

## Marine Natural Products of the Atlantic Zone. Part VI.<sup>1</sup> Base-catalysed Rearrangement of Taondiol

By Antonio G. González,\* Miguel A. Alvarez, José Darías, and Julio D. Martín, Organic Chemistry Department, University of La Laguna, Instituto de Investigaciones Químicas, C.S.I.C., Tenerife, Spain

The base-catalysed isomerisation of taondiol (1; R<sup>1</sup> = R<sup>2</sup> = H), an aromatic terpenoid containing the 1*H*-naphtho[2,1-*a*]xanthen skeleton recently isolated from the marine alga *Taonia atomaria* (Dyctiotaceae), into its C-6a methyl epimer (2) has been studied. A free-radical mechanism is proposed for the reaction. Base-catalysed methyl inversion at C-6a was also carried out on 2-deoxy-9,11-dimethyltaondiol (21; R = H), prepared by condensation of (13*R*)-labda-8(20),14-dien-13-ol (18) with trimethylhydroquinone (19) and subsequent cyclisation.

PREVIOUS communications reported the structure and synthesis of taondiol (2,3,4,4a,4b,5,6,6a,12,12a,12b,13,14,14a-tetradecahydro-1,1,4a,6a,8,12b-hexamethyl-1*H*-naphtho[2,1-*a*]xanthen-2,10-diol) (1; R<sup>1</sup> = R<sup>2</sup> = H), a tocopherol-like compound isolated from the marine alga *Taonia atomaria* (Dyctiotaceae).<sup>2,3</sup> In the present work we report the structure of isotaondiol (2), obtained by base-catalysed rearrangement of taondiol, and discuss the mechanism of its formation.

When heated with 5% methanolic potassium hydroxide, taondiol (1; R<sup>1</sup> = R<sup>2</sup> = H) is smoothly isomerised, in 50% yield, to the dextrorotatory isotaondiol (2), C<sub>27</sub>H<sub>40</sub>O<sub>3</sub>, which was isolated by fractional crystallisation. Its u.v. and mass spectra are identical with those of taondiol.<sup>2</sup> In the <sup>1</sup>H n.m.r. spectrum the presence of two *meta*-coupled protons at  $\tau$  3.54 and 3.60 (each 1H, *s*, *J* 2.3 Hz), two benzylic protons appearing as an octet around  $\tau$  7.38 (AB part of an ABX system), and an aromatic methyl group as a singlet at  $\tau$  7.90 indicate that the 8-methyl-6-chromanol chromophore is also present in isotaondiol. The spectrum further shows a broad signal at  $\tau$  6.80 (1H, *W*<sub>1/2</sub> 14 Hz, >CHOH) and in the high-field region singlets for five tertiary methyl groups (see the Table).

Both taondiol and isotaondiol remain unchanged upon refluxing with hydrochloric acid in methanol. Acetylation of (1; R<sup>1</sup> = R<sup>2</sup> = H) with acetic anhydride in pyridine gave a product, which was homogeneous by t.l.c., but n.m.r. showed that it was a 1 : 1 mixture of two isomers. Separation by fractional crystallisation gave

taondiol diacetate (1; R<sup>1</sup> = R<sup>2</sup> = Ac), identified by comparison with the compound prepared previously,<sup>1</sup> and isotaondiol diacetate (3) which on alkaline hydrolysis yielded (2). Taondiol was also smoothly isomerised by methylation with dimethyl sulphate and potassium carbonate on refluxing in acetone to give a mixture of (1; R<sup>1</sup> = H, R<sup>2</sup> = Me) and (4), in the ratio 1 : 1 (n.m.r.). These were separated by fractional crystallisation of the corresponding iodoacetates. 10-Methoxyisotaondiol (4) was also obtained from (2) by methylation with diazomethane. Treatment of taondiol with benzoyl chloride

Chemical shifts of the methyl groups for isotaondiol and its derivatives \*

Compound	Me group					
	C-8	C-6b	C-12b	C-4a	$\alpha$ -C-1	$\beta$ -C-1
(2)	7.90 (-0.01)	8.79 (0.07)	8.75 (0.37)	9.06 (0.04)	9.00 (0.00)	9.20 (0.02)
(3)	7.89 (0.00)	8.78 (0.07)	8.76 (0.36)	9.03 (0.09)	9.12 (0.00)	9.12 (0.00)
(4)	7.88 (0.00)	8.79 (0.07)	8.75 (0.38)	9.04 (0.06)	8.99 (0.02)	9.20 (-0.01)
(5)	7.82	8.71	8.67	8.91— 8.92	9.01	8.91— 8.92
(6)	7.91	8.80	8.75	8.97— 8.99	9.05	8.97— 8.99
(9)	7.86 (-0.01)	8.90 (-0.04)	8.85 (0.28)	9.03 (0.10)	9.11 (0.02)	9.16 (-0.03)

\*  $\tau$  Values at 100 MHz in CDCl<sub>3</sub> solution [the figures in parentheses are the shift differences from the corresponding taondiol compounds (high-field positive)].

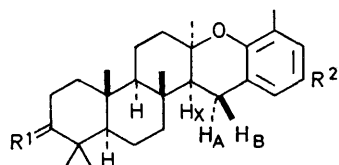
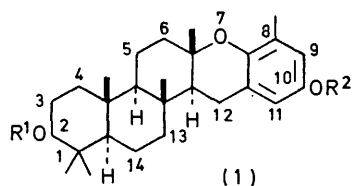
in pyridine gave an almost quantitative yield of isotaondiol dibenzoate (5) which, on refluxing with 5%

<sup>3</sup> A. G. González and J. D. Martín, *Tetrahedron Letters*, 1972, 2259.

