIV) is formed. It is very unlikely that the trimethylamine arose from the upper nitrogen atom in (XII), as this would have produced an aldehyde which would, in turn, have been oxidised to an acid. The important fact is, however, not the structure of (XIV), but the production of this ion from both dimethiodides; evidently the most stable geometric isomer of (XIV) is ultimately obtained during the prolonged boiling with silver oxide. This ether formation during quaternary ammonium hydroxide decomposition is, however, not unique, although very rare : Gabriel and Colman (*Ber.*, 1906, **39**, 2875) have shown that 1 : 1-trimethylenepiperidinium hydroxide, when heated with aqueous potassium hydroxide, gives di-γ-piperidino-*n*-propyl ether, $(C_5H_{10}N{\cdot}[CH_2]_3)_2O$.



$$CH_3{\cdot}C{<}\begin{matrix}CH{\cdot}NMe_3{\cdot}OH\\ CH_2{\cdot}NMe_3{\cdot}OH\end{matrix}$$

(XII.)



$$CH_3{\cdot}C{<}\begin{matrix}CH{\cdot}NMe_3{\cdot}OH\\ CH_2{\cdot}OH\end{matrix}$$

(XIII.)

$$[\overset{+}{N}Me_3{\cdot}CH{:}CMe{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}\overset{+}{N}Me_3]$$

(XIV.)

(*c*) There is some evidence of slow interconversion of the quaternary salts of the " pyro "-base and the synthetic salts at room temperature. A sample of the crystalline " pyro "-base dimethochloride was kept in a securely stoppered tube for 2 years, by which time it had liquefied. When this was boiled in aqueous solution with silver oxide for a short time, and the product precipitated as the picrate, recrystallisation ultimately gave the pure, slightly soluble *dipicrate* of the synthetic salt. The liquefaction was apparently caused by the formation of a mixture of the two dimethochlorides, from which the " pyro "-component was preferentially removed by the silver oxide, the action of the latter being stopped before the second isomeric component had been completely decomposed. This interconversion at room temperature was not observed in any other salt.

Since there is no evidence as to which of the dimethiodides has the *cis*- and which the *trans*-structure, it is proposed for future reference to call the " pyro "-base and its derivatives the α-series, and the synthetic methiodide and its derivatives the β-series.

It should be noted that the synthesis of the dimethiodide (XI) also disposes of the *cyclo*propane structure (IV), since there is no rational mechanism by which the elimination of hydrogen chloride from (X) could give the *cyclo*propane ring.

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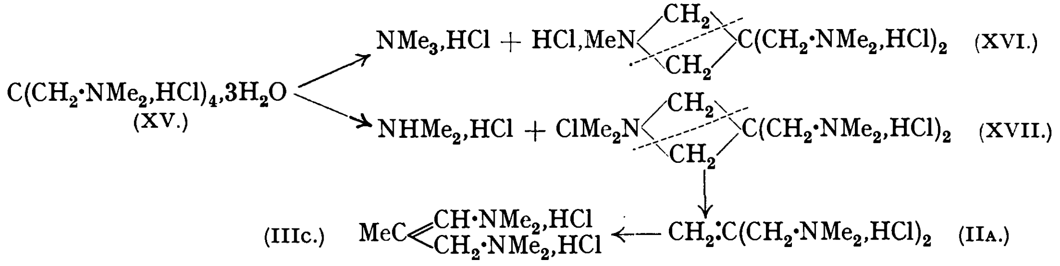
* In view of the close analogy between the two syntheses at all stages, it is remarkable that Ingold and Rothstein's unsaturated dimethiodide on catalytic reduction gave solely the saturated $CH_2(CH_2{\cdot}NEt_2MeI)_2$, whereas our dimethiodide was reduced completely to *iso*butane.

With regard to the mechanism of the formation of the "pyro"-base from the octamethyl tetrahydrochloride, it is significant that several monoalkyl iodides of the octamethyl base readily undergo ring closure to form derivatives of ββ-bisdimethylaminomethyl-*N*-methyltrimethyleneimine (XVI), and that, furthermore, benzyl iodide under certain conditions causes complete disruption into "pyro"-base derivatives (see Part III). These reactions make it highly probable that the first stage of the decomposition of the hydrated tetrahydrochloride (XV) consists of two simultaneous reactions, (*a*) formation of the hydrochlorides of trimethylamine and of (XVI) and (*b*) formation of dimethylamine hydrochloride and the methochloride (XVII) corresponding to (XVI). The ring in (XVI) then undergoes fission as shown in the presence of water to give formaldehyde, monomethylamine hydrochloride, and the unstable methylene base dihydrochloride (IIA), which then passes over into the very stable "pyro"-base dihydrochloride (IIIc). The ring in (XVII) by a similar fission gives the same products, except that di- instead of mono-methylamine is formed. The high yield of dimethylamine and low yield of mono- and tri-methylamine show that reaction (*b*) predominates over (*a*). In view of the close structural analogy between the "pyro"-base (III) and β-methylglutaconic acid, it is noteworthy that Goss, Ingold, and Thorpe (J., 1923, **123**, 327) emphasise "the remarkable tendency to the formation of the mobile glutaconic acids, which is such that groups, for instance $-CO_2Et$ groups, are removed with quite extraordinary ease, and in the presence of reagents which do not usually effect their elimination, when the mobile hydrogen atom necessary for glutaconic tautomerism can thereby be acquired." It is probable that this same tendency underlies the formation of the "pyro"-base and may thus be the dominant factor determining the course of the thermal decomposition.



Many attempts have been made to synthesise an amine of structure (IV) for direct comparison with the "pyro"-base, but all have failed. The preparation and isolation of the three isomeric 1-methyl*cyclo*propane-2 : 3-dicarboxylic acids have been described by Goss, Ingold, and Thorpe (*loc. cit.*; see, however, Feist, *Annalen*, 1924, **436**, 125), but the isolation of the required pure *trans*-dicarboxylic acid in practicable quantities is exceedingly laborious. A mixture of pure diamides or dihydrazides could not be obtained by treating the esterified mixture of *cis*- and *trans*-acids with ammonia or hydrazine respectively. The Curtius degradation of the crude dihydrazide gave, however, 2 : 3-diamino-1-methyl*cyclo*propane, isolated as the *dibenzoyl* derivative, but in spite of many variations in the conditions the yield was uselessly low, and methylation of this diamine was not attempted.

In the early stages of this investigation, when only salts of the "pyro"-base were available and its molecular weight was unknown, it appeared possible that the base was *N*-methyltrimethyleneimine. Trimethyleneimine, prepared by the method of Marckwald *et al.* (*Ber.*, 1898, **31**, 3264; 1899, **32**, 2031), when treated with methyl iodide in cold ethereal solution, gave the *hydriodide* of the unchanged base; when treated with methyl iodide and alcoholic potash it gave N-*methyltrimethyleneimine methiodide*. The insolubility of the latter in all liquids other than water indicated a possibility of polymerisation, however. It was of course quite distinct from the methiodide of the "pyro"-base.

EXPERIMENTAL.

