Tetrahedron, 1966, Vol. 22, pp. 2845 to 2860. Pergamon Press Ltd. Printed in Northern Ireland

CHEMISTRY OF THE PODOCARPACEAE—XI[1]

REDUCTIONS OF TOTAROL

C. R. BENNETT and R. C. CAMBIE
Department of Chemistry, University of Auckland, New Zealand

(*Received* 21 *February* 1966)

Abstract—Methods for the reduction of the aromatic ring of totarol have been examined. Reduction of totaryl methyl ether with lithium in ethylenediamine gives a mixture of totarol (I, R = OH), totara-8,11,13-triene (I, R = H), totar-8(14)-ene (IV), and totar-8-ene (V). Totara-8,11,13-triene is also formed by Kenner desoxygenation of totarol. Friedel-Crafts acetylation of totara-8,11,13-triene yields 12-acetyltotaratriene (XIV, R = $COCH_3$) which has been converted by Baeyer-Villiger oxidation and hydrolysis to 12-hydroxytotaratriene (XIV, R = OH), a partially desoxygenated analogue of pododacric acid and of shonanol. A minor product from the acetylation of totara-8,11,13-triene has been identified as 2,5-diacetyl-3-methyl-7-isopropylindene (XVI). Catalytic hydrogenation of totarol over Pd gives the saturated hydrocarbon totarane (XX), and 13-oxototarane (XXI). The "tetrahydrototarol" of Short and Stromberg is identical with 13-oxototarane and their "dihydrototarol" has been shown to be a mixture of 13-oxototarane and totarol.

INVESTIGATIONS of members of the Podocarpaceae which are endemic to New Zealand have shown that totarol (I, R = OH) comprises the major diterpenoid constituent of the heartwoods of *Podocarpus totara*,[2,3] *P. hallii*,[4] *P. nivalis*,[5] and *Dacrydium cupressinum*.[6] Recently, totarol has also been isolated from the woods of *Podocarpus mannii*,[7] *P. milanjianus*,[8] *P. elongatus*,[9] *P. henckelii*,[9] *P. latifolius*,[9] *P. macrophyllus*,[10] and *P. nagi*,[10] from the wood of *Tetraclinis articulata*,[11] the barks of *Juniperus communis*[12] and *Dacrydium cupressinum*,[13] and the leaves of *Thujopsis dolabrata*.[14] While totarol has been synthesized by two independent routes[15,16] and the position of its phenolic grouping is suited for further synthetic work,[17] few studies have been directed towards the utilization of the readily available natural product for synthetic purposes.[18] As part of an investigation with this aim in view, methods for the

[1] Part X: R. C. Cambie, L. N. Mander, A. K. Bose and M. S. Manhas, *Tetrahedron* **20**, 409 (1965).
[2] T. H. Easterfield, *Trans. New Zealand Inst.* **43**, 53 (1910); T. H. Easterfield and J. C. McDowell, *Trans. New Zealand Inst.* **48**, 518 (1915).
[3] R. C. Cambie and L. N. Mander, *Tetrahedron* **18**, 465 (1962).
[4] R. C. Cambie, W. R. J. Simpson and L. D. Colebrook, *Tetrahedron* **19**, 209 (1963).
[5] C. R. Bennett and R. C. Cambie, unpublished results.
[6] C. W. Brandt and B. R. Thomas, *New Zealand J. Sci. and Tech.* **33B**, 30 (1951).
[7] D. A. H. Taylor, *J. Chem. Soc.* 1553 (1963).
[8] C. W. L. Bevan and D. A. H. Taylor, *J. Chem. Soc.* 6050 (1963).
[9] D. A. H. Taylor, *J. Chem. Soc.* 3495 (1965).
[10] T. Takahashi, personal communication.
[11] Y. L. Chow and H. Erdtman, *Acta Chem. Scand.* **16**, 1291 (1962); L. J. Gough, *Chem. and Ind.* 2059 (1964).
[12] V. P. Arya, *J. Sci. Ind. Res. India* **21B**, 236 (1962).
[13] R. C. Cambie and B. F. Cain, *New Zealand J. Sci.* **3**, 121 (1960).
[14] R. Hodges, *J. Chem. Soc.* 4247 (1961).
[15] J. A. Barltrop and N. A. J. Rogers, *J. Chem. Soc.* 2566 (1958).
[16] G. Pyne, *J. Ind. Chem. Soc.* **40**, 905 (1963).
[17] R. E. Ireland, *Record of Chem. Progress* **24**, 225 (1963).
[18] N. F. Elmore and T. J. King, *J. Chem. Soc.* 4425 (1961); C. P. Falshaw, A. W. Johnson and T. J. King, *J. Chem. Soc.* 2422 (1963); E. A. Adegoke, P. Ojechi and D. A. H. Taylor, *J. Chem. Soc.* 415 (1965).

reduction of the aromatic ring of totarol have now been examined and the present study reports the results, for metal-amine reductions of totaryl methyl ether (I, R = OCH_3), for the Kenner desoxygenation of totarol, and of a reinvestigation of its catalytic hydrogenation.[19]

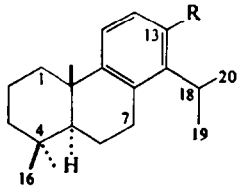
Prior to the present work, Chow and Erdtman[20] had reported the failure of an attempt to reduce the methyl ether and the phenoxyacetic acid derivative of totarol with lithium in liquid ammonia. The lack of reduction was attributed to steric hindrance since it was pointed out that the analogous compound without the isopropyl group had been successfully reduced by this method to a mixture of podocarpenones (II and III).[15] Repetition of Chow and Erdtman's attempted reduction of totaryl methyl ether with lithium and liquid ammonia using Wilds and Nelson's conditions[21] confirmed their observation, the starting material being recovered in quantitative yield. Similar attempts using the technique of Dryden *et al.*[22] with lithium and distilled ammonia in the presence of tetrahydrofuran and t-butanol were also unsuccessful.[23] However, reduction of totaryl methyl ether with the most powerful and least selective of the metal-amine systems, *viz.* lithium in ethylenediamine,[24,25] followed by chromatography on alumina gave four products. The least polar material (3·7% yield), recovered from the column with light petroleum, was a mixture of two isomeric hydrocarbons, $C_{20}H_{34}$, which was separated by preparative GLC. The isomer which was the minor constituent (34%) of the mixture possessed the lowest retention volume and was a solid, m.p. 72·5–73·5°, which showed no double bond absorption in the bending region of the IR spectrum. However, it gave a positive test with tetranitromethane, indicating the presence of a tetrasubstituted double bond. Its integrated NMR spectrum showed the presence of three tertiary methyl peaks (0·85, 0·89 and 0·96 δ) assigned to C_4-*gem* dimethyl and C_{10}-angular methyl groups, and a doublet at 0·90 δ (J = 7 c/s) characteristic of an isopropyl group. Since the spectrum showed no septet, or part thereof, in the region 2·9 δ due to a deshielded allylic C_{18}-methine proton of the isopropyl group[26,27]* it also served to distinguish between the two possible structures (IV and V) in favour of the latter.

* Cf. the position (2·87 δ) of the allylic methine proton in 2,3,4-trimethylpent-2-ene.[28] From a survey of a number of compounds possessing an isopropyl group substituted on a double bond[28] it is apparent that the degree of substitution and the stereochemistry about the double bond can be determined with some accuracy from the chemical shift of the allylic methine proton.[5]

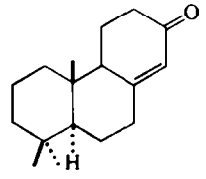
[19] W. F. Short and H. Stromberg, *J. Chem. Soc.* 516 (1937).
[20] Y. L. Chow and H. Erdtman, *Acta Chem. Scand.* **16**, 1305 (1962).
[21] A. L. Wilds and N. A. Nelson, *J. Amer. Chem. Soc.* **75**, 5366 (1953).
[22] H. L. Dryden, G. M. Webber, R. R. Burtner and J. A. Cella, *J. Org. Chem.* **26**, 3237 (1961). See also L. J. Chin and H. L. Dryden, *Ibid.* **26**, 3904 (1961).
[23] Cf. the resistance to reduction of dehydroabietic acid by this method. A. W. Burgstahler and L. R. Worden, *J. Amer. Chem. Soc.* **86**, 96 (1964).
[24] L. Reggel, R. A. Friedel and I. Wender, *J. Org. Chem.* **22**, 891 (1957).
[25] J. D. Brooks, R. A. Durie and H. Silberman, *Aust. J. Chem.* **17**, 55 (1954).
[26] N. S. Bhacca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry* p. 88. Holden-Day, San Francisco (1964).
[27] C. H. Brieskorn, A. Fuchs, J. B-son Bredenberg, J. D. McChesney and E. Wenkert, *J. Org. Chem.* **29**, 2293 (1964).
[28] *A. P. I. Nuclear Magnetic Spectral Data* Serial No. 463. Chemical and Petroleum Institute of Technology, Pittsburgh, Pennsylvania.