<sup>1</sup> Part V, A. G. González, J. Darías, J. D. Martín, and C. Pascual, *Tetrahedron*, 1973, **29**, 1605.

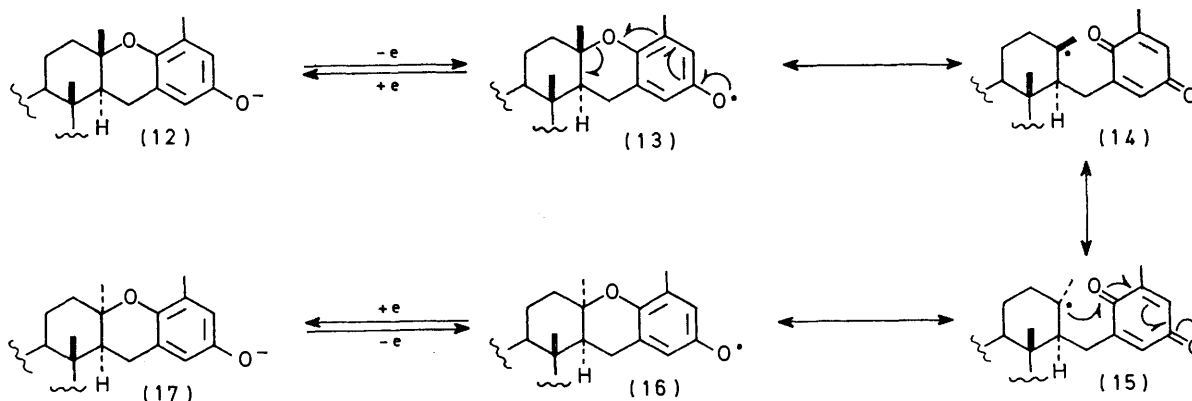
<sup>2</sup> A. G. González, J. Darías, and J. D. Martín, *Tetrahedron Letters*, 1971, 2729.

methanolic potassium hydroxide yielded (2). Alkaline hydrolysis of (5) at 45° gave the monobenzoate (6). The



- (2)  $R^1 = \begin{array}{l} \text{OH} \\ \diagdown \\ \text{H} \end{array}, R^2 = \text{OH}$   
 (3)  $R^1 = \begin{array}{l} \text{OAc} \\ \diagdown \\ \text{H} \end{array}, R^2 = \text{OAc}$   
 (4)  $R^1 = \begin{array}{l} \text{OH} \\ \diagdown \\ \text{H} \end{array}, R^2 = \text{OMe}$   
 (5)  $R^1 = \begin{array}{l} \text{OBz} \\ \diagdown \\ \text{H} \end{array}, R^2 = \text{OBz}$   
 (6)  $R^1 = \begin{array}{l} \text{OBz} \\ \diagdown \\ \text{H} \end{array}, R^2 = \text{OH}$   
 (7)  $R^1 = \text{O}, R^2 = \text{OMe}$   
 (8)  $R^1 = \begin{array}{l} \text{S} \\ \diagdown \\ \text{S} \end{array}, R^2 = \text{OMe}$   
 (9)  $R^1 = \text{H}_2, R^2 = \text{OMe}$   
 (10)  $R^1 = \begin{array}{l} \text{O}_2\text{C}\cdot\text{CH}_2\text{I} \\ \diagdown \\ \text{H} \end{array}, R^2 = \text{OMe}$   
 (11)  $R^1 = \begin{array}{l} \text{O}_2\text{C}\cdot\text{CH}_2\text{Cl} \\ \diagdown \\ \text{H} \end{array}, R^2 = \text{OMe}$

hydroxy-group at C-2 in isotaondiol was removed by conversion of (4) into the thioketal (8), *via* ketone (7),



SCHEME 1

followed by Raney nickel desulphurisation, thus obtaining 2-desoxyisotaondiol methyl ether (9).

The methyl resonances of isotaondiol and some of its

<sup>4</sup> C. E. Johnson, jun. and F. A. Bovey, *J. Chem. Phys.*, 1958, **29**, 1012; C. W. Haigh and R. B. Mallion, *Org. Magn. Resonance*, 1972, **4**, 203.

<sup>5</sup> M. Moreau, R. Longerey, and J. Dreux, *Bull. Soc. chim. France*, 1969, 2490.

derivatives are outlined in the Table, the chemical shifts being assigned on the basis of criteria discussed previously.<sup>2</sup> The numbers in parentheses are the chemical shift differences from the corresponding taondiol compounds. The C-12b methyl group suffers an extremely large down-field shift (0.28–0.38 p.p.m.). This can be explained in terms of two factors: first, the 1,3-*trans*-diaxial configuration of this particular methyl group with respect to the oxygen of the dihydropyran ring and second, the deshielding effect of the aromatic ring.<sup>4</sup> On changing the solvent from deuteriochloroform to hexadeuteriobenzene, the C-12b methyl signal is strongly moved up-field (0.38 p.p.m.), indicating the proximity of the protons to polar groups.

