107. *Alicyclic Diketones and Diols. Part I.* cis- *and* trans-2 : 2 : 5 : 5-*Tetramethyl*cyclo*hexane*-1 : 3-*diol.*

By A. W. Allan, R. P. A. Sneeden, and (in part) J. Colvin.

An improved method of preparing *cis*- and *trans*-2 : 2 : 5 : 5-tetramethyl-*cyclo*hexane-1 : 3-diol is described. The two diols have been characterised by a number of acyl derivatives from which, contrary to Hirsjarvi's findings,[1] the respective parent diols are regenerated on hydrolysis. Again contary to Hirsjarvi's views, the low-melting diol is shown to be the *trans*-isomer by resolution through the bis-(−)-menthoxyacetates.

Hirsjarvi [1] reported the preparation of two isomeric 2 : 2 : 5 : 5-tetramethyl*cyclo*hexane-1 : 3-diols, m. p. 205—206° and 107—108° respectively, by the electrolytic reduction of 2 : 2 : 5 : 5-tetramethyl*cyclo*hexane-1 : 3-dione (dimethyldimedone) to 3-hydroxy-2 : 2 : 5 : 5-tetramethyl*cyclo*hexan-1-one and reduction of the latter with sodium amalgam. The diols were obtained in low overall yield by fractional crystallisation of the resultant mixture.

In the present work the mixed isomeric diols were obtained, in good yield, by reducing dimethyldimedone with lithium aluminium hydride. An initial crystallisation gave substantially pure diol A (m. p. 205—206°). Acetylation of the residue from diol A and chromatography gave a crystalline diacetate which on hydrolysis gave pure diol B (m. p. 107—108°) in low overall yield. Benzoylation of the residue from diol A and chromatography gave two crystalline dibenzoates. The first was identical with diol B dibenzoate and gave diol B on hydrolysis (Hirsjarvi [1] states that diol B dibenzoate gives diol A on hydrolysis). The second was identical with diol A dibenzoate and gave diol A on hydrolysis. On a larger scale the two diols could be separated by fractional crystallisation.

The m. p.s of the diol esters found in the present work agree closely with those reported by Hirsjarvi [except that the di(hydrogen phthalate) was obtained crystalline for the first time]. Hirsjarvi, arguing from the melting points and solubilities of the diols and their derivatives (see Table) assigned the (±)-*trans*-structure to the higher-melting diol, but his attempts to corroborate this by chemical evidence and by optical resolution were unsuccessful. Similarly in the present work, neither di(hydrogen phthalate) gave crystalline diastereoisomers with quinine, brucine, or (+)-1-phenylethylamine.[2]

That the low-melting diol, diol B, has the (±)-*trans*-configuration has now been proved by its resolution through the bis-(—)-menthoxyacetates. Diol B, m. p. 107—108°, with (—)-menthoxyacetyl chloride in pyridine gives an oil which from its infrared spectrum and analytical data is a bis-(—)-menthoxyacetate. Chromatography of this material on alumina yielded two waxy esters, m. p. 59°, $[\alpha]_D^{21}$ $-76{\cdot}5°$ and m. p. 59°, $[\alpha]_D^{21}$ $-54{\cdot}5°$. Hydrolysis of these diastereoisomers gave (—)-, m. p. 134—137°, $[\alpha]_D^{23}$ $-19{\cdot}4°$, and (+)-*trans*-2 : 2 : 5 : 5-tetramethyl*cyclo*hexane-1 : 3-diol, m. p. 125—126°, $[\alpha]_D^{23}$ $+22{\cdot}8°$ respectively.

---

[1] Hirsjarvi, *Ann. Acad. Sci. Fennicae*, **1946**, Series A, **2**, No. 23.

[2] Cf. Rigby, *J.*, 1949, 1588.

That the high-melting diol, A, has the symmetrical *cis*-configuration is confirmed by the fact that it gave a crystalline homogeneous bis-(—)-menthoxyacetate, m. p. 79—80°, $[\alpha]_D^{19}$ −71·69°, unaltered by repeated crystallisation. Hydrolysis of this derivative gave diol A, m. p. 204—207°, $[\alpha]_D^{19}$ 0°.

Differences in reactivity of the diols are under investigation.

