ture. The red solution was diluted with 300 ml. of water and 300 ml. of ether, and, after shaking, the layers were separated. The organic layer was extracted with three portions of 5% sodium hydroxide solution. Acidification of the combined alkaline solutions resulted in separation of the products, which were isolated by extraction with ether–ethyl acetate. Evaporation of the dried organic solutions gave 40 g. of crude product, which crystallized slowly (2 weeks) at ice temperature. Trituration with ether afforded 10.5 g. of colorless crystals (Ib), m.p. 135–139°, raised to 138.5–140.5° by recrystallization from ethanol. The infrared spectrum (chf.) had peaks at 2.85 (OH), 5.73 (ester), and 5.81 $\mu$ (ketone). The compound gave a faint green color with ferric chloride and was slowly soluble in 5% sodium hydroxide solution.

*Anal.* Calcd. for $C_{21}H_{28}O_8$: C, 61.75; H, 6.91. Found: C, 61.63; H, 6.96.

**The 2,4-dinitrophenylhydrazone** was recrystallized from ethyl acetate; bright yellow, fine needles, m.p. 199–201° dec. The infrared spectrum of this derivative (chf.) had peaks at 2.85 (OH), 3.00 (NH), 5.75 (unbonded ester), 5.85 (bonded ester) and 6.16 $\mu$ (unconjugated C=N).

*Anal.* Calcd. for $C_{27}H_{32}O_{11}N_4$: C, 55.10; H, 5.48. Found: C, 55.53; H, 5.56.

The filtrate from the trituration of Ib gave, upon evaporation of the solvents, 25 g. of very viscous orange oil which eventually set to a hard glass and did not crystallize. This material gave a deep purple color with ferric chloride, and was soluble in dilute alkali. Evidently it was an impure mixture of isomers of unsaturated cyclic ketoesters. **The 2,4-dinitrophenylhydrazone** obtained from this material had m.p. 197–199° after recrystallization from ethyl acetate; the mixed m.p. with the 2,4-dinitrophenylhydrazone of Ib was 181–185° (depressed). The infrared spectrum of this derivative had peaks at 3.01 (NH), 5.77 (ester) and 6.18 $\mu$ (C=N).

*Anal.* Calcd. for $C_{27}H_{30}O_{10}N_4$: C, 56.84; H, 5.30. Found: C, 57.13; H, 5.50.

**3-(3′,4′-Dimethoxyphenyl)-5-methylcyclohex-5-ene-1-one.**—Hydrolysis and decarboxylation of both Ib and the glassy enol obtained with it, in 5% sodium hydroxide (reflux) for one hour resulted in each case in formation of neutral, viscous oil. The same **2,4-dinitrophenylhydrazone** was obtained from both products as dense, glittering, deep red crystals from ethyl acetate, m.p. 207–209°.

*Anal.* Calcd. for $C_{21}H_{22}O_6N_4$: C, 59.15; H, 5.20. Found: C, 58.95; H, 5.33.

**2,4-Dicarbethoxy-3-(3′,4′-dimethoxyphenyl)-5-methylcyclohexanone.**—Hydrogenation of 10.3 g. of the glassy enol obtained with Ib, in the presence of 2 g. of 10% palladium–charcoal catalyst in 200 ml. of acetic acid at 80° for 1.5 hours resulted in the formation of 5.2 g. of neutral oil. The remainder of the material obtained after this reaction was a viscous, brown, alkali-soluble gum. **The 2,4-dinitrophenylhydrazone** was prepared from the neutral fraction and was recrystallized from ethanol–ethyl acetate; bright yellow crystals, m.p. 187–189°. The infrared spectrum of the derivative (chf.) had peaks at 3.02, 5.76 (ester) and 6.17 $\mu$.

*Anal.* Calcd. for $C_{27}H_{32}O_{10}N_4$: C, 56.64; H, 5.63. Found: C, 56.49; H, 5.62.

**Condensation of Piperonal and Ethyl Acetoacetate.**—Reaction of 36.5 g. (0.243 mole) of piperonal and 63.5 g. (0.489 mole) of ethyl acetoacetate was carried out in the presence of 22 ml. of 40% Triton B in 60 ml. of ethanol. After 7 days standing, 19.7 g. of crystalline Ic, m.p. 148–150°, and 22 g. of crude, glassy, orange enol were obtained upon treating the mixture in the same way as described for the veratraldehyde products. Further recrystallization of Ic (ethanol) did not raise the melting point. The infrared spectrum (chf.) had peaks at 2.85, 5.73 and 5.80 $\mu$.

*Anal.* Calcd. for $C_{20}H_{24}O_8$: C, 61.21; H, 6.2. Found: C, 60.93; H, 6.6.

**The 2,4-dinitrophenylhydrazone** was recrystallized from ethyl acetate; yellow-orange needles, m.p. 220–222°. The infrared spectrum (chf.) had peaks at 2.85–2.90, 3.02, 5.75, 5.85 and 6.16 $\mu$.

*Anal.* Calcd. for $C_{26}H_{28}O_{11}N_4$: C, 54.54; H, 4.93. Found: C, 54.59; H, 5.05.