Examination of the ABX system involving the benzylic protons provides a good base for the structural and stereochemical elucidation of isotaondiol. The coupling constants calculated using the Karplus equations, for the two possible conformations of the dihydropyran ring with ring fusion B/c being *cis* and the  $\alpha$ -C-6a methyl group equatorial, are  $J_{AX}$  5,  $J_{BX}$  0 Hz for the half-chair conformation and  $J_{AX}$  6.8,  $J_{BX}$  1 Hz for the boat conformation.<sup>5</sup> These agree well with the observed values ( $J_{AX}$  7.1,  $J_{BX}$  0.2 Hz). We therefore conclude that (2) is the only possible structure for isotaondiol.

The fact that C-6a methyl inversion occurs under mild conditions suggests an alkyl-oxy- rather than aryl-oxy-fission of the heterocyclic ring. Taondiol methyl ether (1;  $R^1 = \text{H}$ ,  $R^2 = \text{Me}$ ) does not rearrange on treatment with base even under stringent conditions and hence the rearrangement of taondiol involves the phenolate anion as an intermediate. We would prefer to suggest an oxygen or peroxide catalysed rearrangement in which the initial step is the homolytic oxidation of the anion (12) giving the mesomeric phenoxyl radical (13).<sup>6</sup> Heterocyclic ring opening to form the quinone (14), followed by

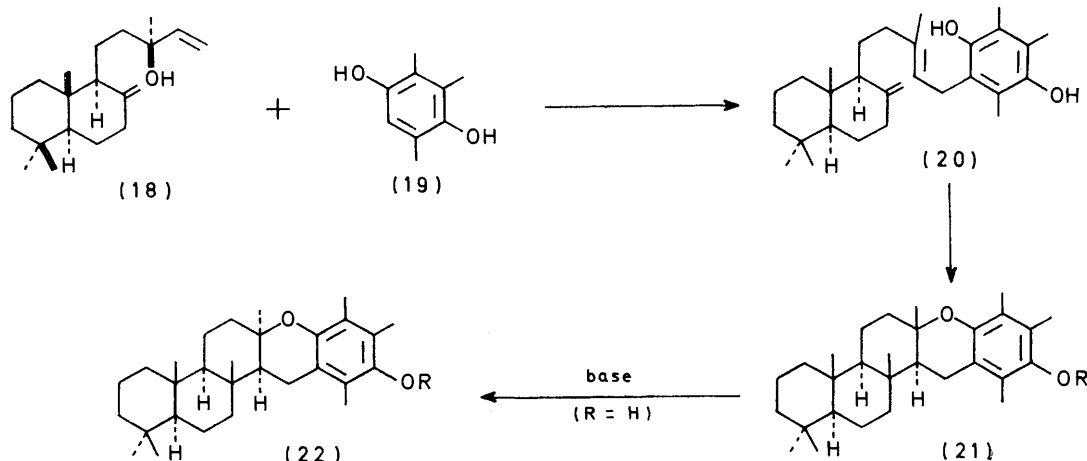
rearrangement to (15) and cyclisation to the 6-chromanoxyl radical (16) would give the anion (17) (Scheme 1).

<sup>6</sup> O. Isler and M. Montavon, *Bull. Soc. chim. France*, 1965, 2403; R. Rügge, H. Mayer, P. Schudel, U. Schweiter, R. Tamm, and O. Isler, *Wissenschaftl. Veröffentlich. Deutsch. Gesellschaft Ernähr.*, 1967, 14; J. L. G. Nilsson, H. Sievertsson, and H. Selander, *Acta Chem. Scand.*, 1969, **23**, 859, and references quoted therein.

This hypothesis is supported by the fact that when the alkaline isomerisation of taondiol is repeated in the presence of a radical scavenger (pyrogallol), in the absence of air and light, the yield of isotaondiol is only 20% (n.m.r.) as compared to the 50% obtained in the original experiment for the same reaction time.

The aim of the present investigation was to establish the generality of this phenomenon, and we were particularly interested in comparing the chemistry of tocopherols. The fact that the position and number of aromatic methyl groups play an important role in the

237 spectrometer. U.v. spectra, measured with a Unicam SP 800 or a Perkin-Elmer 137 spectrometer, refer to ethanol solutions.  $^1\text{H}$  N.m.r. spectra were taken with a Perkin-Elmer R-10 (60 MHz) or a Varian HA-100 (100 MHz) instrument for deuteriochloroform solutions with tetramethylsilane as internal standard;  $W_{1/2}$  refers to the width of a band at half height. Optical rotations were determined for solutions in chloroform with a Perkin-Elmer 141 polarimeter. Mass spectra were recorded on an A.E.I. MS-902 or a Hitachi-Perkin-Elmer RMU-7 instrument. Column and dry column chromatography was performed on silica gel 0.2–0.5 and 0.05–0.2 mm, respectively, and t.l.c. and p.l.c.



