[Contribution from the National Institute for Medical Research and from Oberlin College]

Structures of Some 2-Methoxy-8-keto-4a-methylperhydrophenanthrenes and Related Compounds

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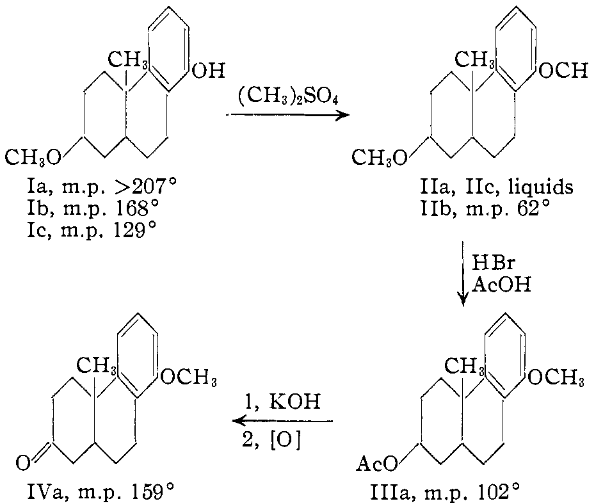
Three stereoisomers of the previously reported 2-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydro-8-phenanthrol (I) have now been separated and evidence obtained for their configurations. Selective demethylation of the dimethyl ethers (II) with hydrogen bromide in acetic acid gave the 2-acetoxy derivatives (III) which have been transformed to the *cis*- and *trans*-2-ketones (IV). The stereoisomers of I have also been hydrogenated and oxidized to give three stereoisomeric 2-methoxy-4a-methyltetradecahydro-8-phenanthrones (VI). The *trans* isomer of I gave VI with the *trans-anti-trans* ring fusion, while the *cis* isomers of I gave the *cis-syn-trans* isomers of VI. The configurations of the latter were established by conversion to the 4a-methyltetradecahydro-2,8-phenanthrenedione "A" (VIII) of Cornforth and Robinson.[3] The former was related to the *trans-anti-trans*-4a,7-dimethyltetradecahydro-2,8-phenanthrenedione (X) prepared from the Koester–Logemann ketone.

An earlier communication[1] described the synthesis of 2-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydro-8-phenanthrol (I) as a mixture of stereoisomerides, of which two were separated in crystalline form. A third isomer (Ic) has crystallized from a cyclohexane solution of the methoxyphenols previously described as non-crystalline. This isomer constitutes about one half of the methoxyphenols prepared.



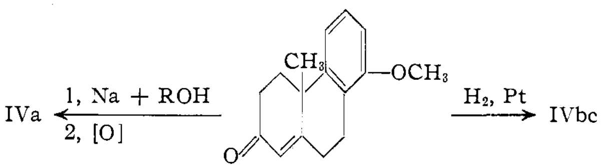
Ia, m.p. >207°
Ib, m.p. 168°
Ic, m.p. 129°

