The Pimarane → Cassane Rearrangement. Synthesis of a Potential Intermediate from Isopimaric Acid

By **James P. Johnston** and **Karl H. Overton,*** Department of Chemistry, University of Glasgow, Glasgow G12 8QQ

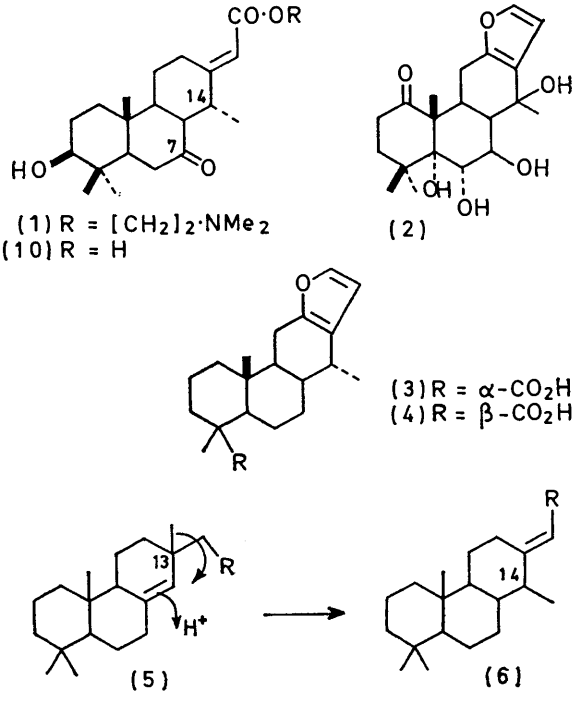
The unstable cisoid enone diester dimethyl 7-oxoisopimar-8(14)ene-16,18-dioate (27), a potential intermediate for the pimarane → cassane rearrangement, has been synthesised regiospecifically from isopimara-7,15-dien-18-oic acid (isopimaric acid) (11) *via* the keto-lactone 18-methoxycarbonyl-7-oxo-18-norisopimaran-16,8α-olactone (25). Several unsuccessful attempts to induce the rearrangement with derivatives of the enone (27) are described.

THE cassane group of diterpenoids is represented in nature by the erythrophlaeum alkaloids [1] [*e.g.* cassaine (1) [2]], the caesalpins [*e.g.* β-caesalpin (2) [3]], and vinhaticoic (3) and vouacapenic (4) acids.[4]

Notionally the cassane framework is most simply derived by shift of the C-13 methyl group of a pimarane to C-14 [(5) → (6)],[5] but to date there is no biochemical experiment on record to support such a relationship. The work which we now describe was motivated by search for a laboratory synthesis of the cassane skeleton modelled on this presumed rearrangement.

With the exception of vinhaticoic and vouacapenic acids, all known natural cassanes [6] bear an oxygen function at C-7. It was therefore tempting to suppose that an oxygen at C-7 might play a part in facilitating the C-13 → C-14 methyl migration, *e.g.* (7) → (8). We describe here the synthesis of the diester (9) [≡ (27)] and a number of unsuccessful attempts to effect the desired rearrangement with substances derived from it.

At the outset of this work the configuration at C-14 in cassaic acid had not been securely established. Subsequently the total synthesis by Turner's group [7] strongly pointed to the 14α-methyl configuration and

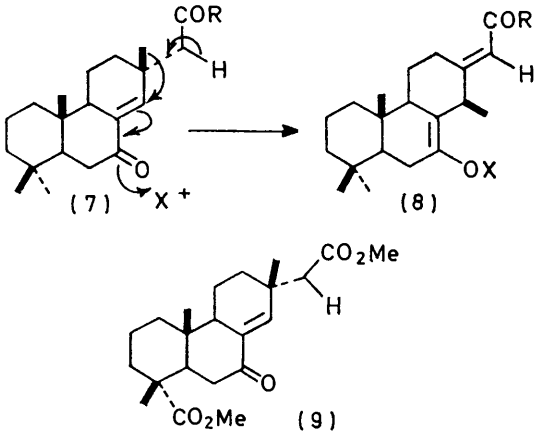


this was confirmed by work in two other laboratories.[8,9] However, this initial uncertainty did not deter us in

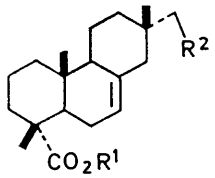
[1] R. B. Morin in ' The Alkaloids,' ed. R. H. F. Manske, vol. X, Academic Press, New York, 1968, p. 287.
[2] L. G. Humber and W. I. Taylor, *J. Chem. Soc.*, 1955, 1044.
[3] A. Balmain, J. D. Connolly, M. Ferrari, E. L. Ghisalberti, U. M. Pagnoni, and F. Pelizzoni, *Chem. Comm.*, 1970, 1244.
[4] F. E. King, T. J. King, and K. G. Neill, *J. Chem. Soc.*, 1953, 1055; F. E. King and T. J. King, *ibid.*, 1953, 4158; F. E. King, D. H. Godson, and T. J. King, *ibid.*, 1955, 1117.
[5] E. Wenkert and J. W. Chamberlin, *J. Amer. Chem. Soc.*, 1959, **81**, 688.
[6] R. McCrindle and K. H. Overton in ' Rodd's Chemistry of Carbon Compounds,' 2nd edn., ed. S. Coffey, vol. IIc, Elsevier, Amsterdam, 1969, p. 391.
[7] R. B. Turner, O. Buchardt, E. Herzog, R. S. Morin, A. Riebel, and J. M. Sanders, *J. Amer. Chem. Soc.*, 1966, **88**, 1766.
[8] H. Hauth, D. Stauffacher, P. Niklaus, and A. Melera, *Helv. Chim. Acta*, 1965, **48**, 1087.
[9] L. Clarke, S. J. Daum, P. E. Shaw, and R. K. Kullnig, *J. Amer. Chem. Soc.*, 1966, **88**, 5865.