Tetrakisaminomethylmethane, $C(CH_2{\cdot}NH_2)_4$.—Van Alphen (*loc. cit.*) has described a monohydrate of this base, having b. p. 278—282°. We, however, ground the disulphate of the tetramine (see Part I, p. 1591) with much powdered potassium hydroxide, extracted the mixture several times with boiling benzene, and fractionally distilled the united filtered extracts; the amine boiled at 282—284° and solidified on cooling to an exceedingly deliquescent, waxy solid. This was recrystallised from benzene, and the *tetrahydrate* of the amine obtained as fine needles, m. p. 100—100·5° (Found: N, 26·9. $C_5H_{16}N_4,4H_2O$ requires N, 27·45%). This compound underwent slow dehydration to the monohydrate when kept over phosphoric oxide in a vacuum (Found: N, 37·0. Calc. for $C_5H_{16}N_4,H_2O$: N, 37·3%).

Tetrakismethylaminomethylmethane, $C(CH_2{\cdot}NHMe)_4$.—This was prepared essentially by van Alphen's method (*loc. cit.*), a mixture of the tetrabromo-compound, $C(CH_2Br)_4$, (40 g.) and a 27% alcoholic methylamine solution (240 c.c.) being heated at 170° for 9 hours. The excess of alcohol and methylamine was then distilled off, and the residue evaporated almost to dryness and treated with much powdered potassium hydroxide. The base was extracted with ether and dried (potash); fractional distillation then gave a *dihydrate* of the tetramethyl-base, of b. p. 245—248°, as a colourless viscous liquid (Found : N, 25·4. $C_9H_{24}N_4,2H_2O$ requires N, 25·0%); yield 11 g. (55%). According to van Alphen, this procedure should give a hemihydrate, b. p. 235—238°. The tetramethyl base gave the monohydrated *tetrahydrochloride*, colourless crystals from alcoholic hydrochloric acid, m. p. 264° (decomp.) (Found : C, 30·7; H, 8·3; N, 15·8; Cl, 40·4. $C_9H_{24}N_4,4HCl,H_2O$ requires C, 30·7; H, 8·5; N, 15·9; Cl, 40·35%), and the monohydrated *tetrahydrobromide*, similar crystals from alcoholic hydrobromic acid, m. p. 266° (decomp.) (Found : Br, 60·4. $C_9H_{24}N_4,4HBr,H_2O$ requires Br, 60·3%), which readily gave the anhydrous *salt* (Found : C, 20·8; H, 5·7. $C_9H_{24}N_4,4HBr$ requires C, 21·1; H, 5·5%). *Tetrakisbenzenesulphonmethylamidomethylmethane*, $C(CH_2{\cdot}NMe{\cdot}SO_2Ph)_4$, was obtained as colourless crystals from acetic acid, m. p. 239° (Found : C, 52·8; H, 5·5. $C_{33}H_{40}O_8N_4S_4$ requires C, 52·9; H, 5·4%).

αγ-Bismethylaminopropane and its Derivatives.—A mixture of trimethylene dibromide (30 g.) and 21% aqueous-alcoholic methylamine solution (160 c.c.) was heated at 120—130° for 8 hours. The excess of methylamine was then removed, and the residue acidified with hydrochloric acid, evaporated to dryness, and treated with potassium hydroxide. The liberated amines were extracted with ether, dried, and fractionally distilled, the αγ-bismethylaminopropane being obtained as a colourless liquid *monohydrate*, b. p. 141—144° (Found : N, 24·5. $C_5H_{14}N_2,H_2O$ requires N, 23·3%); the yield was low owing to considerable formation of bases of b. p. >200°. The *dihydrochloride*, colourless needles from methyl alcohol, had m. p. 262—263° (Found : C, 34·6; H, 9·5; N, 15·7; Cl, 40·9. $C_5H_{14}N_2,2HCl$ requires C, 34·3; H, 9·15; N, 16·0; Cl, 40·6%); the *dipicrate*, pale yellow needles from hot water, turning brown on standing, had m. p. 193—194° (Found : C, 36·3; H, 3·8; N, 20·0. $C_5H_{14}N_2,2C_6H_3O_7N_3$ requires C, 36·4; H, 3·6; N, 20·0%).

Thermal Decomposition of the Tetramethyl Tetrahydrochloride, $C(CH_2{\cdot}NHMe,HCl)_4$.—The powdered tetrahydrochloride (39 g.) was heated at 275° for 45 mins., *i.e.*, until effervescence ceased. The product was treated with potassium hydroxide, extracted with ether, and the extracts dried and distilled. After the ether and much readily volatile amine had been removed, distillation gave the following fractions : (i) b. p. 55—58°/28 mm., 1·5 g.; (ii) b. p. 58—64°/27 mm., 1·0 g.; (iii) b. p. 140—170°/25 mm., 3·5 g.; (iv) b. p. 180—185°/18 mm., 0·8 g. Fractions (i) and (ii) were united, treated with hydrochloric acid, and taken to dryness : the residue, washed with alcohol and recrystallised from methyl alcohol, gave the above αγ-bismethylaminopropane dihydrochloride, m. p. 257° (Found : C, 34·1; H, 9·4; N, 15·4; Cl, 40·3%). The dihydrochloride gave the dipicrate, m. p. 193—194°, unchanged by admixture with the above authentic sample, and also turning brown on standing. Fractions (iii) and (iv) contained chiefly the unchanged tetramethyl base. The low yields of the four fractions show that considerably more extensive decomposition must have occurred during the above heating. When the heating was extended to 1·5 hours to eliminate fractions (iii) and (iv), only very small yields of all fractions were obtained, and the further decomposition had evidently become more complete.

Tetrakisdimethylaminomethylmethane.—The following method of preparation is more expeditious than methylation of the primary tetramine (Litherland and Mann, *loc. cit.*). A mixture of tetrakisbromomethylmethane (90 g.), anhydrous dimethylamine (85 g., 8 mols.), and alcohol (300 c.c.) was heated in a rotating autoclave at 170° for 9 hours. The cold product was diluted with water and then heated to 100° to distil off the excess of dimethylamine. The residual solution was made strongly alkaline, and distilled in steam. The distillate, acidified with hydrochloric acid and evaporated, gave a semi-solid mass of the hydrated tetrahydrochloride, which crystallised when triturated with alcohol. Yield, 52 g. (51%). The free *tetrakisdimethylamino-base* was isolated in the usual way as a colourless liquid, b. p. 157°/45 mm., 248—249°/769 mm. (Found : C, 63·8; H, 13·0; N, 23·2. $C_{13}H_{32}N_4$ requires C, 63·9; H, 13·1; N, 23·0%). The free base remains unchanged in a closed vessel; the tetrahydrochloride very slowly decomposes under these conditions, as shown by a steady fall in m. p., but one recrystallisation usually gives the pure salt.

