Diterpene chemistry. II. The preferential oxidation of the vinyl groups of pimaric and sandaracopimaric acids[1,2]

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The use of the Lemieux – von Rudloff technique for the oxidation of the vinyl groups of pimaric (I*b*) and sandaracopimaric (II*b*) acid methyl esters has been investigated. Although the process leads to the expected C-13 acid V in the case of methyl sandaracopimarate, an unexpected epoxy acid was obtained from methyl pimarate. This product was shown to be the 8β,14β-epoxy-13-α-ketoacid VIII*a*, probably arising from an intramolecular process during oxidation of the vinyl group.

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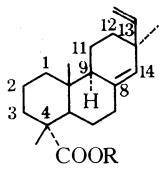
Our interest in diterpene resin acids of the pimaric acid type (I*a*, II*a*) led us to consider these compounds as starting materials for the partial synthesis of other natural products; for instance, novel steroidal derivatives should be available by the formal insertion of one carbon atom, as illustrated in III. The nuclear double bond between C-8 and C-14 and the vinyl group at C-13 represent positions for elaboration of functions for carrying out such transformations (1). Accordingly, we studied the conversion of these groups into those more useful for ring closure.

To achieve a stepwise synthesis, different functionality was required at the double bonds mentioned. The enhanced reactivity of the vinyl group to hydrogenation (2, 4), hydroboration (3), and hydroxylation (4) suggested that a preferential oxidation process should be possible at that site, leading to acids of type IV. A sequence paralleling that of Edwards (4) or a similar method (5) would seem possible, but in our hands this route proved impractical since relatively large amounts of the C-13 acid could not be obtained in a high yield or in a sufficiently pure form for further studies. It was thus decided to attempt a selective oxidation of the vinyl group; the method we considered most amenable to variations in the reaction parameters was that of Lemieux and von Rudloff (6). This technique involves the use of a catalytic amount of potassium permanganate in a buffered solution of sodium metaperiodate. The double bond is attacked by the permanganate, which is continually being regenerated from its reduced state by the periodate. Any glycols or α-ketols (6–9) that are formed are then cleaved by the excess periodate present; further oxidation of aldehydes by permanganate to acids ensues. This method was applied to the methyl esters of pimaric (I*b*) and sandaracopimaric acids (II*b*), and the results are described in this report.

The oxidation of methyl sandaracopimarate (II*b*), using 4 *M* equivalents of periodate with *t*-butyl alcohol as solvent (10), gave 55% of the ester acid V, whereas 6 equivalents of oxidant gave 85% of this product, whose structure was deduced as follows. The infrared spectrum showed absorption characteristic of an acid (3 100 and 1 695 cm^{-1}) and an ester (1 735 cm^{-1}), and the nuclear magnetic resonance (n.m.r.) spectrum showed a single unsplit peak in the olefinic region at 4.43 τ, indicating loss of the vinyl group. The methyl signal attributable to the C-13 methyl group (11, 12), appearing at 8.98 τ in the starting material, had moved downfield to 8.80 τ and now appeared superimposed on the C-4β methyl signal, suggesting that this methyl was now adjacent to a carboxyl group. The β,γ-unsaturated nature of the C-13 carboxyl group was illustrated by the formation of a

[1]For part I in this series, see J. W. ApSimon, P. V. Demarco, and J. Lemke, Can. J. Chem., 43, 2793 (1965).

[2]Presented in part at the 49th Canadian Chemical Conference, Saskatoon, Saskatchewan, June 1966. This work formed part of the B.Sc. thesis of W. G. C. (1963) and the M.Sc. thesis of A. S. Y. C. (1966).