SCHEME 2

course of the oxidation,<sup>7</sup> stimulated us to synthesise 2-deoxy-9,11-dimethyltaondiol (21; R = H), an analogue of  $\alpha$ -tocopherol,<sup>8</sup> in a similar way to that described for taondiol.<sup>3</sup> Condensation of manool (18) with trimethylhydroquinone (17) at room temperature using boron trifluoride-ether afforded the air-unstable compound (20), whose structure was assigned on the basis of n.m.r. data (see Experimental section). Treatment of (20) with formic acid at 70° gave, in 62% yield, an oil with spectroscopic properties which support structure (21; R = H) (Scheme 2). Unless air was carefully excluded, 2-deoxy-9,11-dimethyltaondiol (21; R = H) smoothly rearranged in alkali to give an oil homogeneous by t.l.c. but which was shown by n.m.r. to be a 1:1 mixture of the rearranged compound (20; R = H) and starting material. Treatment of this mixture with benzoyl chloride in pyridine and subsequent separation by p.l.c. afforded the benzoate (21; R = Bz) as a crystalline solid and its isomer (22; R = Bz) as an oil which on basic hydrolysis at room temperature gave pure 2-deoxy-9,11-dimethylisotaondiol (22; R = H). This result is in agreement with the mechanism proposed above (Scheme 1).

#### EXPERIMENTAL

The m.p.s were determined with a Kofler hot-stage apparatus. I.r spectra were recorded with a Perkin-Elmer

\* See Discussion section for systematic name.

<sup>7</sup> J. L. G. Nilsson and H. Selander, *Acta Chem. Scand.*, 1970, **24**, 2885.

on silica gel G, all Merck products. T.l.c. plates were developed by spraying with 6N-sulphuric acid and heating. All solvents were purified by standard techniques. Light petroleum refers to the fraction b.p. 40–60°. Anhydrous sodium sulphate was used for drying solutions.

*Treatment of Taondiol (1; R<sup>1</sup> = R<sup>2</sup> = H) with Base.*—Taondiol\* (98 mg) was heated at reflux with methanolic sodium hydroxide (2%; 30 ml) for 5 h. The methanol was removed and the residue taken up in water (20 ml), extracted with ether (3 × 5 ml), dried, and evaporated to yield a homogeneous (by t.l.c.) crystalline solid (95 mg), which n.m.r. showed to be a 1:1 mixture of two compounds. Mass spectrometry of the mixture gave a single molecular ion at  $m/e$  412 ( $\text{C}_{27}\text{H}_{40}\text{O}_3$ ). The two isomers were separated by fractional crystallisation from methanol, the less soluble compound being identified as starting material (t.l.c.,  $[\alpha]_D$ , i.r. spectrum, and mixed m.p.). From the methanol mother liquors *isotaondiol* (2) crystallised as prisms, m.p. 215–217°,  $[\alpha]_D +60^\circ$  ( $c$  0.47) (Found: C, 78.35; H, 9.7.  $\text{C}_{27}\text{H}_{40}\text{O}_3$  requires C, 78.6; H, 9.75%),  $\lambda_{\text{max}}$  298 nm ( $\epsilon$  3846);  $\nu_{\text{max}}$  (KBr) 3540, 3330, 1620, 1490, 860, and 800  $\text{cm}^{-1}$ ;  $m/e$  (%) 412 ( $M^+$ ), 275 (25), 257 (75), 207 (12), 189 (40), 175 (63), 137 (100), 135 (50), 121 (52), 109 (43), and 95 (44). Further treatment with base did not alter the composition of the epimeric mixture.

*Treatment of Taondiol (1; R<sup>1</sup> = R<sup>2</sup> = H) with Acid.*—The following refluxing media did not affect epimerisation, and taondiol was recovered quantitatively: 2% hydrochloric acid in methanol, or 5% hydrochloric acid in *t*-butyl alcohol.

<sup>8</sup> F. M. Dean and L. E. Houghton, *J. Chem. Soc. (C)*, 1971, 1902.

In a typical experiment, taondiol (2 mg) was dissolved in the acidic medium (2 ml) and refluxed for 3 h. The organic solvent was removed and the residue dissolved in ether (2 ml). The ethereal solution was washed with water (3 × 0.5 ml), dried, and evaporated to give a solid which was shown to be pure starting material (mixed m.p.).

*Isotaondiol Diacetate* (3).—Taondiol (96 mg) in pyridine (5 ml) and acetic anhydride (2.5 ml) was left at room temperature overnight. The solution was poured into water (20 ml) and extracted with ether (3 × 10 ml). The combined extracts were washed with water (3 × 5 ml), dilute hydrochloric acid (3 × 10 ml), and water (2 × 5 ml), dried, and evaporated *in vacuo*. The crude diacetate (94 mg, 82%) was chromatographed using benzene as eluant. N.m.r. showed it to be a 1:1 mixture of two components which could not be separated by t.l.c. or g.l.c.; mass spectrometry gave a single molecular ion at *m/e* 496 (C<sub>31</sub>H<sub>44</sub>O<sub>5</sub>). The mixture was separated by a tedious fractional crystallisation from methanol. *Taondiol diacetate* (1; R<sup>1</sup> = R<sup>2</sup> = Ac) gave needles, m.p. 195–197°, [α]<sub>D</sub> –56° (c 0.82) (Found: C, 74.95; H, 8.95. C<sub>31</sub>H<sub>44</sub>O<sub>5</sub> requires C, 74.95; H, 9.0%), and *isotaondiol diacetate* (3) gave prisms, m.p. 244–246°, [α]<sub>D</sub> +50° (c 0.73) (Found: C, 74.85; H, 9.0%); ν<sub>max.</sub> (CCl<sub>4</sub>) 1760 and 1740 cm<sup>-1</sup>; τ 3.38 (s, H-9 and H-11), 5.51 (m, W<sub>1/2</sub> 14 Hz, H-2'α), 7.42 (m, 12-H<sub>2</sub>), 7.75 and 7.95 (both s, OAc), methyl groups: see the Table; *m/e* (%) 496 (M<sup>+</sup>), 454 (32), 436 (3), 421 (11), 394 (10), 379 (15), 351 (10), 257 (100), 189 (40), 175 (51), 137 (70), and 121 (50). To confirm structure (3) isotaondiol diacetate (5 mg) was dissolved in methanol (5 ml) and water (2 ml) and refluxed with sodium carbonate (10 mg) for 1 h. The methanol was removed *in vacuo* and the product extracted with ether. The ether solution was washed with water, dried, and evaporated *in vacuo*. P.l.c. gave the dihydroxy-compound (2) (3 mg), identical with the authentic sample (i.r. and mixed m.p.).