Thermal Decomposition of the Octamethyl Tetrahydrochloride, $C(CH_2{\cdot}NMe_2,HCl)_4,3H_2O$.—The tetrahydrochloride (120 g., divided into five batches) was heated in an oil-bath at 232—233° until the steady vigorous effervescence subsided (*ca.* 20 mins.); the heating was continued for a further 2—3 mins. (longer heating gave a brown product), and the mixture then allowed to cool. A sample of the gas evolved was dissolved in water and found to be solely formaldehyde, identified by smell and as its 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 166—167°. The cold solidified mixture, on recrystallisation from alcohol, gave the *dihydrochloride* of the " pyro "-base, colourless crystals, m. p. 260° (decomp. with partial sublimation) (Found : C, 44·9; H, 9·7; N, 12·8; ionised Cl, 33·0. $C_8H_{18}N_2,2HCl$ requires C, 44·7; H, 9·3; N, 13·0; Cl, 33·0%); yield 25 g. A sample of the alcoholic mother-liquor was evaporated to a syrup and this was shaken with aqueous sodium hydroxide and benzenesulphonyl chloride; the mixture was then extracted with ether, and the ether in turn extracted with dilute hydrochloric acid. The ether on evaporation left a syrup which, after solidification and recrystallisation from petrol, gave much pure benzenesulphondimethylamide, m. p. 45—47°, unchanged by admixture with an authentic sample. The hydrochloric acid extract was basified, extracted with ether, and the extract treated with methyl iodide; the small amount of precipitate was collected, recrystallised from aqueous alcohol, and identified as tetramethylammonium iodide, unaffected by heating to 300°

(Found : N, 7·0; I, 62·8. Calc. for $C_4H_{12}NI$: N, 7·0; I, 63·2%). The above experiment was repeated, the original syrup being now shaken with sodium hydroxide and *p*-toluenesulphonyl chloride; after extraction with ether, the aqueous solution on acidification gave a very small quantity of *p*-toluenesulphonmethylamide, which, crystallised from aqueous alcohol, had m. p. and mixed m. p. 77°. The production of methyl-, dimethyl-, and trimethyl-amine during the thermal decomposition was thus proved.

The free " pyro "-*base*, obtained by ether extraction of a mixture of the dihydrochloride, powdered potassium hydroxide, and a small quantity of water, was isolated as a colourless liquid, b. p. 150—154°, 50—54°/12 mm., miscible with water (Found : N, 19·7; *M*, by Hofmann's vapour-density method at 100°/196 mm., 157. $C_8H_{18}N_2$ requires N, 19·7%; *M*, 142). This base gave the following salts : *dihydrobromide*, from alcohol, m. p. 243° with darkening (Found : C, 31·7; H, 6·55; Br, 52·6. $C_8H_{18}N_2,2HBr$ requires C, 31·6; H, 6·6; Br, 52·6%); *dihydriodide*, from alcohol, m. p. 203—205° with previous softening, depending on the rate of heating (Found : C, 23·6; H, 5·1; N, 7·15. $C_8H_{18}N_2,2HI$ requires C, 24·1; H, 5·0; N, 7·0%); *dipicrate*, yellow needles from water, m. p. 185·5—187·5° (Found : C, 40·5; H, 4·1; N, 18·6. $C_8H_{18}N_2,2C_6H_3O_7N_3$ requires C, 40·0; H, 4·0; N, 18·7%). When the dihydrochloride was heated at its m. p. a sublimate of unchanged material, m. p. 250° (decomp.), was obtained; this gave a picrate (Found : N, 18·6%), which after recrystallisation from water had m. p. 184—186°, unchanged by admixture with the above preparation.

The dihydrochloride was unaffected by boiling with dilute hydrochloric acid (1 : 1 by vol.) under reflux for 2·5 hours; when the boiling was continued for 12 hours, some decomposition occurred but no indication of hydrogen chloride addition to the unsaturated base could be obtained.

An aqueous solution of the dihydrochloride was treated with silver *d*-α-bromocamphor-π-sulphonate (2 mols.), the mixture boiled and filtered, and the filtrate taken to dryness. The glassy residue, twice recrystallised from alcoholic ethyl carbonate, gave colourless crystals of the *dibromocamphorsulphonate*, m. p. 170—176°, $[M]_D^{10°}$ 556° in water. These were recrystallised five times from *iso*heptyl alcohol, and then had m. p. 165—172°, $[M]_D^{9°}$ 544°; three further crystallisations from *n*-heptyl alcohol gave $[M]_D^{0°}$ 534°, and two more crystallisations led to m. p. 174—178°, $[M]_D^{13°}$ 536° (Found : C, 43·5; H, 6·6; Br, 20·65. $C_8H_{18}N_2,2C_{10}H_{15}O_4BrS$ requires C, 43·85; H, 6·6; Br, 20·85%). Since the bromocamphorsulphonate ion has $[M]_D^{22°}$ 278·7° in aqueous solution (Pope and Read, J., 1910, **97**, 2201), it appeared that no resolution was occurring. This was confirmed by treating an alcoholic solution of the last crop with a saturated alcoholic solution of calcium bromide, whereby the inactive dihydrobromide of the " pyro "-base was precipitated.

The " pyro "-base, treated with methyl iodide in methyl-alcoholic solution, readily gave the *dimethiodide*, colourless crystals from alcohol, m. p. 216—217° (decomp., with preliminary darkening) (Found : C, 28·0; H, 5·6; N, 6·6; I, 59·5. $C_{10}H_{24}N_2I_2$ requires C, 28·2; H, 5·6; N, 6·6; I, 59·6%). An aqueous solution of this compound was shaken with excess of silver oxide, filtered, acidified with hydrochloric acid, and evaporated to a syrup, which solidified when treated with alcoholic acetone; recrystallisation from this mixed solvent gave colourless crystals of the *dimethochloride monohydrate* (Found : Cl, 27·15. $C_{10}H_{24}N_2Cl_2,H_2O$ requires Cl, 27·2%). This dimethochloride when heated melted at 184—186° with slight effervescence, then resolidified and again melted at *ca.* 200°; when heated at 130° for some time, it had m. p. 224° (decomp.). It is possible, therefore, that the preliminary heating gave the anhydrous material, which then had a sharp m. p.

The dimethochloride gave a *dichloroaurate*, m. p. 237—238·5° (decomp.) (Found : N, 3·5; Au, 46·2. $C_{10}H_{24}N_2Cl_8Au_2$ requires N, 3·3; Au, 46·4%), and a *chloroplatinate*, m. p. 245° (decomp.) (Found : C, 20·3; H, 4·7; N, 4·8; Pt, 32·6. $C_{10}H_{24}N_2Cl_6Pt,H_2O$ requires C, 20·1; H, 4·35; N, 4·5; Pt, 32·6%). The *dimethopicrate*, obtained from the dimethiodide and recrystallised from water, had m. p. 257—257·5° (decomp.) (Found : N, 17·8. $C_{22}H_{28}O_{14}N_8$ requires N, 17·8%).

