from O-deuteriomethanol; mass spectrum, *m/e* 389 (d_3), 19%; *m/e* 390 (d_4), 81%.

5α-Cholestan-2β-ol-1,1,3,3-d_4 (XVI) was prepared by lithium tri-*t*-butoxyaluminum hydride[15] reduction of XV as described for the analogous formation of II to provide 5α-cholestan-2β-ol-1,1,3,3-d_4 and a trace of the 2α isomer. Recrystallization of a portion from methanol gave the pure 2β-alcohol, mp 152–154° (for unlabeled alcohol, see ref 21).

Δ²-5α-Cholestene-1,1,3-d_3 (XVII).—The above mixture (465 mg) of 5α-cholestan-2β-ol-1,1,3,3-d_4 and its C-2 epimer was treated with *p*-toluenesulfonyl chloride in pyridine for 25 hr at room temperature and the semisolid which was isolated in the usual manner was dehydrotosylated by heating in 10 ml of dimethyl sulfoxide at 100–103° for 5 hr.[22] The cooled solution was poured into water and extracted with ether, and the ethereal extract was washed with water, 5% sodium bicarbonate (three times), and water (two times), and dried over anhydrous magnesium sulfate. Ether was removed under reduced pressure and a small amount of dimethyl sulfoxide that remained was removed by evaporation at vacuum-pump pressure (0.1 mm). The remaining oil was chromatographed over 60 g of neutral alumina, activity II. Petroleum ether (bp 60–68°) elution furnished 186 mg of Δ²-5α-cholestene-1,1,3-d_3 (XVII), mp 72.5–73° after recrystallization from acetone. Elution with 20% ether in benzene afforded 85 mg of unreacted starting material XVI (mp 155–156° from methanol), and further increasing the eluent polarity to 35% ether in benzene provided 30 mg of 5α-cholestan-2α-ol-1,1,3,3-d_4 (mp 180–181° from methanol).

5α-Cholestan-3α-ol-1,1,3β-d_3 (XIX).—To a solution of 130 mg of XVII in 4 ml of anhydrous ether was added a solution of 85 mg of *m*-chloroperbenzoic acid in 3 ml of anhydrous ether, and the resulting homogeneous solution was kept at room temperature in the dark for 3 days. The ethereal solution was washed well with 5% sodium bicarbonate and water and dried over anhydrous magnesium sulfate. Evaporation of the solvent afforded 132 mg of crystalline material (2α,3α-oxido-5α-cholestane-1,1,3-d_3[21]) which was not purified further but was converted directly to 5α-cholestan-3α-ol-1,1,3β-d_3 (XIX) by heating under reflux for 3 hr with excess lithium aluminum hydride in ether.[21] The crude reduction product was purified by chromatography over 20 g of neutral alumina, activity II, using benzene as eluent, giving 63 mg of crystalline XIX: mp 184–186° after recrystallization from methanol; mass spectrum, *m/e* 389 (d_1), 2%; *m/e* 390 (d_2), 18%; *m/e* 391 (d_3), 80%.

5α-Cholestan-3β-ol-1,1-d_2 (XXI).—The trideuterio alcohol XIX (52 mg) was dissolved in acetone by gentle warming and treated with Jones[18] reagent until an orange color persisted for 1 min. The reaction mixture was concentrated under reduced pressure, poured into water, and extracted with ether. The ethereal extract was washed with water, 5% sodium bicarbonate, and water and dried over magnesium sulfate. Evaporation of solvent under diminished pressure afforded 50 mg of 5α-cholestan-3-one-1,1-d_2 (XX), which after a recrystallization from methanol exhibited a melting point of 127.5–129°.

5α-Cholestan-3β-ol-1,1-d_2 was prepared by lithium tri-*t*-butoxyaluminum hydride[15] reduction of the corresponding ketone as described above (see preparation of II) and was purified by preparative thin layer chromatography in a 3:1 benzene–ether solvent system. Recrystallization from methanol afforded XXI: mp 143–144.5°; mass spectrum, *m/e* 388 (d_0), 3%; *m/e* 389 (d_1), 16%; *m/e* 390 (d_2), 81%.

Acknowledgment.—The work was performed with financial assistance of the National Institutes of Health, U. S. Public Health Service (Grant No. CA07195).

(21) A. Fürst and P. A. Plattner, *Helv. Chim. Acta*, **32**, 275 (1949).
(22) D. N. Jones and M. A. Saeed, *J. Chem. Soc.*, 4657 (1963).

Synthesis and Stereochemistry of Hydrophenanthrenes. IV. 1,2,3,4,4aα,4bβ,5,6,7,9,10,10aβ-Dodecahydro-4,7-dioxo-2α-phenanthrenecarboxylic Acid[1,2]

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Received September 24, 1965

Two synthetic routes leading to the title compound, the racemic *anti–trans* diketo acid IX, are described. Both involve the metal–ammonia reduction of ring A of an octahydrophenanthrene derivative (III or XVII). While the B/C *trans* hydroxy acid XVII could be converted directly to the desired *anti–trans* diketo acid IX, the synthesis from the B/C *cis* hydroxy acid III required the inversion of the 4a-C center. The structural and stereochemical assignments were confirmed by nmr spectroscopy.

In continuation of the work aimed at the synthesis of steroid-like compounds and toward the elucidation of the stereochemistry of hydrophenanthrene derivatives,[4–6] the preparation of the title compound, the racemic *anti–trans* diketo acid IX, is described.