Although also showing no double bond bending absorption and giving a positive test with tetranitromethane, the major isomer (66% of the mixture) was a liquid, b.p. 133–136°/1 mm, whose C_{18}-methine proton resonance was clearly evident in the NMR spectrum as five members of a septet centred at 2·93 δ (J = 7 c/s). For this reason the compound was assigned the alternative structure totar-8(14)-ene (IV).*

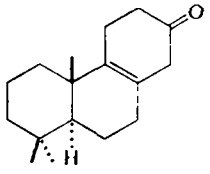
A further hydrocarbon m.p. 78–78·5° (14·4% yield), which was eluted from the column in later light petroleum eluates, was identified as totara-8,11,13-triene (I, R = H). The compound had formula $C_{20}H_{30}$ and the presence of an aromatic ring



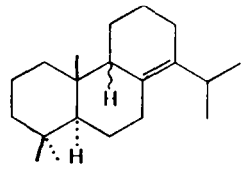
I



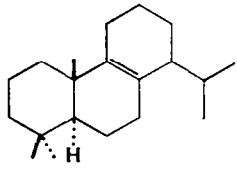
II



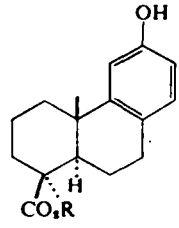
III



IV



V



VI

with three adjacent hydrogen atoms was indicated by bands in the IR spectrum at 1580 and 793 cm^{-1}.[31] The longest wavelength maximum of the UV spectrum occurred

* It should be noted that neither totar-8(14)-ene nor totar-8-ene are identical with a "totarene", isolated from the essential oil of *P. totara*.[29] The latter, a liquid diterpene, b.p. 180°/12 mm, was probably an impure sample of rimuene.[30]

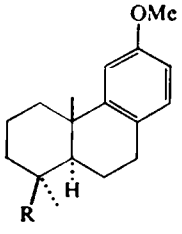
[29] H. A. A. Aitken, *J. Soc. Chem. Ind. Lond.* **48**, 344T (1929).

[30] G. B. Beath, *J. Soc. Chem. Ind. Lond.* **52**, 338T (1933); R. T. Aplin, R. C. Cambie and P. S. Rutledge, *Phytochemistry* **2**, 205 (1963); R. T. Aplin and R. C. Cambie, *New Zealand J. Sci.* **7**, 258 (1964).

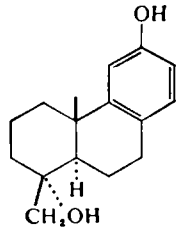
[31] L. J. Bellamy, *The Infrared Spectra of Complex Molecules* (2nd Edition) p. 64. Methuen, London (1958).

at 262·5 mμ and its position was consistent with those of trialkylated aromatic hydrocarbons[32] e.g. 1,2,3-triethylbenzene (λ_{max} 266 mμ) and 4-methyltetralin (λ_{max} 263 mμ) [cf. the 1,2,4-trisubstituted aromatic compound methyl podocarpate (VI, R = CH_3) (λ_{max} 265 mμ)]. Also, the NMR spectrum showed a three-proton singlet at low field (7·02 δ) similar to the A_3 signal given by the three chemically equivalent aromatic protons of 4,5-dimethyl-9,10-dihydrophenanthrene (7·15 δ).[33] By analogy with the spectrum of totarol and its derivatives[4,27] two doublets at 1·22 and 1·18 δ, each with J = 7 c/s, were assigned to the methyls of an isopropyl group differentially shielded by the aromatic ring, while a three-proton peak at 1·20 δ and a six-proton peak at 0·96 δ were assigned to the C_{10}-angular methyl and C_4-*gem* dimethyl groups, respectively.

The major product (52% yield) from the lithium–ethylenediamine reduction was totarol (I, R = OH). The demethylation was not unexpected since Reggel *et al.*[24] have shown that under similar conditions anisole gives phenol (54% yield) as the main product. In the reduction of anisole the primary reaction was considered to be a rapid alkyl-oxygen cleavage of the ether linkage to give methane and phenol which was followed by a slower reduction of the latter compound. While further reduction of totara-8,11,13-triene with lithium in ethylenediamine was found to yield totara-8(14)-ene (IV) and totar-8-ene (V) in the same ratio as obtained during the reduction of totaryl methyl ether, repeated attempts to reduce totarol under a variety of conditions and for long reaction periods were unsuccessful. It would therefore appear that in the reduction of the methyl ether the formation of the desoxy-derivatives (IV, V, and I, R = H) follows a different pathway from that which leads to totarol. When an attempt was made to reduce totaryl methyl ether with the more selective reagent lithium in ethylamine,[34,24] only a mixture of totar-8(14)-ene and totar-8-ene in the ratio 11:9 was obtained but no trace of oxygenated products was found.



VII



VIII

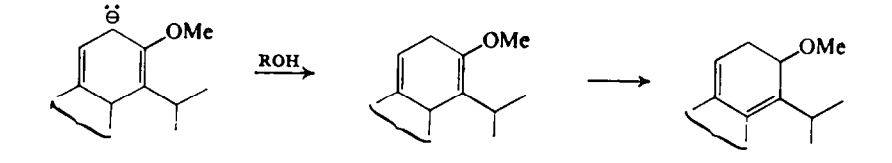
The lack of 1,4-reduction products from the above reductions of totaryl methyl ether is noteworthy. The formation of hydrogenolysed products is similar to, but more marked than, the behaviour of podocarpic acid derivatives during Birch type

[32] A. I. Scott, *Interpretation of the Ultraviolet Spectra of Natural Products* Chap. 3. Pergamon Press London (1964).

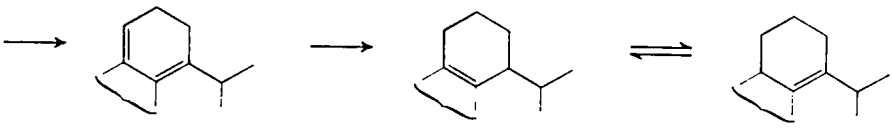
[33] N. S. Bhacca, D. P. Hollis, L. F. Johnson and E. A. Pier, *Varian NMR Spectra Catalog* Vol. 2. spectrum no. 654 (1963).

[34] R. A. Benkeser, R. E. Robinson, D. M. Sauve and O. H. Thomas, *J. Amer. Chem. Soc.* 77, 3230 (1955) and subsequent papers.

reductions.* According to Krapcho and Bothner-By[38] hydrogenolysis products probably arise from protonation of a carbanion intermediate (in this case IX) so as to form a 1,3-diene system which is more favoured for further reduction than a 1,4-diene system. These authors have also pointed out that steric effects can play an important part in the rate and hence the position of proton transfer to the aromatic substrate. Dryden *et al.*[22] have suggested that the formation of hydrogenolysis products from 12-methoxypodocarpa-8,11,13-trien-16-ol (VII, R = CH_2OH) is favoured by final protonation at C_{13} rather than at C_{11} as a result of hindrance by the C_{10}-methyl group. In a similar manner final protonation at C_{12} in the carbanion intermediate (IX) would lead to the totarenes (IV and V) by the following pathway.



IX X



XI V IV

The formation of totaratriene (I, R = H) in the reduction of totaryl methyl ether, however, is unexpected and it is not clear how this compound arises. It could conceivably be formed by an elimination from X or by a disproportionation of XI but neither of these reactions appear to have been hitherto observed during Birch type reductions.