IIa, IIc, liquids
IIb, m.p. 62°

IVa, m.p. 159°
IVbc, m.p. 121°

IIIa, m.p. 102°
IIIb, m.p. 98°
IIIc, liquid

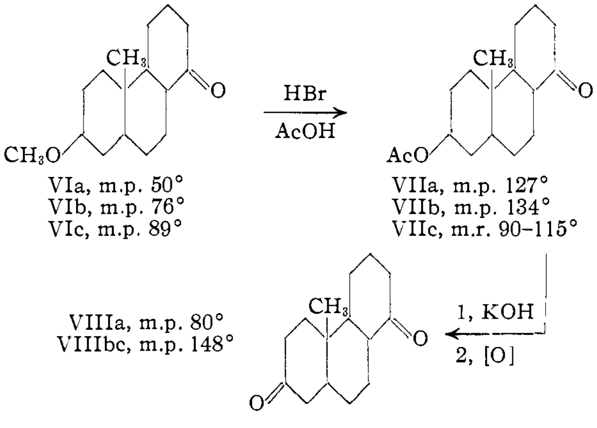
Catalytic hydrogenation of 4a-methyl-8-methoxy-2,3,4,4a,9,10-hexahydro-2-phenanthrone (V), which is available by a different synthetic method,[2] affords 4a-methyl-8-methoxy-1,2,3,4,4a,9,10,10aβ-octahydro-2-phenanthrone (IVbc); the *cis* relationship of the alicyclic rings in this substance is proved by further transformations.[3] We now find that an isomeric ketone which must be 4a-methyl-8-methoxy-1,2,3,4,4a,9,10,10aα-octahydro-2-phenanthrone (IVa), with a *trans* junction of the alicyclic rings, may be obtained by reduction of the unsaturated ketone (V) with sodium and amyl alcohol, followed by an Oppenauer oxidation.



V

Correlation of the methoxyphenols (I) with these ketones of known configuration was effected by the reaction sequence I → IV. The selective cleavage of the alicyclic ether group in IIa, IIb and IIc under mild conditions demonstrates the significance of the work of Burwell, Elkin and Maury[4] for synthetic schemes. The *trans*-ketone (IVa) was obtained from methoxyphenol Ia and the *cis*-ketone (IVbc) from methoxyphenols Ib and Ic. Further, catalytic hydrogenation of the ketone IVa gave two epimeric alcohols, one of which gave an acetyl derivative identical with IIIa.

It was shown previously[1] that hydrogenation of methoxyphenols (I), followed by oxidation, produced 2-methoxy-4a-methylperhydro-8-phenanthrones (VI). We have prepared a methoxy ketone (VIa) from Ia and have obtained the methoxy ketones (VIb and VIc) from Ib and Ic as crystalline solids.



VIa, m.p. 50°
VIb, m.p. 76°
VIc, m.p. 89°

VIIa, m.p. 127°
VIIb, m.p. 134°
VIIc, m.r. 90–115°

VIIIa, m.p. 80°
VIIIbc, m.p. 148°

Treatment of the methoxy ketones (VIa, VIb and VIc) with hydrogen bromide in acetic acid has produced three acetoxy ketones (VIIa, VIIb and VIIc). Saponification followed by oxidation has given two diketones (VIIIa and VIIIbc). The diketone (VIIIbc) obtained from both VIb and VIc is identical with the "A" diketone prepared by Cornforth and Robinson[3] and known to be *dl*-4a-methyl-1,2,3,4,4a,4bβ,5,6,7,8,8aα,9,10,10aβ - tetradecahydro -

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(1) W. B. Renfrow, A. Renfrow, E. Shoun and C. A. Sears, This Journal, **73**, 317 (1951).

(2) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 676 (1946).

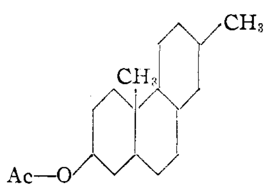
(3) J. W. Cornforth and R. Robinson, *ibid.*, 1855 (1949).

(4) R. L. Burwell, L. M. Elkin and L. G. Maury, This Journal, **73**, 2428 (1951).

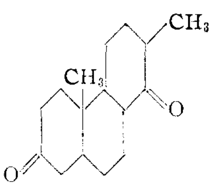
2,8-phenanthrenedione.[5] The configuration of the alicyclic rings in VIb, VIc, VIIb and VIIc is thus established.

The diketone (VIIIa) obtained from VIa may be the same as a diketone of undetermined configuration at the 4b-position reported by Wilds, Ralls, Wildman and McCaleb[6] although there is a considerable discrepancy (18°) in decomposition temperatures of bis-dinitrophenylhydrazones.