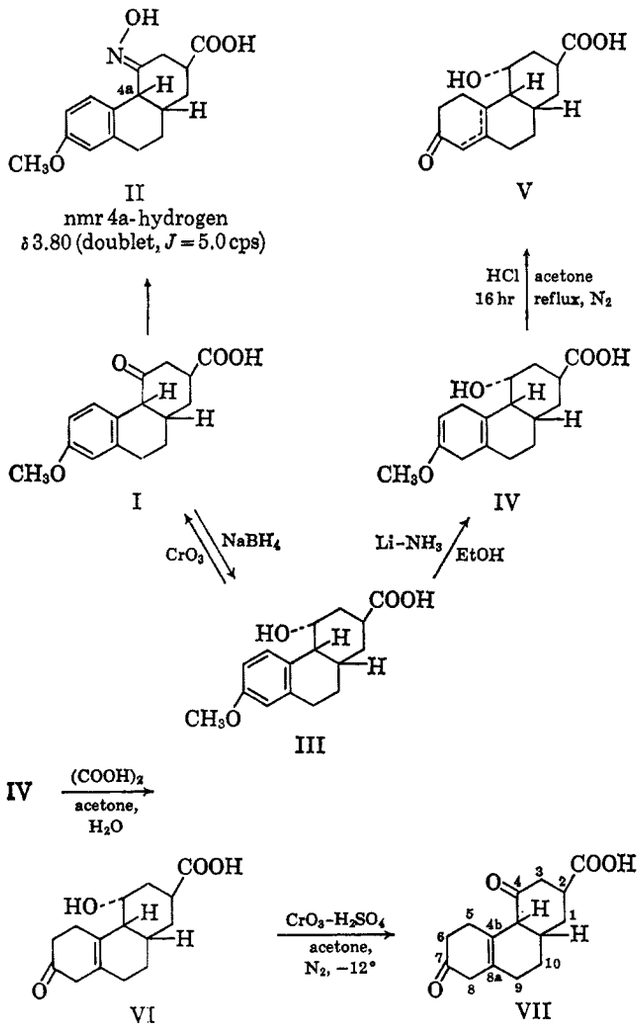
Two synthetic routes have been developed for the preparation of the title compound. One starts with the B/C *cis* keto acid I and the other with the B/C *trans* keto acid XV. The stereochemistry of the starting materials (I and XV) has already been established by chemical means, and by nmr spectroscopy of their respective oximes, II and XVI.[5] The signal of the 4a-hydrogen of II appeared at δ 3.80 (doublet, J = 5.0 cps), whereas the signal of the 4a-hydrogen of XVI is at δ 3.53 (doublet, J = 8.0 cps). This is in agreement with the relationship established between the dihedral angle and the coupling constant of vicinal hydrogens.

The B/C *cis* keto acid I was first reduced with sodium borohydride to the nonlactonizing B/C *cis* hydroxy acid III. This acid III could be oxidized back to the B/C *cis* keto acid I which shows that no change in the configuration occurred during the reduction.[5] The lithium in liquid ammonia reduction of ring A of this hydroxy acid III (rather than the keto acid I) was undertaken to avoid a mixture of stereoisomers at C-4 and C-4a, respectively (see Scheme I).

The use of the original Birch procedure yielded considerable amounts of tetrahydro derivatives with or

(1) Presented before the Organic Chemical Division at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965.
(2) All compounds described in this paper are racemates. As a matter of convenience, only one enantiomeric series (10aβ-hydrogen) has been pictured.
(3) Deceased Feb 17, 1964.
(4) Paper I: Z. G. Hajos, K. J. Doebel, and M. W. Goldberg, *J. Org. Chem.* **29**, 2527 (1964).
(5) Paper II: Z. G. Hajos, D. R. Parrish, and M. W. Goldberg, *ibid.*, **30**, 1213 (1965).
(6) Paper III: Z. G. Hajos, D. R. Parrish, and M. W. Goldberg, *ibid.*, **30**, 2849 (1965).

SCHEME I



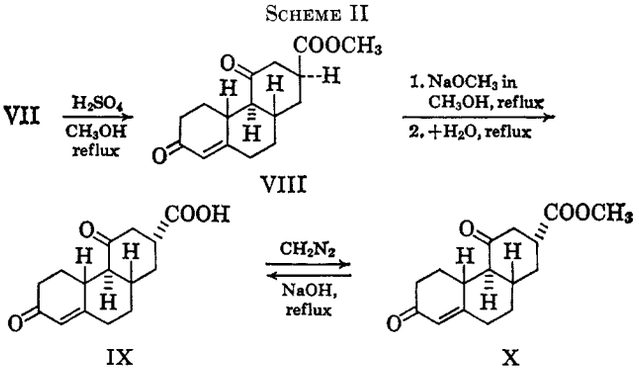
without the loss of the methoxyl group.[7] In order to keep the amount of these secondary products to a minimum, the presence of any considerable excess of lithium metal had to be avoided at all times during the reduction. It was thus possible to isolate the dihydro derivative IV, mp 180–182° dec, in a 50% yield, after recrystallization from acetone.

When IV was refluxed in acetone with aqueous hydrogen chloride for 16 hr under nitrogen, a mixture (V) was obtained which, according to ultraviolet spectroscopy, contained only about 29% α,β-unsaturated ketone. This is in good agreement with previous findings on compounds with a B/C *cis* ring junction,[8] and it is probably due to the greater stability of the double bond at the 4b,8a-position with this configuration.[9]

The enol ether group of IV could be hydrolyzed to a β,γ-unsaturated ketone.[10] Stirring IV at 20° in acetone containing oxalic acid dissolved in a little water gave the ketohydroxy acid VI, mp 200–202°, in a 97% yield. This acid (VI) was then oxidized at −12° under nitrogen[11] (to avoid hydroperoxide formation and oxidation of the double bond) with chromium trioxide–sulfuric acid in acetone to the diketo acid VII, mp 152–153.5°. The position of the double bond was confirmed by the absence of a vinylic proton in the nmr spectrum.

