octant makes a smaller negative contribution, a positive Cotton effect is observed for these ketones.

A comparison of the curves of V and VI is particularly interesting. The *trans* diester V, the thermodynamically more stable product, can be prepared from VI by refluxing in base followed by reesterification with diazomethane. Such an inversion of configuration of a carboxyl grouping is reminiscent of similar changes of stereochemistry performed with 16,17-dicarboxy steroids.[6] This epimerization at C-15 of VI into V is accompanied by a change in the sign of the Cotton effect and can thus be readily followed by optical rotatory dispersion. A possible explanation for the negative Cotton effect observed for VI may be that the unfavorable steric and electronic repulsions of the *cis* C-15 and C-16 carbomethoxy groups in VI induce a conformational modification of the ring system. Further work is, however, desirable in order to permit a safe interpretation for the inversion of the Cotton effect which is observed in going from VI to V.

Finally, in the ethylenic ketone VII, the sign of the Cotton effect is in agreement with the structure and stereochemistry proposed for the β,γ-unsaturated keto chromophore.[3] Indeed, a positive Cotton effect is to be expected[3] if the absolute configuration of this chromophore is as indicated in formula VII. Furthermore, as indicated in Table II, the β,γ double bond greatly enhances the magnitude of the Cotton effect, as previously observed in cases where a nonbonding orbital can overlap the π-system of the neighboring carbonyl chromophore.[3,7,8]

Experimental

All optical rotatory dispersion curves were obtained in methanol (c 0.05–0.15) using the Rudolph photoelectric spectropolarimeter beginning at 700 mμ and continuing to 300 mμ. The preparation and characterization of all compounds used has been described[1] and analytically pure samples were used. In the case of compound VI, both the trough (−4664°) and the peak (+1280°) were obtained in methanol solution, and the curve was unchanged after the addition of a trace of hydrochloric acid, indicative of no hemiketal formation.[9]

(6) J. Romo, L. Rodriguez-Hahn, P. Joseph-Nathan, M. Martinez, and P. Crabbé, *Bull. soc. chim. France*, 1276 (1964).

(7) A. Moscowitz, A. E. Hansen, L. S. Foster, and K. Rosenheck, *Biopolymers*, **1**, 75 (1964).

(8) P. Crabbé, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1965.

(9) C. Djerassi, L. A. Mitscher, and B. J. Mitscher, *J. Am. Chem. Soc.*, **81**, 947 (1959).

Terpenes. XVII.[1] Studies on the Ozonolysis of Methyl Maleopimarate and the Epoxidation of Trimethyl Maleopimarate and Fumaropimarate

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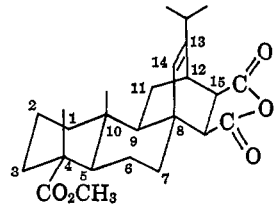
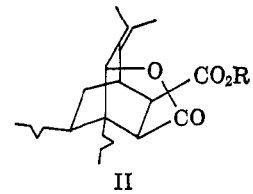
In 1936 Wienhaus and Sandermann[2] reported that ozonolysis of methyl maleopimarate (I), the Diels–Alder adduct obtained from levopimaric acid methyl ester and maleic anhydride, gave a methyl ester,



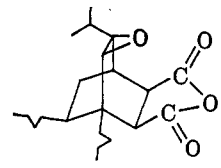
I



II

$C_{25}H_{34}O_8$, m.p. 250°. Several years later Ruzicka and LaLande,[3] after careful re-examination of the reaction, found in addition to the above-mentioned product two other isomeric monomethyl esters of molecular formula $C_{25}H_{34}O_6$, m.p. 289–290° and m.p. 226–227°.[4] The latter workers found that the dimethyl ester of the product of m.p. 226–227° was identical with the dimethyl ester of the product obtained on oxidation of maleopimaric acid with alkaline permanganate. Recent work from our laboratory[5,6] has shown that this product is correctly represented by structure II.

Ruzicka and LaLande[3] concluded that the product of m.p. 289–290° was an acid lactone ester and suggested two possible structures.[4] However, our work does not support the previously assigned structures, and instead we propose structure III for this product.