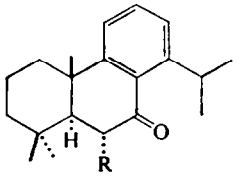
The successful application by Wenkert and Jackson[39] of a Kenner desoxygenation[40] i.e. phosphorylation followed by reduction with lithium in liquid ammonia, for the formation of a desoxy-derivative from podocarpic acid (VI, R = H) offered a further potential route to totara-8,11,13-triene. When the reaction sequence was applied to totarol variable yields of totaratriene were obtained, ranging from 20–53%, which were apparently dependent on the excess of lithium used in the reaction (Experimental), the optimum yield of the aromatic hydrocarbon being obtained when the ratio of lithium to totarol was ca. 25–30:1. Oxidation of the triene with chromium trioxide in acetic acid formed 7-oxototaratriene (XII, R = H) which in turn yielded the

* For the products from the reductions of 12-methoxypodocarpa-8,11,13-trien-16-ol (VII, R = CH_2OH) see ref. 35, for 12-methoxypodocarpa-8,11,13-triene (VII, R = CH_3) see ref. 36, and for O-methylpodocarpic acid (VII, R = CO_2H) see refs. 23 and 37. A preliminary investigation of the products of lithium-ethylenediamine reduction of methyl-O-methylpodocarpate has given *inter alia* podocarpa-8,11,13-trien-12,16-diol (VIII).[5]

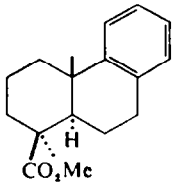
[35] R. H. Bible and R. R. Burtner, *J. Org. Chem.* **26**, 1174 (1961). See also Ref. 22.
[36] F. Sondheimer and M. Gibson, *Bull. Res. Council Israel* **9A**, 204 (1960), *Chem. Abstr.* **55**, 6520 (1961); E. Wenkert, V. I. Stenberg and P. Beak, *J. Amer. Chem. Soc.* **86**, 96 (1964).
[37] K. Crowshaw, R. C. Newstead and N. A. J. Rogers, *Tetrahedron Letters* No. 33, 2307 (1964).
[38] A. P. Krapcho and A. A. Bothner-By, *J. Amer. Chem. Soc.* **81**, 3658 (1959). See also Ref. 22.
[39] E. Wenkert and B. G. Jackson, *J. Amer. Chem. Soc.* **80**, 217 (1958).
[40] G. W. Kenner and N. R. Williams, *J. Chem. Soc.* 522 (1955).

6-bromo-7-oxoderivative (XII, R = Br) on treatment with bromine in acetic acid. From the shift of the carbonyl frequency in the infra-red spectrum from 1678 cm^{-1} to 1696 cm^{-1} on formation of the bromo-derivative from 7-oxototaratriene,[41] from a hypsochromic shift of the n–π^* transition maximum of the carbonyl chromophore in the corresponding UV spectra,[42] from the magnitude of the coupling constant (7·3 c/s) for the C_5 and C_6-protons in the NMR spectrum of the bromo-derivative,[42] and from the ORD curve,[42] the bromo-atom could be assigned an equatorial α-configuration (XII, R = Br).

During their work on podocarpic acid Wenkert and Jackson[39] were able to reconstitute methyl podocarpate (VI, R = CH_3) from its desoxy-derivative (XIII) by acylation with acetyl chloride followed by Baeyer-Villiger oxidation and then hydrolysis of the resulting O-acetyl methyl podocarpate. It was therefore of interest to examine a similar sequence with totara-8,11,13-triene (desoxytotarol). Since Friedel-Crafts acylation of podocarpic acid (VI, R = H) occurs at C_{13} rather than at C_{11}[43] and since the C_{13}-position of totaratriene would be expected to be sterically hindered by the adjacent isopropyl group it could be predicted that acetylation would occur at the C_{12}-position in the latter compound. In the event, two products were obtained after chromatography of the reaction mixture on alumina. The major product (79%), a pale yellow oil with formula $C_{22}H_{32}O$, was an aryl ketone (ν_{max} 1688 cm^{-1}, cf. acetophenone, ν_{max} 1680 cm^{-1} [44]) which was clearly the desired 12-acetyltotara-8,11,13-triene (XIV, R = $COCH_3$). The UV spectrum showed peaks at 220 mμ (log ε 4·37) and 261 mμ (log ε 4·25), the wavelength of the latter peak being close to that of methyl 12-acetylpodocarpa-8,11,13-triene (XV; λ_{max} 258 mμ, log ε 4·28[41]) in which both positions *ortho* to the acetyl group are unsubstituted. This maximum can be compared with those of *ortho*-substituted acetophenones which usually occur at lower wavelength and have lower intensities e.g. 2-methylacetophenone, λ_{max} 242 mμ (log ε 3·94) and 2,4,6-trimethylacetophenone, λ_{max} 242 mμ (log ε 3·55).[32] The IR spectrum was characterized by the lack of absorption in the 800–870 cm^{-1} region associated with the out-of-plane bending of two adjacent aromatic protons.[4,15] From this it follows that the substitution pattern is such that no two hydrogen atoms are adjacent, restricting the location of the acetyl group to the C_{12} position. This was confirmed by the absence of an AB aromatic proton quartet in the NMR spectrum which is characteristic of the C_{11} and C_{12} aromatic protons of totaryl derivatives.[3,4,27] Instead, the spectrum showed two diffuse signals at 6·75 and 6·66 δ corresponding to *meta*-coupled C_{11} and C_{13}-protons.

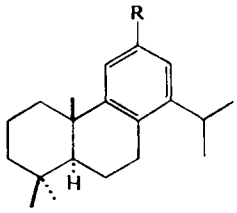


XII

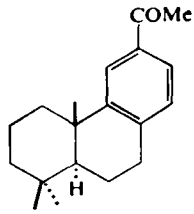


XIII

[41] E. Wenkert, P. Beak, R. W. J. Carney, J. W. Chamberlin, D. B. R. Johnston, C. D. Roth and A. Tahara, *Canad. J. Chem.* **41**, 1924 (1963).
[42] A. K. Bose, M. S. Manhas and R. C. Cambie, *J. Org. Chem.* **30**, 501 (1965).
[43] W. P. Campbell and D. Todd, *J. Amer. Chem. Soc.* **62**, 1287 (1940).
[44] K. Nakanishi, *Infrared Absorption Spectroscopy* p. 162. Holden-Day, San Francisco (1962).



XIV



XV

Treatment of 12-acetyltotara-8,11,13-triene (XIV, R = $COCH_3$) with trifluoroperacetic acid gave 12-acetoxytotara-8,11,13-triene (XIV, R = $OCOCH_3$) which was deacetylated during chromatography on activated alumina to yield 12-hydroxytotara-8,11,13-triene (XIV, R = OH). The IR spectrum of the latter showed a broad band at 3310 cm^{-1} diagnostic of an inter-molecularly hydrogen-bonded phenolic group and is in contrast with the sharp peak at 3600 cm^{-1} shown by the spectrum of totarol (I, R = OH).[45] In the latter case the bulky isopropyl group prevents the molecules from approach, close enough to form strong hydrogen bonding, while in the former case the phenolic group at C_{12} is free from steric protection of adjacent alkyl substituents. The NMR spectrum of the 12-hydroxy-compound showed a two-proton aromatic singlet (somewhat broadened by *meta*-coupling) at 6·56 δ, five members of a C_{18}-methine proton septet at 3·06 δ, two doublets of an isopropyl group at 1·09 δ (J = 7 c/s) and 1·13 δ (J = 7 c/s), a C_{10}-angular methyl peak at 1·13 δ, C_4-*gem* dimethyl signals at 0·92 and 0·95 δ, and a broadened singlet at 6·20 δ due to the phenolic proton whose assignment was confirmed by exchange with deuterium oxide.

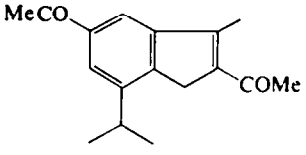
The formation of 12-hydroxytotaratriene by the above sequence of reactions provides a method for the transferrence of a phenolic group from the C_{13}- to the C_{12}-position in totaryl derivatives. This is of interest since pododacric acid, a diterpenoid acid co-occurring with podocarpic acid in the heartwoods of *P. dacrydioides*[46] and *P. totara*,[3] is believed to possess a phenolic group at C_{12} and a dihydroxy substituted isopropyl group at C_{14}.[47] Moreover, shonanol (XIV, R = OH; keto group at C_3) a diterpenoid occurring in the wood of *Libocedrus formosana*, also possesses the same aromatic substitution pattern.[48] 12-Hydroxytotaratriene would thus be a partially desoxygenated derivative of those compounds and its method of formation offers a potential route for a possible synthesis of the acid and of shonanol from the related podocarpic acid.