Refluxing the *cis* diketo acid VII with 0.8 *N* sulfuric acid in methanol gave a product (VIII), which contained approximately 95% α,β-unsaturated ketone as determined by the ultraviolet spectrum of the mixture (see Scheme II). This is in sharp contrast with the

SCHEME II



result obtained with the B/C *cis* 4-hydroxy acid IV, and indicates that a B/C *cis* → *trans* inversion has taken place. This was possible because of the proximity of the 4-keto group to the ring junction in VII. In agreement with published data, the amount of α,β-unsaturated ketone in ring A, therefore, is a good criterion as to the nature of the B/C ring junction.[8,12]

Work-up and recrystallization from acetone gave the B/C *trans* α,β-unsaturated keto ester VIII, mp 158–159°, in 60% yield. The ultraviolet spectrum, λ_{max}^{EtOH} 239 mμ (ε 16,250), confirms the 8,8a-position of the double bond. The nmr spectrum is in agreement with the suggested structure. It shows a vinylic proton at δ 5.85 (singlet), and the C-2 equatorial proton as a multiplet centered at δ 3.22 (Figure 1). Inversion of the B/C *cis* ring junction of the diketo acid VII during the sulfuric acid treatment was therefore not accompanied by a change in the β configuration of the substituent in the 2-position.

Equilibration of the ester group of VIII with refluxing sodium methoxide in methanol, followed by saponification gave the desired *anti-trans* diketo acid IX. Subsequent reesterification with diazomethane gave an isomeric *anti-trans* diketo ester X, mp 128–129.5°. This is in agreement with the aforementioned nmr data and shows that the ester group of the *anti-trans* diketo ester VIII has the thermodynamically less favorable β-axial configuration. Conversely, both the diketo acid IX and its methyl ester X have the thermodynamically stable arrangement, *i.e.*, a B/C *trans* ring junction and a 2α-equatorial substituent. The nmr spectrum of this isomeric diketo ester X shows no band between δ 2.7 and 3.7 in agreement with the equatorial configuration of the ester group and has a singlet at δ 5.96 for the C-8 proton (Figure 2). Saponification of the diketo ester X gave, as expected, the *anti-trans* diketo acid IX.

The assumed 4bβ configuration of the hydrogen is based on analogy with the results with 19-nor steroids, where the β configuration of the corresponding hydro-

(7) A. J. Birch, *J. Chem. Soc.*, 593 (1946); 1642 (1947).
(8) S. K. Balasubramanian, *Tetrahedron*, **12**, 196 (1961).
(9) L. Velluz, J. Valls, and G. Nominé, *Angew. Chem.*, **77**, 185 (1965).
(10) A. L. Wilds and N. A. Nelson, *J. Am. Chem. Soc.*, **75**, 5366 (1953).
(11) C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).
(12) J. A. Zderic, D. C. Limon, H. J. Ringold, and C. Djerassi, *J. Am. Chem. Soc.*, **81**, 3120 (1959).

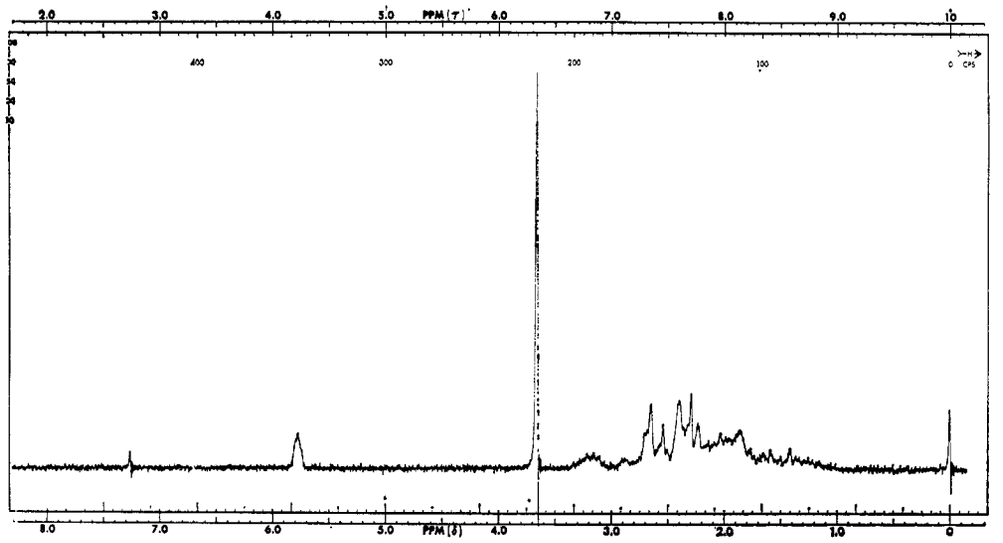


Figure 1.—Nmr spectrum of 1,2,3,4,4aα,4bβ-5,6,7,9,10,10aβ-dodecahydro-4,7-dioxo-2β-phenanthrenecarboxylic acid methyl ester (VIII) in deuteriochloroform.