III

The infrared spectrum of III showed the characteristic five-membered ring anhydride type carbonyl absorption at 1773 and 1842 cm.$^{-1}$ and, in addition, its n.m.r. spectrum showed the proton at C-14 as a singlet centered at δ 3.20 and the isopropyl methyl groups appeared as a pair of doublets (J = 7 c.p.s.) centered at δ 0.72 and 1.07. The most convincing evidence for structure III came from the observation that it could also be prepared from I by treatment with trifluoroperacetic acid[7]; however, other peracids such as monoperphthalic or *m*-chloroperbenzoic were ineffective. The stereochemistry of the epoxide ring in III was assigned on the basis of arguments presented below.

Epoxide III was partially converted into the epoxy triester IV by refluxing in alkali followed by re-esterification with diazomethane. Compound IV was also readily prepared by epoxidation of trimethyl fumaropimarate (V) with trifluoroperacetic acid. A comparison of the n.m.r. spectra of III and IV was of interest. Surprisingly, one of the isopropyl methyl groups in IV is deshielded to a considerable extent (δ 1.32) as compared with those in III. The anhydride ring in III was opened only with great difficulty. Thus, the

(1) (a) The authors gratefully acknowledge financial support of this investigation by the National Science Foundation (GP-233). (b) Terpenes. XVI: L. H. Zalkow, N. N. Girotra, and P. Crabbe, *J. Org. Chem.*, **30**, 1678 (1965).

(2) H. Wienhaus and W. Sandermann, *Ber.*, **69**, 2202 (1936).

(3) L. Ruzicka and W. A. LaLande, *Helv. Chim. Acta*, **23**, 1357 (1940).

(4) The earlier work is described in J. Simonsen, "The Terpenes," Vol. 3, Cambridge University Press, Cambridge, England, 1952, p. 440.

(5) L. H. Zalkow, R. A. Ford, and J. P. Kutney, *J. Org. Chem.*, **27**, 3535 (1962).

(6) L. H. Zalkow and D. R. Brannon, *ibid.*, **29**, 1296 (1964).

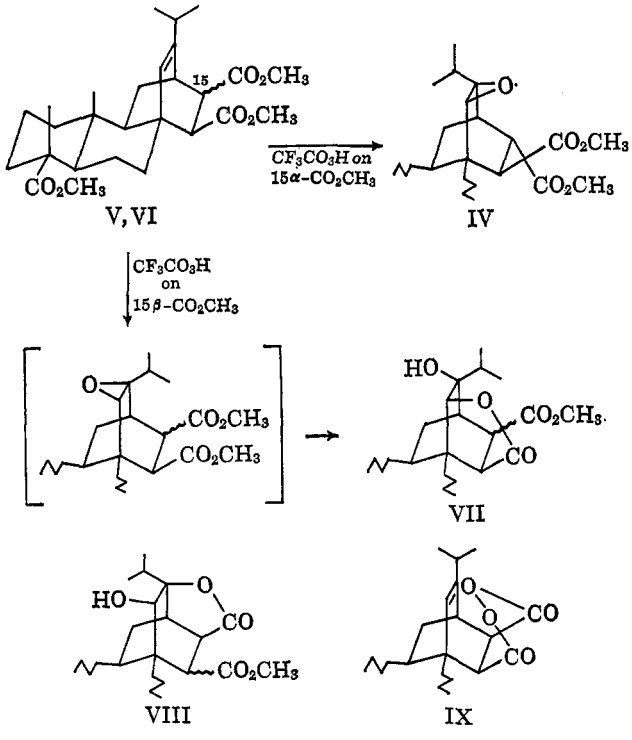
(7) W. D. Emmons and A. S. Pagano, *J. Am. Chem. Soc.*, **77**, 89 (1955).

seemingly similar anhydride ring of I was readily opened with diazomethane–methanol to give the triester VI, whereas the anhydride ring of III was unaffected under these conditions.

In contrast to V, the isomeric triester VI, when treated with trifluoroperacetic acid under identical conditions, did not give an epoxide, but rather a hydroxy lactone ($C_{26}H_{38}O_7$) was obtained. This product has been assigned structure VII on the basis of the following evidence. The infrared spectrum of VII showed that it was a hydroxy-γ-lactone (3400 and 1762 cm.$^{-1}$) and its n.m.r. spectrum confirmed the presence of two methyl ester groups (δ 3.64 and 3.71). Of particular significance was the appearance of a one-proton singlet at δ 3.84 (in the presence of D_2O) which arises from the C-14 proton of VII. The alternative γ-lactone structure of VIII is considered less likely both on mechanistic grounds and on steric grounds. An examination of Dreiding models indicates that in VIII the C-10 methyl group would suffer severe steric interaction with the C-13 isopropyl group and the C-14 hydroxyl group, and, in addition, the C-10 methyl group would be expected to be highly shielded, whereas, in fact, the n.m.r. spectrum showed only a normal C-10 bridgehead methyl group (δ 1.0 or 1.13).

