The Synthesis and Reactions of Branched-chain Hydrocarbons. Part IV. The Synthesis of Ketones with Quaternary Carbon Atoms.*

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The rearrangement of some ditertiary glycols in concentrated sulphuric acid has been examined as a possible route to ketones having two or more quaternary carbon atoms. It is accompanied by varying amounts of fission into olefins and ketones.

The preparation of glycols from hydroxy-ketones has been improved by using lithium alkyls instead of alkylmagnesium halides.

A POSSIBLE synthesis of hydrocarbons with two or more quaternary carbon atoms involves rearrangement of ditertiary glycols (I) to ketones (II or III), followed by reduction of the carbonyl group. The reduction will form the subject of a subsequent paper: an investigation of the rearrangement is now reported, with the object of determining its usefulness.

Preparation of the glycols (I) by reaction of α-hydroxy-ketones (IV) with methylmagnesium halides is unsatisfactory both in yield and in ease of reaction. A considerable

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* Part III, preceding paper.

improvement in yield is obtained by use of methyl-lithium, more particularly if the solution is concentrated by distillation.

Rearrangement of 2 : 3 : 4 : 4-tetramethylpentane-2 : 3-diol (I*b*; $R = Bu^t$) in cold concentrated sulphuric acid gave 3 : 3 : 4 : 4-tetramethylpentan-2-one (III*b*; $R = Bu^t$) and some hexamethylacetone (II*b*; $R = Bu^t$). 2 : 3 : 5 : 5-Tetramethylhexane-2 : 3-diol (I*b*; $R = CMe_3\cdot CH_2$) yielded under similar conditions 3 : 3 : 5 : 5-tetramethylhexan-2-one (III*b*; $R = CMe_3\cdot CH_2$) and a small amount of 2 : 2 : 5 : 5-tetramethylhexan-3-one (II*b*; $R = CMe_3\cdot CH_2$). In both these rearrangements there was evidence of the formation of olefin and a lower-boiling ketone, but the amounts were too small to permit accurate identification. The formation of fission products was noticeably greater during the rearrangement of 2 : 4-dimethyl-3-*iso*propylpentane-2 : 3-diol (I*a*; $R = Pr^i$); acetone corresponding to not more than 4% fission of the glycol was isolated as well as some olefin which could not be precisely identified. The normal products of the rearrangement, 2 : 4 : 4 : 5-tetramethylhexan-3-one (II*a*; $R = Pr^i$) and 2 : 3-dimethyl-3-*iso*propylpentan-4-one (III*a*; $R = Pr^i$), were obtained in good yield.

(*a*) $HO\cdot CR_2\cdot CMe_2\cdot OH$	$R\cdot CO\cdot CRMe_2$	$CR_2Me\cdot COMe$	$HO\cdot CR_2\cdot COMe$
(*b*) $HO\cdot CRMe\cdot CMe_2\cdot OH$	$R\cdot CO\cdot CMe_3$	$CRMe_2\cdot COMe$	$HO\cdot CRMe\cdot COMe$
(I)	(II)	(III)	(IV)

No rearrangement products were obtained by the action of cold sulphuric acid on 2 : 3 : 4 : 4 : 6 : 6-hexamethylheptane-2 : 3-diol (I*b*; $R = CMe_3\cdot CH_2\cdot CMe_2$). Instead, methyl *iso*propyl ketone and a mixture of olefins were obtained. The yield of pure ketone indicates 50% of fission as a minimum while calculations from the yield of crude olefin suggest a much higher figure. Discussion of the factors which may determine the course of the reaction is reserved for a later paper.

EXPERIMENTAL

Preparation of Glycols.—The conditions described by Locquin and Wouseng (*Compt. rend.*, 1923, **176**, 682; cf. Leers, *Bull. Soc. chim.*, 1926, **39**, 423) gave yields of about 20%. Use of methyl-lithium was more satisfactory.