designing our model experiments for two reasons: (*a*) because of the conformational mobility of the cyclohexene ring C in a precursor such as (7), a stereoelectronically favourable conformation for methyl migration can be attained with the C-14 methyl group either α- or β-oriented; (*b*) the rearranged secondary methyl group of the product is vinylogously α to the side chain carbonyl function and therefore epimerisable. Indeed, there is no valid reason to assume that the C-14 configuration in cassaic acid (10) is common to all natural cassanes; moreover, even where the methyl configuration is established as α, as in cassaic,[9] vinhaticoic, and vouacapenic[10] acids, this could be the result of epimerisation after migration. The double allylic *A* [1,3] strain[11] experienced by a 14β-methyl group in, for instance the proximal product of rearrangement (8), could provide a sufficient driving force for epimerisation. In the light of these reflections we set about the synthesis of the diester (9) from the readily available isopimaric acid (11).

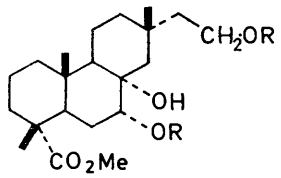
Selective hydroboration with di-isopentylborane[12] of



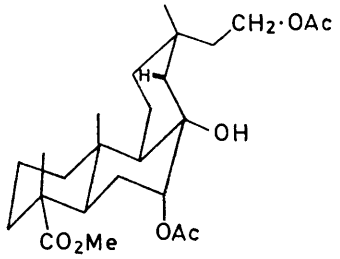
methyl isopimarate (12) afforded the known[12] hydroxyester (13) in 71% yield. Osmylation then furnished a mixture of isomeric triols from which the major crystalline triol (14) could be separated in 51% yield by preparative layer chromatography. We hoped that the derived diacetate (15) [≡ (16)] would eliminate cleanly towards C-14 with phosphoryl chloride in pyridine. In the event there resulted a mixture of the olefinic diacetates (17) and (18) containing the unexpected (and unwanted) $\Delta^{8(9)}$-isomer in excess (65 : 35). Since the mixture was not readily separable by chromatography, an attempt was made to separate the derived diols, However, preparative layer chromatography of the hydrolysis product afforded the oily ester (19) and the crystalline tetrahydrofuran (21) formed from the expected diol (20) on the chromatographic adsorbent. An attempt to capture the desired olefin as the enone (22) by allylic oxidation of the diol mixture with manganese dioxide also failed, since the enone (23) was by far the major product. Formulation of the ' wrong ' olefin (17) in excess during dehydration of the diacetate (15) probably reflects the inaccessibility in conformation



(11) R^1 = H, R^2 = :CH_2
(12) R^1 = Me, R^2 = :CH_2
(13) R^1 = Me, R^2 = CH_2OH



(14) R = H
(15) R = Ac



(16)

(16) of the 14β-H to pyridine and consequent intervention of non-*E*2-type mechanisms.[13,14] To minimise the incidence of such undesirable competitive processes, attention was next directed to dehydration of the ketol (24). Search for a suitable oxidant for the triol (14) led to the discovery of *N*-bromosuccinimide in aqueous dioxan as the most effective reagent, and this serendipitously furnished the crystalline keto-lactone (25) in 73% yield. This product was transformed in an equally clean reaction (80%) with methoxide in dry methanol into the cisoid enone (26), isolated as the crystalline methyl ester (27) [≡ (9)] {$\nu_{max.}$ 1738sh, 1732, 1692, and 1618s cm^{-1}, $\lambda_{max.}$ 250 nm (ε 9600), τ 3·24 [1H, d, C(14)H]}. The carbonyl group at C-7 had evidently played the role assigned to it of enforcing concerted elimination towards C-14 and there is of course no readily available base-catalysed mechanism for isomerisation to the transoid enone. Elimination of the lactone (25) was also effected with dry methanolic sulphuric acid, but then the product, not unexpectedly, consisted of a mixture (1 : 1) of the cisoid and transoid enones.

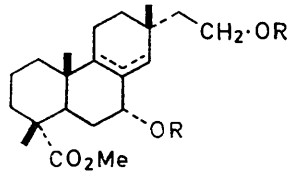
The attempts which we now briefly describe to induce C-13 to C-14 methyl migration revolved round attempts to generate the allylic carbonium ion (28). This is closely related to the product of electrophilic attack on enone (7) and might be expected to undergo the desired rearrangement rather than collapse by one of the more trivial paths open to it.

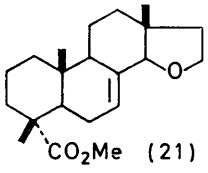
Reaction of the enone (27) with dry methanolic sulphuric acid at reflux caused slow isomerisation to the transoid enone as the only observable reaction. Boron

[10] T. A. Spencer, R. A. J. Smith, D. L. Storm, and R. M. Villarica, *J. Amer. Chem. Soc.*, 1971, **93**, 4856.
[11] F. Johnson, *Chem. Rev.*, 1968, **68**, 375.
[12] W. Herz, D. Melchior, R. N. Mirrington, and P. J. S. Pauwels, *J. Org. Chem.*, 1965, **30**, 1873.
[13] B. Cross and G. H. Whitham, *J. Chem. Soc.*, 1960, 3892.
[14] R. R. Sauers and J. M. Landesburg, *J. Org. Chem.*, 1961, **26**, 964.