The *dimetho*-d-*camphorsulphonate*, prepared from the dimethiodide in the usual manner, was crystallised repeatedly from acetone containing a small quantity of alcohol and finally had m. p. 261—263° with slight preliminary softening (Found : C, 56·3; H, 8·5. $C_{30}H_{54}O_8N_2S_2$ requires C, 56·7; H, 8·6%). A 1·345% aqueous solution had $[\alpha]_D^{12°}$ + 16·0°, hence $[M]_D^{12°}$ + 101°. Since Graham (J., 1912, **101**, 746) found an average value for the camphorsulphonate ion of 50·0° for a 2% aqueous solution and the D-line, it is clear that no resolution was occurring.

The *dibenzyliodide*, obtained by reaction in cold ethereal solution, formed colourless crystals from alcohol, m. p. 168—169° (Found : C, 45·8; H, 6·0; N, 5·0; I, 43·1. $C_{22}H_{32}N_2I_2$ requires C, 45·7; H, 5·6; N, 4·85; I, 43·9%). This compound, treated in warm aqueous methyl-alcoholic solution with sodium picrate, gave the *dibenzylpicrate*, m. p. 199—201° (Found : N, 14·5. $C_{34}H_{36}O_{14}N_8$ requires N, 14·4%) from alcohol. These two compounds were prepared for comparison with those obtained by the decomposition of the benzyliodide of the octamethyl-base (see Part III).

Hydrogenations.—(1) *Of the dihydrochloride of the " pyro "-base.* A solution of the dihydrochloride (0·367 g.) in water (30 c.c.), mixed with Adams's platinum oxide catalyst (0·019 g.), gave an apparent absorption of 86 c.c. of hydrogen at 20·5° and 757 mm. (*i.e.*, 2·10 mols.) in 1·5 hours. The gases were pumped off through calcium chloride and phosphoric oxide and condensed in a liquid-air trap, where solidification occurred; the excess hydrogen was removed, and the solid product (which melted immediately on removal from the trap) was examined by Dr. G. H. Twigg, who reported :

" The specimen was further purified by distillation from liquid air, and was compared with a number of hydrocarbons in respect of its vapour pressure at − 78° and relative thermal conductivity. The apparatus used for these tests was the analyser described by Twigg (*Proc. Roy. Soc.*, 1941, **178**, *A*, 106), and is similar to a McLeod gauge with the closed limb dipping into a bath of solid carbon dioxide–acetone. The method of measuring the vapour pressure is described in this paper. The closed limb of the analyser contains a fine wire stretched down the axis of the tube. The voltage required to keep this wire at a constant temperature in the vapour of the substance, the pressure being the vapour pressure at − 78°, is related to the thermal conductivity, and thus to the mass and specific heat of the substance.

" These two tests were applied to the unknown and other hydrocarbons, and the vapour pressure and voltage values obtained are given below. The *n*- and *iso*-butane used were made by hydrogenating Δ^{β}-butene and *iso*butene respectively, and may contain a small quantity, not more than 5%, of unchanged butene.

Substance.	V. p., mm. at −78°.	Conductivity voltage, v.
Unknown	19·2 ± 0·15	1·1215 ± 0·0005
*iso*Butane	19·2 ± 0·1	1·1223 ± 0·0005
n-Butane	9·7	1·0943
Δ^{α}-Butene	13·1	1·0763
trans-Δ^{β}-Butene	8·7	1·0655
cis-Δ^{β}-Butene	6·6	1·0166
Propane *	131	
n-Pentane *	1·38	

* *International Critical Tables*, 1928, **3**, 218, 220. These values are cited only to show the markedly different values given by the immediate homologues.

" From these results, the unknown substance is clearly identified as *iso*butane."

The alcoholic mother-liquor from the above hydrogenation was evaporated to dryness, and the deliquescent residue, recrystallised from alcoholic acetone, gave dimethylamine hydrochloride, m. p. 171° (Found : N, 17·0. Calc. for C_2H_7N,HCl : N, 17·2%). The mother-liquor from the recrystallisation was evaporated, and the residue, shaken with benzenesulphonyl chloride and sodium hydroxide solution, gave benzenesulphondimethylamide, m. p. 48·5—49°, unchanged by admixture with an authentic sample. After allowance for the evolution of 1 mol. of *iso*butane in the above hydrogenation, the total absorption of hydrogen was 3·1 mols. When similar hydrogenations were carried out in organic solvents, *e.g.*, methyl alcohol, some of the *iso*butane remained dissolved in the solvent, and the apparent absorption was therefore between 2 and 3 mols. of hydrogen.

In repetitions of this experiment in which the hydrogenation was stopped when only 1 or 2 mols. of hydrogen had been absorbed, only the hydrochlorides of dimethylamine and of unchanged " pyro "-base could be detected in the solution.

(2) *Of the free " pyro "-base.* A solution of the free base (0·199 g.) in *cyclo*hexane (15 c.c.) containing the catalyst (0·02 g.) underwent very slow hydrogenation which stopped after absorption of 8·4 c.c. of hydrogen during 3·5 hours. Addition of glacial acetic acid (10 c.c.) caused rapid hydrogenation to occur, total absorption of hydrogen being 78·2 c.c. at 18°/758 mm. (*i.e.*, 2·33 mols.). The initial failure may have been due to poisoning of the catalyst by the free base, but more probably indicates a definite difference in reactivity between the base and its salts.

(3) *Of the dimethiodide of the " pyro "-base.* A solution of the dimethiodide (0·308 g.) in methyl alcohol (20 c.c.), with the catalyst (0·018 g.), similarly absorbed 45·0 c.c. of hydrogen at 21°/771 mm. (*i.e.*, 2·62 mols.). The solution on evaporation gave solely crude trimethylamine hydriodide (Found : I, 68·2. Calc. for C_3H_9N,HI : I, 67·9%), which in turn gave the picrate, m. p. 221—222°, and mixed m. p. with an authentic sample, 219—220°. Many repetitions of this experiment were also made in which only 1 or 2 mols. of hydrogen were actually absorbed, but only trimethylamine hydriodide and the unchanged dimethiodide could be detected.

All attempts to reduce an alcoholic solution of the " pyro "-base with sodium failed.

Oxidation.—(1) *By potassium permanganate.* Initial experiments showed that when the dimethochloride of the " pyro "-base was treated in warm sodium carbonate solution with sufficient permanganate to give 2 atoms of oxygen, much unchanged material could be isolated as the picrate, and the solution gave no semicarbazone. When a similar mixture was titrated with permanganate at 70°, oxidation almost ceased when the equivalent of 9·5 atoms of oxygen had been used, and the solution contained oxalic acid. Consequently, the dimethochloride (1·42 g.) and sodium carbonate (4·0 g.) were dissolved in turn in water (240 c.c.) at 70°, and permanganate (6·18 g. ≡ 10 atoms of oxygen) then added. The filtered solution was concentrated, neutralised with dilute sulphuric acid, and evaporated to dryness in a desiccator. The product was repeatedly extracted with boiling ether. The ethereal extracts on evaporation gave oxalic acid, which when crystallised from petrol–ethyl acetate had m. p. 187°, and when then exposed to the air gave the dihydrate, m. p. 101·5° (efferv.), unchanged on mixing with an authentic sample. The residue from the ether extraction, when dissolved in dilute acetic acid and treated with phenylhydrazine, gave bisphenylhydrazine oxalate, m. p. 180° (decomp.; varying with rate of heating), m. p. when mixed with authentic sample of m. p 184° and heated under the same conditions, 183° (Found : C, 54·4; H, 5·9; N, 18·5. Calc. for $C_{12}H_{16}N_4,C_2H_2O_4$: C, 54·9; H, 5·9; N, 18·3%).