To establish the configuration at the 4b-position in VIa, VIIa and VIIIa, we have used the modified Sen–Mondal methylation procedure[3] to convert VIa to 2-methoxy-4a,7-dimethylperhydro-8-phenanthrone and thence through the 2-acetoxy analog (IX) to 4a,7-dimethylperhydro-2,8-phenanthrenedione (X). The infrared absorption spectrum of X was practically identical with the spectrum[7] of the optically active 4a,7-dimethyl-1,2,3,4,4a,4bα,5,6,7,8,8aβ,9,10,10aα-tetradecahydro-2,8-phenanthrenedione prepared from the Koester–Logemann acetate by the method of Billeter and Miescher,[8] and we conclude that VIa and related compounds have the "natural" or α-configuration at the 4b-position.

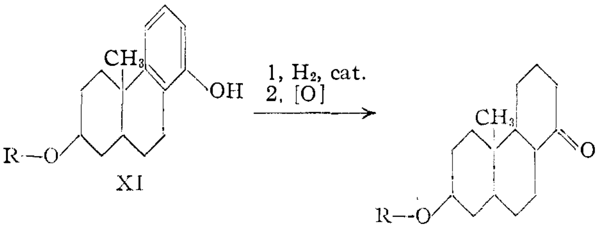


IX



X

Three examples are now known of the transformation XI → XII when the alicyclic rings in XI have the *cis* relationship. In the two cases reported here (R = CH_3) the new alicyclic ring has largely assumed the "unnatural" configuration (4bβ), and in the third (R = Ac) the "unnatural" form predominates over the "natural" by about six to one.[3] From Ia, where the alicyclic rings are in *trans* relationship, the "natural" configuration (4bα) was formed almost exclusively. Thus the configuration at the previously existing bridgehead decisively influences that of the newly-formed bridgehead.



XI XII

The infrared spectrum[9] of IX prepared from VIa was appreciably different in the 7.5 to 12 μ range from that[9] of optically active 2β-acetoxy-4a,7-dimethylperhydro-8-phenanthrone prepared[8] from the Koester–Logemann acetate. Similar differences in infrared spectra have been reported[10] between epimeric 3-acetoxycholestanes. Since it is unlikely that inversion took place during the cleavage of the methoxy group with hydrogen bromide in acetic acid,[4] we conclude that IX and related compounds (Ia, IIIa, VIa and VIIa) have the 2α-configuration.

We are tentatively assigning the β-configuration to the 2-methoxy and 2-acetoxy groups in the b-series (Ib, IIb, IIIb, VIb and VIIb). The acetoxy ketone VIIb was identical with the "A" acetoxy ketone reported by Cornforth and Robinson,[3] for which rotational differences among derivatives of the ketoalcohol suggest a β-configuration for the hydroxyl group.[11] Since the c-series is epimeric at C-2 with the b-series, a tentative assignment of the 2α-configuration to the methoxy and acetoxy groups in Ic, IIIc, VIc and VIIc is made.

Attempts to resolve the methoxy ketone VIa as the 1-menthydrazide[12] and as the ketal of D(levo)-2,3-butanediol have been unsuccessful. The ketal from VIa and D(levo)-2,3-butanediol is a liquid, and the diastereoisomers were not separated by chromatography on alumina.

Experimental

Further Data on Compounds Previously Prepared.[1]—*dl*-2α-Methoxy-4a-methyl-1,2,3,4,4a,9,10,10aα-octahydro-8-phenanthrol (Ia) appears to have no definite and reproducible melting point. Repeated crystallization from ethanol, *n*-butanol or acetic acid gave erratic results, material melting as low as 207–210° and as high as 235–238° having been obtained. The melting range after most crystallizations was somewhere between these extremes. Acetylation of both high- and low-melting specimens (1 g.) with acetic anhydride (1 ml.) and pyridine (0.5 ml.) produced identical acetates (*dl*-2α-methoxy-4a-methyl-8-acetoxy-1,2,3,4,4a,9,10-10aα-octahydrophenanthrene) which crystallized in well-formed platelets from ligroin and melted 100–102°.

Anal. Calcd. for $C_{15}H_{24}O_3$: C, 75.0; H, 8.4. Found: C, 75.3; H, 8.5.