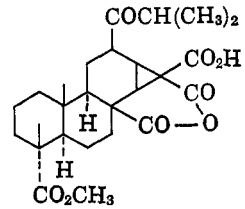
Hydroxy lactone VII undoubtedly arises *via* the intermediate epoxide (see Scheme I), which in the presence of trifluoroacetic acid undergoes displacement by the β-oriented C-16 carbomethoxy group. Compound VII was unchanged after refluxing in alkali followed by re-esterification with diazomethane. Thus the epoxide ring in III and IV must be *trans* to the C-10 bridgehead methyl group, since it is not opened under the acidic epoxidation conditions or by refluxing alkali.

SCHEME I



An explanation for the observed stereospecificity in the epoxidation of I, V, and VI may be as follows. In V the face of the double bond *anti* to the C-10 bridgehead methyl group is less hindered than the *syn* face since the C-15 carbomethoxy group is down, whereas in VI the *syn* face is less hindered, and thus reaction with trifluoroperacetic acid occurs as shown in these two cases. It thus remains to be explained why I leads to epoxidation from the *anti* face. It is postulated that the anhydride ring of I is converted, by trifluoroperacetic acid or by ozone in acetic acid, into the intermediate peroxide IX (see Scheme I), which then reacts intramolecularly to give III.

Ruzicka, *et al.*,[8] originally suggested that the product of m.p. 250° was a keto ester acid anhydride arising simply by cleavage of the double bond in I. However, when they were unable to isolate the expected 1-methyl-6-isobutylphenanthrene on dehydrogenation of this product, these workers suggested two alternative structures arising from oxidation of the double bond without cleavage.[2] Our evidence, together with that of the earlier workers, supports structure X. The infrared spectrum of X showed characteristic glutaric



X

anhydride carbonyl absorption at 1764 and 1802 cm.$^{-1}$, and X was converted into a tetramethyl ester with methanolic diazomethane. That this ester was a tetramethyl and not a trimethyl ester was shown by its n.m.r. spectrum and by its saponification equivalent. The anhydride X apparently arises by cleavage of the double bond as originally surmised,[8] but the more stable six-membered anhydride ring is formed in preference to the five-membered ring during the work-up of the reaction.

It is interesting to compare the results of ozonolysis of I and its corresponding trimethyl ester under the same conditions. In the latter case eight crystalline products were isolated, none of which arose by cleavage of the double bond.[9] However, such an oxidation product might very well have been present to a small extent in the noncrystalline residue.

Experimental

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Analyses were performed by Midwest Microlab, Inc., Indianapolis, Ind. Infrared spectra were recorded with a Beckman IR-5 spectrometer and n.m.r. spectra were recorded with a Varian A-60 n.m.r. spectrometer and are reported as dimensionless "chemical shift" units relative to tetramethylsilane (δ 0).

Ozonolysis of Methyl Maleopimarate. Isolation of II (R = H), III, and X.—Maleopimaric acid (Distillation Products Industries) when treated with ethereal diazomethane gave methyl maleopimarate (I), m.p. 212–213°, lit.[5] m.p. 214–215°. Methyl maleopimarate (15 g.) in 500 ml. of glacial acetic acid was ozonized as previously described by Ruzicka and LaLande[2] and the products II, III, and X were isolated as described by the earlier workers.

Compound X (0.3 g., m.p. 250–251°, lit.[2] m.p. 252–253°) precipitated from the acetic acid solution and gave a negative tetranitromethane test, ν_{max}^{KBr} (cm.$^{-1}$) 1802, 1764, and 1725.

(8) L. Ruzicka, A. G. R. Bacon, R. Lukes, and J. D. Rose, *Helv. Chim. Acta*, **21**, 583 (1938).

(9) L. H. Zalkow and N. N. Girotra, *J. Org. Chem.*, **28**, 2033 (1963).

Anal. Calcd. for $C_{25}H_{34}O_8$: C, 64.99: H, 7.42. Found: C, 65.27: H, 7.38.