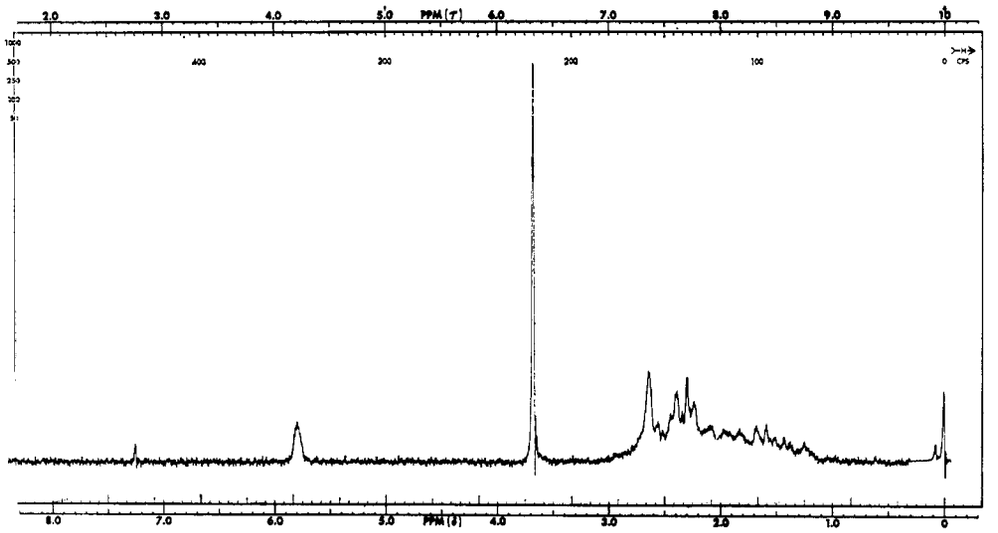


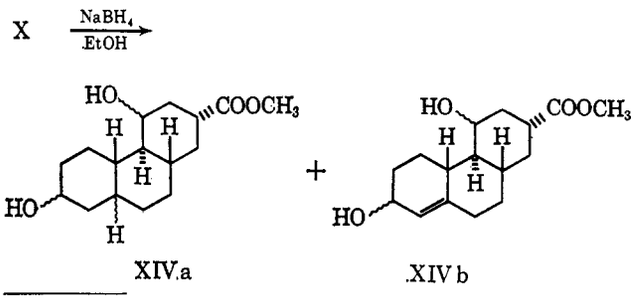
Figure 2.—Nmr spectrum of 1,2,3,4,4aα,4bβ,5,6,7,9,10,10aβ-dodecahydro-4,7-dioxo-2α-phenanthrenecarboxylic acid methyl ester (X) in deuteriochloroform.

gen was confirmed by optical rotatory dispersion studies.[13] Moreover, a 4bα-oriented hydrogen would force ring B into the energetically less favorable boat conformation.

Additional evidence for the assigned configurations of the isomeric diketo esters VIII and X was obtained during the investigation of the sodium borohydride reduction of these compounds. With a large excess of sodium borohydride, the diketo ester VIII gave a mixture of triols (XIIIa and b). No attempt was made to purify the reaction mixture. According to nmr spectroscopy, 70% of the double bond was reduced. It was possible to follow the reaction by infrared spectroscopy, and the appearance of a γ-lactone band indicates the reaction path shown in Scheme III.

If the approach of the reagent along the axial direction is hindered, sodium borohydride reduction of a keto group should give mainly the axial alcohol.[14] With a 2β-axial methyl ester group in the molecule, a strong 1,3-diaxial interaction between this substituent and the approaching bulky reducing agent should lead to a 4β-axial hydroxyl group. The 2,4-diaxial relationship of the hydroxyl and of the methyl ester groups on a rigid B/C *trans* ring system offers an excellent opportunity for spontaneous lactonization.[15] This lactone is then reduced further to the triols XIIIa and b with the excess of the reducing agent.[5,14,15]

The reduction of the isomeric *trans* diketo ester X with a large excess of sodium borohydride gave a mixture of dihydroxy esters (XIVa and b). The lack of



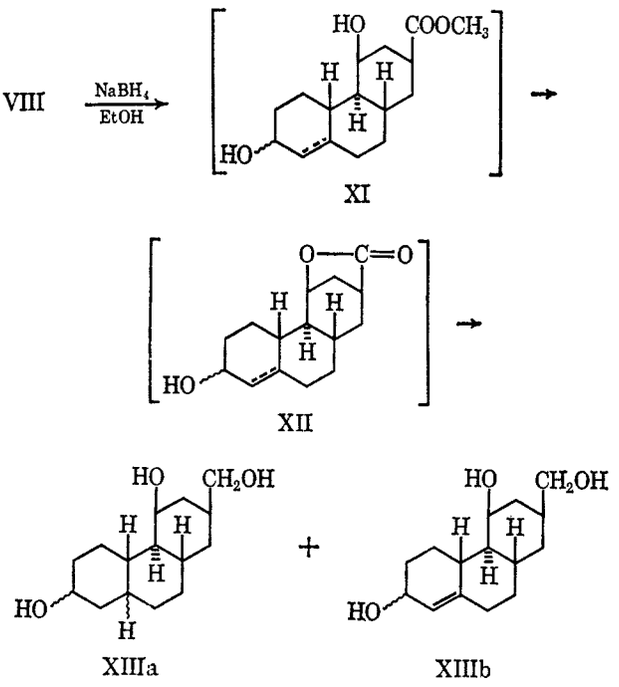
XIVa XIVb

(13) C. Djerassi, R. Riniker, and E. Riniker, *J. Am. Chem. Soc.*, **78**, 6362 (1956).

(14) D. M. S. Wheeler and M. M. Wheeler, *J. Org. Chem.*, **27**, 3796 (1962).

(15) H. O. House, H. Babad, R. B. Toothill, and A. W. Noltes, *ibid.*, **27**, 4141 (1962).

