Oxidation Products of Diïsobutylene. Part II. The Isomerisation of 1 : 2-Epoxy-2 : 4 : 4-trimethylpentane, and Some Products derived from 2 : 4 : 4-Trimethylpentanal.*

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The catalytic isomerisation of 1 : 2-epoxy-2 : 4 : 4-trimethylpentane to 2 : 4 : 4-trimethylpentanal has been studied, in the liquid and in the gas phase, and optimum conditions have been determined. The trimethylpentanal can be readily reduced to 2 : 4 : 4-trimethylpentan-1-ol or oxidised to $\alpha\gamma\gamma$-trimethylvaleric acid. The isomerisation and hydrogenation can be carried out on the crude oxidation product of di*iso*butylene without isolation of the intermediate epoxide or aldehyde. A number of amines have been prepared from reductive amination of trimethylpentanal.

Catalytic isomerisation of 2 : 3-epoxy-2 : 4 : 4-trimethylpentane yields 2 : 4 : 4-trimethylpent-1-en-3-ol, 2 : 4 : 4-trimethylpentan-3-one, and 2 : 2 : 3 : 3-tetramethylbutanal. The 1 : 2-epoxide undergoes isomerisation when heated in the absence of catalyst, giving 2-*neo*pentylprop-2-en-1-ol; some 2 : 4 : 4-trimethylpentan-2-ol is also formed by an unknown mechanism.

The ready availability of 1 : 2-epoxy-2 : 4 : 4-trimethylpentane (see preceding paper) led us to examine a number of its reactions and the products derived therefrom. The present paper deals with products derived from the epoxide by prototropic change, and the following paper will describe those arising from ring-opening without isomerisation.

Catalysed Isomerisation of the Epoxytrimethylpentanes.—The literature gives numerous examples of the isomerisation of 1 : 2-epoxides to aldehydes in the liquid phase under the action of strong acids. Byers and Hickinbottom (*J.*, 1948, 1329, 1331) obtained 2 : 4 : 4-trimethylpentanal 2 : 4-dinitrophenylhydrazone by warming 1 : 2-epoxytrimethylpentane (I) with dilute sulphuric acid in the presence of dinitrophenylhydrazine. In the absence of dinitrophenylhydrazine, however, they obtained no more than a 24% yield of the free aldehyde (II) by reaction with aqueous sulphuric acid, the main products being the 1 : 2-diol and a bimolecular condensation product.

We have found that the aldehyde (II) can be obtained in yields of up to 95% under suitable conditions, by isomerisation with sulphuric acid. The principal requirements for optimum yields were the presence of an inert diluent to protect the aldehyde against the strong acid, and rapid isomerisation to reduce the chance of aldehyde–epoxide interaction. Sulphuric acid (50% v/v) was the most suitable catalyst. In more dilute acid (2N), formation of condensation product (cf. *idem, ibid.*) can largely be avoided by minimising the interaction of epoxide with aldehyde. This can best be done by ensuring a rapid reaction by agitation during the addition of epoxide to the acid, by protection of the aldehyde with an inert solvent, and by continuous steam-distillation of the product.

Other efficient liquid-phase catalysts were syrupy phosphoric acid and solid ferric and zinc chlorides. Numerous other catalysts (see Experimental) gave some isomerisation, but yields were poor.

In the vapour phase, the 1 : 2-epoxide isomerised readily at 200—350° over alumina, fuller's earth, or phosphoric acid on an inert support, giving good yields of trimethylpentanal. A "mixed-phase" technique was also tried, the catalyst being suspended in a hot inert solvent whilst epoxide vapour was passed through. However, at contact times sufficiently long to give complete conversion, the yield of aldehyde was lowered and side-reactions increased.

Isomerisation was also observed when the epoxide was added to acetic anhydride containing a trace of sulphuric acid. The expected glycol diacetate (V) was only detected

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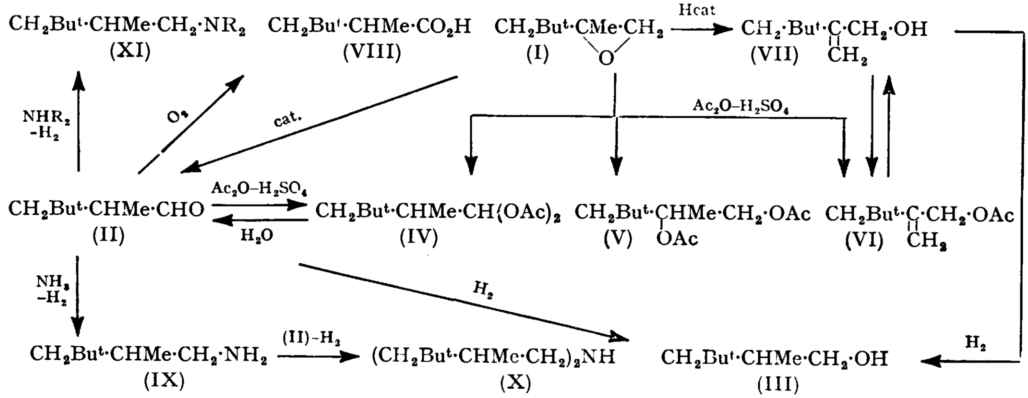
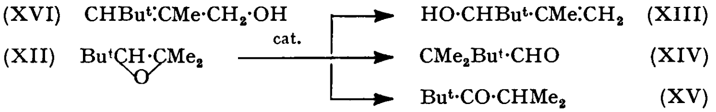
* Part I, preceding paper.

in very small amount; the major product was the isomeric aldehyde diacetate (IV)—identified by hydrolysis and synthesis—along with some 2-*neo*pentylallyl acetate (VI).



Isomerisation of purified 2 : 3-epoxy-2 : 4 : 4-trimethylpentane (XII) in the liquid phase with dilute sulphuric acid gave mainly 2 : 4 : 4-trimethylpent-1-en-3-ol (XIII) accompanied by 2 : 4 : 4-trimethylpentan-2 : 3-diol, in agreement with Hickinbottom (*ibid.*, p. 1331), who also found 2 : 2 : 3 : 3-tetramethylbutanal (XIV). In our experiment the only identified carbonyl product was 2 : 2 : 4-trimethylpentan-3-one (XV). From isomerisation in the vapour phase over alumina at 279—290°, the product was predominantly the ketone (XV), although a similar experiment with crude 2 : 3-epoxide (available in larger quantities) afforded a small amount of the aldehyde (XIV) as well. The 2 : 4-dinitrophenylhydrazones of these two products have the same m. p. (163°), but, as described by Byers and Hickinbottom, the derivative of (XV) forms orange leaflets and that of (XIV) yellow needles; the m. p. of an admixture is lower than that of either compound.