The phenol recovered by hydrolysis of this acetate behaved on crystallization in the same way as before.

The Debye–Scherrer X-ray diffraction patterns of high-, intermediate- and low-melting specimens of Ia were identical.[13]

The melting point previously reported (171°) for *dl*-2β-methoxy-4a-methyl-1,2,3,4,4a,9,10,10aβ-octahydro-8-phenanthrol (Ib) is about 3° higher than we have later obtained (168°) with more carefully purified material. The 3,5-dinitrobenzoate of this methoxyphenol crystallized from ethanol as small needles melting at 139°.

Anal. Calcd. for $C_{23}H_{25}O_7N_2$: C, 62.7; H, 5.5. Found: C, 62.8; H, 5.8.

dl-2α-Methoxy-4a-methyl-1,2,3,4,4a,9,10,10aβ-octahydro-8-phenanthrol (Ic) was isolated from a cyclohexane solution of the methoxyphenols which would not crystallize from ethanol. The material came out of solution slowly at room temperature as a coarse powder melting 108–120°. The yield from 232 g. of mixed isomers was 93 g. Recrystallization from ethyl acetate produced hard, poorly-formed crystals melting 125–129°. The *p*-nitrobenzoate of this methoxyphenol (Ic) melted 125–127° after crystallization from ethyl acetate.

Anal. Calcd. for $C_{23}H_{25}O_6N$: C, 69.9; H, 6.4. Found: C, 69.9; H, 6.4.

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[5] Configurations are indicated according to the suggestions of L. F. Fieser in "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, N. Y., 1949, p. 6.

[6] A. L. Wilds, J. W. Ralls, W. C. Wildman and K. E. McCaleb, THIS JOURNAL, **72**, 5794 (1950).

[7] We are grateful to Drs. H. M. E. Cardwell and F. B. Strauss for determining and interpreting these spectra.

[8] J. R. Billeter and K. Miescher, *Helv. Chim. Acta*, **33**, 388 (1950).

[9] We are grateful to Dr. R. A. Briggs and Mr. J. J. Shipman for determining these spectra.

[10] A. Furst, H. H. Kuhn, R. Scotoni and H. H. Gunthard, *Helv. Chim. Acta*, **35**, 951 (1952).

[11] W. Klyne, private communication.

[12] R. B. Woodward, T. P. Kohman and G. C. Harris, THIS JOURNAL, **63**, 120 (1941).

[13] We are grateful to Mrs. O. Kennard for preparing and interpreting the X-ray photographs.

There was obtained 50 g. of phenolic material from 232 g. of mixed isomers which would not crystallize from cyclohexane. This fraction contains some of the isomer Ic and probably also the isomer with the alicyclic rings *trans* and the configuration of the methoxy group different from Ia.

2,8-Dimethoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrenes (IIa, IIb, IIc).—The methoxyphenol (1.23 g.) was dissolved in a mixture of 2.5 ml. of 2 *N* sodium hydroxide and 3 ml. of methanol. Dimethyl sulfate (0.47 ml.) was added and the solution heated for several minutes. The same quantities of sodium hydroxide and dimethyl sulfate were again added and the heating continued for 20 minutes. The mixture was diluted with water, extracted with ether, the ether layer washed several times with 2 *N* sodium hydroxide, once with water and dried ($MgSO_4$). Removal of the solvent left the diether (about 1 g.). The diether from Ib solidified, and crystallized from petroleum ether as small needles melting 61–62°.

Anal. Calcd. for $C_{17}H_{24}O_2$: C, 78.4; H, 9.3. Found: C, 78.0; H, 9.3.

The diethers from Ia and Ic were liquids and were not further purified.