The glassy material, obtained by evaporation of the filtrates after trituration, gave a deep red-purple color with ferric chloride. Two different orange **2,4-dinitrophenylhydrazones** were obtained by fractional crystallization (ethyl acetate) of the crude derivative from this product. The first one, m.p. 204–206°, evidently contained one ester group and a hydroxyl group, as evidenced by infrared spectrum (peaks at 2.8–2.85, 2.98, 5.77 and 6.16 $\mu$) and analysis.

*Anal.* Calcd. for $C_{28}H_{24}O_9N_4$: C, 55.20; H, 4.83. Found: C, 55.21; H, 4.86.

The second fraction had m.p. 223–225° dec. after numerous recrystallizations; this material was less soluble than the first fraction and had a deeper orange color. A satisfactory analysis could not be obtained. The infrared spectrum was very similar to that of the first derivative except that there was no hydroxyl band (2.85 $\mu$) present, and thus dehydration was indicated.

Hydrogenation of the glassy enol mixture (palladium) resulted in absorption of less than one mole of hydrogen, and no pure derivatives could be obtained from the neutral product. Hydrolysis of Ic (5% alkali) gave a neutral, ketonic product, but no crystalline derivatives could be obtained from this material.

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# COMMUNICATIONS TO THE EDITOR

## THE STRUCTURE OF FRIEDELIN. DEGRADATIVE STUDIES

*Sir:*

The terpenoid ketones, friedelin and cerin ($\alpha$-hydroxy-friedelin) belong to a new class of pentacyclic triterpenes,[1] differing from the known $\beta$-amyrin, $\alpha$-amyrin and lupeol types. We record in this and the following communication the experimental findings which have revealed the structures of these triterpenes.

The starting point for this work was the assumption that friedelin possesses partial carbon skeleton I (1,8-dimethylpicene formed by dehydrogenation[2]) and the information that the unit —CH—CH—CO—$CH_2$—$CH_2$— is present (indicated by the preparation of the $C_{29}$ $\alpha$-diketone, norfriedelendione[3]). These conditions limit the oxo function to two positions, $C_1$ and $C_3$. Proof of the location of oxygen at $C_3$ and a methyl at $C_4$ was obtained in several ways, including: (1) three-step oxidation of friedelin to a $C_{28}$, six-membered lactone (II), m.p. 228–235°, $[\alpha]^{25}D$ +9.6°,[4] infrared max. 1740 cm.$^{-1}$. Found: C, 80.83; H,

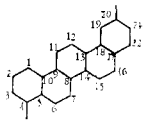
(1) N. L. Drake and R. P. Jacobsen, THIS JOURNAL, **57**, 1570 (1935).

(2) N. L. Drake and W. T. Haskins, *ibid*, **58**, 1684 (1936).

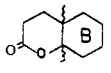
(3) L. Ruzicka, O. Jeger and P. Ringnes, *Helv. Chim. Acta*, **27**, 972 (1944).

(4) All rotations in chloroform solution (*C. ca.* 1.0).

11.07; (2) addition of bromine to $\Delta^2$-friedelene,[5] m.p. 257–258°, followed by dehydrobromination to give the exomethylenic diene III, m.p. 240–244°, $[\alpha]^{25}D$ +48.4°, $\lambda_{max}$ 241 mμ (log ε 4.30), infrared max. 883 cm.$^{-1}$. Found: C, 87.84; H, 12.32.

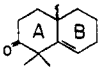


I



II

III

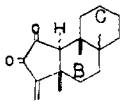


IV

Bromination of friedelin produces a 2-bromofriedelin, m.p. 210° (dec.), $[\alpha]^{25}D$ −140°, infrared, ultraviolet max. 1710 cm.$^{-1}$, 311 mμ (axial Br); found: C, 71.07; H, 9.65; Br, 15.38; location of bromine at $C_2$ proved by conversion to $\Delta^2$-friedelene.[5] Bromination of friedelin enol benzoate furnishes 4-bromofriedelin, m.p. 196–197° (dec.), $[\alpha]^{25}D$ +90.5°, infrared, ultraviolet max. 1715 cm.$^{-1}$, 310 mμ (axial Br); Found: C, 70.44; H, 9.38; Br, 15.70. Although 2-bromofriedelin is unreactive toward silver acetate, 4-bromofriedelin is readily dehydrobrominated to an unsaturated, unconjugated ketone IV, which is not isomerized to a conjugated structure, m.p. 247–248°, $[\alpha]^{25}D$ −48.6°, infrared, ultraviolet max. 1710 cm.$^{-1}$, 290 mμ; Found: C, 84.87; H, 11.20. Wolff–Kishner reduction of IV produces a new olefin, m.p. 221–222°, different from $\Delta^2$- and $\Delta^3$-friedelenes.[5] The production of IV from 4-bromofriedelin indicates that migration of a methyl group at $C_5$ has occurred during dehydrobromination.