Non-catalytic Isomerisation of 1 : 2-*Epoxy*-2 : 4 : 4-*trimethylpentane to* 2-neo*Pentylprop*-2-*en*-1-*ol*.—During attempts to make the 1 : 2-epoxide react with an alcohol in absence of catalyst (cf. Part III, p. 2183), small amounts of a product finally identified as 2-*neo*pentylprop-2-en-1-ol (VII) were isolated when a solution of the epoxide in ethanol was heated for a long time at 200° or above. It appeared unlikely that this was derived from either of the ethoxytrimethylpentanols, and experiments confirmed that these were stable under the conditions of experiment, as was 2 : 4 : 4-trimethylpentane-1 : 2-diol. This left the possibility that it was a direct rearrangement product of the epoxide.

Isomerisation of epoxides to aldehydes or ketones by heat is known, especially in the aromatic series (see, *e.g.*, Tiffeneau *et al.*, *Bull. Soc. chim.*, 1931, **49**, 1709). Isomerisation to unsaturated alcohols by means of special catalysts has been described in patents (Fowler and Fitzpatrick, U.S.P. 2,426,264/1947; Lundsted, Schwoegler, and Jacobs, U.S.P. 2,479,632/1949).

When heated above 200° alone in a sealed tube, the epoxide did indeed give some *neo*pentylpropenol (VII). However, more drastic conditions of temperature or time led to formation of a more complex product, in which 2 : 4 : 4-trimethylpentan-1-ol (III) was found; the high unsaturation values sometimes obtained suggested also the presence of a diene, and much higher-boiling material was formed. Heating the epoxide in an inert solvent (medicinal paraffin) also gave only the trimethylpentanol (III) as identifiable product (small yield), and no unsaturated compounds at all.

The saturated alcohol (III) is presumably formed by a dehydrogenation or disproportionation, so that it should be accompanied by the equivalent amount of a more highly oxidised compound. It is possible that (VII) and (III) are formed simultaneously, but that after long heating the latter is decomposed and unmasks the small amount of (III) which otherwise would escape detection.

In order to prove the structure of the alcohol (VII), samples of it and the isomeric 2 : 4 : 4-trimethylpent-2-en-1-ol (XVI) were prepared by Ponndorff–Meerwein reduction of the corresponding aldehydes, which in turn were obtained from the vapour-phase oxidation of di*iso*butylene; the structure of the aldehydes has been proved (Hadley, Hall, Heap, and Jacobs, *J.*, 1954, 1416). Alcohol (VII) thus prepared was identical with the compound obtained from isomerisation of the epoxide, and also isolated from liquid-phase oxidation of di*iso*butylene (Part I, p. 2162). Alcohol (XVI) is identical with that described by Byers and Hickinbottom (*J.*, 1948, 1328, 1331). However, they described (*loc. cit.*) as (VII) an alcohol, b. p. 170—174°, n_D^{20} 1·4292 (*p*-nitrobenzoate, m. p. 44—45°; 3 : 5-dinitrobenzoate, m. p. 74—75°), the properties of which are at variance with ours (b. p. 72—73·5°/12 mm., n_D^{20} 1·4441; *p*-nitrobenzoate, m. p. 30—35°; 3 : 5-dinitrobenzoate, m. p. 56°). Since the structure of our alcohol is established as (VII) by synthesis, Hickinbottom's compound must be something else, possibly a stereoisomer of (XVI). He (*loc. cit.*, p. 1333) gives m. p. 80° for the dinitrobenzoate of (XVI), but earlier (p. 1330) a dinitrobenzoate, m. p. 51°, was assigned the same probable structure, without comment on the anomaly. The second corresponds in m. p. with that of our (VII).

Products derived from Trimethylpentanal.—Hydrogenation of 2 : 4 : 4-trimethylpentanal (II), suitably in the vapour phase at 200° over a copper–kieselguhr catalyst, provided 2 : 4 : 4-trimethylpentan-1-ol (III). It was indeed possible to treat crude di*iso*butylene oxidation product, from which unchanged olefin had been removed, successively with an isomerisation catalyst and then hydrogen over the appropriate catalyst. The yield of trimethylpentanol so obtained was more than that theoretically possible from the epoxide content of the product, and presumably other compounds, such as the dimeric condensation products, suffered conversion into the aldehyde and thence into trimethylpentanol. Any olefin remaining in the oxidation product was unchanged by this procedure, and the dimethylpentanone was converted into 4 : 4-dimethylpentan-2-ol at less than one-third of the rate that the aldehyde was hydrogenated. Some esters of trimethylpentanol were prepared.

Oxidation of trimethylpentanal (II) with molecular oxygen, with metallic salts as catalysts, gave $\alpha\gamma\gamma$-trimethylvaleric acid (VIII).

A number of amines were prepared by reductive amination of trimethylpentanal (II), and one from 4 : 4-dimethylpentan-2-one (cf. Emerson, *Org. Reactions*, 1948, **4**, 174). High yields of 2 : 4 : 4-trimethylpentylamine (IX) were obtained by hydrogenating (II) in the presence of an excess of methanolic or aqueous ammonia. Raney nickel served as catalyst, and temperatures of 100—140° were necessary in an autoclave. The structure of (IX) was checked by preparing it by reducing the oily oxime of (II) with sodium and ethanol. The secondary amine, bis-2 : 4 : 4-trimethylpentylamine (X), was similarly prepared in excellent yield by reduction of the aldehyde (II) in presence of a twofold excess of the primary amine (IX). The excess of (IX) could be recovered; an excess of only 10% resulted in a much poorer yield. Reductive amination of 4 : 4-dimethylpentan-2-one under similar conditions gave a moderate yield (~50%) of 1 : 3 : 3-trimethylbutylamine.

The preparation of the tertiary amines, *NN*-dimethyl- and *NN*-diethyl-2 : 4 : 4-trimethylpentylamine (XI; R = Me and Et, respectively), by reduction of mixtures of (II) and dimethylamine or diethylamine, was less successful, yields of 27% and 29% respectively being obtained with small excess of amine. With 3 mols. of diethylamine to one of aldehyde, the yield was reduced to 15%.