SCHEME III



reduction of the ester group is in agreement with the assigned configuration.[5,16] No attempt was made to purify the reaction mixture.

The starting material for the other synthesis (see Scheme IV) of the *anti–trans* diketo acid IX was the B/C *trans* keto acid XV. Sodium borohydride reduction gave the B/C *trans* nonlactonizing hydroxy acid XVII. This acid could be oxidized back to the B/C *trans* keto acid XV which shows that no change in the configuration occurred during the reduction.[5] The lithium in liquid ammonia reduction of the B/C *trans* nonlactonizing hydroxy acid XVII gave the corresponding dihydro derivative XVIII in 45% yield, after recrystallization from acetone. Hydrolysis of the enol ether group of XVIII with hydrochloric acid in refluxing tetrahydrofuran was complete after 1 hr, to give an excellent yield of the *anti–trans* α,β-unsaturated keto hydroxy acid XIX, in agreement with the assumed B/C *trans* ring junction in XVIII.

Oxidation of the *anti–trans* α,β-unsaturated keto hydroxy acid XIX with the chromium trioxide–pyridine reagent gave the *anti–trans* diketo acid IX in 88% yield. The compound IX was identical in every respect with the material obtained by the first synthesis. Since there was no possibility for ring inversion throughout the synthesis, the *anti–trans* configuration of the diketo acid IX is thus confirmed.

Experimental Section[17]

1,2,3,4,4aβ,5,8,9,10,10a$\alpha\beta$-Decahydro-4α-hydroxy-7-methoxy-2β-phenanthrenecarboxylic Acid (IV).—The *cis* nonlactonizing hydroxy acid III[5] (16.6 g) was dissolved in 400 ml of refluxing absolute ethyl alcohol. The solution was cooled rapidly, first with an ice bath, then with a Dry Ice–acetone cooling mixture, and 800 ml of liquid ammonia was distilled into the system. A fine precipitate of the ammonium salt of III was thus obtained. Lithium wire (10.72 g) was cut into approximately 160-mg pieces, and the metal was added through a special feeding device in 1.28-g portions at $-70°$. Another piece was not added until after the blue color from the preceding portion had disappeared. If the blue color had not disappeared after 8–10 min, absolute ethyl alcohol was added dropwise to discharge the color. The total time for the addition of lithium was approximately 50 min. Absolute ethyl alcohol (70 ml) was added, and the Dry Ice–acetone bath was replaced with an acetone bath at room temperature. Ice–water (250 ml) was then added very slowly, while the ammonia was boiled off under nitrogen. After most of the ammonia had evaporated, the stirrer was stopped, and most of the alcohol was evaporated under vacuum at about 45°. Approximately 800 ml of water was added to the residue to dissolve the salts, and the solution was acidified in the cold to pH 5 with a cooled 2 *N* hydrochloric acid solution. Acidification to a lower pH precipitates undesired by-products. The crude acid was filtered and dried under high vacuum for 16 hr at 40°; 12.8 g of crude acid IV was thus obtained (77.0%), mp 163–169° dec. Ultraviolet spectroscopy indicated 1.0% starting material in the mixture. The crude product was dissolved in 1850 ml of refluxing acetone, the solution was filtered, and the acetone was concentrated to approximately one-fifth of its original volume by distillation at normal pressure to give 8.9 g (53.5%) of the pure acid IV: mp 180–182° dec; λ_{max} 279 mμ (ϵ 20), 287 mμ (ϵ 19); ν_{max}^{KBr} 3530 (free hydroxyl), 3140, 2500–2700 (bonded OH), 1712 (carboxyl carbonyl) 1686, and 1670 cm^{-1} (dihydroanisole).

Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.82; H, 7.62.

Hydrolysis of the Acid IV with Hydrochloric Acid in Acetone.—Acid IV (140 mg) was stirred and refluxed under nitrogen for 16 hr in a mixture of 10 ml of acetone and 4 ml of 2 *N* hydrochloric acid. It was poured on ice and extracted with ethyl acetate. The ethyl acetate extract was washed with water, dried over magnesium sulfate, and evaporated under vacuum to give 130 mg of an amorphous solid. The ultraviolet absorption, λ_{max} 239 mμ (ϵ 4700), corresponds to 29.4% α,β-unsaturated ketone.

1,2,3,4,4aβ,5,6,7,8,9,10,10aβ-Dodecahydro-4α-hydroxy-7-oxo-2β-phenanthrenecarboxylic Acid (VI).—The acid IV (8.7 g) was suspended in 600 ml of acetone. Oxalic acid dihydrate (7.3 g) in 60 ml of water was added, and the mixture was stirred at room temperature for 4 hr under nitrogen. Ice–water (200 ml) was added to the solution, and most of the acetone was removed under vacuum. The crystalline precipitate was filtered and was recrystallized from acetone to give 8.05 g (97.0%) of the ketohydroxy acid VI: mp 200–202°; λ_{max} 277 mμ (ϵ 25), 287 mμ (ϵ 20); ν_{max}^{KBr} 3500 (free OH), 2500–2700 (bonded OH of acid), 1710 (saturated ketone), and 1700 cm^{-1} (carboxyl carbonyl).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.14; H, 7.33.

