638. *Studies in the Synthesis of Terpenes. Part VI.* Some Reactions of* 3-*Methylbutane*-1,3-*diol.*

By T. G. Halsall and A. R. Hands.

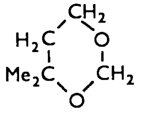
Some reactions of 3-methylbutane-1,3-diol are described.

Synthesis of a monoterpene usually involves the use of a C_5 intermediate. Apart from isoprene the C_5 compound potentially most readily and cheaply available on an industrial scale is 3-methylbutane-1,3-diol (I). This can be prepared by hydrolysis of the product (II) of the Prins reaction between formaldehyde and isobutene.[1] Recently we have studied the reactions of the diol (I) and its conversion into the three alcohols (III), (IV), and (V), and the corresponding chlorides. Some of the new compounds obtained in this work are described.

$X{\cdot}CMe_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$

(I) ; $X = OH$

(VI) ; $X = Cl$



(II)

$HO{\cdot}CMe_2{\cdot}CH{=}CH_2$ (III)

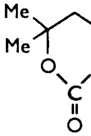
$Me_2C{=}CH{\cdot}CH_2{\cdot}X$ (IV) ; $X = OH$

(VII) ; $X = Cl$

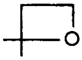
(VIII) ; $X = OAc$

$CH_2 = CMe{\cdot}CH_2{\cdot}CH_2{\cdot}OH$ (V)

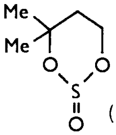
Treatment of the diol (I) with dry hydrogen chloride gave 3-chloro-3-methylbutan-1-ol (VI). Distillation over phosphoric oxide of the crude product gave 1-chloro-3-methylbut-2-ene (VII) which was converted into 3-methyl-2-enyl acetate (VIII) when heated with sodium acetate in acetic acid. Hydrolysis of this acetate gave the corresponding alcohol (IV). Dehydrochlorination of the chloro-alcohol (VI) with *NN*-diethylaniline gave the homoallylic alcohol (V), the pyrophosphate of which is the biogenetic precursor of the terpenes.[2-4]



(IX)



(X)



(XI)

$Me_2CCl{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}SO{\cdot}Cl$

(XII)

The diol (I) readily formed a cyclic carbonate (IX). The band of the infrared spectrum due to its carbonyl group occurred at quite different frequences in carbon tetrachloride (1772 cm.$^{-1}$) and chloroform (1735 cm.$^{-1}$). Pyrolysis of the carbonate gave 3-methylbut-3-en-1-ol (V) (38%) and 2-methylbut-3-en-2-ol (III) (19%). This reaction is, however, not of great preparative value because very careful fractionation is necessary to separate the mixture of alcohols obtained. The formation of the alcohols, rather than of 2,2-dimethyloxetan (X), is in line with the result of Searles, Hummel, Nukina, and Throckmorton[5]

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* Part V, *J.*, 1960, 4931.

[1] Rosen and Arundale, U.S.P. 2,368,494.

[2] Chaykin, Law, Phillips, Tchen, and Bloch, *Proc. Nat. Acad. Sci. U.S.A.*, 1958, **44**, 998.

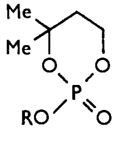
[3] Eggerer, Lynen, Henning, and Kessel, *Angew. Chem.*, 1958, **70**, 738.

[4] Eggerer and Lynen, *Annalen*, 1960, **630**, 59.

[5] Searles, Hummel, Nukina, and Throckmorton, *J. Amer. Chem. Soc.*, 1960, **82**, 2928.

who have shown that if hydrogen is present on the β-carbon of a 1,3-diol its cyclic carbonate is catalytically decomposed by base to an unsaturated alcohol rather than to an oxetan. The corresponding cyclic sulphite (XI) was obtained when the diol (I), thionyl chloride, and pyridine, in a 1 : 1 : 2-molar ratio, were kept in dry benzene. From the chloro-alcohol (VI) the chlorosulphite (XII) was formed.