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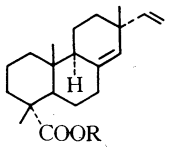
Ib R = Me



IIa R = H
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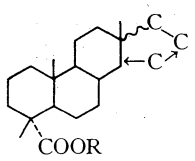
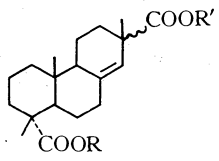
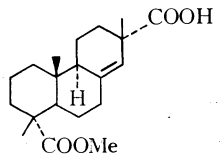


III



IV



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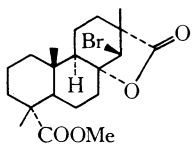
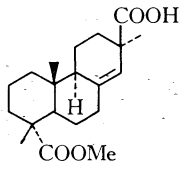


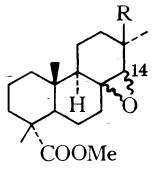
VI

bromo-γ-lactone on treatment with bromine water and sodium bicarbonate solution (13, 14). This lactone, to which we assign structure VI (15), analyzed for $C_{20}H_{39}O_4Br$ and showed infrared absorption at 1 773 cm^{-1} (γ-lactone) and at 1 728 cm^{-1} (ester). Its n.m.r. spectrum showed no olefinic hydrogen resonances, but exhibited a singlet attributable to the *H*—C—Br proton at 6.04 τ.

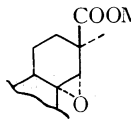
When we turned our attention to the oxidation of methyl pimarate (I*b*), some intriguing results emerged. Oxidation of this compound in the presence of 4 *M* equivalents of sodium periodate gave, besides unchanged methyl pimarate, two major products which were isolated by chromatography on silica gel. Thus, 4.4 g of starting material, on oxidation, yielded 0.9 g of a compound which we assumed was the expected ester acid VII, and 1.6 g of another compound, m.p. 186°, which analyzed for $C_{21}H_{30}O_6$. The structure of the ester acid VII was assigned on the same basis as that described for V obtained from methyl sandaracopimarate (see Experimental for the n.m.r. spectrum and bromolactone formation). The compound with m.p. 186° was unusual, its analysis indicating no loss of carbon and addition of four atoms of oxygen. The material was acidic and its infrared spectrum showed three carbonyl peaks at 1 755, 1 709, and 1 695 cm^{-1}. The n.m.r. spectrum showed no resonance in the olefinic region, but exhibited a singlet at 7.26 τ. Other features of this spectrum indicated a methyl ester, an acid, and three *C*-methyl groups, as expected. One way of accounting for these observations is with structure VIII*a*, where the vinyl group has been oxidized to an α-ketoacid and the double bond between C-8 and C-14 has been epoxidized, both processes being unusual for this type of oxidation. Support for the α-ketoacid structure was obtained by combustion analysis. If the oxidation product was dried at 100° *in vacuo*, it then analyzed for $C_{20}H_{30}O_5$, whereas the $C_{21}H_{30}O_6$ value was obtained on samples dried *in vacuo* at room temperature, intermediate values being obtained under other drying conditions. Further analytical values agreeing with this formulation were obtained for the corresponding cyclohexylamine salts.



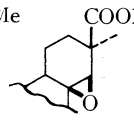
VII



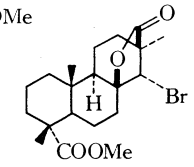
VIIIa R = COCOOH
VIIIb R = COOH
VIIIc R = COOMe



IX



X



XI

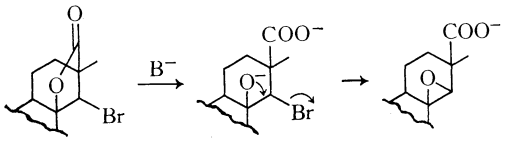
The ease of this decarbonylation was illustrated further by attempts to methylate the oxidation product VIII*a*. With ethereal diazomethane was obtained a crystalline ester analyzing for $C_{21}H_{32}O_5$, whose infrared spectrum showed carbonyl absorption at 1 740 cm^{-1} and whose n.m.r. spectrum indicated a diester (VIII*c*) and a

one-hydrogen singlet at 7.30 τ, which we assign to the C-14 hydrogen in VIII*c*. This latter observation, coupled with the lack of olefinic proton signals in the n.m.r. spectrum and the analytical figures, supports the formulation of the epoxy structure. This time, decarbonylation had apparently occurred on methylation with diazomethane. In subsequent experiments it was more convenient to methylate the oxidation reaction mixture, when the dimethyl ester VIII*c* was obtained directly by chromatography of the reaction mixture.