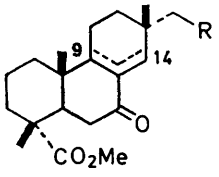
trifluoride–ether complex in benzene [15] at reflux was equally ineffective. Borohydride reduction of the enone (27) afforded as major product the oily 7β-ol (29). Acetolysis in buffered acetic acid of the *p*-nitrobenzoate (30) led to the heteroannular diene (32), $\lambda_{max.}$ 236, 242, and 250 nm (ε 10,000), probably *via* the 6,8(14)-diene. Formolysis of the allylic alcohol (29) with chloroform–formic acid afforded only the 7β-formate (31).

We next studied the acetal (33), which under the influence of a Lewis acid,[16] or even during attempts to form it,[17,18] might be expected to undergo the desired rearrangement. Attempts to acetalise enone (27) under normal conditions (ethylene glycol, toluene-*p*-sulphonic acid) however led only to the isomeric transoid enone and, unexpectedly, to a second product tentatively formulated as (34). Transacetalisation attempts with ethyl methyl ketone were also ineffective. An indirect attempt to obtain the acetal (33) *via* the lactone (25) was next made. Acetalisation did afford the acetal (36), but in poor yield. Its formulation is well supported, *inter alia*, by major fragment ions in its mass spectrum

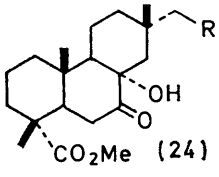


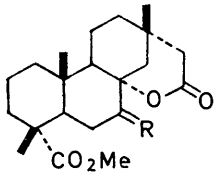


(17) $\Delta^{8(9)}$, R = Ac
(18) $\Delta^{8(14)}$, R = Ac
(19) $\Delta^{8(9)}$, R = H
(20) $\Delta^{8(14)}$, R = H



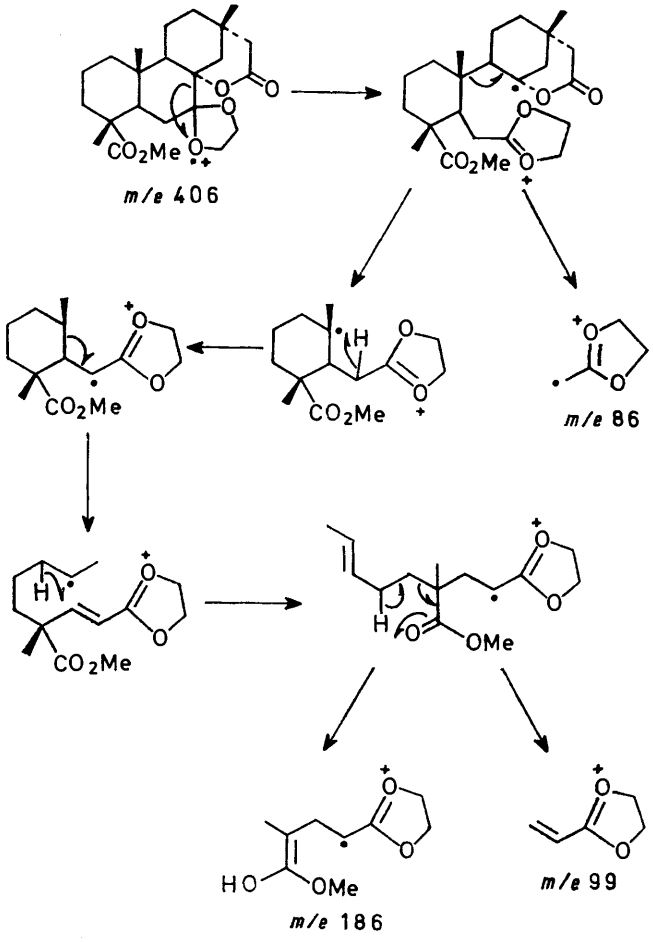
(22) $\Delta^{8(14)}$, R = $CH_2 \cdot OH$
(23) $\Delta^{8(9)}$, R = $CH_2 \cdot OH$
(26) $\Delta^{8(14)}$, R = CO_2H
(27) $\Delta^{8(14)}$, R = CO_2Me
(34) $\Delta^{8(9)}$, R = $CO_2 \cdot [CH_2]_2 \cdot OTs$
(35) $\Delta^{8(14)}$, R = $CO_2 \cdot [CH_2]_2 \cdot OTs$





(25) R = O
(36) R = $O \cdot [CH_2]_2 \cdot O$

at *m/e* 186, 99, and 86 which are readily accommodated [19] as shown in the Scheme. The major product from acetalisation was, however, the enone (35), contaminated by a minor amount of the isomeric enone (34). Treatment of the acetal lactone (36) with methoxide led not to elimination, as hoped, but to methanolysis with formation of the hydroxy-ester (37).