1,2,3,4,4aβ,5,6,7,8,9,10,10aβ-Dodecahydro-4,7-dioxo-2β-phenanthrenecarboxylic Acid (VII).—The ketohydroxy acid V (5.9 g) was dissolved in 840 ml of acetone. The solution was cooled to $-12°$, and 8.35 ml of an 8.0 *N* chromium trioxide–sulfuric acid solution was added within 45 sec, under a strong stream of nitrogen and with vigorous stirring. After stirring for 2.5 min at $-12°$, an ice-cold solution of sodium chloride in water was added, and the mixture extracted four times with ethyl acetate and once with ether. The combined extract was washed with brine, then with ice-water, dried over magnesium sulfate, and evaporated under vacuum to give 5.42 g of crude crystalline material. Recrystallization from acetonitrile gave 3.67 g (62%) of pure diketo acid VII: mp 152–153.5°; λ_{infl} 287 mμ (ϵ 89); ν_{max}^{KBr} 2450–2550 (associated OH of acid), 1710 (ketone carbonyl), and 1699 cm^{-1} (carboxyl carbonyl). The nmr spectrum showed no vinylic proton.

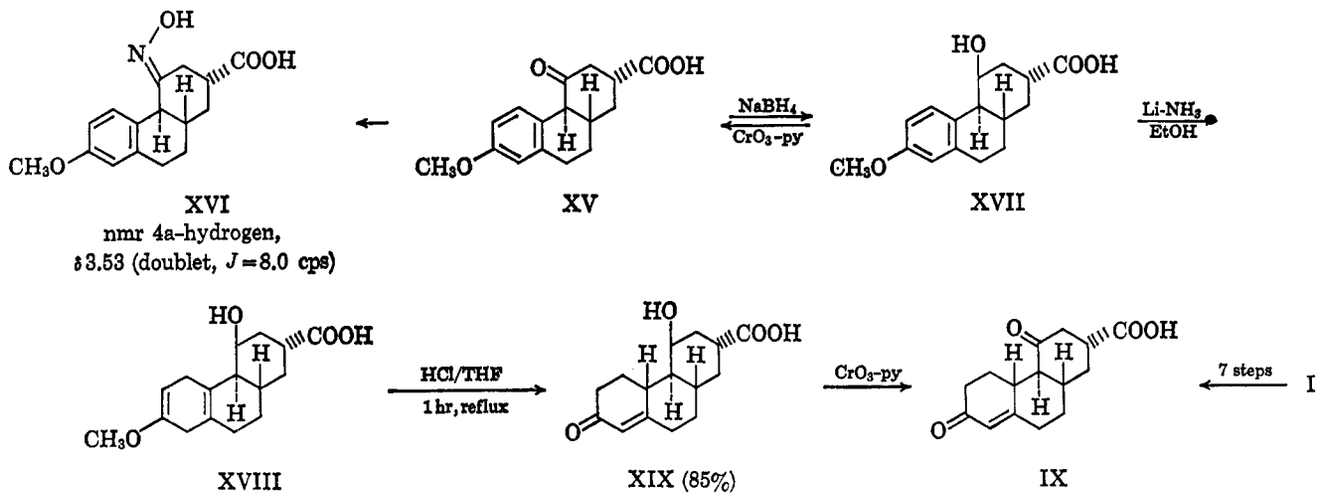
Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.54; H, 7.20.

1,2,3,4,4aα,4bβ,5,6,7,9,10,10aβ-Dodecahydro-4,7-dioxo-2β-phenanthrenecarboxylic Acid Methyl Ester (VIII).—The diketo acid VII (3.67 g) was refluxed for 1 hr under nitrogen in 180 ml of 0.8 *N* sulfuric acid in methanol. The reaction mixture was cooled to 0° and neutralized with 2 *N* sodium hydroxide and most of the methanol was evaporated under vacuum. It was extracted three times with ethyl acetate and once with ether. The combined extract was washed with brine and with water, dried over magnesium sulfate, treated with charcoal, and evaporated under vacuum. The solid residue was treated with a little ether, and the ether-insoluble solid was filtered. It was recrystallized from acetone, to give 2.31 g of the pure diketo ester

(16) R. C. Cookson and N. S. Wariyar, *J. Chem. Soc.*, 2302 (1956).

(17) All melting points were determined in a Thomas–Hoover melting point apparatus and are corrected. All ultraviolet spectra were taken in ethyl alcohol. Nmr spectra were taken with a Varian A-60 spectrometer at 60 Mcps and tetramethylsilane as an internal standard.

SCHEME IV



VIII: mp 158–159°; λ_{max} 239 mμ (ε 16,250); $\nu_{max}^{CHCl_3}$ 1725 (ester carbonyl), 1715 (saturated ketone), and 1660 cm^{-1} (α,β-unsaturated ketone).

Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.72; H, 7.53.

1,2,3,4,4aα,4bβ,5,6,7,9,10,10aβ-Dodecahydro-4,7-dioxo-2α-phenanthrenecarboxylic Acid (IX). A. From the B/C *trans* Diketo Ester VIII.—The diketo ester VIII (5.32 g) was equilibrated by refluxing in 220 ml of 1 *N* sodium methoxide in methanol under nitrogen for 30 min. Water (110 ml) was then added, and the solution was refluxed for another 5 min to saponify the ester. It was cooled with an ice bath and neutralized with 3 *N* hydrochloric acid under nitrogen. Water (120 ml) was added, and most of the methanol was evaporated under vacuum. The mixture was cooled in an ice bath and acidified to pH 2.5–3.0 with 2 *N* hydrochloric acid. The crystalline precipitate was filtered and dissolved in hot ethyl acetate. The mother liquor was extracted with ethyl acetate. The ethyl acetate solutions were combined, washed with brine and with water, dried over magnesium sulfate, and concentrated under vacuum, to give 5.05 g of the crude acid. This was treated with a mixture of 20 ml of ether and 1 ml of acetone and filtered, and the ether-insoluble crystals were recrystallized from acetone, to give 2.63 g of the diketo acid IX: mp 221–223°; λ_{max} 239 mμ (ε 16,700); ν_{max}^{KBr} 2450–2650 (associated OH of acid), 1710 (saturated ketone), 1699 (carboxyl carbonyl), and 1660 cm^{-1} (α,β-unsaturated ketone).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.72; H, 6.82.