We felt that some information on the mode of formation of VIII*a* could be obtained from the orientation of the epoxide grouping. The cleavage (16, 17) of this group in VIII*c* was therefore examined, but we were unable to account for the products on the basis of any particular epoxide stereochemistry. Therefore, the synthesis of the two isomers IX and X of the dimethyl ester VIII*c* was studied.

The "normal" product from the Lemieux oxidation (VII) was available to us from the above reaction, and epoxidation of the nuclear double bond between C-8 and C-14 of this acid would be expected to occur from the least hindered α-face of the molecule, as seen from an examination of Dreiding molecular models and as reported elsewhere (18, 19). Epoxidation of the methyl ester of VII with *m*-chloroperbenzoic acid in ether gave an oxide to which we assign structure IX and which was not identical with the methylated oxidation product VIII*c*.[3]

Confirmation of the β-epoxide structure of X was obtained by a partial synthesis. The "normal" ester acid VII from the Lemieux oxidation of methyl pimarate (I*b*) readily formed a bromo-γ-lactone XI (cf. compound VI) which, we surmised, would open when treated with base, leaving a system ideally oriented for β-epoxide formation, as illustrated in Scheme 1. When the bromo-γ-lactone XI was allowed to stand at room temperature in methanolic potassium hydroxide for 30 min, a product was obtained which was identical with the diester epoxide VIII*c*. Since the stereochemistry of pimaric acid is well established (2, 20, 21), the configuration of its oxidation acid VII and thus that of the derived bromo-γ-lactone XI (13–15) follow. If it is assumed that a process such as depicted in Scheme 2 is reasonable, the stereochemistry of the product obtained (X) is as shown. Thus the epoxide obtained from the permanganate–periodate oxidation of methyl pimarate is β-oriented.

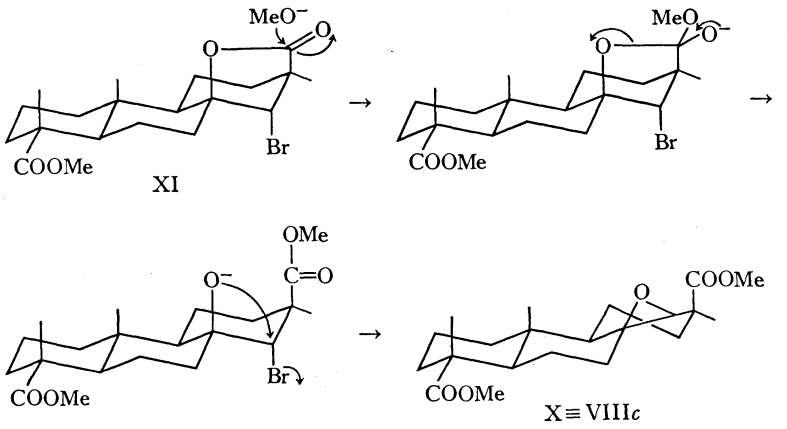


SCHEME 1.

It now remains to consider the mode of formation of compound VIII*a*. The formation of the ketoacid moiety is not difficult to rationalize if we assume that an α-ketol (6–9) or α-glycol or α-hydroxyaldehyde can be oxidized further before cleavage by periodate; there is some evidence that once an α-ketoacid is formed it reacts fairly slowly with periodate (22). Although this type of behavior is unusual, we do not feel that it is unlikely. In later oxidation experiments, we separated the reaction mixture into acidic and neutral fractions before chromatography, and in these cases we could not detect any of the α-ketoacid, but only the decarbonylated material. Similarly, methylation of the reaction product gave decarbonylated material.