In view of the current interest [2,3] in the rôle of C_5 phosphates in the biogenesis of terpenes some phosphates were prepared from the diol (I). Treatment of it (1 mol.) with phenyl phosphorodichloridate (1 mol.) and pyridine (2 mol.) in benzene afforded the cyclic phosphate (XIII). With diphenyl phosphorochloridate, 3-hydroxy-3-methylbutyl diphenyl phosphate (XIV) was obtained. Hydrolysis of the cyclic phenyl phosphate with sodium hydroxide solution gave the cyclic hydrogen phosphate (XV) (42%) and phenyl dihydrogen phosphate (13%), isolated as cyclohexylamine salt. More than one of the P–O bonds of the cyclic phosphate can therefore be split. It was considered possible that treatment of the cyclic phosphate (XV) with sodium t-butoxide would lead to abstraction of a proton from one of the methyl groups followed by fission of the $C_{(3)}$–O bond (cf. XVI) with the formation of the monophosphate of the methylbutenol (V). However, no elimination product was isolated and only the cyclic acid was recovered.

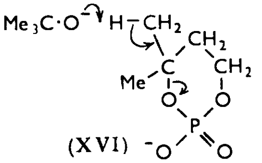


(XIII) ; R = Ph

(XV) ; R = H

$HO{\cdot}CMe_2{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}PO(OPh)_2$

(XIV)



(XVI)

EXPERIMENTAL

M. p.s were determined on a Kofler block and are corrected.

1-Chloro-3-methylbut-2-ene.—3-Methylbutane-1,3-diol (70 g.) was saturated with dry hydrogen chloride (increase in wt., 39 g.). The mixture was distilled under reduced pressure, the fraction (93 g.) of b. p. 20—120°/14 mm. being collected. The upper layer of this distillate was separated and dried ($MgSO_4$; P_2O_5). Redistillation from phosphorus pentoxide (19 g.) gave 1-chloro-3-methylbut-2-ene (37 g., 53%), b. p. 30—40°/14 mm., $n_D^{19\cdot5}$ 1·4490 (lit.: n_D^{20} 1·4480,[6] 1·4485 [7]); $\nu_{max.}$ 838 cm.$^{-1}$ (CH=C), no bands at 890 (=CH_2) or 990 (CH=CH_2) cm.$^{-1}$.

The nitrosochloride formed plates (from carbon disulphide), m. p. 133°, which sublimed at 150° (bath temp.)/15 mm. to give pale blue prisms, m. p. 80—90° immediately after sublimation. After one week at 20° the sublimate was almost colourless and had m. p. 118—119° (lit.,[8] 117°).

The *isothiouronium picrate* formed yellow needles (from ethanol), m. p. 179—180° (decomp.) (Found: C, 38·6; H, 4·3; N, 18·9; S, 8·6. $C_{12}H_{15}N_5O_7S$ requires C, 38·6; H, 4·1; N, 18·7; S, 8·6%).

In a further experiment, 3-methylbutane-1,3-diol (50 g.) was saturated with dry hydrogen chloride at 0° (increase in weight, 29 g.). The excess of hydrogen chloride was removed at 20°/15 mm. The mixture was then dissolved in ether (600 c.c.) and shaken with an excess of sodium carbonate until effervescence ceased. The solution was filtered and dried ($MgSO_4$), and the ether then removed by distillation. Distillation of the residue gave a fraction (13·0 g.; 22%), b. p. 50—65°/15 mm., $n_D^{17\cdot5}$ 1·4490 (Found: C, 48·6; H, 9·0; Cl, 28·5. $C_5H_{11}ClO$ requires C, 49·0; H, 9·0; Cl, 28·9%), which from the analytical data must be essentially *3-chloro-3-methylbutan-1-ol* although the boiling point range is not small. The fraction gave *3-chloro-3-methylbutyl 1-naphthylurethane* as plates (from light petroleum, b. p. 40—60°), m. p. 84° (Found: C, 66·0; H, 6·3; Cl, 12·1; N, 4·7. $C_{16}H_{18}ClNO_2$ requires C, 65·9; H, 6·2; Cl, 12·1; N, 4·8%). A further fraction (30·6 g.; 52%) had b. p. 65—72°/15 mm., $n_D^{17\cdot5}$ 1·4483 (Found: Cl, 25·1%).