Several attempts to make (IX) by reductive amination in the vapour phase were made, but only 20—22% yields of amines were obtained over copper or nickel on kieselguhr catalysts at 200—210° with contact times of 6—22 sec. The use of trimethylpentanal dissolved in 4 volumes of 5N-methanolic ammonia gave better results.

Bis-2 : 4 : 4-trimethylpentylamine (X) was methylated by the Eschweiler–Clarke modification of Leuckart's procedure, formaldehyde and formic acid being used. In addition to the expected product, *N*-methyldi-(2 : 4 : 4-trimethylpentyl)amine (XVII) (66%), two further products, identified as *NN*-dimethyl-2 : 4 : 4-trimethylpentylamine (XI; R = Me) and 2 : 4 : 4-trimethylpentanal (II), were produced. From a number of small-scale experiments it was apparent that these two by-products occurred in approximately equimolar quantities. Corresponding by-products are reported to have occurred in the methylation of dibenzylamine (Clarke *et al.*, *J. Amer. Chem. Soc.*, 1933, **55**, 4571), and an analogous mechanism to that postulated may be applied in the present case.

The tertiary amines (XI; R = Me and Et) readily formed methobromides and methiodides. The amine (XVII) quaternised with more difficulty.

EXPERIMENTAL

Isomerisation of 1 : 2-*Epoxy*-2 : 4 : 4-*trimethylpentane to* 2 : 4 : 4-*Trimethylpentanal.—Liquid-phase.* (*a*) The best conditions for batch operation were as follows: Distilled epoxide (1 vol.) containing 90% of 1 : 2-epoxy-2 : 4 : 4-trimethylpentane, dissolved in *cyclo*hexane or benzene (3 vol.), was added to a stirred mixture of concentrated sulphuric acid (2 vol.) and water (2 vol.), kept below 30° by external cooling. The reaction was preferably conducted under an atmosphere of nitrogen or carbon dioxide. The isomerisation was very rapid, and the epoxide solution could be added as quickly as the removal of heat would allow. When the addition was complete, agitation was continued for a further 5 min. before separating the upper layer and shaking it with a small amount of potassium carbonate solution. The yield of aldehyde, by analysis of the resultant solution, was 89—92% on a 20-g. scale and 77—85% on a 400-g. scale. Equal yields of 2 : 4 : 4-trimethylpentan-1-ol could be obtained by direct hydrogenation of the solution of aldehyde. Distillation of the solution usually gave a somewhat lower yield of aldehyde; the fraction, b. p. 78°/100 mm., was obtained in the expected weight yield, but was only 90—92% pure by analysis by the hydroxylamine hydrochloride method.

(*b*) A 25% solution of epoxide in *cyclo*hexane and 50% aqueous sulphuric acid were fed countercurrent (epoxide at the lower end) into a 38 × 3·8 cm. (internal) glass column packed with porcelain saddles, and cooled externally by a water-jacket. Dispersion of the epoxide solution was effected by feeding in below the blades of a small stirrer operating in the lower part of the column. The two phases were allowed to separate at each end of the column; aldehyde–*cyclo*hexane solution continuously overflowed from the top of the column, and aqueous sulphuric acid was removed from the bottom. With a feed of 2·2 l. of epoxide solution per hr. per l. of reaction space (equivalent to a throughput of 456 g. of epoxide per hr. per l.) and an actual contact time of about 6 min., the yield of aldehyde was 71·4% on crude epoxide, or 82% on the 1 : 2-epoxide fed. No epoxide remained in the product, hence the rather low yields were due to occurrence of side-reactions. The average internal temperature of the column was kept at 20° during the experiment.

(*c*) Distilled epoxide (20·2 g.) containing 88% of the 1 : 2-isomer (by infra-red spectrum analysis), dissolved in an equal weight of *cyclo*hexane, was added slowly during 24 min. to 2N-sulphuric acid (200 ml.) with vigorous stirring under carbon dioxide. Steam was passed in so that the aldehyde steam-distilled out continuously as it was formed, along with the *cyclo*hexane. Analysis of the organic phase of the distillate indicated an aldehyde yield of 74% on epoxide taken, or 82% on the 1 : 2-isomer present.

Isomerisation in dilute sulphuric acid without steam-distillation gave variable yields, owing not only to the greater chance of the aldehyde decomposing, but also to greater formation of trimethylpentanediol.

(*d*) Epoxide stirred with 90% phosphoric acid as described in (*a*) above gave a 92% yield of aldehyde when the volume ratio of acid to epoxide solution was 1 : 100, and 88% when the volumes were equal.

(*e*) Aqueous hydrochloric or toluene-*p*-sulphonic acid gave inferior results.

(*f*) Some solid catalysts, mainly of the Friedel–Crafts type, were examined. In general, 1 : 2-epoxide solutions were dripped slowly on to a fixed amount (2%) of catalyst, then stirred under nitrogen at room temperature for 15 min. and finally heated to 70° for 30 min. The yield of aldehyde was determined by hydroxylamine titration after preliminary neutralisation. Details of the runs are given in Table 1.

The following gave no isomerisation (in *cyclo*hexane): Nickel chloride, mercuric chloride, alumina.

Vapour-phase. The apparatus consisted of a Pyrex U-tube immersed in a fusible-metal bath. One arm, 15 mm. in diameter, was filled with granules of alumina (Peter Spence, 10—18 mesh; previously used; sulphur-free) supported on a sintered-glass plate (catalyst volume 12—18 ml.). Epoxide was introduced into the other arm, which acted as a vaporiser and pre-heater. The epoxide content of the feed was determined by infra-red spectrum analysis, and the degree of isomerisation was measured by titration of aldehyde and epoxide in the product.

TABLE 1.