Compound II (R = H) was isolated by addition of water to the acetic acid filtrate from above: 0.2 g., m.p. 224–225°, lit.[2] m.p. 226–227°, ν_{max}^{KBr} (cm.$^{-1}$) 1730 and 1758. The dimethyl ester II (R = CH_3) was prepared by addition of ethereal diazomethane and was found to be identical with II (R = CH_3) obtained by permanganate oxidation of maleopimaric acid followed by esterification as previously described[5] in melting point (m.p. 180°, alone and on admixture) and by infrared and n.m.r. spectra.

Compound III was isolated from the aqueous acetic acid filtrate as previously described[2] and, after crystallization from hot acetone, gave m.p. 289–290° (100 mg.); ν_{max}^{KBr} (cm.$^{-1}$) 2950, 1777, and 1720; n.m.r. ($CDCl_3$) δ 0.72 (doublet, J = 7 c.p.s.), 0.85, 1.07 (doublet, J = 7 c.p.s.), 1.20, 3.20, (14 H), and 3.71 (OCH_3), no olefinic hydrogen atoms were evident; negative tetranitromethane test.

Anal. Calcd. for $C_{25}H_{34}O_6$: C, 69.83; H, 7.97. Found: C, 69.77; H, 7.91.

Concentration of the filtrate after removal of X, II, and III gave a residue which, by melting point and infrared spectrum, appeared to be almost entirely starting material.

Preparation of the Tetramethyl Ester of X.—An ethereal solution of diazomethane (excess) was added to 250 mg. of X dissolved in 30 ml. of methanol and, after standing overnight, the solution was filtered. Evaporation of the filtrate gave the tetramethyl ester (72%) which melted at 128–132° after recrystallization from water–methanol, ν_{max}^{KBr} (cm.$^{-1}$) 1754–1724 (broad) and 1250–1176. The n.m.r. spectrum of the tetramethyl ester, on integration, showed 30 ± 3% of the total hydrogen present as methoxyl hydrogen (theoretical value 28.5%) by the appearance of three peaks at δ 3.57, 3.63, and 3.69. The saponification equivalent found was 510 (calculated for $C_{28}H_{42}O_9$: 523) assuming four carboxyl groups; if three carboxyl groups are present the saponification equivalent found would have been in the vicinity of 382.

Preparation of III by Direct Epoxidation of I.—A solution containing 3 ml. of trifluoroacetic anhydride and 1 ml. of 90% hydrogen peroxide in 10 ml. of methylene chloride was added dropwise over an interval of 20 min. to a stirred suspension of 4 g. of disodium hydrogen phosphate in 30 ml. of methylene chloride containing 2.5 g. of methyl maleopimarate.[7] The solution was refluxed for 45 min., stirred at room temperature an additional 48 hr., washed with 10% sodium sulfite solution, then filtered; the filtrate was further washed with 10% sodium bicarbonate solution and finally with water. After drying over anhydrous magnesium sulfate, the organic layer was concentrated with a rotary evaporator to give 2.1 g. of crude product which, after recrystallization from acetone, gave 1.5 g. of III identical in melting point (m.p. 289–290°; alone and on admixture) and in infrared and n.m.r. spectra with III obtained by the ozonolysis of I as described above.

Preparation of IV.—Trimethyl fumaropimarate (V,[6] 1.08 g.) was epoxidized with trifluoroperacetic acid as described above to give 0.45 g. of IV: m.p. 179–181° after recrystallization from ether; ν_{max}^{KBr} (cm.$^{-1}$) 1738 and 2950; n.m.r. ($CDCl_3$) δ 0.71, 1.00 (doublet, J = 6 c.p.s.), 1.03, 1.32 (doublet, J = 6 c.p.s.), 3.18 (14 H), 3.66, 3.70, and 3.80.

Anal. Calcd. for $C_{27}H_{40}O_7$: C, 68.12; H, 8.47. Found: C, 68.37; H, 8.43.

Compound III (0.33 g.) was refluxed in a solution of 10 ml. of methanol and 10 ml. of 25% aqueous sodium hydroxide for 34 hr. (shorter reflux times resulted in complete recovery of III). The solution was diluted with water and acidified with dilute hydrochloric acid, and the precipitate was taken up in ether. The ether extract, after drying, was evaporated to give 0.26 g. of product: m.p. 185–198°; ν_{max}^{KBr} 2570–3500 (broad). This material (0.19 g.) was dissolved in 30 ml. of ether and to this solution ethereal diazomethane was added. Evaporation of the ether solution yielded 0.065 g. of unreacted III, m.p. 287–291°, and the remainder as a gummy mass which could not be crystallized. Thin layer chromatography on 25-μ-thick silica gel coated glass plates using 3:7 methyl acetate–n-hexane as the mobile phase and detection by iodine vapors showed that this gummy material was predominantly the same as IV (R_f 0.45), the other components presumably being the C-15 epimer of IV and unreacted III.