3-Chloro-3-methylbutyl Acetate.—3-Chloro-3-methylbutan-1-ol (50 g.) and acetic anhydride (200 c.c.) were heated under reflux for 3 hr. After it had cooled, the mixture was added to

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[6] Nazarov and Azerbaev, *J. Gen. Chem.* (*U.S.S.R.*), 1948, **18**, 414.

[7] Ultee, *Rec. Trav. chim.*, 1949, **68**, 125.

[8] Jones and Chorley, *J.*, 1946, 832.

ice (800 g.) and stirred vigorously for 2 hr. An excess of potassium carbonate was added and the mixture was extracted with ether (2 × 200 c.c.), and the product fractionally distilled under reduced pressure to give 3-*chloro*-3-*methylbutyl acetate* (5·9 g., 9%), b. p. 47—51°/14 mm., n_D^{18} 1·4350 (Found: C, 50·8; H, 8·5; Cl, 21·7. $C_7H_{13}ClO_2$ requires C, 51·1; H, 8·0; Cl, 21·6%).

Conversion of 1-*Chloro*-3-*methylbut*-2-*ene into* 3-*Methylbut*-2-*enyl Acetate.*—1-Chloro-3-methylbut-2-ene (12·5 g.), anhydrous sodium acetate (20·2 g.), and acetic acid (100 c.c.) were stirred and heated at 60—70° for 2 hr. The cooled product was poured into water (250 c.c.) and an excess of potassium carbonate was added. Ethereal extraction afforded a product which was distilled under reduced pressure to give 3-methylbut-2-enyl acetate (12·5 g., 81%), b. p. 40—44°/15 mm., n_D^{17} 1·4304, $\nu_{max.}$ 824w cm.$^{-1}$ (Found: C, 65·65; H, 9·6. Calc. for $C_7H_{12}O_2$: C, 65·5; H, 9·45%) (lit.:[9] b. p. 74°/55 mm., n_D^{20} 1·4298).

The acetate was hydrolysed to 3-methylbut-2-en-1-ol, b. p. 45—52°/15 mm., n_D^{24} 1·4400; $\nu_{max.}$ 834m cm.$^{-1}$ (–C=CH–) (lit.: n_D^{19} 1·4439). The 1-*naphthylurethane* crystallised from light petroleum as long needles, m. p. 104° (Found: C, 74·95; H, 6·7; N, 5·7. $C_{16}H_{17}NO_2$ requires C, 75·3; H, 6·7; N, 5·5%).

3-*Methylbut*-3-*en*-1-*ol.*—A mixture of 3-chloro-3-methylbutan-1-ol (50 g.) and *NN*-diethylaniline (250 c.c.) was distilled, the fraction boiling between 70° and 180° being collected. The upper layer of the distillate was separated, dried, and fractionally distilled to give 3-methylbut-3-en-1-ol (23 g., 65%), b. p. 129—133°, n_D^{15} 1·4371; $\nu_{max.}$ (liq. film), 1650s (C=C), and 886s (C=CH$_2$) cm.$^{-1}$ (lit.:[10] b. p. 130°, n_D^{16} 1·4354).

The 1-*naphthylurethane* crystallised from light petroleum as needles, m. p. 66° (Found: C, 75·3; H, 6·6; N, 5·2. $C_{16}H_{17}NO_2$ requires C, 75·3; H, 6·7; N, 5·5%).