Catalyst	Solvent	Concn. of epoxide, %	Yield of aldehyde, %	Catalyst	Solvent	Concn. of epoxide, %	Yield of aldehyde, %
$ZnCl_2$ ...	None	—	41	$SnBr_4$ [5]	*cyclo*Hexane	25	78 [1, 3]
,, ...	*cyclo*Hexane	25	73 [1]	$SnCl_2$ [6]	Di*iso*butylene	25	75 [7]
,, ...	,,	12·5	84	BF_3,Et_2O	,,	25	62 [7]
,, ...	Benzene	25	84 [1]	$TiCl_4$	*cyclo*Hexane	25	66 [7]
,, ...	Di*iso*butylene	25	88 [2]	NaH_2PO_4	,,	25	6
$FeCl_3$ ...	None	—	25	$Al_2(SO_4)_3$	,,	25	8
,, ...	*cyclo*Hexane	25	91 [3]	Potash alum ...	,,	25	4 [7]
,, ...	,,	12·5	87·5	Zeocarb H.I. ...	,,	25	8
,, ...	Benzene	25	87·5 [4]	,, ...	Benzene	25	22
,, ...	Di*iso*butylene	25	48 [2]	Supercel	*cyclo*Hexane	25	4 [1]
$MgCl_2$ ...	*cyclo*Hexane	25	5·5	Fuller's earth [8]	,,	25	58
$CoCl_3$ ...	,,	25	5				

[1] Reaction is substantially complete after 15 min. at room temp. [2] Reaction is substantially complete after 15 min. at room temp., then 15 min. at 70°. [3] Final heating at 80° (30 min.). [4] Final heating for 15 min. at 70°; only 62% yield after 30 min. [5] 5% on epoxide. [6] 1% on epoxide. [7] Not heated. [8] Fulmont 700.

This procedure was adequate for a comparison of results under different conditions. The epoxide analysis (by hydrogen chloride–ether) would give a low result (cf. Part I, p. 2163), and applied to a first approximation only to the 1 : 2-isomer. The carbonyl analysis would also include dimethylpentanone which was originally present in known quantity in the epoxide fed and so could be allowed for in the result. The 2 : 3-epoxide gives only small amounts of keto-compounds which react with hydroxylamine in the cold (see below). In all runs except those in which obvious decomposition occurred, the weight balance was quantitative.

Highest aldehyde yields were obtained between 280° and 340°, and varied between 83 and 87% by weight, or 95—99·5% on the 1 : 2-epoxide used. The yield was unchanged over a variation in contact time (calculated as the vapour flow at the reaction temperature through an empty reaction vessel) between 2 sec. and about 100 sec. The catalyst had a life of $>$100 hr., although it became covered with a thin film of carbon. The average aldehyde yield, from an epoxide fraction of 92·7% purity, was 95% on the 1 : 2-epoxide fed; the total epoxide isomerised was 1075 g. per g. of catalyst.

Larger-scale experiments were carried out in an electrically-heated inclined Pyrex tube, 75 × 2·5 cm. (internal). The heat removal was not so efficient, and a hot zone formed in the catalyst at the feed end. Nevertheless, provided that contact time was sufficiently long (above 4 sec.) to prevent gross overheating, results as favourable as in the smaller apparatus were attained.

Granulated acid-washed fuller's earth (8—10 mesh) gave, after an initial period of rather lower yields, 98% of aldehyde on 1 : 2-epoxide fed. It appeared to be less vigorous and easier to control than alumina, but its catalytic life was not determined. Pumice or kieselguhr impregnated with phosphoric acid gave up to 90% yields under suitable controlled conditions; it was necessary to dilute the entering epoxide vapour, and to avoid the combination of high acid content and high feed rate, which resulted in charring. Oxidised aluminium (Dural) turnings gave a 76% yield.

Of vapour-phase catalysts, sulphur trioxide gave a 74% yield with considerable charring; dibutyl hydrogen phosphate 10—12%; and sulphur dioxide, although it entered into reaction with the epoxide at room temperature with evolution of heat, gave only 3—4% of aldehyde at 250°.

Reaction with acetic anhydride and sulphuric acid. Epoxide (128 g.) was added dropwise to stirred acetic anhydride (200 g.) containing sulphuric acid (2 g.). The reaction was highly exothermic, and the temperature was controlled below 60° by the rate of addition. After an hour, the sulphuric acid was neutralised with an excess of powdered anhydrous sodium acetate, and after filtration most of the acetic anhydride was removed under reduced pressure. The residue was partitioned between ether and water, and the alkali-washed ethereal layer distilled to give two main fractions, (i) b. p. 76°/12 mm., n_D^{20} 1·4338 (22·1 g.), and (ii) b. p.114°/12 mm., n_D^{20} 1·4296 (82·9 g.). Fraction (i) had a hydrolysis equivalent of 177 (calc., 170), and was shown spectroscopically to be impure 2-*neo*pentylallyl acetate (see below). This was confirmed by hydrolysis to the alcohol, b. p. 75—80°/20 mm., n_D^{20} 1·4440 (3 : 5-dinitrobenzoate, m. p. 47—48° undepressed by authentic material).

Fraction (ii) gave hydrolysis equivalent 122 (calc. for the glycol diacetate, 115), but was not identical with 2 : 4 : 4-trimethylpentane-1 : 2-diol diacetate (Part III, p. 2190). When warmed with 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid, it gave a precipitate of 2 : 4 : 4-trimethylpentanal 2 : 4-dinitrophenylhydrazone, but the glycol diacetate does likewise. It was rather resistant to alkaline hydrolysis; 40 g. of fraction (ii) were refluxed for 6 hr. with 20 g. of sodium hydroxide in 200 ml. of water and 50 ml. of ethanol, and the product was extracted and separated roughly into two fractions, boiling above and below 50°/12 mm., by rapid distillation without a column. The first fraction (10·1 g.) on refractionation through a column gave almost exclusively 2 : 4 : 4-trimethylpentanal, b. p. 42°/12 mm., n_D^{20} 1·4138 (dinitrophenylhydrazone, m. p. 145°). The second fraction yielded a little 2 : 4 : 4-trimethylpentane-1 : 2-diol, b. p. 104—105°/10 mm. (3·0 g.; solidified on cooling). The presence of 15% of diol in the hydrolysis product was also inferred from periodate titration.

Fraction (ii) was therefore presumed to consist of 15% of 2 : 4 : 4-trimethylpentane-1 : 2-diol diacetate (V) and the remainder of 2 : 4 : 4-*trimethylpentylidene diacetate* (IV). The latter was synthesised as follows: 2 : 4 : 4-trimethylpentanal (50 g.) was added slowly to acetic anhydride (100 ml.) containing sulphuric acid (2 g.), and, by the procedure of the last experiment, 37·8 g. of the diacetate were obtained, b. p. 112—114°/10 mm., n_D^{20} 1·4274 (Found: C, 63·4; H, 9·8%; equiv., 119. $C_{12}H_{22}O_4$ requires C, 62·5; H, 10·1%; equiv., 115). Infra-red spectroscopy showed that this was identical with the main component of fraction (ii) above. It did not give better analytical figures after repeated redistillations.