As noted above two products were obtained from the Friedel-Crafts acetylation of totarol. The second and minor product (6% yield) of the reaction was isolated from ether eluates during chromatography on alumina. It was an optically inactive crystalline solid, m.p. 151–152°, which analysed for $C_{17}H_{20}O_2$ in agreement with the proton count from the integrated NMR spectrum. As the spectrum showed the presence of an isopropyl group [6-proton doublet centred at 1·38 δ (J = 7 c/s) and a one-proton septet at 3·26 δ (J = 7 c/s)] it was clear that degradation of rings A and/or B had occurred during the acetylation. The compound was assigned the

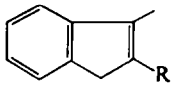
[45] W. F. Short and H. Wang, *J. Chem. Soc.* 2979 (1951).
[46] L. H. Briggs, R. C. Cambie, R. N. Seelye and A. D. Warth, *Tetrahedron* **7**, 270 (1959).
[47] A. R. Cashmore, M.Sc. thesis, University of Auckland (1963); L. D. Colebrook, personal communication.
[48] Y. T. Lin and K. T. Liu, *J. Chinese Chem. Soc. Taiwan* **12**, 51 (1965); *Chem. Abs.* **63**, 16772 (1965).

structure 2,5-diacetyl-3-methyl-7-isopropylindene (XVI) from the following physical evidence. Absorption maxima at 1675 cm^{-1} and 1665 cm^{-1} in the IR spectrum showed that two carbonyl groups were present in the molecule, the former band corresponding in position to that of an aryl ketone[44] and the latter to that of an $\alpha\beta$-unsaturated ketone. A single peak at 877 cm^{-1} is associated with the out-of-plane bending of an isolated aromatic proton and thus no two aromatic hydrogen atoms were adjacent in the compound. The UV spectrum showed absorption maxima at 249 mμ (log ε 4·29) and 301·5 mμ (log ε 3·22) and was similar to that of 2-aldehydo-3-methylindene (XVII, R = CH=O) [λ_{max} 234 mμ (log ε 3·99) and 307 mμ (log ε 4·33)][49] whose chromophore bore the closest available analogy to that of the acetylated indene.

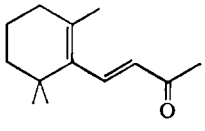
Weilder *et al.*[50] have noted that in the NMR spectrum of 3-methylindene (XVII, R = H) the C_3-methyl signal is split by the olefinic C_2-proton (J = 1·6 c/s) and also (J = 2·2 c/s) by homoallylic coupling with the C_1-methylene protons to give three doublets. The C_1-methylene protons are magnetically equivalent and hence *geminal* coupling does not occur but they give rise to a multiplet by the homoallylic coupling above and by coupling to the C_2-ethylenic proton (J = 1·8 c/s). The methyl resonance is deshielded slightly and occurs at 2·06 δ.



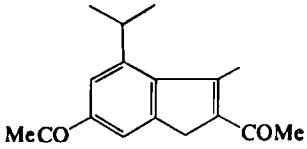
XVI



XVII



XVIII



XIX

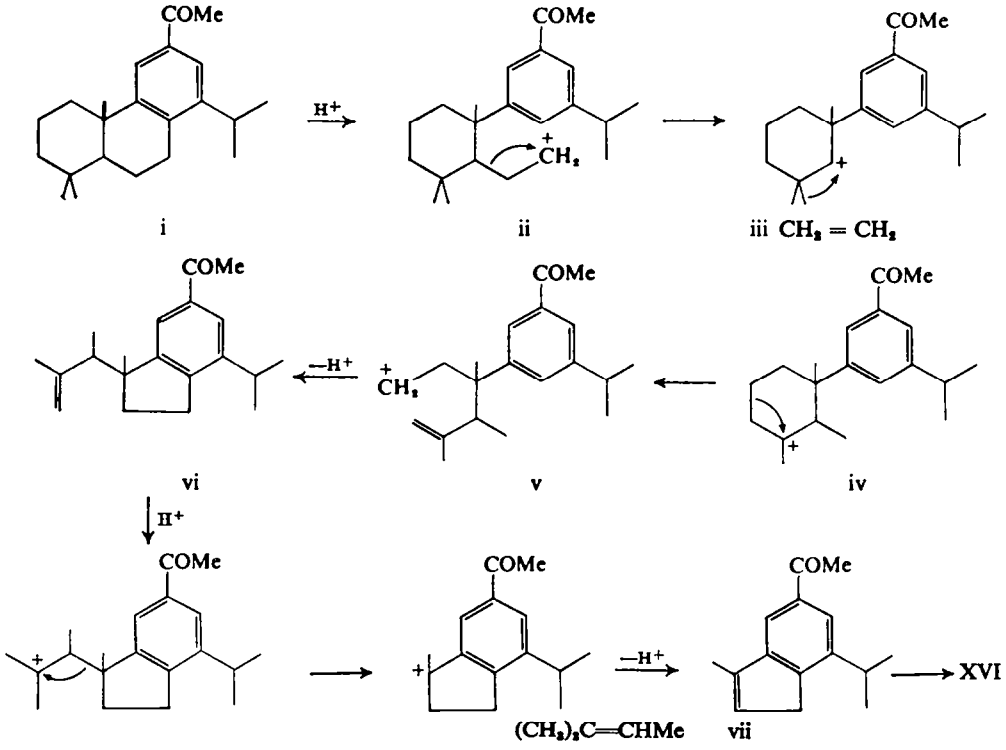
By analogy with the spectrum of 3-methylindene, a triplet at 2·58 δ in that of 2,5-diacetyl-3-methyl-7-isopropylindene was assigned to the methyl peak, the splitting arising from homoallylic coupling with the C_1-methylene protons. The coupling constant of 2·3 c/s agrees closely with that for 3-methylindene and for related systems,[50] while the larger paramagnetic shift suffered by the methyl signal is due to the deshielding effect of the acetyl group at C_2. A quartet at 3·72 δ (J = 2·3 c/s) corresponds to the signal of the C_1-methylene protons which are coupled to the protons of the methyl group. The spectrum also showed a two-proton aromatic singlet at 8·01 δ and its large paramagnetic shift is due to the presence of electron-withdrawing acetyl groups in close proximity to the aromatic protons. Two remaining peaks at 2·67 and 2·50 δ were assigned to the protons of the vinylic and aryl acetyl groups at C_2 and C_5, respectively. The signal at 2·67 δ can be compared with the

[49] T. Fujita and A. Ayada, *Tanabe Seiyaku Kenyku Nempô* **3**, 1 (1958); *Chem. Abstr.* **52**, 20016 (1958).

[50] A. M. Weidler, B. Mathiasson and G. Bergson, *Arkiv Kemi* **21**, 187 (1963); A. M. Weidler, *Acta Chem. Scand.* **17**, 2724 (1963).

corresponding acetyl methyl resonance of β-ionone (XVIII) which occurs at 2·31 δ.[51] The large paramagnetic shift of the acetyl signal in the substituted indene derivative is to be expected as that group is also conjugated with the aromatic ring while the chemical shift of the aryl acetate peak (2·50 δ) agrees favourably with that (2·59 δ) of acetophenone.[52] The mutual coupling of the protons of the C_3-methyl and C_1-methylene groups was confirmed by a spin decoupling experiment. Irradiation of the quartet at 3·72 δ at a frequency of ca. −68 c/s caused the collapse of the methyl triplet to a singlet while irradiation of the triplet at 2·58 δ at a frequency of ca. +68 c/s caused the corresponding collapse of the quartet.

The formation of an indene derivative during a Friedel-Crafts acylation of a diterpenoid is unexpected. However, a scheme leading to the formation of the substituted indene in terms of a rational mechanism is outlined below. The primary carbonium ion (ii)* formed by protonation of an acylated totaratriene (i) could eliminate a molecule of ethylene to give a secondary carbonium ion (iii). This in turn could provide a more stable tertiary carbonium ion (iv) by a 1:2-methyl shift. Ring opening followed by intramolecular acylation of the aromatic nucleus by the resulting primary carbonium ion in (v) would give the indene derivative (vi). Further



* Cf. The formation of a primary carbonium ion during isomerisation of 9-acetyl-s-octahydrophenanthrene in the presence of aluminium chloride.[53]

[51] Ref. 33, spectrum no. 617.

[52] N. S. Bhacca, L. F. Johnson and J. N. Shoolery, *Varian NMR Spectra Catalog* Vol 1 spectrum no. 192 (1962).