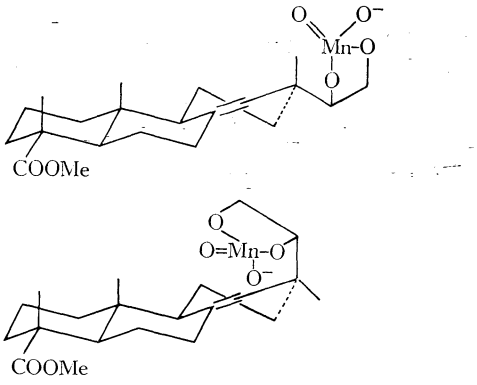
The formation of the β-epoxide can be rationalized if the intervention of an intramolecular complex between the two double bonds of methyl pimarate (I*b*) and the permanganate ion is postulated. Analogy for this type of process exists (23), and the formation of epoxides during permanganate oxidation has been reported elsewhere (24–28). It will be recalled that methyl sandaracopimarate (II*b*) underwent normal oxidation of the vinyl group to yield the acid V, whereas methyl pimarate (I*b*) gave

[3]This α-epoxide is very labile, rearranging when chromatographed or even when warmed in a hexane solution. It was obtained in an analytically pure form by rapid crystallization from hexane (see Experimental). Its chemistry, together with that of X, will be described when our studies are complete.



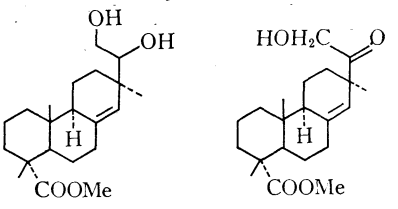
SCHEME 2.

a predominance of the unusual product VIII*a*. This can be explained on the basis of the C-13 stereochemistry of the parent resin acids and the formation of such a permanganate–diolefin complex[4] as illustrated below. The epoxide formed from this intermediate in the pimaric acid case would be β-oriented, whereas in the sandaracopimaric acid derivative the geometry is not favorable for oxide formation. There is a



possibility that oxide formation is a consequence of further oxidation of a normal oxidation product. We do not favor this alternative, since we have treated both the glycol XII and the ketol XIII under the oxidizing conditions described and have obtained only compound VII under conditions (vapor-phase chromatography) where we could observe less than 0.5% of the epoxidized material. This latter compound (VII) does not yield any epoxide on similar oxidation.[5]

The diol ester XII was obtained by the reaction of osmium tetroxide and methyl pimarate (I*b*) (29). The α-ketol was obtained during a series of oxidations on methyl pimarate with varying amounts of oxidant or by stopping an oxidation before completion. Its formation is unexceptional (6–9), and the pertinent features of its characterization are described in the Experimental.



Our opinion, at present, is that two pathways exist in this oxidation of methyl pimarate: firstly, the normal cleavage mode of the vinyl double bond and, secondly, via an intramolecular permanganate–diolefin complex leading to epoxidized material. Our studies in this field are continuing in an effort to obtain more information on the existence of such a complex.

[4]A possible alternate is a stepwise process involving transfer of the oxidizing agent, which again would be possible only for closely placed double bonds.

[5]Control reactions with only periodate gave no evidence of epoxidation, cleavage of the α-glycol or α-ketol being the only observed reaction.

EXPERIMENTAL

Infrared spectra were determined on Perkin–Elmer Infracord 137 and 237 spectrophotometers in Nujol mulls. Nuclear magnetic resonance spectra were determined at 60 Mc/s on a JEOLCO C-60 spectrometer; chemical shifts are given in τ units relative to tetramethylsilane as an internal standard (s is used to signify singlets). Only those signals deemed to be of interest in assigning structures have been quoted. Sample concentrations were approximately 10% (w/v) in deuteriochloroform as solvent. All optical rotations were taken with absolute ethanol as solvent at room temperature. Melting points are uncorrected and were determined on a Kofler hot stage. Mass spectra were obtained on the Perkin–Elmer–Hitachi instrument of McMaster University through the courtesy of Professors R. A. Bell and D. B. McLean.