2-Acetoxy-8-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrenes (IIIa, IIIb, IIIc).—The diethers were treated with a 5% excess of a 30% solution of hydrogen bromide in glacial acetic acid. The flasks were tightly stoppered and placed in a warm room at 38°. The reaction time was 24 hours for IIa and IIc; 48 hours were necessary for IIb. The reaction mixtures were diluted with water, extracted with ether, washed twice with water, once with aqueous sodium bicarbonate, dried ($MgSO_4$), and the solvent removed. The products from IIa and IIb solidified, and were recrystallized from 60–80° ligroin. Yields were 50–60% of the theoretical amounts. *dl*-2α-Acetoxy-8-methoxy-4a-methyl-1,2,3,4,4a,9,10,10aα-octahydrophenanthrene (IIIa) crystallized as small needles melting 101–102°.

Anal. Calcd. for $C_{18}H_{24}O_3$: C, 75.0; H, 8.4. Found: C, 75.1; H, 8.4.

dl-2β-Acetoxy-8-methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-β-octahydrophenanthrene (IIIb) crystallized as irregular plates melting 96–99°.

Anal. Calcd. for $C_{18}H_{24}O_3$: Found: C, 74.8; H, 8.2.

8-Methoxy-4a-methyl-1,2,3,4,4a,9,10,10a-octahydro-2-phenanthrones (IVa and IVbc) from IIIa, IIIb and IIIc.—The crystalline acetoxy ethers (IIIa and IIIb), and the crude product from the cleavage of IIc were saponified with potassium hydroxide in aqueous methanol. The reaction mixtures were distilled from a steam-bath to remove most of the methanol, diluted with water, extracted with ether and the ether layer washed with water. The residues from evaporation of the ether solutions were taken up in benzene and the benzene distilled to ensure removal of traces of methanol. The methoxy alcohols so obtained from IIIa and IIIb were oxidized without further purification. The alcoholic material from crude IIIc was isolated *via* the acid succinate before oxidation. The crude hydroxy ketone (1 g.) was mixed with succinic anhydride (0.7 g.) and pyridine (3 ml.) and heated on a boiling water-bath for 1 hour. The cooled reaction mixture was treated with 2 *N* sodium carbonate solution (15 ml.), water (20 ml.) and extracted twice with ether. Sodium hydroxide (2 g.) was added to the aqueous layer and the solution boiled gently for 30 minutes. The thick oil which came out of solution was extracted with ether, the ether layer washed with water, dilute hydrochloric acid, water and dried ($MgSO_4$). Evaporation of the ether left the hydroxy ketone (0.6 g.).

The oxidation procedures are illustrated by the following example. The methoxy alcohol from IIIa (740 mg.), toluene (25 ml.), cyclohexanone (3 ml.) and aluminum isopropoxide (500 mg.) were refluxed about 90 minutes. A small amount of water was added to precipitate aluminum oxides. The organic layer was separated by decantation and steam distilled. The residue from the steam distillation was extracted with ether and the ether layer washed, dried ($MgSO_4$) and evaporated. Crystallization of the residue from ethanol gave IVa (400 mg., 64%) as well formed needles melting 156–158°.

The methoxy ketone obtained from both IIIb and IIIc melted 120–121° and was identical with the 8-methoxy-4a-methyl-1,2,3,4,4a,9,10,10aβ-octahydro-2-phenanthrone prepared by Cornforth and Robinson.[2,3]

8-Methoxy-4a-methyl-1,2,3,4,4a,9,10,10aα-octahydro-2-phenanthrone (IVa) from 8-Methoxy-4a-methyl-2,3,4,4a,-9,10-hexahydro-2-phenanthrone (V).—A solution of the unsaturated ketone (V, 20 g.) in boiling amyl alcohol (750 ml.) was stirred and sodium (55 g.) added over a period of 15 minutes. Stirring and refluxing were continued until practically all the sodium had reacted. Water (300 ml.) was added cautiously to the hot, stirred solution. The organic layer was separated, washed with water (75 ml.) and steam distilled. The residue from the steam distillation was extracted with ether, washed with water and distilled. The yield of viscous oil boiling 150–155° at 0.05 mm. was 19.8 g. The distillate was refluxed with toluene (400 ml.), cyclohexanone (60 ml.) and aluminum isopropoxide (8 g.) for 2 hr., and the reaction mixture worked up as described above for the same reaction. Crystallization from ethanol gave 4.4 g. (20%) of small needle-shaped crystals melting 156–158°. This compound is identical with the methoxy ketone obtained from IIIa.