4,4-*Dimethyl*-1,3-*dioxan*-2-*one.*—3-Methylbutane-1,3-diol (50 g.), diethyl carbonate (60 g.), and sodium (0·3 g.) were heated at 130° (bath temp.) for 2 hr. The temperature was then raised to 170° during 1 hr. The mixture was cooled, and the resulting solid was filtered off and recrystallised from ethanol to give 4,4-*dimethyl*-1,3-*dioxan*-2-*one* (47 g., 76%) as prisms, m. p. 78—79°; $\nu_{max.}$ (CCl$_4$), 1772s (CHCl$_3$), 1735s, (Nujol) 1725s cm.$^{-1}$ [Found: C, 55·2; H, 7·9%; *M* (micro-Rast), 116. $C_6H_{10}O_3$ requires C, 55·4; H, 7·85%; *M*, 130].

Pyrolysis of 4,4-*Dimethyl*-1,3-*dioxan*-3-*one.*—4,4-Dimethyl-1,3-dioxan-2-one (50 g.) was placed in a 150 c.c. distilling flask which was then immersed in Wood's metal previously heated to 300—320°. The material (29·5 g.; n_D^{19} 1·4385) distilling at 180—200° was collected, starting material (5·3 g.) remaining in the flask. The distillate was redistilled through a 12-cm. fractionating column packed with stainless steel gauze to give 2-methylbut-3-en-2-ol (6·2 g., 19%), b. p. 98—108°, n_D^{18} 1·4180; $\nu_{max.}$ 990s, 918s cm.$^{-1}$ (CH=CH$_2$) (lit.:[11] b. p. 96—98°/744 mm., n_D^{20} 1·4168), and 3-methylbut-3-en-1-ol (12·6 g., 38%), b. p. 130—135°, n_D^{18} 1·4365; $\nu_{max.}$ 886s cm.$^{-1}$ (C=CH$_2$) (lit.:[10] b. p. 130°, n_D^{16} 1·4384). A further fraction (7%), b. p. 139—145°, was collected. 4,4-Dimethyl-1,3-dioxan-2-one (6·9 g., 14%) remained in the distilling flask.

4,4-*Dimethyl*-1,3,2-*dioxathian*-2-*one.*—3-Methylbutane-1,3-diol (10·4 g.) was dissolved in dry benzene (200 c.c.), and dry pyridine (15·8 g.) was added. Thionyl chloride (11·9 g.) in benzene (50 c.c.) was added dropwise during 1 hr., the mixture being stirred and cooled in ice. It was kept at 20° for ½ hr. and then filtered, and the filtrate evaporated at 35°/13 mm. The residue was distilled to give 4,4-*dimethyl*-1,3,2-*dioxathian*-2-*one* (10 g., 67%), b. p. 79—80°/13 mm., n_D^{14} 1·4545 (Found: C, 39·95; H, 6·75; S, 21·3. $C_5H_{10}O_3S$ requires C, 40·0; H, 6·7; S, 21·35%).

3-*Chloro*-3-*methylbutyl Chlorosulphite.*—3-Chloro-3-methylbutan-1-ol (12 g.) was dropped during ½ hr. into thionyl chloride (70 g.), and the mixture was then heated under reflux for 2½ hr. The thionyl chloride was distilled off at atmospheric pressure and the residue was distilled twice to give 3-*chloro*-3-*methylbutyl chlorosulphite* (12·8 g., 64%), b. p. 108—110°/15 mm., n_D^{15} 1·4845 (Found: C, 29·6; H, 5·0; Cl, 34·3; S, 15·3. $C_5H_{10}Cl_2O_2S$ requires C, 29·3; H, 4·9; Cl, 34·6; S, 15·6%).