Methyl Sandaracopimarate (IIb)

Sandaracopimaric acid (4) was methylated with excess ethereal diazomethane, and the methyl ester was crystallized from aqueous methanol to give colorless needles, m.p. 57°, $[\alpha]_D$ −15.4° (*c*, 1.1); ν_{max} 1 725 (ester), 1 640, 1 005, and 917 (vinyl), and 836 cm^{-1} (trisubstituted double bond).

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.57; H, 10.13.

Methyl Pimarate (Ia)

Methyl pimarate prepared in a similar manner was first passed through a column of alumina (Woelm, neutral, grade IV) in benzene, and then crystallized from aqueous methanol to give needles, m.p. 68–69°, $[\alpha]_D$ +17.5° (*c*, 0.98); ν_{max} 1 728 (ester), 1 640, 1 000, and 915 (vinyl), and 838 cm^{-1} (trisubstituted double bond) (reported m.p. 69° (26, p. 445)).

General Procedure for the Lemieux – von Rudloff (6) Oxidation

This procedure was used for all the oxidations described in this work.

The methyl ester (1 g) in 250 ml of *t*-butyl alcohol was treated, with stirring, with a solution of the requisite number of molar equivalents of sodium metaperiodate and 20 mg of potassium permanganate in water (ca. 500 ml). The reaction mixture was kept at pH 8 by the addition of 5% aqueous potassium carbonate solution, and the mixture was stirred until the color of the permanganate was discharged (1–4 h), then acidified with 2 *N* sulfuric acid, and extracted with ether several times. The ethereal extract was washed well with water, dried, and evaporated to give the reaction product, which was worked up as described below in the individual cases.

Oxidation of Methyl Sandaracopimarate

Methyl sandaracopimarate (8 g) was oxidized with 4 equivalents of sodium metaperiodate to yield a gum which was separated into neutral and acidic fractions. The neutral fraction was chromatographed on alumina (Woelm, neutral, grade IV), when elution with benzene gave 3.2 g of unchanged methyl sandaracopimarate. The acidic fraction, on crystallization from methanol, gave the ester acid V (4.8 g), m.p. 154–156°, $[\alpha]_D$ +4° (*c*, 1.0); ν_{max} 1 695 (acid), 1 728 (ester), and 830 cm^{-1} (trisubstituted double bond).

Anal. Calcd. for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.53; H, 8.86.

The cyclohexylamine salt was prepared by the addition of 0.1 ml of cyclohexylamine to an acetone solution of the acid (300 mg). The precipitate was crystallized from 2-butanone to yield colorless needles, m.p. 153–154°.

Anal. Calcd. for $C_{26}H_{43}NO_4$: N, 3.09. Found: N, 3.36.

On oxidation with 6 equivalents of periodate, 0.87 g of the ester acid V was obtained from 1 g of methyl sandaracopimarate.

Bromo-γ-lactone VI Derived from Methyl Sandaracopimarate

The oxidation product V (0.5 g) was dissolved in 15% sodium bicarbonate solution (10 ml), and saturated bromine water was added until a brownish-red color remained after the mixture was shaken. The solution was extracted with ether, washed with water, dried, and evaporated to yield a product which crystallized slowly from ether to give the bromo-γ-lactone VI (0.38 g) as colorless needles, m.p. 198°; ν_{max} 1 773 (γ-lactone), 1 728 (ester), and 670 cm^{-1} (C—Br); n.m.r. signals at 6.04 (1H, H—C—Br), 6.32 (3H, s, methyl ester), and 8.80, 8.83, and 8.88 τ (3H, s, *C*-methyl groups). A Beilstein test for halogen was positive.

Anal. Calcd. for $C_{20}H_{29}O_4Br$: C, 58.18; H, 7.03; Br, 19.21. Found: C, 58.18; H, 7.15; Br, 19.3.