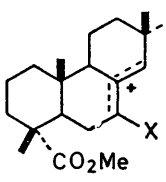


SCHEME Mass spectrometric fragmentation of the acetal (36)

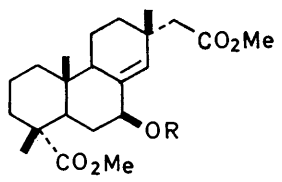
A final attempt to effect the desired methyl migration resorted to a more conventional approach and involved the αβ-epoxy-ketone (38) as an intermediate. The α-epoxide, which is properly oriented for a concerted migration, should be the major epoxide formed from the enone (27) and there is literature precedent for the desired direction of epoxide opening [20] and concomitant methyl migration.[21] The epoxide (38) was formed smoothly and was readily isolated when appropriate care was taken during work-up to avoid its hydrolytic decomposition. It was unaffected by prolonged contact with Grade III acidic alumina in benzene. On the other hand, exposure to boron trifluoride–ether complex in dry benzene converted it into two products readily separable by preparative layer chromatography. The minor more polar product was readily identified by its i.r. spectrum as the unexceptional γ-lactone (39).

[15] See R. S. Atkinson, *Chem. Comm.*, 1969, 735.
[16] W. S. Johnson, *Accounts Chem. Res.*, 1968, **1**, 1.
[17] J. W. Dean and R. G. Christianson, *J. Org. Chem.*, 1963, **28**, 2110.
[18] R. Antonucci, S. Benstein, R. Littell, K. J. Sax, and J. H. Williams, *J. Org. Chem.*, 1952, **17**, 1341.
[19] H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Mass Spectrometry of Organic Compounds,' Holden-Day, San Francisco, 1967, p. 265.
[20] D. N. Kirk, V. Petrov, and D. M. Williamson, *J. Chem. Soc.*, 1961, 2821.
[21] A. K. Ganguly, T. R. Govindachari, and A. Manmade *Tetrahedron*, 1967, **23**, 3847.

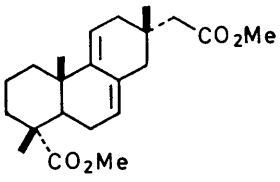
The major product, more unexpectedly, turned out to be the stable boron difluoride-complexed β-diketone (40).[22]



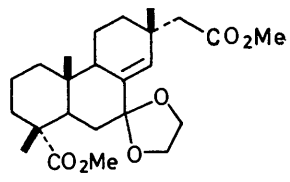
(28)



(29) R = H
(30) R = *p*-$O_2N{\cdot}C_6H_4{\cdot}CO$
(31) R = CO·H

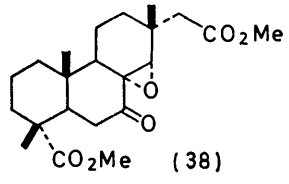


(32)

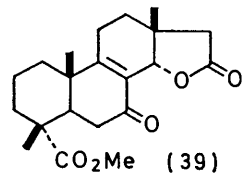


(33) $\Delta^{8(14)}$
(37) 8α-OH

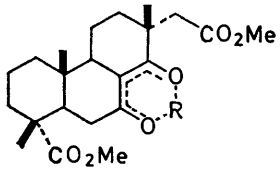
In accordance with this formulation the mass spectrum, which showed no molecular ion, exhibited fragments at *m/e* 420 (M^+ — HF) and 409 (M^+ — BHF). The u.v.



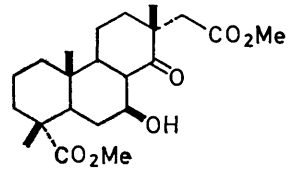
(38)



(39)



(40) R = BF_2
(41) R = H



(42)

[$\lambda_{max.}$ 297 nm (ε 8900)] and i.r. [$\nu_{max.}$ 1350s cm^{-1} (B–O str.)] spectra added further support.[23] The parent β-diketone (41), obtained from the epoxy-ketone with hydrogen iodide in refluxing benzene, had $\lambda_{max.}$ 297 nm (ε 8800) in ethanol and $\lambda_{max.}$ 316 nm (ε 17,600) in ethanolic base. The complex was stable to dilute acid at 20° but was reduced with borohydride to the β-hydroxy-ketone (42), the i.r. spectrum of which showed evidence of a strong H-bond [$\nu_{max.}$ 3560 (bonded OH) and 1698 cm^{-1} (bonded cyclohexanone)].

EXPERIMENTAL

For general experimental directions see ref. 24.

Methyl Isopimara-7,15-dien-18-oate (12).—Isopimaric acid (11), isolated [25] from American Gum Rosin, was methylated with diazomethane in ether. Recrystallisation from methanol afforded methyl isopimarate (12), m.p. 62—62·5° (lit.,[26] 62—62·5°).

Methyl 16-Hydroxyisopimar-7-en-18-oate (13).[12]—This was obtained from methyl isopimarate (12) (1·482 g, 0·005 mol) with di-isopentylborane [12] in 71% yield and after prep. layer chromatography and crystallisation from ethyl acetate–light petroleum (1 : 3) had m.p. 90—91° (lit.,[12] 90—90·5).