Isomerisation of 1 : 2-*Epoxy*-2 : 4 : 4-*trimethylpentane to* 2-neo*Pentylprop*-2-*en*-1-*ol*.—*In alcohol*. (*a*) The epoxide (100 g.) was heated in ethanol (500 ml.) to 220° in an autoclave for 5 hr. Distillation under reduced pressure removed alcohol and much unchanged epoxide, and the remainder was fractionated through a column. A main fraction (15·7 g.), b. p. 71—74°/12 mm., n_D^{20} 1·4409, was obtained, which had the properties of an unsaturated primary alcohol. It yielded a *p*-nitrobenzoate, m. p. 30—35° (crystallised from alcohol between 20° and −50°), and a 3 : 5-dinitrobenzoate, m. p. 52—53°. The carbon skeleton was proved by hydrogenation, over Adams's catalyst at room temperature and pressure, to 2 : 4 : 4-trimethylpentan-1-ol (3 : 5-dinitrobenzoate, m. p. 74° not depressed by authentic material). The unsaturated alcohol formed an acetate, b. p. 73°/15 mm., n_D^{20} 1·4280 (Found: equiv., 170. Calc. for $C_{10}H_{18}O_2$: equiv., 170). It was identified by comparison with synthetic material (see below) as 2-*neo*pentylprop-2-en-1-ol.

(*b*) A similar experiment but with methanol in place of ethanol gave the same product, with additional indications of some methoxytrimethylpentanol; the latter could not, however, be definitely identified.

Without solvent. In the following experiments, 10 g. of the epoxide were heated in a Carius tube and then distilled, the following fractions being collected: (i) b. p. 40—50°/10 mm. (unchanged epoxide, aldehyde), (ii) 50—72°/10 mm. (intermediate), (iii) 72—85°/10 mm. (trimethylpentenol and -pentanol), (iv) above 85°/10 mm., (v) undistillable residue. The product (iii) was identified by conversion into the 3 : 5-dinitrobenzoate, which was either that of 2-*neo*pentylprop-2-en-1-ol or of 2 : 4 : 4-trimethylpentan-1-ol. No attempt was made to fractionate the esters, so that it is possible that the more readily formed and crystallised trimethypentanol derivative may mask the presence of the trimethylpentenol. Attempts to estimate the percentage of unsaturated alcohol by bromide–bromate titration gave high and inconsistent values, sometimes well over 100% of apparent trimethylpentenol. Results are collected in Table 2.

Isomerisation in liquid paraffin. Epoxide (10 g.) was heated in medicinal paraffin (20 ml.) for 18 hr. at 275°, and in the same way gave (i) 1·2, (ii) 1·2, (iii) 1·5 g. Fraction (iii) showed only 10% of trimethylpentenol by titration, and gave the dinitrobenzoate of the trimethylpentanol.

2 : 4 : 4-*Trimethylpent*-2-*en*-1-*ol*.—β-*tert*.-Butyl-α-methylacraldehyde (αγγ-trimethylcrotonaldehyde) (23·5 g.; Hall, Hadley, Heap, and Jacobs, *loc. cit.*) was heated with 3N-aluminium *iso*propoxide in *iso*propanol (63 ml.) at the base of a fractionating column. Acetone was withdrawn from the head of the column until nearly the calculated amount had collected. The residue in the base was acidified and worked up to yield 2 : 4 : 4-trimethylpent-2-en-1-ol, b. p. 75—77°/20 mm. (13·0 g., 55%), n_D^{20} 1·4501. The 3 : 5-dinitrobenzoate formed flat needles,

m. p. 80° (Hickinbottom, *J.*, 1948, 1333, gives b. p. 177·5—178·5°/760 mm., n_D^{20} 1·4459; dinitrobenzoate, m. p. 80°).

2-neo*Pentylprop*-2-*en*-1-*ol*.—α-*neo*Pentylacraldehyde (22·3 g.) was similarly reduced with *iso*propoxide solution (60 ml.), yielding of 2-neo*pentylprop*-2-*en*-1-*ol* (7·0 g., 31%), b. p. 72—73·5°/12 mm., n_D^{20} 1·4441 (Found: C, 74·7; H, 12·2. $C_8H_{16}O$ requires C, 75·0; H, 12·6%). This was identical in infra-red spectrum with the unsaturated alcohol obtained by heating the 1 : 2-epoxide. It formed a 3 : 5-*dinitrobenzoate*, m. p. 56° not depressed by the derivative obtained by heating the epoxide (Found: C, 55·8; H, 5·6. $C_{15}H_{18}O_6N_2$ requires C, 55·8; H, 5·7%), and a 1-*naphthylurethane*, m. p. 83—85° (from light petroleum) (Found: C, 76·7; H, 7·8. $C_{19}H_{23}O_2N$ requires C, 76·8; H, 7·8%).

TABLE 2.

Conditions:		Wt. of products, g.					Identification of (iii) by dinitrobenzoate
Time, hr.	Temp.	(i)	(ii)	(iii)	(iv)	(v)	
24	200°	5·4	1·0	1·3	0	1·2	Trimethylpentenol
1·75	250	6·7	0	2·2	0	0	Unidentified
4	250	2·1	1·1	3·0	1·1	1·5	Trimethylpentenol
7	250	1·8	1·6	2·9	0·9	1·3	Trimethylpentanol (?)
18	250	0	0·6	3·1	2·6	1·7	Trimethylpentanol
2	275	3·1	2·3	3·6	0	0·8	Mixture

Isomerisation of 2 : 3-*Epoxy*-2 : 4 : 4-*trimethylpentane*.—(*a*) (cf. Hickinbottom, *J.*, 1948, 1333). The 2 : 3-epoxide, shaken for 1 hr. with 10% (wt.) aqueous sulphuric acid, gave mainly 2 : 4 : 4-trimethylpent-1-en-3-ol (XIII), identified as its 3 : 5-dinitrobenzoate, m. p. 120—121° (Hickinbottom, *loc. cit.*, gives 123°), and a little 2 : 4 : 4-trimethylpentane-2 : 3-diol, m. p. 62—63° (Byers and Hickinbottom, *ibid.*, p. 286, give m. p. 65—66°). The mixed product yielded a small amount of the orange-red 2 : 4-dinitrophenylhydrazone of 2 : 2 : 4-trimethylpentan-3-one (XV), m. p. and mixed m. p. 154—156°.