In an attempt to isolate the intermediate products, the experiment was repeated, " pyro "-base (0·35 g.), sodium carbonate (1·0 g.), and permanganate (1·30 g. ≡ 5 atoms of oxygen) being used. A portion of the filtered solution, treated with phenylhydrazine, gave the above oxalate; a second portion, treated with excess 1% alcoholic 2 : 4-dinitrophenylhydrazine containing 10% of concentrated hydrochloric acid to prevent separation of the oxalate, gave formaldehyde-2 : 4-dinitrophenylhydrazone; when twice recrystallised from alcohol, this had m. p. 163°, unchanged on admixture with an authentic sample (Found : N, 25·9. Calc. for $C_7H_6N_4O_4$: N, 26·65%).

(2) *By ozone.* A solution of the dimethochloride in water or in acetic acid was unaffected by the passage of ozone for 3 hours. An aqueous solution of the dihydrochloride, when ozonised for 5 hours, underwent decomposition (probably by oxidation of the dimethylamino-groups) but no hydrazone or semicarbazone could be isolated.

Action of Bromine.—A bromine solution (2·24 c.c., 1 mol. Br_2), prepared by mixing bromine (2·50 c.c.) and chloroform (30 c.c.), was added dropwise to one of the " pyro "-base (0·5 g.) in chloroform (10 c.c.). Each drop gave a transient orange precipitate, which rapidly redissolved to a yellow solution; towards the end of the addition, colourless crystals separated and the solution ultimately became colourless. The crystals, when collected and recrystallised from alcohol, had m. p. 239—239·5°, unchanged by admixture with the dihydrobromide of the " pyro "-base (Found : C, 31·4; H, 6·8; Br, 53·4. Calc. for $C_8H_{18}N_2,2HBr$: C, 31·6; H, 6·6; Br, 52·6%). The chloroform filtrate was extracted with dilute hydrochloric acid and the extract warmed with charcoal, an odour of formaldehyde being evolved. The aqueous filtrate, evaporated in a desiccator, gave a brown viscous syrup from which no crystalline compound could be isolated. When this experiment was repeated but with 0·67 mol. of bromine, the same dihydrobromide and unchanged base were isolated. When 2 mols. of bromine were employed, a heavy red oil was immediately precipitated, and on treatment with alcohol this gave the dihydrobromide again. These results contrast markedly with the addition of bromine to a chloroform solution of the octamethyl base, $C(CH_2{\cdot}NMe_2)_4$, which causes an immediate stable orange precipitate, presumably of a perbromide.

Addition of bromine water to an aqueous solution of the dihydrochloride of the " pyro "-base gave at first a yellow solution, and ultimately an orange precipitate, apparently of a perbromide. [The compound $C(CH_2{\cdot}NMe_2,HCl)_4$ behaved similarly.] No decolorisation or apparent reaction occurred when methyl-alcoholic solutions of bromine and of the dihydrochloride of the " pyro "-base were mixed; a similar result was obtained when warm acetic acid solutions of bromine and the dimethiodide of the " pyro "-base were mixed.

αγ-Bisdimethylamino-β-methylpropane, $CH_3{\cdot}CH(CH_2{\cdot}NMe_2)_2$.—Pure αγ-dibromo-β-methylpropane (33 g.), prepared by Faworski's method (*Annalen*, 1907, **354**, 384), and 30% alcoholic dimethylamine (150 c.c.) were heated together at 130° for 10 hours. The product was diluted with water, neutralised, and ether-extracted to remove neutral impurities; it was then concentrated, basified, and the base extracted with ether and twice distilled. The above *amine* was thus obtained as a colourless liquid (8 g.), b. p. 151—152° (Found : N, 16·8. $C_8H_{20}N_2$ requires N, 19·4%). It gave a *dihydrochloride*, m. p. 233—234° (Found : Cl, 32·4. $C_8H_{20}N_2,2HCl$ requires Cl, 32·7%); a *dimethiodide*, m. p. 267—268° (Found : I, 59·3. $C_{10}H_{26}N_2I_2$ requires I, 59·3%); a dibenzyliodide, obtained as a syrup and as a glass, which could not be purified, but readily gave a *dibenzylpicrate*, m. p. 169—171° (Found : N, 14·6. $C_{34}H_{38}O_{14}N_8$ requires N, 14·4%). These three derivatives were all purified by recrystallisation from alcohol.

All attempts to reduce the dimethiodide catalytically under precisely the same conditions as those employed for the dimethiodide of the " pyro "-base failed.

Synthesis of αγ-Bistrimethylammonium-β-methylpropenylene Di-iodide (XI).—A Grignard reagent prepared from methyl bromide (70 g.) and magnesium (16·6 g., 1·2 atoms) in ether (300 c.c.) was added slowly with stirring and cooling to a suspension of *s*-dichloroacetone (72 g.) in ether (200 c.c.). Next day, the mixture was treated with dilute hydrochloric acid, the ethereal layer removed, the aqueous layer extracted with ether, the ethereal extracts united, concentrated, shaken with sodium bisulphite solution, dried, and distilled. *αγ-Dichloro-β-methyl*iso*propyl alcohol* (VI) was obtained as a colourless liquid (33 g.), b. p. 71—72°/18 mm. (Found : Cl, 49·0. $C_4H_8OCl_2$ requires Cl, 49·7%). A high-boiling residue proved to be a mixture and was disregarded. The carbinol was characterised by boiling with an alcoholic solution of sodium 2-naphthoxide, the *β-hydroxy-β-methyltrimethylene-αγ-bis-2-naphthyl ether* being obtained as colourless crystals from alcohol, m. p. 151—152° (Found : C, 80·2; H, 6·2. $C_{24}H_{22}O_3$ requires C, 80·4; H, 6·1%).