Osmylation of the Hydroxy-ester (13).—The hydroxy-ester (13) (0·765 g, 0·0023 mol) in dry ether (15 mol) was added to osmium tetroxide (0·7 g, 0·0028 mol) in a mixture of dry ether (10 ml) and anhydrous pyridine (1 ml). Dark brown crystals of the osmate complex separated after a few minutes. After 5 days at 20°, the ether was replaced by benzene and hydrogen sulphide was bubbled through the solution for 15 min. Removal of osmium sulphide by filtration and evaporation of solvent *in vacuo* left the crude glycol mixture as a dark brown crystalline mass, consisting of two products and a little starting material. Preparative t.l.c. [ethyl acetate–light petroleum (7 : 3)] afforded *methyl 7α,8α,16-trihydroxyisopimaran-18-oate* (14) (0·429 g, 51%), which, recrystallised from light petroleum–chloroform, had m.p. 166—168°, $[\alpha]_D$ −2° (*c* 0·86), $\nu_{max.}$ 3637, 3496, 3427, 1726, 1717sh, 1256, 1245, 1168, 1079, and 1039 cm^{-1}, τ 9·10, 8·93, and 8·81 (each 3H, s), 6·65 (1H, t, J_{AX} 3 Hz), 6·34 (3H, s), 6·31 (2H, t, J_{AX} 8 Hz), and 6·18br (2 or 3H, s, OH by D_2O exchange) (Found: C, 68·2; H, 10·05. $C_{21}H_{36}O_5$ requires C, 68·45; H, 9·85%). The less polar β-triol ester was isolated as a brownish semicrystalline compound (0·040 g, 5%). However, further purification and characterisation was hindered by rapid decomposition.

Acetylation of the α-Triol Ester (14).—The α-triol ester (14) (0·100 g, 0·27 mmol) in anhydrous pyridine (2 ml) and acetic anhydride (2 ml) was kept at 20° for 20 h. Evaporation of the solvent *in vacuo* and purification by preparative t.l.c. [ethyl acetate–light petroleum (1 : 1)] yielded *methyl 7α,16-diacetoxy-8α-hydroxyisopimaran-18-oate* (15) (0·091 g, 75%), m.p. 110—111° [from ether–light petroleum (40 : 60)], $[\alpha]_D$ −28° (*c* 1·02), $\nu_{max.}$ 3592, 3552, 1744vb, 1365, 1239br, and 1023 cm^{-1}, τ 9·08, 8·96, 8·81, 7·97, 7·88, and 6·36 (each 3H, s), 5·83 (2H, t, J_{AX} 8 Hz), and 5·32 (1H, t, J_{AX} 5 Hz) (Found: C, 66·45; H, 8·85. $C_{25}H_{40}O_7$ requires C, 66·35; H, 8·9%).

Dehydration of the Hydroxy-diacetate (15) *with Phosphoryl Chloride*.—To a solution of the hydroxy-diacetate (15) (50 mg, 0·11 mmol) in dry pyridine (2 ml), freshly distilled phosphoryl chloride (20 drops) was added dropwise with swirling and cooling, and the mixture was set aside at 20° overnight. Careful solvent removal and extraction of the residue with ether afforded an oil, from which the oily olefin diacetate mixture [(17) and (18)] (26 mg, 53%) was recovered by preparative t.l.c. with ethyl acetate–light petroleum (3 : 7). This mixture could not be resolved by further t.l.c. and showed $\nu_{max.}$ 1730—1740br, 1230, 1030, 1365, and 1675 cm^{-1}, τ 9·10, 9·03, 8·82, 9·20 (all s), 7·98 (6H, s), 6·38 (3H, s), 5·90 (t, J_{AX} 7 Hz), 5·93 (t, J_{AX} 7 Hz), 5·05 (m), 4·78 (m), and 4·40 (d, *J* 2 Hz). Integration of the relevant n.m.r. peaks showed that it contained *ca.* 65% of the $\Delta^{8(9)}$-isomer.

[22] M. W. Roomi, *Canad. J. Chem.*, 1969, **47**, 1099 and references therein.
[23] A. N. Sagredos, *Annalen*, 1966, **700**, 29.
[24] J. P. Johnston and K. H. Overton, *J.C.S. Perkin I*, 1972, 1490.
[25] D. E. Baldwin, B. M. Loeblich, and R. V. Lawrence, *J. Org. Chem.*, 1958, **23**, 25.
[26] G. C. Harris and T. F. Sanderson, *J. Amer. Chem. Soc.*, 1948, **70**, 2079.

Hydrolysis of the Mixture of Olefin Diacetates (17) *and* (18). —The olefin diacetate mixture (100 mg, 0·23 mmol) in ethanol (2 ml) and ethanolic 10% potassium hydroxide solution (2 ml) was left at 20° for 24 h. Dilution with water and extraction with ether afforded an oily residue (70 mg), which consisted of two major compounds [t.l.c., in ethyl acetate–light petroleum (7 : 3)]. These were separated by preparative t.l.c. (triple development). The less polar material was the oily $\Delta^{8(9)}$-isomer (19) (36 mg, 44%), $\nu_{max.}$ 3620, 3400br, 1728, 1230, 1175, 1150, 1118, 1062, and 1045 cm^{-1}, τ 9·10, 9·05, and 8·81 (each 3H, s), 7·87br (s, OH by D_2O exchange), 6·35 (3H, s), and 6·92 (2H, t, J_{AX} 8 Hz). The more polar material, the $\Delta^{8(9)}$-isomer (20) (14 mg; 17%) cyclised on elution from the Kieselgel, to the much less polar tetrahydrofuran (21), m.p. 115—116·5° (from light petroleum), $\nu_{max.}$ 1730, 1232, 1189, 1179, 1142, 1115, and 1044 cm^{-1}, τ 9·18, 9·03, 8·75, and 6·43 (each 3H, s), 6·15 (2H, t, J_{AX} 8 Hz), and 4·28 (1H, m), M^+ 332 (Calc. for $C_{21}H_{32}O_3$: *M*, 332·47).