[53] G. Baddeley and A. C. Pendleton, *J. Chem. Soc.* 807 (1952).

protonation followed by elimination of a molecule of 2-methylbut-2-ene and then de-protonation would give vii which would be expected[54] to undergo Friedel-Crafts acetylation to give 2,5-diacetyl-3-methyl-7-isopropylindene (XVI). An alternative structure (XIX) for the indene which is also possible from the above evidence is ruled out on the grounds that no reasonable mechanism can be postulated which leads to an indene derivative with the spatial arrangement of methyl and isopropyl groups as in XIX.

In addition to the metal-amine reductions, a re-investigation of the products from catalytic hydrogenation of totarol was also carried out. Short and Stromberg[19] had shown that although totarol was resistant to catalytic hydrogenation at room temperature, reduction in acetic acid at 70° and 30 lb/sq in. over Pd–C gave a saturated laevorotatory hydrocarbon, totarane and a smaller yield of a "dihydrototarol". The dihydro-compound was slowly reduced by further hydrogenation to a "tetrahydrototarol" but all attempts to isolate the saturated alcohol were unsuccessful.

In the present work, at 60° and 500 lb/sq in. totarol was partly converted to totarane (XX) and 13-oxototarane (XXI). The elemental analysis and melting point of 13-oxototarane are in agreement with those quoted by Short and Stromberg for "tetrahydrototarol" and the compounds are almost certainly the same. The IR spectrum of the ketone showed carbonyl absorption at 1720 cm^{-1} [cf. 12-oxopodocarpan-16-ol (XXII; R = CH_2OH), 1715 cm^{-1}][35] but no absorption typical of aromatic or double bonds. Reduction of the compound with LAH gave 13-hydroxytotarane whose hydroxyl group probably possessed an equatorial conformation since a broad peak (half-height width 28 c/s) at 3·31 δ in the NMR spectrum was characteristic of an axial proton on an alcohol-bearing carbon atom flanked by two other protons.[55,56]

The configuration of 13-oxototarane cannot be assigned with certainty but from the following considerations it is probably that represented by XXI.* The ketone was unaffected by heating under reflux with methanolic sodium methoxide and thus the isopropyl group is in the thermodynamically more stable quasi-equatorial conformation. From Dreiding models and applying the octant rule[57] only structure (XXI) with a *trans*-anti-*trans* configuration and a quasi-equatorial isopropyl group would be predicted to give the strong positive effect [amplitude (*a*) +81] which is observed on measurement of the ORD curve.† A compound similar to 13-oxototarane

* The uncertainty arises from the fact that assignment of configuration to a similar ketone (XXIII) based on the octant rule would lead to the wrong stereochemistry.[55] This ketone, prepared by hydrogenation and subsequent oxidation of 12-hydroxyabietic acid, has been shown to be correctly represented by XXIII from chemical evidence, and the anomalous ORD curve has been suggested to reflect a distortion of ring C from the normal chair conformation.[55]

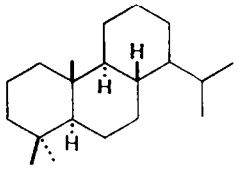
† In the absence of any evidence to the contrary it is assumed that ring C of 13-oxototarane adopts a normal chair conformation. A compound with a *trans*-anti-*cis* configuration possessing ring B in a boat form would also be expected to give a moderately strong positive Cotton effect. However, such a model is ruled out by the large interactions which would be introduced (cf. ref. 55).

[54] F. H. Howell and D. A. H. Taylor, *J. Chem. Soc.* 3011 (1957); H. Weiland and L. Bettag, *Chem. Ber.* **55**, 2246 (1922).

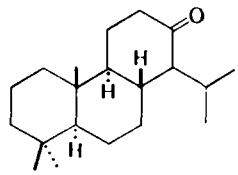
[55] W. Herz, H. J. Wahlborg, W. D. Lloyd, W. H. Schuller and G. W. Hedrick, *J. Org. Chem.* **30**, 3190 (1965).

[56] H. Feltkamp and N. C. Franklin, *Tetrahedron* **21**, 1541 (1965).

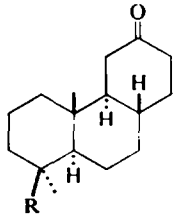
[57] C. Djerassi, *Optical Rotatory Dispersion* p. 181. McGraw-Hill, New York (1960); W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne and C. Djerassi, *J. Amer. Chem. Soc.* **83**, 4013 (1961).



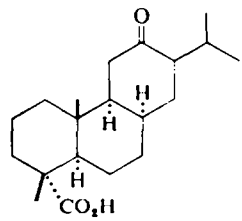
XX



XXI



XXII



XXIII

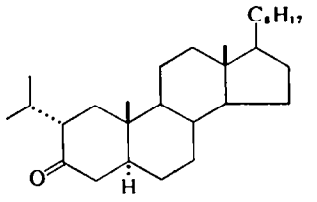
(XXVIII of ref. 58) which also possesses a *trans*-anti-*trans* fused backbone but a β-methyl group at C_{14} has an ORD curve ($a + 61$)[58] which is almost superimposable on that of the oxototarane. Djerassi *et al.*[59] have estimated that the contribution (Δa) of an equatorial isopropyl group to the amplitude of the ORD curve of cyclohexanone derivatives possessing an isopropyl group adjacent to the carbonyl group, is 15–20 units while that for an axial isopropyl group is approximately 90 units. The contribution of the quasi-equatorial isopropyl group to the amplitudes of the ORD curve of 13-oxototarane is found from the difference in amplitude of the curves of 13-oxototarane and 13-oxopodocarpane (XXII, R = CH_3; $a + 48$). The value of +33 units is in reasonable agreement with that predicted. Moreover, since the isopropyl group is to the left in the projection (XXIV) of 13-oxototarane the sign of its contribution to the amplitude is as expected. This follows from analogy with the contribution of the quasi-equatorial isopropyl group of 2α-isopropylcholestan-3-one (XXV) (projection formula XXVI) which has been shown to be −15 units.[59]

It appears probable that totarane (XXI) also possesses a *trans*-anti-*trans* configuration and an equatorial isopropyl group since reduction of the thioketal of 13-oxototarane with Raney nickel, a method which proceeds without affecting the stereochemistry at the carbon atom *alpha-* to a carbonyl group[60,61] afforded a hydrocarbon which was identical with totarane. It should be noted that both 13-oxototarane and totarane are products of *trans*-addition of hydrogen, presumably in the latter stage, to a species possessing an 8,9- or 8,14- double bond. There are many cases in the literature of this phenomenon[62] including the recent report[60] of the formation of *trans*-products from the Pt-catalysed hydrogenation of pimaric, sandaracopimaric and isopimaric acids. This latter paper also reports the formation of large percentages of *trans*-products from the catalytic hydrogenation of a podocarpic

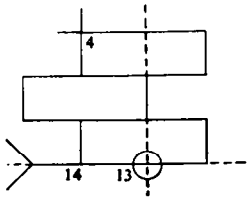
[58] C. Djerassi and W. Klyne, *J. Chem. Soc.* 4929 (1962).
[59] C. Djerassi, P. A. Hart and C. Beard, *J. Amer. Chem. Soc.* **86**, 85 (1964).
[60] J. W. ApSimon, P. V. Demarco and J. Lemke, *Canad. J. Chem.* **43**, 2793 (1965).
[61] R. E. Ireland and J. A. Marshall, *J. Org. Chem.* **27**, 1620 (1962).
[62] S. Siegel and G. V. Smith, *J. Amer. Chem. Soc.* **82**, 6082, 6087 (1960); S. Siegel, P. A. Thomas and J. T. Holt, *J. Catalysis* **4**, 73 (1965); J. F. Sauvage, R. H. Baker and A. S. Hussey, *J. Amer. Chem. Soc.* **82**, 6090 (1960); **83**, 3874 (1961); S. Bory and C. Asselineau, *Bull. Soc. chim. Fr.* 1355 (1961).

acid derivative, an even closer relative of totarol. ApSimon *et al.*[60] have discussed the formation of *trans*-products in the resin acid series in detail and have suggested that in the case of inaccessible double bonds transfer of hydrogen as a proton from the solvent is a "vital step in the reaction sequence". They suggest that this protonation, possibly while the olefin is associated with the catalyst surface, yields a tertiary carbonium ion which then adds hydrogen from the catalyst surface as a hydride ion to give an overall *trans*-addition product.