Anal. Calcd. for $C_{16}H_{20}O_2$: C, 78.7; H, 8.3. Found: C, 78.7; H, 8.3.

The 2,4-dinitrophenylhydrazone crystallized as small rods from dioxane–water, and melted 203–204°.

Anal. Calcd. for $C_{22}H_{24}O_5N_4$: C, 62.3; H, 5.7. Found: C, 62.1; H, 5.9.

Catalytic hydrogenation of IVa with a platinum catalyst in acetic acid produced two epimeric methoxy alcohols which we were unable to separate by crystallization. However, the acetates of these alcohols, corresponding to III, were separable by crystallization. From 1 g. of mixed epimers there was obtained 0.34 g. of flattened needles (from ligroin) melting 106–107° and 0.11 g. of stout, pointed needles (from ligroin) melting 101–102°. A mixed melting point was strongly depressed. The isomer melting 101–102° gave no depression of the melting point when mixed with IIIa. The isomer melting 106–107° must be *dl*-2β-acetoxy-8-methoxy-4a-methyl-1,2,3,4,4a,9,10,10aα-octahydrophenanthrene.

Anal. Calcd. for $C_{18}H_{24}O_3$: C, 75.0; H, 8.4. Found: C, 74.6; H, 8.3.

2α-Methoxy-4a-methyl-1,2,3,4,4a,4bα,5,6,7,8,8aβ,9,10aα-tetradecahydro-8-phenanthrone (VIa).—The aromatic ring in Ia was hydrogenated in the presence of Raney nickel and potassium hydroxide as previously described.[1] Nickel catalysts which have been thoroughly digested and washed with alkali to remove aluminum give better results in these hydrogenations than catalysts[14] from which all the aluminum has not been removed.

The product (12 g.) from hydrogenation of Ia (13 g.) was dissolved in 100 ml. of acetic acid. A solution of chromium trioxide (5.5 g.) in a small amount of water was diluted with 50 ml. of acetic acid and added in portions to the solution of perhydrophenanthrol. The reaction mixture was allowed to stand about 20 hours at room temperature, diluted with water (800 ml.) and extracted three times with ether. The ether solution was washed three times with water, once with 2 *N* sodium hydroxide, once with water and dried ($MgSO_4$). The residue from evaporation of the ether (10.2 g.) boiled 162–164° at 0.5 mm. The distillate (8.5 g.) was dissolved in an equal volume of ligroin, cooled in Dry Ice to induce crystallization and the solid filtered on to a funnel cooled with Dry Ice. The yield of methoxy ketone melting 49–51° was 6.5 g. The mother liquor from the crystallization was concentrated and the residue converted to an oxime. The oxime crystallized from *n*-butanol as well-formed needles which melted sharply at 206–208°. There was obtained 1.3 g. of oxime, which gave an additional 1.1 g. of methoxyketone after treatment with pyruvic acid. The total yield of purified methoxy ketone was 7.6 g. (62%).

Anal. Calcd. for $C_{16}H_{26}O_2$: C, 76.8; H, 10.5. Found: C, 76.7; H, 10.4. Calcd. for $C_{16}H_{27}O_2N$: C, 72.4; H, 10.3. Found: C, 72.1; H, 10.4.