Oxidation of the Mixture of Olefinic Diols (19) *and* (20) *with Manganese Dioxide.*—The crude oily olefin diol mixture (20 mg) was dissolved in ether (5 ml), powdered manganese dioxide (500 mg) was added, and the suspension was stirred at 20° for 18 h. Removal of manganese dioxide and the ether left an oil (15 mg). Preparative t.l.c. [ethyl acetate–light petroleum (1 : 1)] afforded an oil (7 mg), which was mainly the $\Delta^{8(9)}$-ketone (23), $\nu_{max.}$ 3632, 1730, 1691w, 1668, and 1162 cm^{-1}, $\lambda_{max.}$ 250 nm (ε 8000) (calc. $\lambda_{max.}$ 249 nm).

Oxidation of the Triol (14) *with* N-*Bromosuccinimide.* 4-*Methoxycarbonyl*-7-*oxo*-18-*norisopimaran*-16,8α-*olactone* (25). —A solution of the triol (14) (380 mg, 1·03 mmol) in aqueous dioxan (10 ml) was mixed with a solution of *N*-bromosuccinimide (2 g, 11·23 mmol) in 90% aqueous dioxan (10 ml) and set aside in the dark at 20° for 48 h. Water was added and the solution extracted thoroughly with chloroform. The combined extracts were washed with water and brine, and dried. Solvent removal and preparative t.l.c. [ethyl acetate–light petroleum (7 : 3)] afforded the *keto-lactone* (25) (0·273 g, 73%), which after several recrystallisations from ethyl acetate–light petroleum (40 : 60) had m.p. 215—224°, $[\alpha]_D$ −12° (*c* 0·69), $\nu_{max.}$ (KBr) 1720, 1735sh, 1253, 1230, 1225sh, 1198, 1091, and 1031 cm^{-1}, τ 8·98 (3H, s), 8·82 (6H, s), 7·81 (1H, s), 7·64 (d, *J* 1 Hz) + 7·69sh (3H in all), and 6·36 (3H, s) (Found: C, 69·4; H, 8·35. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·35%).

Reaction of the Lactone (25) *with Sodium Methoxide.*—To a refluxing solution of the lactone (25) (100 mg, 0·276 mmol) in dry methanol (30 ml) was added sodium metal (0·6 g) in small pieces during 5 min. The solution was refluxed for a further 30 min under nitrogen and then evaporated to low bulk *in vacuo*. Dilute hydrochloric acid was added (to pH 5) and the precipitate quickly extracted into ether, which was washed with water and dried. Methylation of the ether layer and evaporation *in vacuo* gave a semi-crystalline material, which contained two products [t.l.c. in ethyl acetate–light petroleum (3 : 7)]. The less polar, major product, separated by preparative t.l.c. in the same solvent system, was dimethyl 7-*oxoisopimar*-8(14)-*ene*-16,18-*dioate* (27) (83 mg, 80%), which, from ethyl acetate–light petroleum (40 : 60), had m.p. 116—118°, $[\alpha]_D$ +2° (*c* 0·63), τ 9·14, 8·89, and 8·76 (each 3H, s), 7·72 (2H, s), 7·66 (2H, s), 6·38 (6H, s), and 3·24 (1H, d, J_{AX} 2·5 Hz) (Found: C, 70·0; H, 8·55. $C_{22}H_{32}O_5$ requires C, 70·2; H, 8·55%).

Reaction of the Lactone (25) *with Methanol–Sulphuric Acid.*—A solution of the lactone (25) (10 mg, 0·028 mmol) in dry methanol (5 ml) and concentrated sulphuric acid (0·5 ml) was refluxed under nitrogen for 2 days, then evaporated to low bulk *in vacuo*, neutralised with aqueous sodium hydroxide, and extracted with ethyl acetate. The combined extracts were washed with water and brine, and dried. Solvent removal afforded an oil (9 mg), consisting of one major component [t.l.c. in ethyl acetate–light petroleum (7 : 3)]. This was separated by preparative t.l.c. and found to be a 1 : 1 mixture of the enone (27) and the $\Delta^{8(9)}$-isomer which could not be resolved by t.l.c.; $\nu_{max.}$ 1732, 1737sh, 1692, 1668, 1226, 1152, and 1111 cm^{-1}, $\lambda_{max.}$ 249 nm (ε 9000).

Reduction of the Cisoid Enone (27) *with Sodium Borohydride.*—The cisoid enone (27) (20 mg, 0·053 mmol) and sodium borohydride (5 mg) in ethanol (1 ml) were stored at 20° for 30 min. Extraction of the product into ethyl acetate afforded the oily allylic alcohol (29) (18 mg, 90%), homogeneous by t.l.c., $\nu_{max.}$ 3610, 1734, 1739sh, 1234, 1178, 1150, 1121, 1082, and 1010 cm^{-1}, τ 9·19, 8·93, and 8·80 (each 3H, s), 7·73 (2H, s), 6·33, 6·36 (3H, s), 6·06 (1H, q, poorly resolved), and 4·26br (1H, s), M^+ 378 (Calc. for $C_{22}H_{34}O_5$: *M*, 378·49).