A mixture of the carbinol (VI; 32 g.), dimethylamine (50 g., 4 mols.), and alcohol (100 g.) was heated at 115—125° for 8 hours. The cold product was concentrated, diluted with water, neutralised, extracted with ether to remove non-basic impurities, and the aqueous layer basified and extracted with ether. Fractional distillation gave *αγ-bisdimethylamino-β-methyl*iso*propyl alcohol* (VII; 27 g.), b. p. 80—81°/20 mm. (Found : N, 17·7. $C_8H_{20}ON_2$ requires N, 17·5%); an uninvestigated high-boiling residue remained. This amine gave a *dihydrochloride*, colourless deliquescent crystals from acetone–alcohol (1 : 1 by vol.), m. p. 250° (efferv.) (Found : Cl, 30·3. $C_8H_{20}ON_2,2HCl$ requires Cl, 30·5%); a *dipicrate*, yellow crystals from water, m. p. 172—173° (Found : N, 18·3. $C_8H_{20}ON_2,2C_6H_3O_7N_3$ requires N, 18·1%); and a *dimethiodide*, which crystallised from acetone containing a small quantity of alcohol as a *monohydrate*. The latter on direct heating dissolved in its water of crystallisation at 105—110°, but on slow heating it became anhydrous between 90° and 120° and then had m. p. 176—177°; confinement in a vacuum over phosphoric anhydride also gave the anhydrous material (Found, for the hydrate: C, 25·8; H, 6·0. $C_{10}H_{26}ON_2I_2,H_2O$ requires C, 26·0; H, 6·1%. Found, for the anhydrous product: C, 27·2; H, 6·2; N, 6·1. $C_{10}H_{26}ON_2I_2$ requires C, 27·0; H, 5·9; N, 6·3%).

Two other syntheses of the amine (VII) were also investigated. It was hoped to convert *s*-dichloroacetone into bisdimethylaminoacetone, $CO(CH_2{\cdot}NMe_2)_2$, and this by the action of methylmagnesium iodide into the amine (VII); the interaction of the dichloroacetone with dimethylamine gave, however, a dark product which could not be distilled or purified. The second method entailed the conversion of αγ-dichlorohydrin into αγ-bisdimethylamino*iso*propyl alcohol, oxidation of the latter to the ketone, and the conversion of this by the Grignard reagent as above into the amine (VII). A mixture of the dichlorohydrin (25 g.), dimethylamine (50 g., 4 mols.), and alcohol (100 g.) was heated in an autoclave at 115—120° for 7 hours. Alcohol and excess dimethylamine were then distilled off, and the residue, when worked up in the usual manner, gave the *αγ-bisdimethylamino*iso*propyl alcohol* as a colourless liquid (16 g.), b. p. 80—82°/17 mm. (Found: N, 18·9. $C_7H_{18}ON_2$ requires N, 19·2%). This amine was characterised as its *dimethiodide*, colourless crystals from alcohol, decomposing at 250° without melting (Found: C, 24·9; H, 5·5; N, 6·5; I, 59·3. $C_9H_{24}ON_2I_2$ requires C, 25·1; H, 5·6; N, 6·5; I, 59·1%). Oxidation of the amino-alcohol to the corresponding ketone could not be achieved, however, and this route to the compound (VII) was not further investigated.

All attempts to dehydrate the amine (VII) by heating with 70% sulphuric acid, powdered potassium hydroxide, or zinc chloride failed. When the dihydrochloride was heated at 260° for 5 mins., some decomposition appeared to occur, but the residue on purification gave the unchanged dihydrochloride (Found: Cl, 30·0%). When, however, the dimethiodide was heated at 185—190° for 10 mins., and the brown syrupy residue then extracted with boiling methyl alcohol until colourless, the insoluble crystalline product, which was unmelted at 350°, proved to be tetramethylammonium iodide (Found: C, 24·6; H, 6·2; N, 6·7; I, 62·4. Calc. for $C_4H_{12}NI$: C, 23·9; H, 6·0; N, 7·0; I, 63·2%).

To prepare the chloro-base (VIII), a solution of thionyl chloride (16 c.c., *ca.* 2 mols.) in chloroform (16 c.c.) was added rapidly with stirring to one of the amine (VII; 16 g.) also in chloroform (80 c.c.). A vigorous reaction caused the clear brown solution to boil and deposit crystals. The mixture was then boiled under reflux for 10 mins., and the chloroform and excess thionyl chloride were removed by distillation. The residue was dissolved in water (25 c.c.), mixed with ether (250 c.c.), and cooled in ice-water whilst a solution of sodium hydroxide (80 g.) in water (160 c.c.) was slowly added with stirring. The ethereal layer was separated, dried, and fractionally distilled, the *β-chloro-αγ-bisdimethylamino-β-methylpropane* (VIII; 12·7 g.) being obtained as a colourless liquid, b. p. 81°/15 mm. (Found: Cl, 19·4. $C_8H_{19}N_2Cl$ requires Cl, 19·9%). This amine gave a *dipicrate*, yellow crystals from alcohol, m. p. 155—156° (Found: N, 17·5. $C_8H_{19}N_2Cl,2C_6H_3O_7N_3$ requires N, 17·6%), and a *dimethiodide* (X), obtained as a brown crystalline material, which, when washed with cold acetone until colourless and then crystallised from alcohol containing a small quantity of water, had m. p. 195—196° (decomp.) (Found: C, 26·3; H, 5·6; N, 6·0. $C_{10}H_{25}N_2ClI_2$ requires C, 25·9; H, 5·4; N, 6·1%). This is very sparingly soluble in boiling absolute alcohol. It is noteworthy that the base (VIII) would not combine with methyl chloride in methyl-alcoholic solution at room temperature.

When this chloro-base (VIII) was boiled with alcoholic potash, potassium chloride was precipitated, but the product was *αγ-bisdimethylamino-β-ethoxy-β-methylpropane* (IX), b. p. 91—92°/15 mm. (Found: N, 14·5. $C_{10}H_{24}ON_2$ requires N, 14·9%), which was characterised as its *dimethiodide*, slightly hygroscopic crystals from a mixture of methyl and ethyl alcohols, melting to a viscous mass between 140° and 150° with effervescence and preliminary softening (Found: C, 30·3; H, 6·7; N, 5·8. $C_{12}H_{30}ON_2I_2$ requires C, 30·5; H, 6·4; N, 5·9%). Several other attempts to eliminate hydrogen chloride from the chloro-base by boiling it with powdered potash or with quinoline all failed. When, however, the dimethiodide (6·2 g.) was added to a boiling solution of pure potassium hydroxide (1 g., 1 mol.) in methyl alcohol (50 c.c.), and the mixture boiled under reflux for 30 mins., elimination of hydrogen chloride occurred smoothly. The precipitated potassium chloride was removed, and the filtrate neutralised with methyl-alcoholic hydrogen chloride, and evaporated to a syrup. This was dissolved in boiling methyl alcohol, and the solution filtered and diluted with alcohol until precipitation of a brown syrup was complete. The latter solidified on standing, and recrystallisation from alcohol gave *αγ-bistrimethylammonium-β-methylpropenylene di-iodide* (XI) as colourless crystals, m. p. 203—204° with darkening and slight preliminary softening (Found: C, 27·9; H, 5·8; N, 6·4; I, 59·6. $C_{10}H_{24}N_2I_2$ requires C, 28·2; H, 5·6; N, 6·6; I, 59·6%). A mixed m. p. determination using equal quantities of this compound and the dimethiodide of the "pyro"-base (m. p. 216—217°) gave 206—210° with darkening and preliminary softening precisely as with the two pure compounds. Since these m. p.'s were affected by both the age of the specimen and the rate of heating, the above values were determined side by side in the same bath with freshly crystallised and dried samples.