3-Hydroxy-3 : 4 : 4-trimethylpentan-2-one (38 g.) in ether (100 c.c.) was added to a stirred solution of methyl-lithium (from 9 g. of lithium, 115 g. of methyl iodide, and 600 c.c. of ether) at 0°. Reaction was completed by 2 hours' stirring at room temperature and 6 hours' refluxing. The mixture was poured into dilute acetic acid and ice, and extracted with ether. The extracts were washed with aqueous sodium carbonate and sodium thiosulphate, dried, and distilled. 2 : 3 : 4 : 4-Tetramethylpentane-2 : 3-diol had b. p. 98—100°/17 mm., m. p. 22°, n_D^{20} 1·4597 (supercooled) (yield 24·5 g., 58%). Locquin and Wouseng (*loc. cit.*) give b. p. 99—100°/13 mm., melting in the hand. Fission of the glycol by periodic acid and separation of the products by the method described on p. 2535 gave acetone and pinacolone, identified by comparison of their 2 : 4-dinitrophenylhydrazones with genuine specimens.

The following glycols were prepared by adding 3-hydroxy-3 : 4 : 4-trimethylpentan-2-one to the appropriate alkyl-lithium in ether, replacing the solvent by benzene, and heating under reflux : 2 : 2 : 3 : 4-*Tetramethylhexane*-3 : 4-*diol* (25%), m. p. 29°, b. p. 109°/17 mm. (Found : C, 69·2; H, 12·6. $C_{10}H_{22}O_2$ requires C, 68·9; H, 12·7%). 2 : 2 : 3 : 4 : 5-*Pentamethylhexane*-3 : 4-*diol* (31%), m. p. 50°, b. p. 103—104°/3 mm. (Found : C, 70·4; H, 12·6. $C_{11}H_{24}O_2$ requires C, 70·2; H, 12·8%). 2 : 2 : 3 : 4-*Tetramethyloctane*-3 : 4-*diol* (20%), m. p. 59°, b. p. 94/2 mm. (Found : C, 71·2; H, 12·65. $C_{12}H_{26}O_2$ requires C, 71·2; H, 12·95%). Each of these glycols was oxidised by periodic acid in aqueous methanol to pinacolone and a ketone corresponding to the structure of the glycol. They were converted into 2 : 4-dinitrophenylhydrazones which were separated by chromatography on silica.

Preparation of other glycols is described below.

Rearrangement of 2 : 3 : 4 : 4-*Tetramethylpentane*-2 : 3-*diol.*—The diol (190 g.) was added slowly to concentrated sulphuric acid (2100 g.) at −10°, with efficient stirring. Next morning, the solution was poured on crushed ice (3 kg.) and steam-distilled. The yellow volatile oil was separated, dried, and resolved by precise distillation into 3 : 3 : 4 : 4-tetramethylpentan-2-one, b. p. 165—168° (117 g.), which solidified, and fractions containing hexamethylacetone. After draining on porous earthenware and crystallising from light petroleum, 3 : 3 : 4 : 4-tetramethylpentan-2-one had m. p. 62°, b. p. 168° (semicarbazone, m. p. 207—208°). Locquin and

Wouseng (*ibid.*, 1924, **35**, 753) give m. p. 63—64°, b. p. 167·4° (semicarbazone, m. p. 207—208°). The 2 : 4-dinitrophenylhydrazone formed orange needles, m. p. 188·5° (Found : C, 56·0; H, 7·1; N, 17·8. Calc. for $C_{15}H_{22}O_4N_4$: C, 55·9; H, 6·9; N, 17·4%) (Howard *et al.*, *J. Res. Nat. Bur. Stand.*, 1947, **38**, 365, give m. p. 182—183°).

Preparation and Rearrangement of 2 : 3 : 5 : 5-*Tetramethylhexane*-2 : 3-*diol*.—3-Hydroxy-3 : 5 : 5-trimethylhexan-2-one (190 g.) in ether was added slowly to methyl-lithium [from lithium (42 g.) and methyl bromide in ether (2600 c.c.)] at room temperature. The bulk of the ether (2000 ml.) was then distilled off and the concentrated residue heated under reflux for 10 hr., then decomposed by water. The *glycol*, removed by extraction with ether and distilled, had m. p. 39°, b. p. 100°/13·5 mm., n_{D}^{20} 1·4538 (supercooled) (Found : C, 68·7; H, 12·8. $C_{10}H_{22}O_2$ requires C, 68·9; H, 12·75%). The yield was 90%, but about 60% if concentration of the ethereal reaction mixture was omitted.