(*b*) In the vapour phase over alumina at 279—290°, the 2 : 3-epoxide (34 g.) gave a liquid product (26 g.), which was distilled to give the following fractions: (i) b. p. 123·5—127° (4 g.; 7·3% of C_8 ketone by titration), (ii) 127—135° (18 g.; 25% of ketone), (iii) 135° (8 g.; 29% of ketone), (iv) 110°/130 mm. (4 g.; 61% of ketone). In spite of the low carbonyl values, no other functional groups were detectable by infra-red analysis of the fractions, whereas the C=O bands were strong. It appeared that a carbonyl compound that did not react readily with hydroxylamine had been produced. Fractions (iii) and (iv) both yielded the orange-red dinitrophenylhydrazone, m. p. and mixed m. p. 158—160°, of 2 : 2 : 4-trimethylpentan-3-one. Fractions (i) and (ii) yielded dinitrophenylhydrazones which melted over a range; from (ii) was eventually obtained a derivative, m. p. 97—100°, depressed by admixture with the hydrazone of 4 : 4-dimethylpentan-2-one.

(*c*) From similar isomerisation (on a larger scale) of the dimethylpentanone–2 : 3-epoxide azeotrope were obtained the same products, and also a small quantity of a volatile solid, m. p. 109—119°, b. p. 46—52°/12 mm., with a strong odour of camphor. It gave a yellow 2 : 4-dinitrophenylhydrazone, m. p. 157—159°. When kept in contact with air for 2—3 months the original substance changed into an odourless acidic solid, m. p. 195—197° (sealed tube) after one recrystallisation from ethyl acetate. This was probably ααββ-tetramethylbutyric acid (cf. Byers and Hickinbottom, *ibid.*, p. 1336), and so the camphoraceous solid was 2 : 2 : 3 : 3-tetramethylbutanal (XIV), which is recorded as having a yellow dinitrophenylhydrazone, m. p. 163—164° (*idem, ibid.*, p. 286).

A sample of 2 : 2 : 4-trimethylpentan-3-one was synthesised by Favorsky and Fritzmann's method (*J. Russ. Phys. Chem. Soc.*, 1912, **44**, 1351); this gave the 2 : 4-dinitrophenylhydrazone as orange-red leaflets, m. p. 161—162° (Byers and Hickinbottom, *J.*, 1948, 287, record m. p. 163—164°).

Hydrogenation of 2 : 4 : 4-*Trimethylpentanal to Trimethylpentanol*.—The apparatus used was an electrically-heated Pyrex tube, 2·5 cm. in internal diameter, packed with 290 g. of copper–kieselguhr catalyst in the form of pellets (3 mm. diameter × 1 mm. thick). The liquid feed was first passed through a heated copper coil where it was vaporised and mixed with the hydrogen. The optimum conditions were: reaction temperature, 200° ± 10°; 6—7 moles of hydrogen per mole of aldehyde fed; and a contact time of *ca.* 20 sec. The product was separated by fractional distillation.

It was advantageous to carry through the preparation by removing unchanged di*iso*butylene from the oxidation product as far as possible by distillation, passing the residue through the isomerisation process under the conditions indicated above, and then hydrogenating the product by the procedure just described. Thus, crude isomerised oxidation product (518 g.) gave 508 g. of liquid product, which by distillation followed by chemical and infra-red analysis was shown to consist of di*ïso*butylene (4·8%), dimethylpentanone (5·7%), trimethylpentanone (8·7%), trimethylpentanal (1·5%), 4 : 4-dimethylpentan-2-ol (4·6%), 2 : 4 : 4-trimethylpentan-3-ol (4·5%), 2 : 4 : 4-trimethylpentan-1-ol (59·9%), and unknown material (10·1%, mainly in the distillation residue). The main fraction of 2 : 4 : 4-trimethylpentan-1-ol (267·2 g.), b. p. 168—169°/740 mm., was substantially pure.

The vapour pressure of 2 : 4 : 4-trimethylpentan-1-ol was as follows :

Pressure, mm.	20	40	60	100	200	400	760
Temp.	79·7°	93·1°	101·6°	113·6°	131·2°	151·2°	172·4°

Esters of 2 : 4 : 4-*Trimethylpentan*-1-*ol*.—A number of esters were prepared as in the following example : Adipic acid (36·5 g.; 0·25 mole), trimethylpentanol (100 g.; 0·77 mole), benzene (19 g.), and concentrated sulphuric acid (0·1 ml.) were heated under reflux, the water being removed by means of a Dean and Stark head. When the reaction was completed (6 hr.) the benzene was removed, and the crude ester washed and distilled. Other esters were prepared in a similar manner, except the phosphate which was made by slowly adding trimethylpentanol (109 g.) to a stirred solution of phosphorus oxychloride (38 g.) in benzene (107 g.); when the addition was complete the mixture was warmed on the steam-bath until evolution of hydrogen chloride ceased. The ester was then washed and distilled. The following esters were thus prepared :

			Equiv.	
	B. p./mm.	n_D^{20}	Reqd.	Found
Adipate	178°/1	1·4452	185	186
αγγ-Trimethylvalerate	92—93°/1	1·4307	256	259
Fumarate	168—172°/2	1·4540	170	168
Maleate	167°/3	1·4518	170	171
Pimelate	192°/1·5	1·4461	192	189
Orthophosphate	184°/2	1·4395	—	—
Oleate	208°/1	1·4547	394	378
cyclo*Hexene*-3-*carboxylate*	112°/2	1·4600	239	240

Oxidation of 2 : 4 : 4-*Trimethylpentanal to αγγ-Trimethylvaleric Acid*.—Oxygen was passed through trimethylpentanal (410 g.) containing manganese naphthenate (" Novenate," A. Boake Roberts & Co.; 1 g.) with rapid stirring, until absorption became very slow. Water separated during oxidation. The product was fractionally distilled, and trimethylvaleric acid came over at 90—94°/2 mm.; a higher fraction, b. p. 110—120°/1 mm., may have been the anhydride. Some material boiling below the aldehyde was always obtained, but could not be separated or identified. The results obtained at different oxidation temperatures may be summarised :

		O_2 absorbed	Peroxide, mole/l.		Yield of acid (% on
Temp.	Time, hr.	(% of theory)	Max.	Final	aldehyde charged)
50°	8	33	0·48	—	42
10—20	12·5	73	0·33	0·13	60
0	4·5	76	—	0·05	73·5

The oxidation rate decreased and degradation increased with increase of temperature. It appeared from further results that at low temperatures (0—10°) an unstable peroxide was formed (probably aldehyde peroxide), which decomposed (particularly on heating) to give mainly acid, whilst at higher temperatures (30—50°), a more stable peroxide was formed which was not greatly decomposed under the conditions of reaction.