***dl*-2β-Methoxy-4a-methyl-1,2,3,4,4a,4bβ,5,6,7,8,8aα,9,-10,10aβ-tetradecahydro-8-phenanthrone (VIb) and *dl*-2α-Methoxy-4a-methyl-1,2,3,4,4a,4bβ,5,6,7,8,8aα,9,10,-10aβ-tetradecahydro-8-phenanthrone (VIc).**—These compounds were originally reported[1] as liquids, but have crystallized after purification through the oximes. Recrystallization of VIb from ligroin at low temperature produced

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[14] H. R. Billica and H. Adkins, *Org. Syntheses*, **29**, 24 (1949).

thin, irregular platelets melting 74–76°. The oxime of VIb crystallized from ethanol as thin, irregular plates melting 184–186°.

Anal. Calcd. for $C_{16}H_{27}O_2N$: C, 72.4; H, 10.3. Found: C, 72.8; H, 10.3.

Recrystallization of VIc from ligroin produced well-formed rods melting 88–89°. The oxime of VIc crystallized from ethanol as small needles melting 204–206°.

Anal. Calcd. for $C_{16}H_{27}O_2N$: as above. Found: C, 72.0; H, 10.2.

2-Acetoxy-4a-methylperhydro-8-phenanthrones (VIIa, VIIb, VIIc).—Cleavage of the methoxy group in the methoxy ketones (VIa, VIb, VIc) with hydrogen bromide in acetic acid was carried out as described above for diethers.

dl-2α-Acetoxy-4a-methyl-1,2,3,4,4a,4bα,5,6,7,8,8aβ,9,-10,10aα-tetradecahydro-8-phenanthrone (VIIa) crystallized from ethanol as small, irregular plates melting 125–127°.

Anal. Calcd. for $C_{17}H_{26}O_3$: C, 73.4; H, 9.4. Found: C, 73.1; H, 9.0.

dl-2β-Acetoxy-4a-methyl-1,2,3,4,4a,4bβ,5,6,7,8,8aα,9,-10,10aβ-tetradecahydro-8-phenanthrone (VIIb) crystallized from benzene–ligroin as large rods and melted 133–134°. The melting point was not depressed by admixture with a sample of the "A" acetoxy ketone prepared by Cornforth and Robinson.[3] A solvated form of this acetate was previously reported[3] to melt at 129–130°. Recrystallization of the original specimen from benzene–ligroin gave material m.p. 133–134°.

dl-2α-Acetoxy-4a-methyl-1,2,3,4,4a,4bβ,5,6,7,8,8aα,9,-10,10aβ-tetradecahydro-8-phenanthrone (VIIc) crystallized as irregular fragments from ligroin, and melted gradually over the range 90–115°.

Anal. Calcd. for $C_{17}H_{26}O_3$: Found: C, 73.5; H, 9.4.

4a-Methylperhydro-2,8-phenanthrenediones (VIIIa, VIIIbc).—The acetoxy ketones were saponified to hydroxy ketones with potassium hydroxide in aqueous methanol. The procedure for oxidation of the hydroxy ketones to diketones was the same as described above for oxidation of 2-methoxy-4a-methylperhydro-8-phenanthrol. Yields of diketones from acetoxy ketones were 30–60%.

dl-4a-Methyl-1,2,3,4,4a,4bα,5,6,7,8,8aβ,9,10,10aα-tetradecahydro-2,8-phenanthrenedione (VIIIa) crystallized from cyclohexane or ligroin as thin, fragile plates melting 79–81°. The bis-dinitrophenylhydrazone of VIIIa was prepared by gently boiling for 30 min. a solution of the diketone (13 mg.), dinitrophenylhydrazine (30 mg.) and one drop of sulfuric acid in 10 ml. of *n*-butanol. The bis-dinitrophenylhydrazone crystallized from the reaction mixture as small needles melting with decomposition at 245°. The bis-ethyleneketal of VIIIa crystallized from ligroin as thin needles melting 149–150°.

Anal. Calcd. for $C_{15}H_{22}O_2$: C, 76.9; H, 9.5. Found: C, 76.5; H, 9.7. Calcd. for $C_{27}H_{30}O_8N_4$: C, 54.5; H, 5.1. Found: C, 54.3; H, 5.3. Calcd. for $C_{19}H_{30}O_4$: C, 70.8; H, 9.4. Found: C, 70.5; H, 9.5.