Dimethyl 7β-p-*Nitrobenzoyloxyisopimar*-8(14)-*ene*-16,18-*dioate* (30).—The allylic alcohol (29) (8 mg, 0·021 mmol) and freshly recrystallised *p*-nitrobenzoyl chloride (25 mg) in the minimum of anhydrous pyridine were set aside at 20° for 72 h. Dilution with aqueous sodium hydrogen carbonate and extraction into ethyl acetate afforded on preparative t.l.c. [ethyl acetate–light petroleum (1 : 1)] the pure *p*-nitrobenzoate (30) (10 mg, 91%), $\nu_{max.}$ 1730, 1737sh, 1350, 1275, 1240, 1178, 1153, 1119, 1104, 1066, 1010, and 874 cm^{-1}, τ 9·10, 8·92, and 8·77 (each 3H, s), 7·82 (2H, s), 6·50 (3H, s), 6·33 (3H, s), 4·43br (1H, s), and 1·72br (4H, s) (1H under the 6·50 and 6·33 peaks).

Acetolysis of the p-*Nitrobenzoate* (30).—The *p*-nitrobenzoate (30) (10 mg, 0·019 mmol) and urea (15 mg) in dry acetic acid were refluxed under nitrogen for 20 h. Cooling, careful neutralisation with sodium hydrogen carbonate, and ethyl acetate extraction afforded an oil (7 mg) (one major component by t.l.c.). Preparative t.l.c. (ethyl acetate–light petroleum) afforded this least polar component (3 mg), dimethyl isopimara-7,9(11)-diene-16,18-dioate (32), $\nu_{max.}$ 3020sh, 1732, 1739sh, 1350, 1340, 1275, 1235, 1190, 1150, 1110, and 1074 cm^{-1}, τ 8·92, 8·80, and 8·75 (each 3H, s), 7·73 (s), 6·36 and 6·33 (both 3H, s), and *ca.* 4·60 (m), M^+ 360 (Calc. for $C_{22}H_{32}O_4$: *M*, 360·48).

Attempted Rearrangement of the Allylic Alcohol (29) *with Formic Acid.*—Formic acid (99%; 0·2 ml) was added to a stirred solution of the allylic alcohol (29) (5 mg, 0·014 mmol) in chloroform (0·5 ml) at 0°. The temperature of the solution was allowed to rise to 20° and stirring was continued for 72 h. Neutralisation with sodium hydrogen carbonate and extraction with ethyl acetate furnished an oil (5 mg). The formate (31) was separated from unchanged alcohol by preparative t.l.c. [ethyl acetate–light petroleum (1 : 1)] and had $\nu_{max.}$ 1733, 1739sh, 1236, 1177, 1152sh, 1133, 1107, and 1064 cm^{-1}. Hydrolysis on an acid-washed alumina column regenerated the allylic alcohol (29) (t.l.c., i.r.).

Attempted Acetalisation of the Enone (27).—The enone (27) (15 mg, 0·040 mmol) was treated with ethylene glycol (10 drops) and toluene-*p*-sulphonic acid (15 mg) in dry benzene (10 ml) at reflux. After 18 h work-up afforded an oil (25 mg), whose three components were separated by preparative t.l.c. [ethyl acetate–light petroleum (2 : 3)].

Each compound was identified by its i.r. spectrum. The most polar was the oily monotosylate of ethylene glycol (9 mg). That of intermediate polarity was the enone tosylate (34) (5 mg) and the most mobile component was the $\Delta^{8(9)}$-isomer of the ester (27) (5 mg).

Attempted Acetalisation of the Keto-lactone (25).—The keto-lactone (25) (40 mg, 0·11 mmol), toluene-*p*-sulphonic acid (40 mg), and dry ethylene glycol (1 ml) in sodium-dried benzene were refluxed for 18 h with continuous water separation. The solution was quenched in aqueous sodium hydrogen carbonate and thoroughly extracted with ethyl acetate. Analytical t.l.c. of the product (55 mg) revealed two major components. Preparative t.l.c. [ethyl acetate–light petroleum] afforded the more mobile enone tosylate (35) (30 mg, 0·054 mmol) contaminated by a small amount of the isomeric $\Delta^{8(9)}$-ketone (34), $\nu_{max.}$ 1733, 1740sh, 1692, 1670vw, 1619, 1380, 1225, 1191, 1181, 1153, 1123, 1100, 1025, 962, and 910 cm^{-1}, τ 9·15, 8·94, and 9·79 (each 3H, s), 7·91 (m), 7·72 (4H, s), 7·55 (3H, s), 6·37 (3H, s), 5·82 (4H, s), 3·36 (1H, d), and 2·50 (4H, q). The more polar 7,7-ethylenedioxy-4-methoxycarbonyl-18-norisopimaran-16,8α-olactone (36) (15 mg) was contaminated by the monotosylate of ethylene glycol. Purified by preparative t.l.c. and recrystallisation from ether–light petroleum (40 : 60), it had m.p. 209—209·5°, $\nu_{max.}$ 1731, 1740sh, 1322, 1283, 1245, 1198, 1162, 1145, 1124, 1051, 1040, 1030, 1018, and 950 cm^{-1}, τ 9·00, 8·94, and 8·85 (each 3H, s), 7·73br, 6·34 (3H, s), and 6·07 (4H, m), M^+ 406 (Calc. for $C_{23}H_{34}O_6$: *M*, 406·50).