A vanadium naphthenate catalyst gave more irregular results and one explosion. At low temperatures oxygen was taken up rapidly, but the catalyst was apparently incapable of decomposing the peroxide formed.

In order to convert it into the chloride, 100 g. of trimethylvaleric acid were warmed with 70 ml. of thionyl chloride until gas evolution had ceased and the mixture was boiling. The product was fractionated through a short column, and the acid chloride collected at 164—165°/750 mm. The yield was 107 g. (95% of theory).

Amines derived from 2 : 4 : 4-*Trimethylpentanal and* 4 : 4-*Dimethylpentan*-2-*one*.—2 : 4 : 4-

Trimethylpentylamine (IX). (*a*) 2 : 4 : 4-Trimethylpentanal (200 g., 1·56 moles) and 10N-methanolic ammonia (500 ml., 5 moles) were hydrogenated at 30 atm. and 120° in the presence of Raney nickel. Reduction was complete after 2 hr. The methanol was evaporated from the filtered solution, and then benzene was added and water removed as the azeotrope. Finally 2 : 4 : 4-trimethylpentylamine, b. p. 79—84°/78 mm. (173·2 g., 84%), was distilled out. The picrate gave no depression of m. p. in admixture with that prepared as in (*c*) below.

(*b*) Trimethylpentanal dissolved in four times its volume of 4N-methanolic ammonia was passed, with a tenfold excess of hydrogen, over pelleted nickel on kieselguhr (28% Ni) at 200°. The contact time was 20 sec. Conversions of 45% into 2 : 4 : 4-trimethylpentylamine and 16% into bis-2 : 4 : 4-trimethylpentylamine were thus attained.

(*c*) Trimethylpentanal (10 g.), hydroxylamine hydrochloride (10 g.), potassium acetate (15 g.), methanol (100 ml.), and water (50 ml.) were refluxed together for 1 hr. The mixture was poured into water, the oily layer extracted with ether, the extract washed successively with water, 2N-hydrochloric acid, water, aqueous sodium hydrogen carbonate, and water, dried, and concentrated to yield the oily oxime. This was dissolved in dry ethanol (500 ml.) and added in one portion to sodium (50 g.) cut in small pieces in a 2-l. flask fitted with an efficient reflux condenser. The reaction was allowed to proceed vigorously with only occasional cooling to prevent flooding of the condenser. The mixture was finally heated on the steam-bath until all the sodium had reacted, poured into a large quantity of water, and the basic fraction isolated in ether. From it, 2 : 4 : 4-*trimethylpentylamine* (22%) was obtained, b. p. 45—47°/12 mm., 150—152°/735 mm., n_{D}^{20} 1·4280 (Found: C, 73·5; H, 14·5; N, 10·9%; equiv., 130. $C_8H_{19}N$ requires C, 74·3; H, 14·8; N, 10·8%; equiv., 129). The carbon values for this compound were persistently low. The *picrate* crystallised from aqueous ethanol in yellow plates, m. p. 190° (Found: C, 47·2; H, 5·9; N, 15·6. $C_8H_{19}N,C_6H_3O_7N_3$ requires C, 46·9; H, 6·2; N, 15·6%). The *sulphate* crystallised in colourless plates, m. p. 268—272°, from hot water on dilution with ethanol (Found: N, 7·6. $2C_8H_{19}N,H_2SO_4$ requires N, 7·9%).

Bis-2 : 4 : 4-*trimethylpentylamine* (X).—2 : 4 : 4-Trimethylpentylamine (197 g.; 88% pure; 1·34 mole), 2 : 4 : 4-trimethylpentanal (105 g.; 85% pure; 0·70 mole), methanol (150 ml.), and Raney nickel were hydrogenated at 50 atm. and 110—125°. Reaction was complete after 6 hr. Distillation of the filtered product afforded the secondary *amine*, b. p. 121—124°/11 mm., n_{D}^{20} 1·440 (154 g., 92% based on aldehyde) (Found: C, 79·0; H, 14·3; N, 5·8. $C_{16}H_{35}N$ requires C, 79·6; H, 14·5; N, 5·8%). The *hydrochloride* had m. p. 134—137° after recrystallisation from ethyl acetate (Found: N, 4·8. $C_{16}H_{35}N,HCl$ requires N, 5·0%).

N-*Methylbis*-2 : 4 : 4-*trimethylpentylamine*.—98% Formic acid (50 ml.) was added carefully to bis-2 : 4 : 4-trimethylpentylamine (50 g.), so that the temperature of the mixture remained below 40°. 40% Aqueous formaldehyde (50 ml.) was then added, and the mixture warmed until evolution of carbon dioxide began. When this was substantially complete, the mixture was refluxed for 2 hr., then poured into a large volume of water and basified with sodium hydroxide. The oil which separated was isolated, by use of ether, and distilled. The main fraction, b. p. 120—130°/12 mm. (b. p. 127—128°/13 mm., n_{D}^{20} 1·4377, after redistillation) was the tertiary *amine* (XVII) (34·8 g., 66%) (Found: C, 80·3; H, 14·7; N, 5·2%; equiv., 258. $C_{17}H_{37}N$ requires C, 79·9; H, 14·6; N, 5·5%; equiv., 255). The *picrate* crystallised from ethanol in yellow plates, m. p. 128—129° (Found: C, 57·2; H, 8·2; N, 11·7. $C_{17}H_{37}N,C_6H_3O_7N_3$ requires C, 57·0; H, 8·3; N, 11·6%), and the *hydrobromide* had m. p. 238° (from aqueous ethanol) (Found: C, 60·2; H, 11·1; N, 4·1. $C_{17}H_{37}N,HBr$ requires C, 60·7; H, 11·4; N, 4·2%).