Oxidation of Methyl Pimarate

Methyl pimarate (4.4 g) was reacted with 4 equivalents of sodium metaperiodate as described above, and the reaction mixture was chromatographed on silica gel (125 g). Benzene eluted 0.24 g of methyl pimarate. Chloroform–ether (9:1) eluted 0.88 g of an oil which could not be induced to crystallize even though thin-layer chromatography indicated a single compound (VII). The cyclohexylamine salt of this material was prepared as described above, and on recrystallization from 2-butanone yielded colorless plates, m.p. 127–129°, $[\alpha]_D$ +24° (*c*, 1.0). Regeneration of the acid (VII) from this salt gave an oil which distilled at 130° and 0.2 mm and then crystallized when scratched, m.p. 52–54°. This material could not be recrystallized, but a redistilled sample was used as an analytical sample.

Anal. Calcd. for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.77; H, 8.96.

ν_{max} 1 728 (ester), 1 695 (acid), and 823 cm^{-1} (trisubstituted double bond); n.m.r. signals at 4.36 (1H, s, olefinic hydrogen), 6.33 (3H, s, methyl ester), and 8.71, 8.79, and 9.17 τ (3H, s, *C*-methyl groups).

Chloroform–ether (4:1) eluted 1.56 g of a crystalline compound (VIII*a*) which was recrystallized from ether–hexane to give colorless needles, m.p. 185–186°, $[\alpha]_D$ +41° (*c*, 0.70); ν_{max} 1 755 (ketone), 1 709 (ester), and 1 695 cm^{-1} (acid).

Anal. Calcd. for $C_{21}H_{30}O_6$: C, 66.68; H, 7.99. Found: C, 66.95; H, 7.95.

The cyclohexylamine salt of this acid was made by adding excess cyclohexylamine (0.1 ml) to the acid (70 mg) in acetone, and was recrystallized from 2-butanone, giving fine matted colorless needles, m.p. 145–147°, $[\alpha]_D$ +25° (*c*, 1.14), ν_{max} 1 720 (ketone + ester) and 1 620 cm^{-1} (carboxylate).

Anal. Calcd. for $C_{27}H_{43}NO_6$: C, 67.89; H, 9.07; N, 2.93. Found: C, 67.89; H, 9.19; N, 3.01.

When an analytical sample of this acid (VIII*a*) was dried overnight at 100° and 0.4 mm, it had m.p. 186–189°, ν_{max} 1 715 (ester) and 1 702 cm^{-1} (acid), $[\alpha]_D$ +13° (*c*, 0.59).

Anal. Calcd. for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63. Found: C, 68.48; H, 8.49.

This indicated the loss of CO on heating *in vacuo*.

This decarbonylated product (VIII*b*) formed a cylohexylamine salt as colorless needles after crystallization from acetone, m.p. 147–148°, ν_{max} 1 730 (ester) and 1 620 cm^{-1} (carboxylate).

Anal. Calcd. for $C_{26}H_{43}NO_5$: C, 69.45; H, 9.60; N, 3.12. Found: C, 69.80; H, 9.75; N, 3.28.

Methylation of VIII*a* (49 mg) with an excess of ethereal diazomethane gave, after evaporation of the solvent, a crystalline product, which was recrystallized from ether–hexane as colorless needles, m.p. 147°, $[\alpha]_D$ +28° (*c*, 0.97), ν_{max} 1 740 cm^{-1} (ester); n.m.r. signals at 6.24 and 6.35 (3H, s, methyl esters) and 7.3 τ (C-14 H), but no signals in the olefinic region.

Anal. Calcd. for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 68.94; H, 8.76.