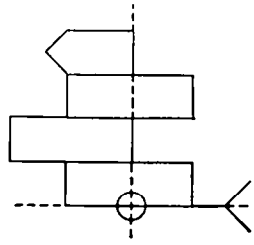
Finally, repeated attempts were made to obtain "dihydrototarol" under a variety of hydrogenation conditions. From the chromatography of reduction products on silica gel a crystalline material, $[\alpha]_D^{25}$ +24°, was obtained which possessed a constant m.p. 151·5–152·5° and whose description fitted that of Short and Stromberg's "dihydrototarol" (i.e., m.p. 151–151·5°, $[\alpha]_D$ +20°).[19] Closer investigation by TLC and NMR spectroscopy, however, revealed that the material was a mixture of 13-oxototarane and totarol in the ratio 1:3, which could be separated by chromatography on activated alumina. A synthetic "dihydrototarol" with m.p. and mixed m.p. 150–151·5° could be prepared by crystallizing a 1:3 mixture of 13-oxototarane and totarol from light petroleum–chloroform. It is noteworthy that the m.p. of "dihydrototarol" is higher than that of each constituent of the mixture. A similar elevation of the m.p. of totarol when mixed with 16-hydroxytotarol has been observed by Taylor[63] and confirmed by workers in this laboratory.[4]



XXV



XXIV



XXVI

EXPERIMENTAL

Microanalyses were by Dr. A. D. Campbell and his associates, University of Otago, New Zealand. IR spectra were measured with Perkin-Elmer 237 or Infracord instruments and UV spectra were determined for EtOH solutions with a Perkin-Elmer 137 UV spectrophotometer. ORD curves and optical rotations were determined with a Jasco ORD/UV-5 spectrophotometer at 25° and, unless otherwise stated, are for solutions in MeOH. NMR spectra were determined on a Varian A60 spectrometer in $CDCl_3$ with TMS as internal reference.

[63] D. A. H. Taylor, *Chem. & Ind.* 1712 (1961).

Light petroleum refers to the fraction b.p. 50–60° and alumina used for chromatography was P. Spence Type H material.

Reduction of totaryl methyl ether (I, R = OMe_3) *in ethylenediamine*

A solution of I (12·0 g) in ethylenediamine (200 ml) was heated to 100° in an atm. of N_2, and Li (4·5 g) was added to the stirred solution in portions (0·6 g) at 15 min intervals over a period of 2 hr. After the fourth addition the blue colour of the cation persisted throughout the remaining additions. The solution was heated gently under reflux for 2 hr, until it became colourless, water (800 ml) was then added, and the mixture was extracted with ether. The aqueous layer was acidified and re-extracted with ether, and the combined ethereal extracts were washed with dil HCl, sat NaClaq, and dried. The semi-crystalline concentrate was chromatographed on alumina (500 g) to afford 3 products which were contained in initial light petroleum, later light petroleum, and ether eluates, respectively. The product from the ether eluate was identified as totarol, which formed prisms (6·2 g), m.p. and mixed m.p. 127° (identical IR spectrum).

Totar-8-ene (V) *and totar-8(14)-ene* (IV)

Concentration of the initial light petroleum eluate gave a mixture (0·44 g) of two isomeric alkenes as a colourless mobile oil, b.p. 146–147°/0·25 mm, which was separated by preparative GLC using a Wilkens Autoprep instrument, Model A-700 with a 20′ SE30 column operating at 270°.

Totar-8-ene (retention vol. 7·5 L) was collected as a solid which crystallized from EtOH–$CHCl_3$ as needles, m.p. 72·5–73·5°, $[\alpha]_D$ +175° (*c* 0·75). (Found: C, 87·8; H, 12·8. $C_{20}H_{34}$ requires: C, 87·5; H, 12·5%.) ν_{max} (CCl_4) 2920 (CH_2), 1465 (C—H), 1380 and 1365 cm^{-1} (*gem* dimethyl). NMR 0·85, 0·89 and 0·96 (C_4-*gem* dimethyl, C_{10}-angular methyl), and 0·90 δ (doublet, J = 7·0 c/s, isopropyl methyls).

Totar-8(14)-ene (retention vol. 8·3 l.) was isolated as an oil, b.p. 133–136°/1 mm, $[\alpha]_D$ +30° (*c* 0·67 in $CHCl_3$). (Found: C, 87·65; H, 12·5. $C_{20}H_{34}$ requires: C, 87·5; H, 12·5%.) ν_{max}(film) 2960, 2870 (CH_3), 1650 (C=C), 1465 (C—H), 1375 and 1365 cm^{-1} (*gem* dimethyl). NMR 0·85, 0·89, 0·89 (C_4-*gem* dimethyl, C_{10}-angular methyl), 0·92 (doublet J = 7·0 c/s, isopropyl methyls), and 2·93 δ (5 members of a septet, J = 7·0 c/s, C_{18}-methine proton).

Both isomers gave positive tests for unsaturation with tetranitromethane and were recovered quantitatively after attempted hydrogenations at 20° and 40 lb/sq in. for 140 hr.

Totara-8,11,13-triene (I, R = H)

The concentrate (1·71 g) from later light petroleum eluates was crystallized from EtOH to give *totara*-8,11,13-*triene* as needles, m.p. 78–78·5°, $[\alpha]_D$ +30·6° (*c* 2·6). (Found: C, 88·7; H, 11·45. $C_{20}H_{30}$ requires: C, 88·8; H, 11·2%.) λ_{max} 220 (log ε 3·84) and 262·5 mμ (log ε 3·37). ν_{max}(CCl_4) 3070, 1580 (aromatic C=C), 1370 and 1365 cm^{-1} (*gem* dimethyl); ν_{max}(CS_2) 793 cm^{-1} (3 adjacent aromatic hydrogen atoms). NMR 0·96 (6 protons, C_4-*gem* dimethyl), 1·20 (C_{10}-angular methyl), 1·18 and 1·22 (two doublets, each with J = 7·0 c/s, isopropyl methyls), 2·86 (2 proton multiplet, C_7-methylene protons), 3·12 (5 members of a septet, J = 7·0 c/s, C_{18}-methine proton), and 7·02 δ (3 proton singlet, aromatic protons).

Reduction of totara-8,11,13-triene in ethylenediamine

Compound I (R = H) (5·0 g) in ethylenediamine (150 ml) was treated with Li (4·8 g) as for I(R = OMe). The mixture was heated under reflux for 6 hr and afforded after chromatography on alumina, a mixture (3·64 g, 73%) of V and IV, b.p. 137°/0·15 mm. (Found: C, 87·65; H, 12·5. Calc. for $C_{20}H_{34}$: C, 87·5; H, 12·5%) in the ratio of ca. 1:2 as determined by GLC and NMR spectroscopy.

Reduction of totaryl methyl ether (I, R = OMe_3) *in ethylamine*

Li (1·6 g) was added to a well stirred solution of I(R = OMe) (1·5 g) in t-amyl alcohol (40 ml) and anhydrous ethylamine (250 ml). After 1½ hr the Li had dissolved and further metal (1·65 g) was added to the blue solution which was stirred for 3 hr. t-Amyl alcohol (50 ml) was then added and the ethylamine allowed to evaporate. The residue was dissolved in water (200 ml) and extracted with ether. The ethereal solution was washed with 80% HClaq, sat NaClaq, and then dried. Removal of

solvent gave a colourless oil which contained no oxygenated material and which, after percolation through alumina, gave a mixture (77% yield) of V and IV whose ratio (9:11) of components was determined by comparative GLC.

Kenner desoxygenation of totarol (I, R = OH)

A mixture of I(R = OH) (5·0 g), anhydrous tetrahydrofuran (40 ml), redistilled Et_3N (12 ml), anhydrous CCl_4 (35 ml), and diethyl phosphite [prepared from PCl_3 (19·5 g), anhydrous EtOH (20 ml) and CCl_4 (30 ml)] was heated under reflux for 6 hr. The cooled mixture was washed successively with 5% HClaq, 8% NaOHaq, and water, and then dried. Removal of the solvent gave totaryl diethyl phosphate as a yellow viscous oil (7·14 g), $\nu_{max}(CCl_4)$ 1275 (P═O), 1205 (P—O—C_{aryl}), and 1050–1030 cm^{-1} (P—O—C_{alkyl}), which was used directly in the following reaction without further purification.