Reaction of VI with Trifluoroperacetic Acid. Preparation of VII.—Trimethyl ester VI (2.58 g.) was treated with trifluoroacetic anhydride and hydrogen peroxide as described above. After the usual work-up 2.6 g. of white glassy product was obtained which, after three recrystallizations from methanol, gave 1.5 g. of VII: m.p. 146–148°; ν_{max}^{KBr} (cm.$^{-1}$) 3400, 1762, and 1709; n.m.r. (CCl_4) δ 1.00, 1.02 (doublet, J = 6 c.p.s.), 1.13, 1.20 (doublet, J = 6 c.p.s.), 3.64, 3.71, 3.84 (14 H, after addition of D_2O).

Anal. Calcd. for $C_{26}H_{38}O_7$: C, 67.59; H, 8.29. Found: C, 67.42; H, 8.38.

VI was unchanged after refluxing in methanolic sodium hydroxide for 8 hr. followed by acidification and re-esterification with diazomethane.

Relative Shielding of *cis* and *trans* Methyls of Some Substituted Methylcyclopropanes[1]

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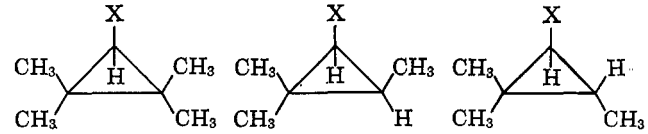
The n.m.r. spectra of **1**–**9** are the subject of this Note. In particular the relative chemical shifts of methyls *cis* and *trans* to the X functions are discussed.



1, X = CO_2CH_3 **2**, X = CO_2CH_3 **3**, X = CO_2CH_3
4, X = CH_2OH **5**, X = CH_2OH **6**, X = CH_2OH
7, X = $C(CH_3)_2OH$ **8**, X = $C(CH_3)_2OH$ **9**, X = $C(CH_3)_2OH$

The three esters **1**, **2**, and **3** were obtained *via* copper-catalyzed addition of diazoacetic ester to 2,3-dimethyl-2-butene[2] and 2-methyl-2-butene.[3] Isomers **2** and **3**, arising from addition to 2-methyl-2-butene, could unfortunately not be separated by the vapor phase chromatography equipment available at the time. However, mixtures enriched in **2** (70%) and **3** (90%) were obtained by partial saponification, the stereochemical assignments of *cis* and *trans* being made on the basis of relative saponification rates.[4] Primary alcohol **4** and mixtures enriched in **5** and **6** were derived from **1** and the mixtures enriched in **2** and **3** by reduction with lithium aluminum hydride. Tertiary alcohol **7** and mixtures enriched in **8** and **9** were formed from the same starting materials by treatment with methyllithium. Spectra of the mixtures of tertiary alcohols were consistent with **8** (80%) and **9** (80%) predominating in the mixtures derived from **2** (70%) and **3** (90%), respectively. The stereochemistry of the major isomer in each mixture was clearly revealed by the two coupling constants of 9.5 and 6.0 c.p.s. observed for the cyclopropyl hydrogen at τ *ca.* 9.9, the *cis* isomer being

(1) This investigation was supported in part by Petroleum Research Fund Grant 1116-A4. Acknowledgment is also made of National Science Foundation Grant G 19108 which contributed to the purchase of the n.m.r. spectrometer used in this research.

(2) A. P. Meschcheryakov and I. E. Dolgii, *Izv. Akad. Nauk. SSSR, Otd. Khim. Nauk.*, 931 (1960).

(3) P. S. Skell and R. M. Etter [*Chem. Ind.* (London), 624 (1958)] performed this addition in a competitive rate study but gave no experimental details and did not refer to the individual isomers **2** and **3**.

(4) See P. S. Skell and R. M. Etter, *Proc. Chem. Soc.*, 443 (1961); W. von E. Doering and T. Mole, *Tetrahedron*, **10**, 65 (1960); T. V. Van Auken and K. L. Rinehart, *J. Am. Chem. Soc.*, **84**, 3736 (1962).