Another diketone (VIIIbc) was obtained from both VIIb and VIIc. This diketone crystallized from cyclohexane as well-formed prisms melting 146–148°, and was identical with the "A" diketone prepared by Cornforth and Robinson.[2,3]

***dl*-4a,7-Dimethyl-1,2,3,4,4a,4bα,5,6,7,8,8aβ,9,10,10aα-tetradecahydro-2,8-phenanthrenedione (X).**—The methoxy ketone (VIa, 2.00 g.) was formylated, methylated with methyl iodide in the presence of potassium carbonate and, after separation of O-methylated material, the formyl group was removed by alkaline hydrolysis in the manner described previously.[3] The 2-methoxy-4a,7-dimethylperhydro-8-phenanthrone (0.9 g., 41%) so obtained melted 78–79° after crystallization from ligroin.

Anal. Calcd. for $C_{17}H_{28}O_2$: C, 77.2; H, 10.7. Found: C, 77.3; H, 10.6.

Cleavage of the methoxy group with hydrogen bromide in acetic acid afforded an acetoxy ketone (IX, 0.6 g., 60%) which melted 129–132° after crystallization from ligroin. A small part of the acetoxy ketone was recrystallized from ethanol and the melting point raised to 134–135°.

Anal. Calcd. for $C_{18}H_{28}O_3$: C, 73.9; H, 9.7. Found: C, 73.7; H, 9.7.

The acetoxy ketone (IX, 0.6 g.) was saponified and oxidized as described above for VII. The dimethylperhydro-2,8-phenanthrenedione (0.4 g., 78%) thus obtained crystallized from ligroin as flat, rectangular plates and melted 87–88°.

Anal. Calcd. for $C_{16}H_{24}O_2$: C, 77.4; H, 9.7. Found: C, 77.4; H, 9.8.

2β-Acetoxy-4a,7-dimethyl-1,2,3,4,4a,4bα,5,6,7,8,8aβ,-9,10,10aα-tetradecahydro-8-phenanthrone and 4a,7-dimethyl-1,2,3,4,4a,4bα,5,6,7,8,8aβ,9,10,10aα-tetradecahydro-2,8-phenanthrenedione were prepared from the Koester-Logemann acetate by the procedure of Billeter and Miescher.[8]

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[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY]

The Structure of Ketene Dimer

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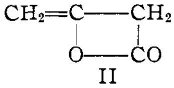
The isotope exchange reactions of ketene dimer, the liquid methylketene dimer, and related acetoacetic esters with methanol-*d* have been studied. Exchanges with the α-hydrogens of the acetoacetic esters are extremely rapid, while with ketene dimer the exchange is quite slow (even at reflux temperature) and with methylketene dimer the rate is exceedingly slow. Methanolysis of these dimers leads to acetoacetic esters in which a substantial proportion of deuterium enters into the γ-position. This evidence is used to support the conclusion that ketene dimer is a single molecular species to be represented as 3-butenoic β-lactone (II). Methylketene dimer, and presumably the liquid dimers of other alkylketenes, can be represented as 2,4-dialkyl-3-butenoic β-lactone structures.

The structure of ketene dimer has been the subject of considerable investigation and controversy since the first appearance of its description in the chemical literature in 1908.[1] The following five formulas have at one time or another received serious consideration.[2]

$CH_3—CO—CH=C=O$

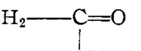
I

acetylketene



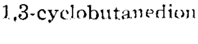
II

3-butenoic β-lactone



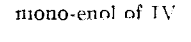
III

2-butenoic β-lactone



IV

1,3-cyclobutanedione



V

mono-enol of IV

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[1] F. Chick and N. T. M. Wilsmore, *J. Chem. Soc.*, **93**, 946 (1908).

[2] For a review of the earlier work see: W. E. Hanford and J. G. Sauer, "Organic Reactions," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 127.