Fission of the glycol into acetone and 4 : 4-dimethylpentan-2-one was brought about by shaking a solution of the glycol (2 g.) in methanol (7 c.c.) and water (12 c.c.) with periodic acid (1·5 g.). A yellow oil separated when the solution was diluted after 4 hr.; it consisted of a mixture of two ketones which were separated by chromatography of their 2 : 4-dinitrophenylhydrazones on silica. The less strongly adsorbed hydrazone, m. p. 101°, gave no depression with that of 4 : 4-dimethylpentan-2-one. The other was acetone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 126°.

The finely powdered glycol (348 g.) was added to concentrated sulphuric acid (3700 g.) at −10° to −15°, efficiently stirred. After being kept overnight, the solution was poured on ice (1·5 kg.), and the volatile products were removed by steam-distillation. The oil thus obtained was taken up in ether and fractionated after washing and drying. The main fraction, 3 : 3 : 5 : 5-*tetramethylhexan*-2-*one* (220 g.), n_{D}^{20} 1·4324, was collected at 74—77°/18 mm. The lower-boiling fractions were distilled again to give approximately pure 2 : 2 : 5 : 5-tetramethylhexan-3-one, b. p. 160—161°, n_{D}^{20} 1·4200 (15 g.). Unsaturated material was condensed in the cold traps of the earlier distillations but no pure substance was isolated.

3 : 3 : 5 : 5-Tetramethylhexan-2-one, b. p. 70—71°/13 mm., n_{D}^{20} 1·4326, d_{20}^{20} 0·8441 (Found : C, 76·8; H, 13·1. $C_{10}H_{20}O$ requires C, 76·85; H, 12·9%) is a mobile liquid of faint camphoraceous odour and gives a 2 : 4-*dinitrophenylhydrazone*, orange-yellow, m. p. 109·5—110° (Found : C, 57·3; H, 7·1; N, 16·6. $C_{16}H_{24}O_4N_4$ requires C, 57·1; H, 7·2; N, 16·7%), and a *semicarbazone*, m. p. 188° (Found : C, 62·25; H, 11·0; N, 19·5. $C_{11}H_{23}ON_3$ requires C, 61·9; H, 10·9; N, 19·7%). Reduction of the ketone in ether with lithium aluminium hydride gives 3 : 3 : 5 : 5-*tetramethylhexan*-2-*ol*, b. p. 87—87·5/27 mm., n_{D}^{20} 1·4458 (Found : C, 76·0; H, 13·9. $C_{10}H_{22}O$ requires C, 75·85; H, 14·0%) [3 : 5-*dinitrobenzoate*, m. p. 83·5—84° (Found : C, 58·0; H, 6·6; N, 8·4. $C_{17}H_{24}O_6N_2$ requires C, 57·9; H, 6·9; N, 8·0%)]. The ketone (3 g.) was added slowly to nitric acid (*d* 1·42; 25 c.c.) diluted with an equal volume of water, and then heated under reflux for 8 hr. The mixture was diluted with water and extracted with benzene. Unchanged ketone and 2 : 4 : 4-trimethylpentane-2-carboxylic acid, b. p. 119—121°/13 mm., m. p. 43—45°, were obtained. The m. p. of the acid was unchanged on admixture with an authentic specimen (Whitmore, Wheeler, and Surmatis, *J. Amer. Chem. Soc.*, 1941, **63**, 3237); the p-*toluidide* had m. p. 116° (Found : C, 77·6; H, 10·5; N, 5·9. $C_{16}H_{25}ON$ requires C, 77·7; H, 10·2; N, 5·7%).