The dimethiodide (XI), treated in aqueous solution with sodium picrate, gave the *dimethopicrate*, yellow crystals from hot water, m. p. 245—246° (decomp.) (Found: C, 42·2; H, 4·5; N, 18·2. $C_{22}H_{28}O_{14}N_8$ requires C, 42·0; H, 4·5; N, 17·8%); mixed m. p. with the dimethopicrate of the "pyro"-base (m. p. 257—257·5°), 250—253° (decomp.).

When the dimethiodide (X) of the chloro-base was boiled with excess methyl-alcoholic potash (4 mols.), decomposition occurred with formation of trimethylammonium iodide, m. p. 254—255° (Found: C, 19·3; H, 5·4; N, 6·9; I, 68·4. Calc. for C_3H_9N,HI: C, 19·3; H, 5·3; N, 7·5; I, 67·9%); prolonged boiling of the original mixture caused the evolution of all the nitrogen as trimethylamine, and the filtrate gave a minute quantity of a red 2 : 4-dinitrophenylhydrazone, m. p. 174—177°. It is probable that the excess potash converted the ion of (X) first into that of (XI), then into (XII), and finally complete elimination of trimethylamine gave an aldehyde which clearly would be unstable in the presence of the hot potash.

Hydrogenation of the Dimethiodide (XI).—(A) A solution of this compound (0·519 g.) in water (25 c.c.), mixed with the platinum catalyst (0·1 g.), gave an apparent absorption of 62·0 c.c. of hydrogen at 17·5°/760 mm. (2·15 mols.), the absorption being rapid and complete. The filtered aqueous solution, evaporated to dryness, gave solely crude trimethylammonium iodide (0·431 g., 95% of theoretical), m. p. 242—245°, raised to 253—254° by warming with acetone and then unchanged by admixture with an authentic sample of m. p. 255—257°. This compound was further identified by conversion into the picrate, m. p. 217—220°, also unchanged by admixture with an authentic sample. The gaseous hydrocarbon evolved during hydrogenation was not analysed, as the source of the dimethiodide (XI) precluded the gas being other than *iso*butane.

(B) A similar reduction was performed in methyl-alcoholic solution to ensure that the *iso*butane remained dissolved and that an accurate measure of the hydrogen absorption was made. The dimethiodide (0·268 g.) in methyl alcohol (40 c.c.) with the catalyst (0·01 g.) absorbed 45·5 c.c. of hydrogen at 20°/761 mm., *i.e.*, 2·96 mols. The filtered solution on evaporation gave trimethylammonium iodide (0·195 g., 91%).

Oxidations.—(A) *Of the dimethiodide* (XI). Solutions of the dimethiodide (1·4 g.) in water (10 c.c.) and of silver sulphate (0·9 g., 1 mol.) in water (100 c.c.) were mixed, filtered, and the filtrate treated at 70° with a solution of potassium permanganate (3·1 g.) and anhydrous sodium carbonate (2 g.) in water (100 c.c.). The mixture was shaken for 10 mins. at this temperature and then filtered, evaporated to 10 c.c., refiltered, and treated with an acetic acid solution of phenylhydrazine. The phenylhydrazine oxalate which separated had, after crystallisation from water, m. p. 182—183°, mixed m. p. with authentic sample, 182—184°.

(B) *Of pyruvic acid.* (*a*) A solution of freshly distilled pyruvic acid (b. p. 70—72°/18 mm., 1·602 g.) and sodium carbonate (5 g.) was similarly treated at 70° with one of potassium permanganate (6·5 g.) in water (200 c.c.). The experiment was then completed precisely as in (A). Yield of phenylhydrazine oxalate, 4·07 g. (73%).

(*b*) A similar oxidation was performed with pyruvic acid (1·532 g.), but the oxalic acid was now precipitated as calcium oxalate and estimated volumetrically. Yield of oxalic acid, 1·470 g. (91%).

It would appear therefore that the oxidation to oxalic acid is not strictly quantitative and some acetic acid may be formed. Oxalic acid itself was found to be unaffected by boiling alkaline permanganate.

Action of Silver Oxide.—(A) *On the dimethiodide of the pyro-base.* The silver oxide used in all these experiments was prepared by interaction of silver nitrate and potassium hydroxide, both in hot aqueous solution; it was collected, washed repeatedly with boiling water, then with alcohol and ether, and dried in a vacuum at room temperature.

A solution of the dimethiodide (8 g.) in water (30 c.c.), mixed with silver oxide (14 g., 3·3 mols. Ag_2O), was boiled for 2 hours, the vapours evolved being absorbed in dilute hydrochloric acid; this was subsequently found to contain trimethylamine (identified as picrate, m. p. 216°) but no other amines or formaldehyde. The main solution was filtered, evaporated in an open dish to half-bulk, cooled, filtered again, and treated with aqueous picric acid. The precipitated *dipicrate* of (XIV) was thrice recrystallised from water and obtained as yellow needles, which were unaffected by exposure to phosphoric anhydride in a vacuum; m. p. 173—174° (Found: C, 44·7; H, 5·25; N, 16·1. $C_{26}H_{34}O_{15}N_8$ requires C, 44·7; H, 4·9; N, 16·0%). Yield of recrystallised picrate, 1 g. Trimethyl*iso*butylammonium picrate has the same m. p. (Hanhart and Ingold, J., 1927, 1017) and almost the same composition; a mixture of the two picrates had, however, m. p. 160—167°.

To identify the ion (XIV) further, the dipicrate was decomposed by hydrochloric acid, the picric acid removed with ether, and the colourless solution concentrated and divided into two portions. (*a*) Excess of chloroauric acid was added to one portion, and the *dichloroaurate* of (XIV), which was immediately precipitated, was collected and, after recrystallisation from dilute acetone, obtained as yellow needles, m. p. 201—202° (Found: for material dried in vacuum over phosphoric anhydride, Au, 42·8; for that dried in a vacuum at 130° for 10 hours, C, 18·5; H, 3·6; N, 3·15; Au, 42·95. $C_{14}H_{30}ON_2Cl_8Au_2$ requires C, 18·2; H, 3·3; N, 3·0; Au, 42·9%). The chloroaurate is sparingly soluble in hot water, readily so in hot acetone.

(*b*) The second portion, similarly treated with chloroplatinic acid, gave the *chloroplatinate* of (XIV), reddish-orange crystals from hot water, m. p. 206—207° (decomp.; efferv.) (Found: for material dried in a vacuum over phosphoric anhydride, Pt, 29·8; for material dried in a vacuum at 130° for 10 hours, C, 25·8; H, 4·7; N, 4·2; Pt, 30·05. $C_{14}H_{30}ON_2Cl_6Pt$ requires C, 25·8; H, 4·6; N, 4·3; Pt, 30·1%). The analytical figures in (*a*) and (*b*) show clearly that the oxygen is not present as a molecule of water of crystallisation.

(B) *On the synthetic dimethiodide* (XI). The dimethiodide (2 g.), water (10 c.c.), and silver oxide (4 g.) were treated precisely as in (A). The dipicrate, similarly recrystallised, had m. p. 173—174°, unchanged by admixture with that from (A) (Found: C, 44·5; H, 5·2; N, 16·2%).