*Methylation of Taondiol*.—A solution of taondiol (300 mg) and dimethyl sulphate (2 ml) in dry acetone (50 ml) was refluxed over anhydrous potassium carbonate (5 g) for 20 h. The solid was filtered off and the solution evaporated *in vacuo*, and the residue taken up in water (40 ml) and extracted with ether (3 × 15 ml). The combined extracts were washed with 2N-sodium hydroxide (3 × 10 ml) and water (3 × 10 ml), dried, and evaporated *in vacuo*. Crystallisation of the residue from methanol gave large needles (293 mg, 94%) of a 1:1 mixture (by n.m.r.) of 10-methoxytaondiol (1; R<sup>1</sup> = H, R<sup>2</sup> = Me) and 10-methoxyisotaondiol (4) which could not be separated by recrystallisation from methanol or by t.l.c. or g.l.c. The mass spectrum of the mixture showed a single molecular ion at *m/e* 426 (C<sub>28</sub>H<sub>40</sub>O<sub>3</sub>) (Found: C, 79.05; H, 10.05. Calc. for C<sub>28</sub>H<sub>40</sub>O<sub>3</sub>: C, 78.85; H, 9.9%).

*10-Methoxytaondiol Iodoacetate* (1; R<sup>1</sup> = ICH<sub>2</sub>CO, R<sup>2</sup> = Me) and *10-Methoxyisotaondiol Iodoacetate* (10).—The above mixture of the methyl ethers (1; R<sup>1</sup> = H, R<sup>2</sup> = Me) and (4) (287 mg) in chloroform (20 ml) and pyridine (2 ml) was cooled to 0°. An excess of chloroacetyl chloride (3 ml) in chloroform (10 ml) was added slowly and the solution was stirred at 0° for 1 h, after which it was poured onto crushed ice and the product was extracted with methylene chloride (3 × 15 ml). The combined extracts were washed with water (2 × 10 ml), sodium carbonate solution (2 × 5 ml), 2N-hydrochloric acid (2 × 5 ml), and water (2 × 5 ml), dried, and evaporated *in vacuo* to give the chloroacetates (1; R<sup>1</sup> = ClCH<sub>2</sub>CO, R<sup>2</sup> = Me) and (11) (294 mg, 90%),

τ 6.00 (2H, s, Cl·CH<sub>2</sub>·CO<sub>2</sub>). All attempts to separate them by t.l.c. and fractional crystallisation failed.

The mixture of the chloroacetates (282 mg) in dry acetone (40 ml) was refluxed with finely powdered potassium iodide (2 g) for 3 h and worked up in the usual way to give the corresponding iodoacetates (326 mg, 98%), which were separated by fractional crystallisation from methanol; the *iodoacetate* (1; R<sup>1</sup> = ICH<sub>2</sub>CO, R<sup>2</sup> = Me) had m.p. 226–228°, [α]<sub>D</sub> –45° (c 0.56) (Found: C, 60.7; H, 7.3; I, 21.5. C<sub>30</sub>H<sub>43</sub>IO<sub>4</sub> requires C, 60.6; H, 7.25; I, 21.4%); ν<sub>max.</sub> (KBr) 1740 cm<sup>-1</sup>; τ 3.47 and 3.57 (both d, *J* 3 Hz, H-9 and H-11), 6.23 (s, MeO·Ar), 6.26 (2H, s, I·CH<sub>2</sub>·CO<sub>2</sub>), 7.86 (3H, s), 8.86 (3H, s), and 9.12 (12H, s); the *iodoacetate* (10) had m.p. 191–193°, [α]<sub>D</sub> +53° (c 0.63) (Found: C, 60.65; H, 7.35; I, 21.45%); ν<sub>max.</sub> (KBr) 1735 cm<sup>-1</sup>; τ 3.44 and 3.57 (both d, *J* 3 Hz, H-9 and H-11), 6.23 (s, MeO·Ar), 6.30 (2H, s, I·CH<sub>2</sub>·CO<sub>2</sub>), 7.92, 8.73, 8.82, 9.03, 9.06, and 9.10 (each 3H, s).

*10-Methoxytaondiol* (1; R<sup>1</sup> = H, R<sup>2</sup> = Me).—The iodoacetate (1; R<sup>1</sup> = ICH<sub>2</sub>CO, R<sup>2</sup> = Me) (60 mg) in methanolic potassium hydroxide (5%; 30 ml) was stirred at 40–50° for 2 h. The methanol was removed and the residue was taken up in water (20 ml) and extracted with ether (3 × 10 ml). The combined extracts were washed with water (3 × 5 ml), dried, and evaporated to give *10-methoxytaondiol* (1; R<sup>1</sup> = H, R<sup>2</sup> = Me) as prisms (33 mg, 80%), m.p. 203–204°, [α]<sub>D</sub> –67° (c 0.27), which was identical with an authentic sample obtained by methylation of taondiol (1; R<sup>1</sup> = R<sup>2</sup> = H) with diazomethane.