In a typical experiment Li wire (2·0 g) was added to a mixture of totaryl diethyl phosphate (3·6 g) and anhydrous tetrahydrofuran (50 ml) in liquid ammonia (180 ml) over a period of 5 min. When the Li had dissolved the blue solvated cation was decolourized by the addition of NH_4Cl (9·9 g). The ammonia was evaporated and the residue was partitioned between 5% HClaq and ether. The ethereal extract was washed successively with 5% HClaq, 8% NaOHaq, and sat NaClaq, and then dried. Removal of solvent gave a yellow oil which when chromatographed on alumina afforded I(R = H) as needles (1·16 g), m.p. and mixed m.p. 77–78° (identical IR spectrum), from light petroleum eluates. Totarol (0·9 g) was recovered from the ether eluate as prisms (identical IR spectrum).

In a series of experiments using 10·6, 26, 33, and 40 moles per mole of totaryl diethyl phosphate the yields of I(R = H) were 19·9%, 53·2%, 51·0%, and 38·8%, respectively.

7-*Oxototara*-8,11,13-*triene* (XII, R = H)

A solution (5 ml) of chromic acid in 80% AcOH[64] was added to a stirred solution of I(R = H) (700 mg) in glacial AcOH (5 ml). The mixture was kept at 70–80° for 10 min, diluted with ice-water, and extracted with ether. The organic layer was washed with water and sat NaClaq and dried. Chromatography of the concentrate on alumina gave crystals (230 mg) from the benzene eluate. Purification by sublimation gave 7-*oxototara*-8,11,13-*triene* as long needles, m.p. 123–124° (Found: C, 84·4; H, 10·1. $C_{20}H_{28}O$ requires: C, 84·45; H, 9·9%.) λ_{max} 218 (log ε 3·96), 254 (log ε 3·92), and 296 mμ (log ε 3·28). $\nu_{max}(CCl_4)$ 1678 (aryl CO), 1595, 1580 (aromatic stretching) and 1375, 1360 cm^{-1} (*gem* dimethyl); $\nu_{max}(CS_2)$ 785 cm^{-1} (3 adjacent aromatic hydrogen atoms). NMR 0·94 (C_4-axial methyl), 1·04 (C_4-equatorial methyl), 1·16 (C_{10}-angular methyl), 1·15 and 1·29 (2 doublets, J = 7·0 c/s, isopropyl methyls), 2·60 (AB part of ABC multiplet, C_5 and C_6 protons), 3·83 (5 members of a septet, J = 7·0 c/s, C_{15}-methine proton) and 7·22 δ (3-proton multiplet, C_{11-13} aromatic protons). RD (*c* 0·159) $[\phi]_{450}$ +462°, $[\phi]_{354}$ +8210°, $[\phi]_{336}$ 0°, $[\phi]_{314}$ −15,850°, $[\phi]_{260}$ −1068°, a_{314}^{354} +181.

6α-*Bromo*-7-*oxototara*-8,11,13-*triene* (XII, R = Br)

Bromine (65 mg) in glacial AcOH (0·5 ml) was added over a period of 10 min to a stirred solution of XII (R = H) (106 mg) in glacial AcOH (5 ml) containing a drop of 48% HBr. Isolation of the product by precipitation with water followed by ether extraction gave an oil which solidified at 0°. Crystallization from MeOH afforded 6α-*bromo*-7-*oxototara*-8,11,13-*triene* (90 mg, 66%) as irregular plates, m.p. 102·5–104°. (Found: C, 66·4; H, 7·6; Br, 22·1. $C_{20}H_{27}BrO$ requires: C, 66·1; H, 7·5; Br, 22·0%.) λ_{max} 217 (log ε 3·89), 261 (log ε 3·87), 292 mμ (sh., log ε 3·46). $\nu_{max}(CCl_4)$ 1696 cm^{-1} (aryl COCHBr); $\nu_{max}(CS_2)$ 790 cm^{-1} (3 adjacent aromatic hydrogen atoms). NMR 1·08 (C_4-axial methyl), 1·17 (C_4-equatorial methyl), 1·28 (C_{10}-angular methyl), 1·45 and 1·51 (2 doublets, J = 7·0 c/s, isopropyl methyls), 2·14 (doublet, J = 7·3 c/s, C_5-proton), 3·42 (5 members of a septet, J = 7·0 c/s, C_{15}-methine proton), 4·43 (doublet, J = 7·3 c/s, C_6-proton) and 7·23 δ (3 proton multiplet, C_{11-13} aromatic protons). RD (*c* 0·209) $[\phi]_{400}$ +255°, $[\phi]_{360}$ +4020°, $[\phi]_{345}$ 0°, $[\phi]_{317}$ −16,880°, $[\phi]_{270}$ −15,840° a_{317}^{360} +199°.

[64] R. H. Bible, U.S. Pat. 2,759,014; *Chem. Abstr.* **51**, 5838 (1957).

12-*Acetyltotara*-8,11,13-*triene* (XIV, R = COMe)

To a stirred solution of anhydrous $AlCl_3$ (1·99 g) in dry CS_2 (25 ml) was added totara-8,11,13-triene (2·23 g) in anhydrous AcCl (1 ml) and dry CS_2 (25 ml) over a period of 15 min. The crimson mixture was stirred and heated under reflux for 1½ hr, the solvent was evaporated, and the residue was treated with 5% HClaq (50 ml). The mixture was extracted with ether and the extracts were washed successively with water, sat NaClaq, and then dried. The solvent was removed and the viscous oily residue (2·68 g) was chromatographed on alumina.

Concentration of the benzene eluate gave 12-*acetyltotara*-8,11,13-*triene* (2·03 g) as a pale yellow oil, b.p. 188–190°/0·9 mm, $[\alpha]_D$ −20·7° (*c* 3·6). (Found: C, 84·2; H, 10·5. $C_{22}H_{32}O$ requires: C, 84·6; H, 10·3%.) λ_{max} 220 (log ε 4·37) and 261 mμ (log ε 4·25). ν_{max}(CCl_4) 1688 (aryl CO), 1600 1570 (aromatic stretching) and 885 cm^{-1} (isolated aromatic hydrogen atom). NMR 0·97 (6 protons, C_4-*gem* dimethyl), 1·18 and 1·23 (2 doublets, J = 7·0 c/s, isopropyl methyls), 1·21 (C_{10}-angular methyl), 2·50 (ArCOMe), 2·77 (2 proton multiplet, C_7-methylene protons), 3·20 (5 members of a septet, J = 7·0 c/s, C_{15}-methine proton), 6·66 and 6·75 δ (C_{11} and C_{13}-protons, *meta* coupled).

2,5-*Diacetyl*-3-*methyl*-7-*isopropylindene* (XVI)

Concentration of the ether eluate from chromatography of the Friedel-Crafts acetylation, followed by crystallization of the residue from light petroleum gave 2,5-*diacetyl*-3-*methyl*-7 *isopropylindene* (127 mg) as glistening needles, m.p. 151–152°, $[\alpha]_D$ 0° (*c* 2·0). (Found: C, 79·6; H, 8·1. $C_{17}H_{20}O_2$ requires: C, 79·65; H, 7·9%.) λ_{max} 261 (log ε 4·29) and 301·5 mμ (log ε 4·22). ν_{max}(nujol) 1675 (aryl CO), 1665 ($\alpha\beta$-unsaturated CO), 1220 or 1185 (aryl CO) and 887 cm^{-1} (isolated aromatic hydrogen atom). NMR 1·38 (6 proton doublet, J = 7·0 c/s, isopropyl methyls), 2·50 (ArCOMe), 2·58 (3 proton triplet, J = 2·3 c/s, ArC(Me)=C, homoallylic coupling with C_1-methylene protons), 2·67 (vinyl COMe), 3·26 (1 proton septet, J = 7·0 c/s, C_7-methine proton), 3·77 (2 proton quartet, J = 2·3 c/s, homoallylic coupling to ArC(Me)=C) and 8·01 δ (2 proton singlet, C_4 and C_6 aromatic protons).