(C) *On the chloro-dimethiodide* (X). (*a*) The dimethiodide (1 g.) in water (10 c.c.), with silver oxide (2·0 g., 4 mols.), was boiled for 1 hour, and then treated as in (A). The picrate obtained was notably less soluble in hot water than that of (XIV), and after recrystallisation had m. p. 243—246° (decomp.), unchanged by admixture with the synthetic dimethopicrate of m. p. 245—246° (Found : C, 42·6; H, 4·6; N, 18·5%).

(*b*) The experiment was repeated but with 4 g. of silver oxide and 3 hours' boiling. The dipicrate of (XIV) was now obtained, m. p. 173—174°. It is clear, therefore, that small quantities of the oxide merely abstract hydrogen chloride from (X) to give the ion of the synthetic dimethiodide (XI), which then with excess of oxide undergoes the usual degradation to (XIV).

(D) *On an old sample of the "pyro"-base dimethochloride.* This liquid sample (p. 166), similarly treated with silver oxide with limited boiling, also gave the synthetic dimethopicrate, which, thrice recrystallised from water, had m. p. 242—244° (decomp.), unchanged by admixture with authentic sample (Found : C, 42·3; H, 5·1; N, 18·6%).

Both trimethylamine and tetramethylammonium hydroxide were found to be unaffected by boiling in aqueous solution with excess silver oxide for 3 hours.

Acetonyltrimethylammonium picrate, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}NMe_3{\cdot}O{\cdot}C_6H_2(NO_2)_3$, was prepared for comparison with the picrate of (XIV). 30% Aqueous trimethylamine (5 c.c.) was added to a solution of chloroacetone (2 g.) in alcohol (40 c.c.); next day, the solution was evaporated to a syrup and then treated with alcoholic picric acid. The precipitated picrate, recrystallised from alcoholic acetone, formed large yellow needles, m. p. 149—150° (Found : C, 42·3; H, 4·1; N, 16·5. $C_{12}H_{16}O_8N_4$ requires C, 41·9; H, 4·6; N, 16·3%).

Attempted Preparation of 2 : 3-*Bisdimethylamino*-1-*methyl*cyclo*propane*.—For this purpose, 1-methyl*cyclo*propane-*trans*-dicarboxylic acid was required. The synthetic approach from ethyl crotonate (Goss, Ingold, and Thorpe, *loc. cit.*) gave a mixture of the *trans*- and the (*cis*)*cis*-acid, from which the pure *trans*-acid, being present in low proportion, could be isolated only in very small yield. The following experiments were therefore performed with the mixed ethyl esters of the two acids.

Amide. When a mixture of the ester (2 c.c.) and ammonia (30 c.c., *d* 0·88) was shaken for 15 hours and then allowed to evaporate to small bulk at room temperature, white crystals of the crude *amide-ammonium salt*, $C_4H_6(CO{\cdot}NH_2)(CO_2NH_4)$, m. p. 167—169° with effervescence and preliminary softening, separated out (Found: C, 45·5; H, 7·9; N, 17·8. $C_6H_{12}O_3N_2$ requires C, 45·0; H, 7·5; N, 17·5%). The same product was obtained with alcoholic ammonia, and in spite of a wide variation in conditions, a pure diamide could not be isolated.

Hydrazide. When hydrazine hydrate (15 g., 4 mols.) was added with stirring and cooling to a solution of the ester (10 g.) in alcohol (50 c.c.), a white solid was precipitated; recrystallisation of this substance from aqueous alcohol gave only a crude *dihydrazide*, m. p. 167—170°, which could not be further purified (Found : N, 30·4. $C_6H_{12}O_2N_4$ requires N, 32·6%). If the reaction was performed at room temperature, a product of lower nitrogen content, presumably contaminated with the cyclic hydrazide, was obtained. The Curtius degradation was therefore performed on this crude dihydrazide.

Ether (50 c.c.) was added to a solution of the dihydrazide (8·6 g.) in a mixture of water (70 c.c.) and concentrated hydrochloric acid (9 c.c.). The mixture was chilled in ice–salt and stirred whilst a solution of sodium nitrite (7 g.) in water (15 c.c.) was added during 30 mins. A vigorous effervescence of nitrogen finally occurred, and the diazide dissolved in the ether which acquired a pungent odour. The ethereal layer was boiled with alcohol, but a crystalline urethane could not be isolated. The alcoholic solution was evaporated to a syrup, and the latter boiled with hydrochloric aid. The solution on benzoylation furnished 2 : 3-*bisbenzamido*-1-*methyl*cyclo*propane* as colourless needles, m. p. 197—200° (Found : C, 73·5; H, 6·7; N, 9·8. $C_{18}H_{18}O_2N_2$ requires C, 73·5; H, 6·4; N, 9·5%). Many other attempts were made to prepare the pure azide, but all failed. Since the major difficulty in this work was clearly the presence of the *cis*-dicarboxylic acid, the conversion of this acid into the *trans*-isomeride was attempted by the method of Buchner (*Annalen*, 1895, **284**, 218), who showed that *cyclo*propane-*cis*-dicarboxylic acid on potash fusion gave a high yield of the *trans*-acid. A similar potash fusion on the mixed methyl-dicarboxylic acids gave, however, a syrupy mixture of acids, apparently consisting mainly of propionic acid. Attempts to synthesise the amine (IV) were therefore abandoned.

Methylation of Trimethyleneimine.—(*a*) A sample of the imine, b. p. 65—70°, reacted vigorously with undiluted methyl iodide, and gave only a sticky product. When ethereal solutions of the base and of excess methyl iodide were mixed at 0°, a white crystalline product slowly separated; two recrystallisations from alcohol gave *trimethyleneimine hydriodide*, m. p. 146·5°, suddenly resolidifying and melting again at 240—250° (decomp.) (Found : C, 20·1; H, 4·4; N, 7·4; ionised I, 68·1. C_3H_8NI requires C, 19·5; H, 4·3; N, 7·6; I, 68·6%).

(*b*) A solution of trimethyleneimine (0·39 g.) in methyl alcohol (5 c.c.) was treated with 15% methyl-alcoholic potash (2·6 c.c., 1 mol. KOH) and then with methyl iodide (2 c.c., 4 mols.) at 0°. After 2 hours the solution was evaporated to dryness on the water-bath, and the product extracted with much boiling ethyl alcohol to remove potassium iodide. The residual white solid, m. p. 225° (decomp., varies with rate of heating), was freely soluble in water, slightly soluble in glycol monomethyl ether, and insoluble in boiling methyl and ethyl alcohol, acetone, chloroform, acetonitrile, and ethyl carbonate. Analysis indicated that it was N-*methyltrimethyleneimine methiodide* still contaminated with a trace of potassium iodide (Found : C, 27·1;

H, 6·15; N, 6·35; ionised I, 60·0. $C_5H_{12}NI$ requires C, 28·2; H, 5·6; N, 6·6; I, 59·6%). This compound was unchanged after boiling with excess methyl iodide for 5 hours.

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