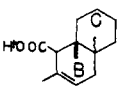
2-Bromofriedelin is not epimerized by hydrogen bromide, which proves the *trans*-locking of rings A and B and the presence of a hydrogen at $C_{10}$.[6] The change in molecular rotation due to axial bromine at $C_2(\Delta M_D$ −651°) is opposite in direction to that due to axial bromine at $C_1(\Delta M_D$ +614°). These data together with data on axial α-bromoketosteroids[7] reveal that (1) bromine is α-oriented in both 2- and 4-bromofriedelins and (2) the methyl at $C_5$ is β and the hydrogen at $C_{10}$ is α.

Stepwise oxidation of norfriedelendione (V)[5] by hydrogen peroxide and ozone produces a tetracyclic saturated ketone, $C_{25}H_{42}O^8$ (VI), which possesses the oxo function at $C_{10}$ (original numbering). Treatment of VI with excess deuterium bromide results in incorporation of only one deuterium atom/molecule proving the presence of a methyl group at $C_9$ and confirming the presence of a methyl group at $C_5$.

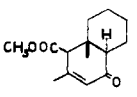


V

VI



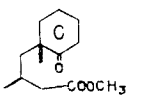
VII



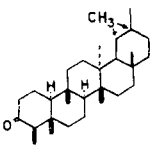
VIII

Oxidation of norfriedelendione with alkaline peroxide produces a β,γ-unsaturated acid,[8] $C_{26}H_{42}O_2$, VII. Sodium dichromate oxidation of the methyl ester of VII yields the unsaturated keto ester VIII, m.p. 150–151°, $[\alpha]^{25}D$ −42.7°, ultraviolet max. 247 mμ (log ε 3.97), infrared max. 1742; Found: C, 78.49; H, 10.05. Alcoholysis of VIII provides an unsaturated ketone (IX), m.p. 191–192°, $[\alpha]^{25}D$ −19.5°, ultraviolet max. 248 mμ (log ε 3.94), infrared max. 1664 cm.$^{-1}$; Found: C, 84.33; H, 11.38, which upon hydrogenation yields the corresponding saturated ketone X, m.p. 195–197°, $[\alpha]^{25}D$ +42.5°, infrared max. 1707 cm.$^{-1}$; Found: C, 84.02; H, 11.88.

X



XII



XIII

The presence of a hydrogen at the original $C_8$ is indicated by deuterium exchange of X with deuterium bromide (2.9 deuterium atoms/molecule) and by the three-step conversion of X via the keto acid XI to the keto methyl ester XII, m.p. 132–133°, $[\alpha]^{25}D$ +21.1°, infrared max. 1736, 1713, 1696 (weak) cm.$^{-1}$; Found: C, 77.38, H, 10.91.

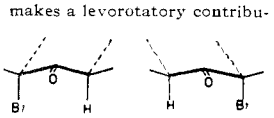
It is apparent that rings B and C and rings C and D in friedelin are *trans*-locked, both from chemical evidence[5] and from the molecular dimensions (1/4 unit cell) of friedelan-3α-ol chloroacetate, 16.5 × 6.5 × 6.9 Å. as determined by X-ray studies.[5,9]

The four remaining methyl groups of friedelin may be located as follows. Methyl groups must be present at $C_{13}$ and at $C_{14}$ since 1,2,7-trimethylnaphthalene and 1,2,8-trimethylphenanthrene are formed by selenium dehydrogenation of friedelan-3α-ol.[2] The presence of a third methyl group at $C_{17}$ and the fourth at $C_{19}$ or $C_{20}$ is highly probable on biosynthetic grounds[10] because of the probable common genesis of friedelin and the other pentacyclic triterpenes from squalene. Thus, expanded structure XIII follows for friedelin.

(5) To be described in full later.

(6) Otherwise the 2(axial)-bromoketone would be epimerizable, E. J. Corey, *ibid.*, **76**, 175 (1954).

(7) An axial bromine in the unit (a) makes a levorotatory contribution whereas that in the unit (b) makes a dextrorotatory contribution. For example, *e.g.* $\Delta M_D$ for 5α-bromo-6-ketocholestanyl acetate is −645° while that for 7α-bromo-6-ketocholestanyl acetate is +269°.



(a) (b)

(8) G. W. Perold, K. Meyerhans, O. Jeger and L. Ruzicka, *Helv. Chim. Acta*, **32**, 1246 (1949).

(9) *Cf.* methyl iodoacetyloleanolate 16.1 × 6.3 × 7.7 Å. [A. M. Abd El Rahim and C. H. Carlisle, *Chem. and Ind.*, 279 (1954)].

(10) L. Ruzicka, A. Eschenmoser and H. Heusser, *Experientia*, **9**, 357 (1953).

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RECEIVED MAY 19, 1955

## PROOF OF THE CONSTITUTION OF FRIEDELIN BY MULTI-GROUP REARRANGEMENT OF FRIEDELAN-3β-OL TO OLEAN-13(18)-ENE

*Sir:*

Formula I has been derived for friedelin by the studies described in the previous communication.[1] This structure bears a most interesting relationship to the three known classes of pentacyclic triterpenes and suggests a biosynthetic pathway starting from α- or β-amyrin which involves a series of consecutive 1,2-shifts of methyl groups and hydrogen

(1) E. J. Corey and J. J. Ursprung, THIS JOURNAL, **77**, 3667 (1955).