EXPERIMENTAL

Optical rotations were taken in $CHCl_3$.

cis- *and* trans-2 : 2 : 5 : 5-*Tetramethyl*cyclo*hexane*-1 : 3-*diol*.—A suspension of lithium aluminium hydride (2·5 g.) in dry ether (250 c.c.) was heated (2 hr.) under reflux, the returning condensate passing through a thimble containing 2 : 2 : 5 : 5-tetramethyl*cyclo*hexane-1 : 3-dione[3] (8·5 g.). The mixture was then cooled, and excess of lithium aluminium hydride destroyed by ethyl acetate before addition of water and dilute sulphuric acid. Removal of the ether from the dried organic layer resulted in a semi-crystalline residue (7·4 g.) which on crystallisation from chloroform gave 2 : 2 : 5 : 5-tetramethyl*cyclo*hexane-1 : 3-diol A as prisms (2·1 g.), m. p. 205—206° (from benzene) (Found: C, 70·0; H, 11·3. Calc. for $C_{10}H_{20}O_2$: C, 69·7; H, 11·7%).

Separation via *the Diacetates*.—The mixture of diols (4·8 g.) recovered from the chloroform mother-liquors was treated with acetic anhydride in pyridine, and the mixture of isomeric diacetates (5·1 g.) chromatographed on alumina. Elution with light petroleum (b. p. 40—60°) gave one diacetate as prisms [from light petroleum (b. p. 60—80°)], m. p. 64—66° (Found: C, 65·2; H, 9·2. Calc. for $C_{14}H_{24}O_4$: C, 65·6; H, 9·4%).

The diacetate (900 mg.) on hydrolysis with potassium hydroxide (0·4 g.) in water (5 c.c.) and methanol (25 c.c.) gave the second diol (B) as prisms (100 mg.) [from light petroleum (b. p. 60—80°)], m. p. 107—108° (Found: C, 69·7; H, 11·5%).

Separation via *the Dibenzoates*.—Benzoylation of the residue from diol A in the usual manner gave a semicrystalline mass, which (27 g.) was chromatographed on alumina (500 g.). The product (14 g.) eluted with light petroleum (b. p. 60—80°) was the dibenzoate B, plates, m. p. and mixed m. p. 112—114° (from methanol); a second product (1·57 g.) was the dibenzoate A, prisms, m. p. and mixed m. p. 111—112° (from methanol), sharply depressed on admixture with dibenzoate B. On hydrolysis with aqueous-methanolic potassium hydroxide the dibenzoate of m. p. 112—114° gave diol B, m. p. 107—108°, and the dibenzoate of m. p. 111—112° gave diol A, m. p. 205—206°, neither m. p. being depressed on admixture with the appropriate diol.

Separation by Crystallisation.—The crude reduction product from dimethyldimedone (33·6 g.) in ether was concentrated to 1 l.; crystals of diol A (6·55 g.), m. p. 203—205°, were removed and the filtrate concentrated to 300 c.c.; a second crop of diol A (0·43 g.), m. p. 205—206°, was obtained. The ether was removed from the filtrate, and the residue crystallised from acetone. Subsequent fractional crystallisation from acetone–light petroleum (b. p. 40—60°) gave diol B (12·28 g.), m. p. 107—108°. The m. p. of the diols and their derivatives as prepared in the present work and those reported by Hirsjarvi are tabulated.

	Diol	Diacetate	Dibenzoate	Di(hydrogen phthalate)
Diol A	205—206°	83·5—84·5°	110·5—111°	208—209° (H)
	205—206 [a]	84—85 [c]	111—112 [d]	207—210 [b] (*)
Diol B	107—108	64—65	111—111·5	151—153 (H)
	107—108 [b]	64—66 [c]	112—114 [e]	193—194 [b] (*)

(*) Present work. (H) Hirsjarvi.[1] Solvents: [a] Benzene; [b] acetone–light petroleum (b. p. 40—60°); [c] light petroleum (b. p. 60—80°); [d] methanol; [e] acetone–methanol.

Diol B Di(hydrogen Phthalate).—Diol B (1 g.) and phthalic anhydride (1·8 g.) in pyridine (3 c.c.) were heated on a steam-bath for 3 hr., set aside overnight, poured into aqueous sodium carbonate, and extracted three time with ether; the aqueous layer was acidified with concentrated hydrochloric acid, and the product isolated with the aid of ether. The *diester* crystallised from acetone–light petroleum (b. p. 40—60°) as prisms, m. p. 193—194° (Found: C, 66·9; H, 6·3. $C_{26}H_{28}O_8$ requires C, 66·65; H, 6·0%).

---

[3] Halsall and Thomas, *J.*, 1956, 2431.