1,1-*Dimethyltrimethylene Phenyl Phosphate.*—3-Methylbutane-1,3-diol (14·4 g.) was dissolved in benzene (100 c.c.)–pyridine (21·4 g.), and phenyl phosphorodichloridate (29·3 g.) was added. The mixture was kept at 20° for 24 hr. and then filtered. The filtrate was evaporated to give 1,1-*dimethyltrimethylene phenyl phosphate* (33·5 g., 100%) as an oil, n_D^{26} 1·5113, which solidified, m. p. 64—72°, after 4 days (Found: C, 54·4; H, 6·25. $C_{11}H_{15}O_4P$ requires C, 54·55; H, 6·25%);

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[9] Young and Webb, *J. Amer. Chem. Soc.*, 1951, **73**, 780.

[10] Laforgue, *Compt. rend.*, 1948, **227**, 352.

[11] Campbell and Eby, *J. Amer. Chem. Soc.*, 1941, **63**, 2683.

$\nu_{max.}$ 1294s cm.$^{-1}$ (P=O) (Jones and Katritzky [12] give 1290 cm.$^{-1}$ from ν(P=O) in ethyl trimethylene phosphate).

3-*Hydroxy*-3-*methylbutyl Diphenyl Phosphate.*—3-Methylbutane-1,3-diol (10·4 g.) in benzene (20 c.c.)–pyridine (7·9 g.) was kept at 20° for 24 hr. with diphenyl phosphochloridate (26·85 g.). The mixture was filtered and the filtrate evaporated to give 3-*hydroxy*-3-*methylbutyl diphenyl phosphate* (33·5 g., 100%) as an oil, n_D^{20} 1·5280 (Found: C, 60·4; H, 6·6. $C_{17}H_{21}O_5P$ requires C, 60·7; H, 6·3%).

1,1-*Dimethyltrimethylene Hydrogen Phosphate.*—1,1-Dimethyltrimethylene phenyl phosphate (67 g.) was heated at 100° for 30 min. with 27% aqueous sodium hydroxide (150 c.c.). The mixture was cooled and acidified with concentrated hydrochloric acid, and ether (250 c.c.) was added. After the mixture had been cooled it was filtered and the separated solid was extracted with ether in a Soxhlet apparatus. On cooling of the extract, 1,1-*dimethyltrimethylene hydrogen phosphate* crystallised as short needles (19·5 g., 42%), m. p. 63—68° (decomp.) (Found: C, 36·1; H, 6·7; active H, 0·6. $C_5H_{11}O_4P$ requires C, 36·15; H, 6·7; active H, 0·6%). The *cyclohexylamine salt* formed needles, m. p. 198—199° (from ethanol) (Found: C, 49·3; H, 8·5. $C_{11}H_{24}NO_4P$ requires C, 49·8; H, 9·1%).

The filtrate described above was separated, and the ether layer was evaporated to give a residue which was taken up in ethyl acetate. Addition of cyclohexylamine gave *di*(*cyclohexylammonium*) *phenyl phosphate* as needles (8·8 g.), m. p. 214° (from ethanol) (Found: C, 57·85; H, 9·1; N, 7·2. $C_{18}H_{33}N_2O_4P$ requires C, 58·1; H, 8·95; N, 7·55%). Treatment of the salt with 2N-hydrochloric acid, followed by extraction with ether, afforded phenyl dihydrogen phosphate, m. p. 97—98° (sealed tube).

Action of Sodium t-Butoxide on 1,1-*Dimethyltrimethylene Hydrogen Phosphate.*—The acid ester (3·32 g., 0·02 mole) was added to a solution of sodium (0·92 g., 0·04 g.-atom) in t-butyl alcohol (125 c.c.), and the mixture was heated under reflux for 24 hr. Acidification of the cooled mixture with concentrated hydrochloric acid (3·56 c.c., 0·04 mole) and evaporation to dryness at 60°/16 mm. gave a solid. Extraction of this with ether (Soxhlet) afforded only unchanged material (0·1 g., 3%), m. p. 76—78°.

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[12] Jones and Katritzky, *J.*, 1960, 4376.