Synthesis of the α-Epoxide IX

The "normal" oxidation product VII of methyl pimarate (0.57 g) was first methylated with excess ethereal diazomethane and evaporated to dryness. The reaction product showed one spot on thin-layer chromatography, and was dissolved in ether (5 ml, anhydrous) and treated with *m*-chloroperbenzoic acid (0.30 g) at 0° for 3 days. The reaction mixture was poured into sodium carbonate solution, and extracted with ether to yield an oil (0.49 g) which crystallized from hexane as needles, m.p. 90–92°. This compound was very labile, changing, even on recrystallization from hexane, to another compound, m.p. 208°. The study of this is proceeding. Rapid crystallization of the epoxidized material from hexane yielded an analytical sample, m.p. 96°; ν_{max} 1 730 (slightly split, indicating two esters) and 1 435, 1 240, and 1 130 cm^{-1} (epoxide?), but no absorption around 823 cm^{-1} attributable to the trisubstituted double bond; n.m.r. signals at 6.2 (2 × 3H, s, two methyl esters) and 6.8 τ (1H, s, C-14 H), but no signal in the olefinic region; molecular weight (mass spectral) 364.

Anal. Calcd. for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 69.17; H, 8.62.

Bromo-γ-lactone XI Derived from Methyl Pimarate

The ester acid VII (0.52 g) was treated with 15% aqueous sodium bicarbonate solution (10 ml) followed by saturated bromine water. Extraction with ether and evaporation after drying gave the crystalline bromo-γ-lactone XI, which was recrystallized from ether–hexane to give oblong plates, m.p. 202°; ν_{max} 1 774 (γ-lactone), 1 726 (ester), and 675 cm^{-1} (C—Br); n.m.r. signals at 6.03 (1H, s, H—C—Br) and 6.28 τ (3H, s, methyl ester). A Beilstein test for halogen was positive.

Anal. Calcd. for $C_{20}H_{29}O_4Br$: C, 58.18; H, 7.03; Br, 19.3. Found: C, 58.37; H, 6.88; Br, 19.59.

Synthesis of the β-Epoxide X

The above bromo-γ-lactone XI (15 mg) dissolved in methanol (3 ml) was treated with two drops of 50% methanolic potassium hydroxide. After 30 min, water (5 ml) was added and, when the solution was left at room temperature, colorless needles separated, m.p. 138–141°. Recrystallization from methanol gave the epoxy diester X, identical in all respects (melting point, mixture melting point, thin-layer chromatography, and infrared and mass spectra) with that obtained on methylation of the oxidation product of methyl pimarate; molecular weight (mass spectrum) 364.

α-Ketol XIII

Methyl pimarate (8.0 g) (I*b*) was treated with 4 equivalents of sodium metaperiodate in the manner described above, except that the reaction was stopped after 30 min (permanganate color still present). The reaction mixture was worked up in the usual manner and separated into acidic and neutral fractions. The acidic fraction contained both compounds VII and VIII*a*. The neutral fraction (2.58 g) was chromatographed on silica gel (100 g), when benzene eluted methyl pimarate (0.94 g). Chloroform and chloroform–ether (9:1) eluted the ketol XIII (1.60 g), m.p. 126° after recrystallization from ether–hexane, $[\alpha]_D$ 0° (*c*, 1.0); ν_{max} 3 450 (hydroxyl), 1 742 (ester), 1 695 (carbonyl), and 823 cm^{-1} (trisubstituted double bond); n.m.r. signals at 4.61 (1H, s, C-14 olefinic proton), 5.63 (2H, s, $R—\overset{\overset{O}{\|}}{C}—CH_2—O—H$), 6.32 (3H, s, methyl ester), and 8.78, 8.83, and 9.32 τ (3 × 3H, s, angular methyl groups).

Anal. Calcd. for $C_{21}H_{32}O_4$: C, 72.39; H, 9.20. Found: C, 72.62; H, 9.35.

The same product was not present when the reaction was allowed to run to completion. Further oxidation of the α-ketol XIII by the described technique or with Jones' reagent (30, 31) gave VII as the only product in greater than a 90% yield of purified material.