*10-Methoxyisotaondiol* (4).—The iodoacetate (10) (142 mg) was refluxed in methanolic potassium hydroxide (1%; 20 ml) for 3 h. Then the mixture was cooled and evaporated and the residue was partitioned between water and ether. Work-up in the usual way gave *10-methoxyisotaondiol* (4) (98 mg), as plates (from methanol), m.p. 180–181°, [α]<sub>D</sub> +44° (c 0.10) (Found: C, 79.1; H, 9.95%; M<sup>+</sup>, 426.3095. C<sub>28</sub>H<sub>42</sub>O<sub>3</sub> requires C, 78.85; H, 9.9%; M, 426.3133); ν<sub>max.</sub> (KBr) 3400 and 1620 cm<sup>-1</sup>; τ 3.47 and 3.57 (both d, *J* 3 Hz, H-9 and H-11), 6.28 (3H, s, MeO·Ar), methyl groups: see the Table; *m/e* (%) 426 (M<sup>+</sup>), 275 (19), 257 (64), 189 (70), 175 (29), 151 (100), 131 (40), and 121 (50).

*Methylation of Isotaondiol (2) with Diazomethane*.—Isotaondiol (2) (100 mg) was allowed to stand with ethereal diazomethane (50 ml) at room temperature overnight. Usual work-up gave (4) as crystals (65 mg, 64%), m.p. 181–182°, [α]<sub>D</sub> +44° (c 0.28), identical with 10-methoxyisotaondiol (4) obtained above (t.l.c., i.r. spectrum, and mixed m.p.).

*Isotaondiol Dibenzoate* (5).—Taondiol (148 mg) in pyridine (5 ml) was left with benzoyl chloride (3 ml) at room temperature overnight. The solution was poured into water and the product extracted with ether. The combined extracts were washed with water, aqueous sodium hydrogen carbonate, dilute hydrochloric acid, and water, dried, and evaporated *in vacuo*. Recrystallisation from methanol gave *isotaondiol dibenzoate* (5) (142 mg), m.p. 280–282° (Found: C, 79.2; H, 7.75. C<sub>41</sub>H<sub>43</sub>O<sub>5</sub> requires C, 79.35; H, 7.75%); ν<sub>max.</sub> (KBr) 1740 and 1720 cm<sup>-1</sup>; τ 1.9–2.5 (m, Ar), 3.22 (s, H-9, and H-11), 5.23 (m, W<sub>1/2</sub> 14 Hz, H-2α), 7.3 (m, 12-H<sub>2</sub>), methyl groups: see the Table; *m/e* (%) 620 (M<sup>+</sup>), 498 (5), 257 (32), 241 (12), 161 (13), 135 (15), and 105 (100). The dibenzoate (5) under reflux with 5% methanolic potassium hydroxide gave isotaondiol (2), identical with an authentic sample (mixed m.p., t.l.c., i.r. and n.m.r. spectra).

*Isotaondiol 2-Monobenzoate* (6).—The dibenzoate (5) (120

mg) in aqueous methanolic potassium hydroxide (5%; 30 ml) was stirred at 40–45° for 2 h. The methanol was removed and the residue was taken up in water and extracted with ether. Work-up in the usual way and separation by column chromatography on silica gel (20 g), with benzene as eluant, gave *isotaondioliol 2-monobenzoate* (6) (48 mg), m.p. 247–248° (Found: C, 78.8; H, 8.4.  $C_{34}H_{44}O_4$  requires C, 79.05; H, 8.6%;  $\nu_{\max}$  (KBr) 3540 and 1740  $cm^{-1}$ ;  $\tau$  1.9–2.5 (m, Ar), 3.45 (s, H-9 and H-11), 5.13 (m,  $W_{1/2}$  14 Hz, H-2 $\alpha$ ), 7.4 (m, 12-H $_2$ ), methyl groups: see the Table. Further elution (benzene–ethylacetate, 95:5) afforded *isotaondioliol* (s) (46 mg), identical with an authentic sample. Unchanged dibenzoate (5) (12 mg) was also recovered.

*2-Oxoisotaondioliol Methyl Ether* (7).—10-Methoxyisotaondioliol (4) (93 mg) in acetone (20 ml) was treated at room temperature with Jones reagent (0.15 ml). After 10 min the solution was poured into water and the product was extracted with ether. The ether solution was washed with water, aqueous sodium hydrogen carbonate, and water. Evaporation *in vacuo* and separation by p.l.c. gave the *keto-ether* (7) (83 mg, 89%), as needles, m.p. 207–209° (from methanol–chloroform),  $[\alpha]_D + 161^\circ$  (*c* 0.10) (Found: C, 79.0; H, 9.35.  $C_{28}H_{40}O_3$  requires C, 79.2; H, 9.5%;  $\nu_{\max}$  (KBr) 1720  $cm^{-1}$ ;  $\tau$  3.46 and 3.54 (both d, *J* 3 Hz, H-9 and H-11), 6.25 (3H, s), 7.5 (m, 12-H $_2$  and 3'-H $_2$ ), 7.88, 8.72, 8.79, 8.93, 8.97, and 9.19 (each 3H, s); *m/e* (%) 424 ( $M^+$ ), 273 (32), 205 (19), 151 (100), and 137 (22).