Baeyer-Villiger oxidation of 12-*acetyltotara*-8,11,13-*triene;* 12-*hydroxytotara*-8,11,13-*triene* (XIV, R = OH)

Trifluoroperacetic acid, prepared by the addition of trifluoroacetic anhydride (4·7 ml) to 83% H_2O_2 (0·83 ml) in a stirred solution of dichloromethane, was added to a stirred suspension of anhydrous Na_2HPO_4 (15·7 g) and 12-acetyltotara-8,11,13-triene (3·7 g) in dichloromethane (200 ml). The mixture was stirred and heated under reflux for 3·5 hr, cooled, washed with Na_2CO_3 (100 ml), and dried. Concentration yielded a yellow viscous oil which was chromatographed on activated alumina. XIV (R = COMe) (0·77 g, 21%) was recovered from the light petroleum–benzene (2:1) eluate while concentration of the benzene–ether (7:3) eluate afforded 12-*hydroxytotara*-8,11,13-*triene* (2·6 g, 70%) as an oil, b.p. 171–173°/0·4 mm, $[\alpha]_D$ −8·6° (*c* 3·5). (Found: C, 83·4; H, 10·5. $C_{20}H_{30}O$ requires: C, 83·9, H, 10·6%.) λ_{max} 226 (log ε 3·88) and 282 mμ (log ε 3·58). ν_{max}(CCl_4) 3310 (OH), 1603, 1595 (aromatic stretching), 1380, 1370 (*gem* dimethyl), 1180 (phenolic CO) and 864 cm^{-1} (isolated aromatic hydrogen atom). NMR 0·92, 0·94 (C_4-*gem* dimethyl), 1·13 (C_{10}-angular methyl), 1·09 and 1·13 (2 doublets each with J = 7·0 c/s, isopropyl methyls), 2·75 (2 proton multiplet, C_7-methylene protons), 3·06 (5 members of a septet, J = 7·0 c/s, C_{15}-methine proton), 6·20 (broad singlet, phenolic OH), and 6·56 δ (broad 2 proton singlet, C_{11} and C_{13}-aromatic protons).

12-*Acetoxytotara*-8,11,13-*triene* (XIV, R = $OCOCH_3$)

12-*Acetoxytotara*-8,11,13-*triene* was obtained as a pale yellow oil by acetylation (93% yield) of XIV (R = OH) with Ac_2O–pyridine (100°, 3 hr). It had b.p. 156–157°/0·2 mm, $[\alpha]_D$ −16·2° (*c* 3·6). (Found: C, 80·2; H, 9·9; Ac, 13·2. $C_{22}H_{32}O_2$ requires: C, 80·4; H, 9·8; Ac, 13·1%.) λ_{max} 218 (log ε 4·02), 268·5 (log ε 2·99) and 275 mμ (log ε 2·98). ν_{max}(film) 1770 (aryl acetate), 1380, 1360 (*gem* dimethyl), 1192–1223 (ester CO) and 905 cm^{-1} (isolated aromatic hydrogen atom). NMR 0·93 (6 protons, C_4-*gem* dimethyl), 1·18 and 1·23 (2 doublets each with J = 7·0 c/s, isopropyl methyls), 1·26 (C_{10}-angular methyl), 2·18 (aryl acetate), 2·77 (2 proton multiplet, C_7-methylene protons), 3·12 (5 members of a septet, J = 7·0 c/s, C_{15}-methine proton), 6·70 and 6·76 δ (C_{11} and C_{13}-aromatic protons).

Saponification of the acetate (1·84 g) in EtOH (250 ml) by heating under reflux with 5% KOHaq (50 ml) for 4½ hr, followed by acidification, extraction with ether and chromatography on alumina,

gave XII (R = OH) (1·24 g, 76·5%), b.p. 170–173°/0·4 mm, from benzene–ether eluates (identical IR spectrum).

Hydrogenation of totarol; Totarane (XX) *and* 13-*oxototarane* (XXI)

A solution of totarol (10·5 g) in glacial AcOH (80 ml) was shaken with H_2 over a 10% $PdCl_2$-C catalyst for 6 hr at 60° and 500 lb/sq. in. Removal of the solvent and chromatography of the product on alumina gave totarane (1·13 g, 12·5%) from light petroleum eluates. Totarane crystallized from light petroleum as thick plates, m.p. 71–72·5°, $[\alpha]_D$ −41·5° (*c* 1·7) (lit[19] m.p. 74·5–75°, $[\alpha]_D$ −31·06 in 4% EtOH). ν_{max}(CCl_4) 1383 and 1365 cm^{-1} (*gem* dimethyl). NMR 0·83 δ (15 proton singlet, C_4-*gem* dimethyl, C_{10}-angular and C_{18}, C_{19}-isopropyl methyls), total protons 36.

Concentration of the benzene eluate yielded 13-*oxototarane* (2·23 g, 21%) which crystallized from light petroleum as glistening needles, m.p. 135–135·5°, $[\alpha]_D$ +4·4°, $[\alpha]_{400}$ +66·4° (*c* 1·0). (Found: C, 82·8; H, 12·2. $C_{20}H_{34}O$ requires: C, 82·7; H, 11·8%.) ν_{max}(CCl_4) 1720 (6 membered ring CO), 1380, 1365 (*gem* dimethyl), and 1206 cm^{-1} (CO). NMR 0·85 (9 proton singlet, C_{10}-angular methyl and C_4-*gem* dimethyl), 2·09–2·22 δ (3 proton multiplet, C_{14}-methine and C_{13}-methylene protons). RD (*c* 0·241) $[\phi]_{490}$ +561°, $[\phi]_{311}$ +3670°, $[\phi]_{294.5}$ 0°, $[\phi]_{278}$ −4560°, $[\phi]_{340}$ −2895°, a_{278}^{311} +82·3.

13-Oxototarane was recovered quantitatively after treatment of a methanolic solution with MeONa for 7½ hr.

Totarol (6·11 g, 58%) was recovered from ether eluates during the chromatography.

Attempted hydrogenations of totarol at temp and press lower than 50° and 100 lb/sq in. for 6 hr gave no reduced material. It was also recovered quantitatively from attempted hydrogenation in the presence of Raney Ni (B.D.H. stabilised) for 9 hr at 50° and 500 lb/sq in.

13-*Hydroxytotarane*

A solution of XXI (200 mg) in anhydrous ether (15 ml) was added to a stirred refluxing solution of LAH in dry ether (30 ml). The mixture was heated under reflux for 7 hr and then kept at 20° for 15 hr. Isolation of the product by pouring the mixture into acidified ice-water and extraction with ether gave, after washing the ethereal solution with water and sat NaClaq, a semi-crystalline solid (201 mg). Recrystallization from light petroleum gave 13-*hydroxytotarane* (101 mg) as needles, m.p. 140–141° with sublimation, $[\alpha]_D$ −8° (*c* 0·85). (Found: C, 82·5; H, 12·5; O, 5·75. $C_{20}H_{36}O$ requires: C, 82·1; H, 12·4; O, 5·5%.) ν_{max} 3550 (OH), 1380, 1365 (*gem* dimethyl) and 1050 cm^{-1} (OH deformation). NMR 0·81, 0·83, 0·85 (C_4-*gem* dimethyl, C_{10}-angular methyl), 0·97 and 1·05 (2 doublets each with J = 7·0 c/s, isopropyl methyls), 1·04 (OH, exchanged with D_2O), 2·04 (multiplet C_{18}-methine proton) and 3·31 δ (diffuse multiplet, C_{13} proton).

Reduction of the dithioketal of 13-*oxototarane*

13-Oxototarane (105 mg) in AcOH (5 ml) was mixed with BF_3-etherate (0·5 ml) and ethanedithiol (0·5 ml)[65] and the mixture was allowed to stand at 20° for 2 days. Filtration of the crystalline precipitate and recrystallization from EtOH–$CHCl_3$ gave the *dithioketal* (97 mg, 74%) as needles, m.p. 178° with sublimation (Found: C, 72·4; H, 10·65; S, 17·4. $C_{22}H_{38}S_2$ requires: C, 72·1; H, 10·45; S, 17·5%.) NMR 0·84 (C_4-*gem* dimethyl), 0·86 (C_{10}-angular methyl), 1·06 and 1·12 (2 doublets each with J = 7 c/s, isopropyl methyls), 2·37 (5 members of a septet, J = 7 c/s, C_{18}-methine proton) and 3·22 δ [4 proton multiplet, $C(SCH_2)_2$].

The dithioketal (65 mg) in purified dioxan (8 ml) was heated under reflux in the presence of freshly prepared Raney Ni for 27 hr. Filtration and working up of the mixture gave totarane (29 mg) as plates, m.p. and mixed m.p. 68·5–70° (identical IR spectrum).

Acknowledgements—The authors are grateful to Professor W. Klyne for an ORD measurement on 13-oxototarane and to Dr. B. E. Swedlund for helpful discussions.

[65] L. F. Fieser, *J. Amer. Chem. Soc.* **76**, 1945 (1954).