2 : 2 : 5 : 5-Tetramethylhexan-3-one, b. p. 160—161°, gives no ketonic derivatives. Whitmore and Heyd (*J. Amer. Chem. Soc.*, 1938, **60**, 2030) claim that a 2 : 4-dinitrophenylhydrazone, m. p. 123·5—124·5°, is formed with considerable difficulty. We are unable to confirm this. The ketone is best identified by reduction to 2 : 2 : 5 : 5-tetramethylhexan-3-ol, m. p. and mixed m. p. 50—51° (Whitmore and Heyd, *loc. cit.*, give m. p. 49·4°) [3 : 5-*dinitrobenzoate*, m. p. 146° (Found : C, 57·8; H, 6·8; N, 8·0. $C_{17}H_{24}O_6N_2$ requires C, 57·9; H, 6·9; N, 8·0%)].

Preparation and Rearrangement of 2 : 4-*Dimethyl*-3-iso*propylpentane*-2 : 3-*diol*.—Methyl-lithium [from lithium (21 g.), methyl bromide, and ether (1300 c.c.)] with 3-hydroxy-4-methyl-3-*iso*propylpentan-2-one (95 g.) gave crystalline 2 : 4-*dimethyl*-3-iso*propylpentane*-2 : 3-*diol* (52·5 g.) with lower-boiling fractions of unchanged ketol. In subsequent preparations the yield was raised to 80% by distilling off the ether, replacing it with dry benzene, and refluxing for 8 hr. The pure glycol, m. p. 68° (from light petroleum, b. p. 40—60°), b. p. 119°/18 mm. (Found : C, 68·9; H, 12·55. $C_{10}H_{22}O_2$ requires C, 68·9; H, 12·75%), was oxidised by periodic acid in aqueous methanol to acetone and di*iso*propyl ketone, identified as 2 : 4-dinitrophenylhydrazones.

The glycol (100 g.) was added slowly to concentrated sulphuric acid (1000 g.) at −10° to 0°, with stirring. The mixture was kept at −5° for 3 hr., then poured on crushed ice (2 kg.), and steam-distilled after further dilution. The volatile product was removed with ether, washed with aqueous sodium carbonate, dried, and fractionated into two main fractions: (*a*) b. p. 79°/22 mm., n_D^{20} 1·4284 (52 g.), (*b*) b. p. 84—88°/22 mm., n_D^{20} 1·4398—1·4416 (14·3 g.); residue, 4·6 g. The most volatile fractions were collected in a cold trap, and amounted to 4·8 g., of which 1·7 g. had b. p. 60—65°, n_D^{20} 1·3604, and consisted essentially of acetone. No other compound could be identified with certainty; some olefinic compounds were present; no di*iso*propyl ketone was found.

Refractionation of (*a*) gave pure 2 : 4 : 4 : 5-*tetramethylhexan*-3-*one*, b. p. 79°/22 mm., n_D^{20} 1·4275, a colourless liquid of camphoraceous odour (Found: C, 77·3; H, 13·0. $C_{10}H_{20}O$ requires C, 76·9; H, 12·9%). No carbonylic derivatives could be prepared from it, but reduction with lithium aluminium hydride gave 2 : 4 : 4 : 5-*tetramethylhexan*-3-*ol*, b. p. 85—86°/16 mm., n_D^{20} 1·4492 (Found: C, 76·1; H, 14·0. $C_{10}H_{22}O$ requires C, 75·9; H, 14·0%) [3 : 5-*dinitrobenzoate*, m. p. 76° (Found: C, 58·0; H, 7·15; N, 8·0. $C_{17}H_{24}O_6N_2$ requires C, 57·9; H, 6·9; N, 8·0%)]. With boiling nitric acid (*d* 1·42) diluted with half its volume of water the ketone gave ααβ-trimethylbutyric acid, characterised as the amide, m. p. 129° (Found: C, 65·3; H, 11·4; N, 10·2. Calc. for $C_7H_{15}ON$: C, 65·1; H, 11·6; N, 10·8%), and p-*toluidide*, m. p. 91—92° (Found: C, 77·0; H, 10·0; H, 6·3. $C_{14}H_{21}ON$ requires C, 76·7; H, 9·7; N, 6·4%).