B. From the B/C *trans* Keto Hydroxy Acid XIX.—To 1.3 ml of anhydrous pyridine at 15° was added 100 mg of chromium trioxide in about 15-mg portions over a period of 10 min with magnetic stirring. Stirring was continued at 20° for 5 hr to obtain a uniform suspension of the reagent. The unsaturated keto hydroxy acid XIX (100 mg) in 1.0 ml of anhydrous pyridine was added at once at 5°. The cooling bath was removed after 5 min, and the mixture was stirred at 20° for 2.5 hr. It was poured into ice–water and acidified in the cold to pH 3.0 with 2.0 *N* hydrochloric acid. The mixture was shaken with ethyl acetate and filtered through a pad of Celite. The precipitate was washed carefully with warm ethyl acetate. The water phase, after separation, was reextracted with ethyl acetate and with ether. The combined extracts were dried over magnesium sulfate, filtered, and evaporated under vacuum to give 88 mg of crude diketo acid IX, mp 213–217° (89% yield). Recrystallization from acetone gave pure IX, mp 221–223°. The product was identical with the compound prepared by method A, as shown by mixture melting point determination and by the identity of the ultraviolet and infrared spectra.

C. From the Isomeric B/C *trans* Diketo Ester X.—The ester X (100 mg) was stirred and refluxed under nitrogen in 10 ml of 1 *N* sodium hydroxide solution for 1 hr. The solution was cooled to 20° and extracted with ether to remove any unsaponified ester. The basic solution was acidified to pH 5 with 2 *N* hydrochloric acid and extracted with ethyl acetate. The ethyl acetate extract was washed with a saturated sodium chloride solution, dried over magnesium sulfate, and evaporated under vacuum. The crystalline residue gave 90 mg of the pure diketo acid IX, mp 221–223°, after recrystallization from acetone. The compound was identical in every respect with the sample prepared by method A.

1,2,3,4,4aα,4bβ,5,6,7,9,10,10aβ-Dodecahydro-4,7-dioxo-2α-phenanthrenecarboxylic Acid Methyl Ester (X).—The diketo acid IX (250 mg) in 10 ml of ether was treated at 0° with 250 mg of diazomethane in 15 ml of ether. After stirring for 30 min, 10 ml of ice–water was added. When the color had faded, the ether layer was separated, washed with a dilute sodium bicarbonate solution, then with brine, dried over magnesium sulfate, and evaporated under vacuum. The solid residue was recrystallized from acetone–hexane to give 203 mg of the pure ester X: mp 128–129.5°; λ_{max} 239 mμ (ε 16,900); $\nu_{max}^{CHCl_3}$ 1730 (ester carbonyl), 1710 (saturated ketone), and 1660 cm^{-1} (α,β-unsaturated ketone).

Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.79; H, 7.27.

Sodium Borohydride Reduction of the Diketo Ester VIII. A. With Twice the Theoretical Amount of Sodium Borohydride.—The diketo ester VIII (276 mg) was dissolved in 30 ml of absolute ethyl alcohol. Sodium borohydride (40 mg) was added, and the mixture was stirred for 18 hr at 20°. Ice–water (30 ml) was added, and the system was neutralized with 1 *N* hydrochloric acid. It was then extracted three times with ethyl acetate and once with ether. The combined extract was washed with a saturated sodium chloride solution, dried over magnesium sulfate, and evaporated under vacuum to give 260 mg of an oil: λ_{max} 240 mμ (ε 150); $\nu_{max}^{CHCl_3}$ 3600, 3350–3500 (OH groups), 1780 (five-membered lactone), and 1725 cm^{-1} (ester group).

B. With Ten Times the Theoretical Amount of Sodium Borohydride.—The diketo ester VIII (276 mg) was dissolved in 30 ml of absolute ethyl alcohol. Sodium borohydride (200 mg) was added. The mixture was stirred for 72 hr at 20° and worked up as in A to give 245 mg of an oil: $\nu_{max}^{CHCl_3}$ 3600 and 3250–3550 cm^{-1} (OH groups). There was no carbonyl absorption.

Sodium Borohydride Reduction of the Isomeric Diketo Ester X.—The diketo ester X (276 mg) was dissolved in 30 ml of absolute ethyl alcohol. Sodium borohydride (80 mg, four times theory) was added, the mixture was stirred for 72 hr at 20° and was worked up as in the previously described reduction of the isomeric diketo ester VIII to give 270 mg of an oil: λ_{max} 240 mμ (ε 36); $\nu_{max}^{CHCl_3}$ 3650, 3350–3500 (OH groups), and 1730 cm^{-1} (ester carbonyl).