The fore-runnings of the distillation (b. p. 30—120°/12 mm.) were separated into basic and neutral material. Distillation of the former gave *NN*-dimethyl-2 : 4 : 4-trimethylpentylamine, b. p. 47—50°/10 mm., n_{D}^{20} 1·4220, equiv., 158, m. p. and mixed m. p. of picrate, 107° (cf. below). The neutral fraction boiled mainly at 143—148°, n_{D}^{20} 1·4178, and contained aldehyde equivalent to 80% of 2 : 4 : 4-trimethylpentanal. The 2 : 4-dinitrophenylhydrazone, m. p. 136—137°, gave no depression of m. p. when mixed with the derivative of authentic 2 : 4 : 4-trimethylpentanal.

Quaternisation of methylbis-2 : 4 : 4-trimethylpentylamine (2 g.) with methyl iodide (5 g.) at 110° for 2 hr. in a Carius tube gave the *methiodide* (1·35 g.), which had m. p. 198° (decomp.) after recrystallisation from aqueous ethanol (Found: N, 3·0. $C_{18}H_{40}NI$ requires N, 2·8%).

Quaternisation of the amine (XVII) (20 g., 0·0785 mole) with methyl bromide (16 g., 0·168 mole) in ethyl acetate (50 ml.) containing sodium iodide (1 crystal) at 110° for 4 hr. in Carius tubes afforded a crude solid (23·0 g.) insoluble in the solvent. The mother-liquor contained unchanged amine (18%). The solid was taken up in chloroform and washed with 2N-sodium hydroxide to decompose the amine hydrobromide which it contained. The chloroform layer was reconcentrated, and the residual sticky solid triturated with ethyl acetate. On recrystallisation from ethanol–ethyl acetate the m. p. of the *methobromide* (18·9 g.) was raised to 209—210° (Found: C, 62·0; H, 11·4. $C_{18}H_{40}NBr$ requires C, 61·7; H, 11·5%); a mixed m. p. with hydrobromide described above was 186—189°.

1 : 3 : 3-*Trimethylbutylamine*.—4 : 4-Dimethylpentan-2-one (68 g., 0·60 mole) and 10N-methanolic ammonia (150 ml., 1·5 moles) were hydrogenated at 55 atm. and 120—140° over Raney nickel. 1 : 3 : 3-Trimethylbutylamine, b. p. 118—121°, n_D^{20} 1·416, was fractionated out of the product (49%). The *picrate* crystallised from aqueous ethanol in yellow needles, m. p. 181—182° (Found: C, 45·6; H, 6·0; N, 16·5. $C_7H_{17}N,C_6H_3O_7N_3$ requires C, 45·3; H, 5·9; N, 16·3%).

NN-*Diethyl*-2 : 4 : 4-*trimethylpentylamine* (XI; R = Et).—A mixture of trimethylpentanal (400 g., 3·1 moles), diethylamine (235 g., 3·2 moles), methanol (200 ml.), and Raney nickel was reduced at 100° and 50 atm. pressure of hydrogen in the usual way. The main fraction had b. p. 71—76°/14 mm. (93·5 g., 16%) and redistillation afforded NN-*diethyl*-2 : 4 : 4-*trimethylpentylamine*, b. p. 70—71°/10 mm., n_D^{20} 1·4272, K_b 10^{-4} (Found: C, 77·7; H, 14·6; N, 7·9%; equiv., 182. $C_{12}H_{27}N$ requires C, 77·8; H, 14·7; N, 7·6%; equiv., 185). The *picrate*, after recrystallisation from aqueous ethanol, had m. p. 96—97° (Found: N, 13·4. $C_{12}H_{27}N,C_6H_3O_7N_3$ requires N, 13·5%). From the high-boiling residue of the distillation, some *NN*-diethyl-2-hydroxy-2 : 4 : 4-trimethylpentylamine, b. p. 90—100°/10 mm. (7·0 g.), was obtained, and identified with the material otherwise prepared (Part III) by a mixed m. p. of the picrate, m. p. 104—105°.

The amine was quaternised by refluxing it with excess of methyl iodide on a steam-bath for 1 hr. The *methiodide* obtained had m. p. 101—102° after recrystallising from acetone–ether and drying at 0·2 mm. for 3 hr. (Found: C, 47·6; H, 9·2; I, 39·3. $C_{13}H_{30}NI$ requires C, 47·7; H, 9·2; I, 38·8%). The *methobromide*, prepared from the amine and methyl bromide in benzene at 110° for 5 hr., had m. p. 110° after recrystallisation from acetone–ethyl acetate, and was very hygroscopic (Found: Br, 28·8. $C_{13}H_{30}NBr$ requires Br, 28·6%).

NN-*Dimethyl*-2 : 4 : 4-*trimethylpentylamine* (XI; R = Me).—A mixture of 2 : 4 : 4-trimethylpentanal (240 g., 1·87 moles), 33% aqueous dimethylamine (350 ml., 1·33 moles), ethanol (400 ml.), and Raney nickel was reduced as in the experiment described above, giving *NN*-dimethyl-2 : 4 : 4-trimethylpentylamine, b. p. 53—63°/11 mm., n_D^{20} 1·423 (79 g., 27%; 96% pure by base titration). The *picrate* had m. p. 105—196° after recrystallisation from ethanol (Found: C, 49·4; H, 6·2; N, 14·5. $C_{10}H_{23}N,C_6H_3O_7N_3$ requires C, 49·7; H, 6·7; N, 14·5%). The *hydrochloride* had m. p. 167—168° after recrystallisation from *iso*propanol–ether (Found: N, 6·9. $C_{10}H_{23}N,HCl$ requires N, 7·2%).

The amine was quaternised by leaving it with an excess of methyl iodide in ethyl acetate for 2 days. The *methiodide* which separated as a white solid (7·7 g., 73%) had m. p. 238° (decomp.) after recrystallisation from acetone–ethyl acetate (Found: C, 44·2; H, 8·5. $C_{11}H_{26}NI$ requires C, 44·1; H, 8·8%).

The amine (30 g.), methyl bromide (20 g.), and ethyl acetate (100 ml.) were heated in a silver-lined autoclave to 140—150° for 4 hr. The crystalline, hygroscopic *methobromide* was filtered off and recrystallised from ethanol–ethyl acetate; the yield was 35·1 g. (73%) (Found: Br, 31·9. $C_{11}H_{26}NBr$ require Br, 31·7%). By further recrystallisation a m. p. of 275° (decomp.) was attained.

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