*2-Deoxyisotaondioliol Methyl Ether* (9).—(a) *Ethylenedithioacetal* (8). To a solution of (7) (78 mg) in glacial acetic acid (2 ml) were added ethanedithiol (0.1 ml) and boron trifluoride–ether (2 drops). After 2 h at room temperature, the solution was cooled to 0° and poured into cold 4*N*-sodium hydroxide. The product was extracted with ether and the ether solution was washed several times with water, dried, and evaporated *in vacuo*. The dithioacetal (8) was separated by p.l.c. as a crystalline solid (39 mg, 60%), m.p. 195–197° (large needles from methanol),  $\tau$  6.72 (4H, s,  $S-[CH_2]_2 \cdot S$ ).

(b) *Reduction of the dithioacetal* (8). The dithioacetal (35 mg) in absolute ethanol (15 ml) was refluxed with an excess of Raney nickel for 20 h. The cooled mixture was filtered and evaporated *in vacuo*. Separation by p.l.c. gave the *2-deoxy-ether* (9) (20 mg, 72%) which crystallised from methanol as needles, m.p. 121–122°,  $[\alpha]_D + 30^\circ$  (*c* 0.22) (Found: C, 82.1; H, 10.5.  $C_{28}H_{42}O_2$  requires C, 81.95; H, 10.25%;  $\nu_{\max}$  (KBr) 1620 and 860  $cm^{-1}$ ;  $\tau$  3.32 and 3.43 (both d, *J* 3 Hz, H-9 and H-11), 6.21 (3H, s, MeO·Ar), methyl groups: see the Table; *m/e* (%) 410 ( $M^+$ ), 259 (91), 206 (27), 191 (54), 151 (87), 135 (28), and 121 (30).

*Deuterium Exchange Experiments*.—Taondioliol (10 mg) in dry triethylamine (2 ml) was treated with deuterium oxide (1–5 ml) and the reaction was allowed to proceed to completion (50% isomerisation) by refluxing for 1–5 h. The solvent was evaporated off *in vacuo* and the residue (after isotopic exchange of  $-O[^2H]$  for  $-OH$ ) was examined by mass spectrometry.

*Attempted Isomerisation of 10-Methoxytaondioliol* (1;  $R^1 = H$ ,  $R^2 = Me$ ) with Base.—The following refluxing media did not affect isomerisation, and the starting material was recovered quantitatively: potassium carbonate in acetone, 5% methanolic potassium hydroxide, or pyridine. In a typical experiment, 10-methoxytaondioliol (1;  $R^1 = H$ ,  $R^2 = Me$ ) (5 mg) was dissolved in the alkaline medium (5 ml) and refluxed for 10 h. The organic solvent was removed and the residue was dissolved in ether (3 ml). The ether solution was washed with water (3  $\times$  2 ml), dried, and evaporated

to yield a solid which proved to be pure starting material (mixed m.p.).

*Treatment of Taondioliol with Base in the Absence of Air*.—A solution of pyrogallol (100 mg) in methanolic potassium hydroxide (5%; 20 ml) was deoxygenated by passing nitrogen through it for 1 h. Taondioliol (20 mg) was added and the solution was heated on a steam-bath for 5 h, under nitrogen and with protection from light. It was then poured into water and the product was extracted with ether. Work-up in the usual way and separation by p.l.c. gave a 4:1 mixture (by n.m.r.) of taondioliol and isotaondioliol. Attempts to decrease the extent of isomerisation by changing the conditions (amount of pyrogallol, flow of nitrogen) were ineffective.

*Synthesis of 2-Deoxy-9,11-dimethyltaondioliol* (21;  $R = H$ ).—(a) *Condensation of manool (18) with trimethylhydroquinone* (19). To a solution of trimethylhydroquinone (19) (5.0 g, 0.03 mol) in freshly distilled dioxan (40 ml) was added dropwise, with stirring at room temperature and under nitrogen, a solution of manool [(13*R*)-labda-8(20),14-dien-13-ol] (18) (5.8 g, 0.02 mol) in dioxan (25 ml). After the addition was complete, stirring was continued overnight. The reaction mixture was poured onto crushed ice and extracted with ether (3  $\times$  25 ml). The ether solution was washed with water, sodium hydrogen carbonate solution, and water, dried, and evaporated *in vacuo*. The residue was partitioned between *n*-hexane (150 ml), methanol (100 ml), and water (45 ml). The *n*-hexane solution was washed with aqueous methanol (70%; 3  $\times$  50 ml) and water, dried, and evaporated *in vacuo*. The air-unstable residue, crystallised from deoxygenated *n*-hexane–methylene chloride (4:1), gave the *prenyl phenol* (20) (6.7 g, 80%) as long needles, m.p. 52–53°,  $\tau$  4.80 (1H, t, *J* 8 Hz), 5.11 and 5.40 (each 1H, s), 6.63 (2H, d, *J* 8 Hz), 7.84 (9H, s), 8.20, 9.12, 9.20, and 9.34 (each 3H, s).