Diol B Bis-(−)-menthoxyacetates.—(−)-Menthoxyacetyl chloride (20·2 g.) was added slowly to a cooled solution of diol B (6 g.) in pyridine (25 c.c.), and the whole kept overnight. The product (15·5 g.) isolated with the aid of ether was a mixture of the diastereoisomeric bis-(−)-menthoxyacetates of diol B, b. p. 210°/0·1 mm. (Found: C, 72·6; H, 10·7. Calc. for $C_{34}H_{60}O_6$: C, 72·3; H, 10·7%). The infrared spectrum (liquid film) showed no absorption in the OH region and an ester band at 1743 cm.$^{-1}$.

The above derivative was chromatographed on alumina; elution with *n*-hexane gave a viscous oil (5·97 g.), $[\alpha]_D^{20}$ −66·37°, and elution with ether gave a second viscous oil (6·33 g.), $[\alpha]_D^{20}$ −59·02°. The ether eluate was rechromatographed on alumina, and from the similarities in the rotation of successive eluates they were combined into three main fractions: (1) 0·96 g., $[\alpha]_D^{17}$ −71·3°; (2) 1·3 g., $[\alpha]_D^{17}$ −64° to −68°; (3) 1·20 g., $[\alpha]_D^{17}$ −56·5°. Fraction (2) was combined with the original hexane eluate, and the whole rechromatographed on alumina, and from the similarities in the rotation of successive fractions two main eluates were collected: (4) 0·6 g., $[\alpha]_D$ −75·6°, (5) 3·20 g., $[\alpha]_D$ −74° to −58·7°. Fraction (4) set to a wax, m. p. 59°, which could not be crystallised; on distillation one diastereoisomer of the *bis-(−)-menthoxyacetate of diol B*, b. p. 210°/0·1 mm., $[\alpha]_D^{21}$ −76·5° (*c* 0·9), was obtained (Found: C, 72·9; H, 10·8%). The infrared spectrum (liquid film) was identical with that of the original mixture.

Fraction (3) set to a wax, m. p. 59°, which could not be crystallised, but distillation gave the other diastereoisomer of the *bis-(−)-menthoxyacetate* of diol B, b. p. 210°/0·1 mm., $[\alpha]_D^{24}$ −54·5° (*c* 1·1) (Found: C, 72·2; H, 10·8%). The infrared spectrum (liquid film) was identical with that of the original mixture and that of the other diastereoisomer.

(+)- and (−)-Form of Diol B.—Hydrolysis of the ester diastereoisomer, $[\alpha]_D^{21}$ −76·5° (0·180 g.), with aqueous-methanolic potassium hydroxide gave crystals (0·018 g.); these on sublimation gave *(−)-diol B*, m. p. 134—137°, $[\alpha]_D^{23}$ −19·4° (*c* 0·5) (Found: C, 69·6; H, 11·5%). The infrared spectrum in CCl_4 was identical with that of the racemic diol B.

Hydrolysis of the diastereoisomer, $[\alpha]_D^{21}$ −54·5° (0·633 g.), gave a crystalline product (0·096 g.) and this on sublimation gave *(+)-diol B*, m. p. 125—126°, $[\alpha]_D^{23}$ +22·8° (*c* 0·9) (Found: C, 69·7; H, 11·7%). The infrared spectrum in CCl_4 was identical with that of (−)-diol B.

Diol A Bis-(−)-menthoxyacetate.—Diol A (1 g.) was treated as described for diol B; the crude product (2·07 g.) solidified. Recrystallisation from acetone–methanol gave the *bis-(−)-menthoxyacetate* as prisms, m. p. 79—80°, $[\alpha]_D^{19}$ −71·69° (*c* 1·1) (Found: C, 72·1; H, 11·1%). The infrared spectrum in Nujol showed no absorption in the OH region and an ester band at 1743 cm.$^{-1}$. The rotation of this derivative did not change with recrystallisation.

Hydrolysis of Diol A Bis-(−)-menthoxyacetate.—The derivative (0·25 g.) was hydrolysed with aqueous-methanolic potassium hydroxide, and the product crystallised from chloroform. In this way diol A (0·057 g.) was obtained as prisms, m. p. 204—207°, $[\alpha]_D$ 0°.

One of us (A. W. A.) thanks the Department of Scientific and Industrial Research for a maintenance allowance. All of us thank Dr. G. Eglinton for the infrared spectra and Mr. J. M. L. Cameron for the microanalyses.

THE UNIVERSITY, GLASGOW. [*Received, June 13th,* 1957.]