Fraction (*b*) gave pure 3 : 4-*dimethyl*-3-iso*propylpentan*-2-*one* on further distillation, as a pale yellow liquid, b. p. 87—88°/22 mm., n_D^{20} 1·4415 (Found: C, 77·1; H, 12·8. $C_{10}H_{20}O$ requires C, 76·9; H, 12·9%). Neither semicarbazone nor 2 : 4-dinitrophenylhydrazone could be prepared. The nitroprusside test was positive. Reduction with lithium aluminium hydride afforded 3 : 4-*dimethyl*-3-iso*propylpentan*-2-*ol*, b. p. 100°/16 mm., n_D^{20} 1·4619 (Found: C 76·1; H, 13·9. $C_{10}H_{22}O$ requires C, 75·9; H, 14·0%) [3 : 5-*dinitrobenzoate*, m. p. 80—81° (Found: C, 58·0; H, 7·3; N, 7·7. $C_{17}H_{24}O_6N_2$ requires C, 57·9; H, 6·9; N, 8·0%)]. With hot nitric acid (1 : 1) the ketone gave αβ-dimethyl-α-*iso*propylbutyric acid [p-*toluidide*, m. p. 116° (Found: C, 78·1; H, 10·2; N, 5·5. $C_{16}H_{25}ON$ requires C, 77·7; H, 10·2; N, 5·7%)].

2 : 3 : 4 : 4 : 6 : 6-*Hexamethylheptane*-2 : 3-*diol and its Fission by Sulphuric Acid*.—A solution of 3-hydroxy-3 : 4 : 4 : 6 : 6-pentamethylheptan-2-one (260 g.) in dry ether (200 c.c.) was added dropwise to methyl-lithium (from 45·5 g. of lithium and 3 l. of ether), so that gentle reflux was maintained. The mixture was then heated under reflux for 2 hr., the bulk of the solvent (2200 c.c.) was distilled off, and the residue heated under reflux for 10 hr. The product was worked up as usual to give 2 : 3 : 4 : 4 : 6 : 6-*hexamethylheptane*-2 : 3-*diol*, b. p. 104—106°/1·8 mm., n_D^{20} 1·4672, a very viscous liquid (Found: C, 72·13; H, 12·95. $C_{13}H_{28}O_2$ requires C, 74·15; H, 13·0%). It is oxidised by periodic acid in aqueous methanol to acetone and 3 : 3 : 5 : 5-tetramethylhexan-2-one, identified as 2 : 4-dinitrophenylhydrazones, m. p.s and mixed m. p.s 125° and 110° respectively.

The diol (230 g.) was added slowly to concentrated sulphuric acid (1·5 l.) at −10° to 0°, stirring and cooling being continued for 2 hr. after the addition. The solution was then poured on crushed ice and steam-distilled after further dilution. The volatile products were collected with ether, washed, dried, and fractionally distilled. In the cold trap, distillate (A) (55·6 g.) was collected; the remainder (B) (92 g.) distilled between 40°/8 mm. and 90°/2 mm. There was a considerable tarry residue. The material (A) distilled between 90° and 95° (47·3 g.) and the fraction of b. p. 94—95° was substantially pure methyl *iso*propyl ketone, n_D^{20} 1·3889 (semicarbazone, m. p. and mixed m. p. 112—113°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 117°). There was a small amount of unsaturated material in the fraction of b. p. 95—100°. The distillate (B) showed a steady rise in b. p. and refractive index without much evidence of separation. All the fractions were unsaturated and the following analyses show that they consisted substantially of unsaturated hydrocarbons:

Fraction	B. p./mm.	n_D^{20}	C (%)	H (%)	*M*	Fraction	B. p./mm.	n_D^{20}	C (%)	H (%)	*M*
3	50—58°/8	1·4303	84·0	14·25	170	9	60—66°/2	1·4528	85·5	13·5	185
5	50—54°/4	1·4450	84·4	13·7	166	11	72—76°/2	1·4589	85·7	13·3	189
7	60—68°/4	1·4483	85·1	13·6	173	13	82—90°/2	1·4660	85·5	13·3	203

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