Reaction of the Acetal Lactone (36) *with Sodium Methoxide*.—The acetal lactone (36) (12 mg, 0·030 mmol) was treated with sodium methoxide in methanol under the conditions used for the keto-lactone (25). Work-up yielded the hydroxy-acetal (37) (10 mg, 77%), shown to be almost pure by analytical t.l.c. [ethyl acetate–light petroleum (2 : 3)], $\nu_{max.}$ 3545, 3460, 1731, 1739, 1230, 1200, 1155, 1096, 1054, 1042, 1034, and 950 cm^{-1}, τ 8·99, 8·92, and 8·83 (each 3H, s), 7·30 [3H, s, including OH (by D_2O exchange)], 6·36 and 6·33 (both 3H, s), and 6·03 (4H, m).

Epoxidation of the Enone (27).—To the enone (27) (300 mg, 0·798 mmol) in methanol (20 ml) and 4N-sodium hydroxide (1·5 ml) at 0°, 30% hydrogen peroxide (2·3 ml) was added dropwise with stirring. After 48 h at 25° the solution was evaporated to low bulk at 25° *in vacuo* and carefully neutralised with N-hydrochloric acid. The organic material was rapidly extracted into ether and immediately methylated with diazomethane. Removal of excess of diazomethane, filtration through Celite, and evaporation of the ether *in vacuo* afforded an oil (300 mg). T.l.c. [ethyl acetate–light petroleum (2 : 3)] revealed one major product, slightly more polar than the starting enone, and three minor products. Preparative t.l.c. in the same solvent system furnished the oily dimethyl 8α,14α-epoxy-7-oxoisopimarane-16,18-dioate (38) (152 mg, 49%), $\nu_{max.}$ 1730, 1721, 1230, 1194, and 1150 cm^{-1}, τ 8·90, 8·82, and 8·69 (each 3H, s), 7·59 (4H, m), 6·60 (1H, s), and 6·34 (6H, s), M^+ 392 (Calc. for $C_{22}H_{32}O_6$: *M*, 392·48).

Cleavage of the Epoxy-ketone (38).—(a) *Boron trifluoride–Ether*. Redistilled boron trifluoride–ether (10 drops) was added with swirling to a solution of the epoxy-ketone (38) (30 mg, 0·077 mmol) in dry benzene (5 ml) at 0°. After 24 h at 25°, the reaction was quenched with sodium hydrogen carbonate solution and extracted into ethyl acetate as usual, affording an oil (26 mg), shown by analytical t.l.c. [ethyl acetate–light petroleum (2 : 3)] to contain two products in addition to a little starting material. Preparative t.l.c. afforded the oily boron difluoride complex (40) (10 mg), $\nu_{max.}$ 1730br, 1493, 1385, 1350, 1170br, and 1046 cm^{-1}, τ 9·15, 8·73, and 8·70 (each 3H, s), complex centred at 7·55 (3H), 6·90 (1H, half of AB system, J_{AB} 16 Hz, other half contained in τ 7·55 region), and 6·29 and 6·27 (both 3H, s), highest *m/e* 420 (M^+ — HF) (Calc. for $C_{22}H_{30}BFO_6$: 420·277).

The boron difluoride complex was slightly unstable; one of the decomposition products was shown to be the β-diketone (41), by comparison with material prepared later.

A solution of the boron difluoride complex in chloroform was shaken with dilute hydrochloric acid for several min. Separation and work-up of the organic phase in the usual manner afforded material identical by analytical t.l.c. and i.r. with the starting material.

Sodium borohydride (50 mg) was added with swirling to a solution of the boron difluoride complex (15 mg, 0·034 mmol), in methanol (3 ml) and the resultant solution set aside at 0° for 4 h. Work-up provided an oil (12 mg), shown to consist of one major and four minor components by t.l.c. [ethyl acetate–light petroleum (2 : 3)]. The major component, the β-hydroxy-ketone (42) (6 mg) was separated by preparative t.l.c.; $\nu_{max.}$ 3560, 1736, 1698, 1200—1140vbr, 1104, 1079, and 1058 cm^{-1}, τ 8·99, 8·80, and 8·78 (each 3H, s), 7·78 and 7·34 (2H, AB system, J_{AB} 16 Hz), and 6·40 (6H, s), M^+ 394 (Calc. for $C_{22}H_{34}O_6$: *M*, 394·49).

The more polar component of the mixture (3 mg) was assigned the γ-lactone structure (39); $\nu_{max.}$ 1785, 1730, 1676, 1163, and 1112 cm^{-1}, M^+ 360 (Calc. for $C_{21}H_{28}O_5$: *M*, 360·44).

(b) *Hydrogen iodide*. A solution of the epoxy-ketone (38) (30 mg, 0·077 mmol) in benzene containing concentrated hydriodic acid (1 drop) was heated under reflux for 60 h. Evaporation of the solvent *in vacuo* and preparative t.l.c. [ethyl acetate–light petroleum (2 : 3)] yielded the β-diketone (41) (10 mg) as an oil, $\nu_{max.}$ 3430vbr, 1730, 1610 (band disguised by carbon tetrachloride opaque region), 1215br, 1168, 1150, and 1107 cm^{-1}, τ 9·16, 8·80, and 8·75 (each 3H, s), 7·78br (2H, s), 7·70 and 7·02 (2H, AB system, J_{AB} 16 Hz), and 6·35 and 6·33 (both 3H, s), $\lambda_{max.}$ 297 nm (ε 8800) [changed to 316 (ε 17,600) in base]. The remainder of the material isolated was unchanged epoxy-ketone (38).

We thank the Carnegie Trust for the Universities of Scotland for Scholarship support (to J. P. J.).

[2/2422 *Received*, 24*th October*, 1972]