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REFERENCES

1. W. E. BACHMANN, W. COLE, and A. L. WILDS. J. Am. Chem. Soc. **61**, 974 (1939); **62**, 824 (1940); **62**, 2750 (1940).
2. O. E. EDWARDS and R. HOWE. Can. J. Chem. **37**, 760 (1959), and references therein.
3. O. E. EDWARDS and R. S. ROSICH. Private communication.
4. O. E. EDWARDS, A. NICOLSON, and M. N. RODGER. Can. J. Chem. **38**, 663 (1960).
5. R. PAPPO, D. S. ALLEN, JR., R. U. LEMIEUX, and W. S. JOHNSON. J. Org. Chem. **21**, 478 (1956).
6. R. U. LEMIEUX and E. VON RUDLOFF. Can. J. Chem. **33**, 1701 (1955); **33**, 1710 (1955); **33**, 1714 (1955).
7. K. B. WIBERG and K. A. SAEGEBARTH. J. Am. Chem. Soc. **79**, 2822 (1957).
8. R. STEWART. *In* Oxidation in organic chemistry. K. Wiberg (*Editor*). Academic Press, Inc., New York. 1965. p. 41.
9. S. WOLFE. Ph.D. Thesis, University of Ottawa, Ottawa, Canada. 1957.
10. E. VON RUDLOFF. Can. J. Chem. **34**, 1413 (1956).
11. J. W. APSIMON, W. G. CRAIG, P. V. DEMARCO, D. W. MATHIESON, and W. B. WHALLEY. Chem. Commun. 361 (1966).
12. J. W. APSIMON, W. G. CRAIG, P. V. DEMARCO, D. W. MATHIESON, and W. B. WHALLEY. Tetrahedron. In press.
13. A. WINTERSTEIN and R. EGLI. Z. Physiol. Chem. **202**, 207 (1931).
14. W. HERZ, D. MELCHOIR, R. N. MIRRINGTON, and P. J. S. PAUWELS. J. Org. Chem. **30**, 1873 (1965).
15. H. O. HOUSE, R. G. CARLSON, and H. BABAD. J. Org. Chem. **28**, 3359 (1963).
16. J. G. PHILLIPS and V. D. PARKER. *In* Steroid reactions. C. Djerassi (*Editor*). Holden-Day, Inc., San Francisco. 1963. p. 593.
17. R. E. PARKER and N. S. ISAACS. Chem. Rev. **59**, 737 (1959).
18. W. HERZ, H. J. WAHLBORG, W. D. LLOYD, W. H. SCHULLER, and S. W. HEDRICK. J. Org. Chem. **30**, 3190 (1965).
19. W. H. SCHULLER and R. V. LAWRENCE. J. Am. Chem. Soc. **83**, 2563 (1961).
20. R. E. IRELAND and P. W. SCHIESS. J. Org. Chem. **28**, 6 (1963).
21. R. MCCRINDLE and K. OVERTON. *In* Advances in organic chemistry. Vol. 5. R. A. Raphael (*Editor*). Interscience Publishers, Inc., New York. 1965. p. 70.
22. G. W. PEROLD and K. G. R. PACHLER. J. Chem. Soc., C, 1918 (1966).
23. E. KLEIN and W. ROJAHN. Tetrahedron, **21**, 2353 (1965).
24. E. VON RUDLOFF. Tetrahedron Letters, 993 (1966).
25. S. W. PELLETIER. J. Am. Chem. Soc. **87**, 761 (1965).
26. J. SIMONSEN and D. H. R. BARTON. The terpenes. Vol. 3. Cambridge University Press, London, England. 1952. pp. 438 and 439.
27. H. WIENHAUS and B. MARCHLAND. Chem. Ber. **91**, 401 (1958).
28. M. EHRENSTEIN and M. T. DECKER. J. Org. Chem. **5**, 544 (1940).
29. O. E. EDWARDS and R. HOWE. Chem. Ind. London, 537 (1959).
30. K. BOWDEN, I. M. HEILBRON, E. R. H. JONES, and B. C. L. WEEDON. J. Chem. Soc. 39 (1946).
31. C. DJERASSI, R. R. ENGLE, and A. BOWERS. J. Org. Chem. **21**, 1547 (1956).