(b) *Acid-catalysed cyclisation of (20)*. To the phenol (20) (6.3 g) formic acid (98%; 10 ml) was added with stirring under nitrogen. After the addition, stirring was continued for 12 min at 25°, and then the mixture was gradually heated to 70° to give a clear solution. It was then refluxed for 1 h. After cooling, it was poured into water and extracted with ether (3  $\times$  10 ml). The ether extract was washed with water, sodium hydrogen carbonate solution, and water, dried, and the solvent evaporated *in vacuo*. The oily residue was chromatographed on silica gel (50 g), elution with benzene–light petroleum (3:1) affording *2-deoxy-9,11-dimethyltaondioliol* (21;  $R = H$ ) (4.5 g, 72%) as an oil,  $[\alpha]_D - 52^\circ$  (*c* 0.44),  $\lambda_{\max}$  194 nm ( $\epsilon$  3105),  $\nu_{\max}$  (KBr) 3500, 1480, 1390, and 1090  $cm^{-1}$ ;  $\tau$  7.6 (m, 12-H $_2$ ), 7.83 (3H, s) and 7.88 (6H, s) (*MeAr*), 8.89 and 9.09 (each 3H, s, Me-6a and Me-4a), 9.14 (6H, s, Me-12b and Me-1 $\alpha$ ), and 9.17 (3H, s, Me-1 $\beta$ ); *m/e* (%) 424 ( $M^+$ , 20), 259 (11), 191 (87), 165 (100), and 149 (30).

*Treatment of (21; R = H) with Base*.—2-Deoxy-9,11-dimethyltaondioliol (21;  $R = H$ ) (3 g) was heated under reflux with methanolic sodium hydroxide (5%; 30 ml) for 5 h. The methanol was removed and the residue was taken up in water (20 ml) and extracted with ether (3  $\times$  10 ml). Work-up in the usual way gave a homogeneous (by t.l.c.) oil, but n.m.r. showed it to be a 1:1 mixture of two compounds. Mass spectrometry of the mixture gave a single molecular ion at *m/e* 424 ( $C_{29}H_{44}O_2$ ).

*2-Deoxy-9,11-dimethyltaondioliol Benzoate* (21;  $R = Bz$ ) and *2-Deoxy-9,11-dimethylisotaondioliol Benzoate* (22;  $R = Bz$ ).—The above mixture (2.5 g) in pyridine (5 ml) and benzoyl chloride (3 ml) was left at room temperature overnight. The

solution was poured onto crushed ice and the product was extracted with ether. Work-up in the usual way gave a mixture of the two *benzoates* (21; R = Bz) and (22; R = Bz) which were separated by multiple elution p.l.c. The *benzoate* (21; R = Bz) had m.p. 176–177° (from *n*-hexane),  $[\alpha]_D -24^\circ$  (*c* 0.85) (Found: C, 81.65; H, 9.15.  $C_{36}H_{48}O_3$  requires C, 81.8; H, 9.1%);  $\nu_{\max}$  (KBr) 1730  $cm^{-1}$ ;  $\tau$  1.5–2.5 (m, Ar), 7.6 (m, 12-H<sub>2</sub>), 7.85, 7.87, and 7.90 (each 3H, s, *Me*·Ar), 8.84 and 9.08 (each 3H, s, Me-6a and Me-4a), 9.11 (6H, s, Me-12b and Me-1 $\alpha$ ), and 9.14 (3H, s, Me-1 $\beta$ ); *m/e* (%) 528 (*M*<sup>+</sup>, 100), 269 (40), 259 (38), 191 (92), and 105 (36). Basic hydrolysis of (21; R = Bz) at room temperature and under nitrogen gave pure (21; R = H) (t.l.c. and i.r. spectrum). The *benzoate* (22; R = Bz) was an oil which was purified by chromatography on silica gel,  $[\alpha]_D +60^\circ$  (*c* 0.93);  $\nu_{\max}$  (KBr) 1730  $cm^{-1}$ ;  $\tau$  1.5–2.5 (m, Ar), 7.54 (m, 12-H<sub>2</sub>), 7.84, 7.92, and 7.96 (each 3H, s, *Me*·Ar), 8.72 (6H, s, Me-6a and Me-12b), 9.04, 9.12, and 9.17 (each 3H, s, Me-4a,

Me-1 $\alpha$ , and Me-1 $\beta$ ); *m/e* (%) 528 (*M*<sup>+</sup>, 100), 269 (42), 259 (37), 191 (95), and 105 (41). Basic hydrolysis of (22; R = Bz) at room temperature gave pure 2-deoxy-9,11-dimethylisotaondiol (22; R = H) as an oil,  $[\alpha]_D +30^\circ$  (*c* 0.72);  $\lambda_{\max}$  294 nm ( $\epsilon$  3204);  $\nu_{\max}$  (KBr) 3600, 1480, 1390, and 1090  $cm^{-1}$ ;  $\tau$  7.54 (m, 12-H<sub>2</sub>), 7.87 (9H, s, *Me*·Ar), 8.75 (6H, s, Me-6a and Me-12b), 9.07, 9.12, and 9.17 (each 3H, s, Me-4a, Me-1 $\alpha$ , and Me-1 $\beta$ ); *m/e* (%) 424 (*M*<sup>+</sup>, 20), 259 (15), 191 (88), 165 (100), and 149 (27).

We thank Professor D. H. R. Barton and Dr. T. J. King for helpful comments. Dr. C. Pascual is thanked for recording some of the spectra and the Ministerio de Educación y Ciencia for a fellowship (Formación de Personal Investigador) (to J. D.). This work was performed within the Programme of Chemistry 1971 conceded by the Foundation Juan March.

[3/349 Received, 15th February, 1973]