1,2,3,4,4aα,5,8,9,10,10aβ-Decahydro-4β-hydroxy-7-methoxy-2α-phenanthrenecarboxylic Acid (XVIII).—The *trans* nonlactonizing hydroxy acid[5] XVII (1.6 g) was dissolved in 40 ml of refluxing absolute ethyl alcohol. The solution was cooled rapidly, first with an ice bath, then with a Dry Ice–acetone cooling mixture, and 80 ml of liquid ammonia was distilled into the system. A fine precipitate of the ammonium salt of XVII was thus obtained. Lithium wire (1.08 g) was cut into approximately 80-mg pieces, and the metal was added through a special feeding device one piece at a time at −70°. Another piece was not added until after the blue color from the preceding portion had disappeared. The total time for the addition of lithium was approximately 1 hr. The Dry Ice–acetone bath

was replaced with an acetone bath at room temperature, and 40 ml of ice–water was added very slowly, while the ammonia was evaporated under nitrogen. After most of the ammonia had been removed, the stirrer was stopped, and most of the alcohol was evaporated under vacuum at about 45°. Water (50 ml) was added to the residue to dissolve the salts, and the solution was acidified in the cold to pH 4.5 with a cooled 2 *N* hydrochloric acid solution. After stirring for 1 hr at ice-bath temperature, the crude acid was filtered and dried under high vacuum for 16 hr at 40° to give 0.99 g of crude acid XVIII. Recrystallization from acetone gave the analytical sample of XVIII: mp 141–142° dec; ν_{max}^{KBr} 3450 (hydroxyl group), 2500–2700 (associated OH of acid), 1710 (carboxyl carbonyl), 1680, and 1670 cm^{-1} (dihydroanisole).

Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.13; H, 7.88.

1,2,3,4,4aα,4bβ,5,6,7,9,10,10aβ-Dodecahydro-4β-hydroxy-7-oxo-2α-phenanthrenecarboxylic Acid (XIX).—The foregoing acid XVIII (560 mg) was refluxed under nitrogen for 1 hr in a mixture of 15 ml of tetrahydrofuran and 5 ml of 2 *N* hydrochloric acid. Distilled water (60 ml) was added to the cold mixture, and most of the THF was evaporated under vacuum. The crystalline precipitate was filtered and dried under high vacuum for 16 hr to give 528 mg of crude unsaturated ketohydroxy acid XIX. Recrystallization from acetone gave 450 mg (85%) analytically pure acid: mp 222.5–223°; λ_{max} 240 mμ (ε 16,700); ν_{max}^{KBr} 3350 (OH group), 2500–2700 (associated OH of acid), 1699 (carboxyl carbonyl), and 1660 cm^{-1} (α,β-unsaturated keto group).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.30; H, 8.01.

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Reactions of α,β-Unsaturated Acid Chlorides with Tertiary Amines

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Solvolysis of the acyl quaternary ammonium salt (II) formed from 3,3-dimethylacrylyl chloride and trimethylamine gave 3-hydroxy-2-isopropylidene-5-methyl-3,5-hexadienoic acid β-lactone (V) in 62% yield. In the presence of ethyl vinyl ether, the ketene intermediate(s) initially formed underwent cycloaddition to give unsaturated cyclobutanones (VI and VII). Several reactions of V are described.

The dehydrochlorination of an acid chloride through use of a tertiary amine is a classical method for the generation of a ketene.[1] Surprisingly, however, no

$$R_2CH{-}COCl + R_3'N \longrightarrow R_2C{=}C{=}O + R_3'N\cdot HCl$$

report in the chemical literature was found describing the reaction of α,β-unsaturated acid chlorides with tertiary amines.

It was anticipated that dehydrohalogenation might occur by removal of an α-hydrogen atom to yield an alkylidene ketene (A) or, just as likely, by 1,4 elimination to give an α,β-unsaturated ketene (B).

$$R_2CH{-}CH{=}CH{-}COCl \xrightarrow{R_3'N} \begin{matrix} R_2CH{-}CH{=}C{=}C{=}O \\ \text{A} \\ \text{or} \\ R_2C{=}CH{-}CH{=}C{=}O \\ \text{B} \end{matrix}$$

Initial experiments were carried out with the readily available *trans*-crotonyl chloride. With tripropyl-, triethyl-, and trimethylamines under a variety of conditions, reaction occurred to give tertiary amine hydrochlorides. However, only a dark viscous polymeric product was obtained, and efforts to trap an unsaturated ketene intermediate with dihydropyran[2] were fruitless.

Substitution of 3,3-dimethylacrylyl chloride (3-methyl-2-butenoyl chloride, (I) for *trans*-crotonyl chloride led to the isolation of a pure product, but not until trimethylamine had been used in place of the unsatisfactory triethyl- and tripropylamines.

Under optimum conditions, a slight excess of dry trimethylamine gas was bubbled into a stirred solution of acid chloride in hexane. The acyl quaternary ammonium salt (II) thus formed precipitated in almost quantitative yield and was pumped free of excess amine and solvent.[3] It was then allowed to stir overnight at room temperature with dry acetone containing a catalytic amount of sodium iodide.[4] Filtration of trimethylamine hydrochloride, followed by concentration and recrystallization, gave a novel dimeric product, 3-hydroxy-2-isopropylidene-5-methyl-3,5-hexadienoic acid β-lactone (V), in 62% yield.

The β-lactone structure V was assigned on the basis of elemental, molecular weight, infrared, and nmr analyses (see Experimental Section). The last, in particular, was useful in distinguishing between V and the alternative β-lactone structures IVa and IVb expected from the dimerization of isopropylideneketene (IIIa) or isopropenylketene (IIIb) unaccompanied by allylic shifts into conjugation (see Chart I).

Lactone V may have been formed to a large extent, if not exclusively, by path b (1,4 elimination) rather than by path a (1,2 elimination), since an isopropenylketene intermediate (IIIb) could be trapped by ethyl vinyl ether to give the cycloaddition product, 3-ethoxy-2-isopropenylcyclobutanone (VI). The latter was isolated by fractional distillation as an approximately 1:1 mixture with its conjugated isomer, VII, to which it isomerized slowly at room temperature.[5] Attempts to isolate a pure sample of VI by glpc trapping were not

(1) W. E. Hanford and J. C. Sauer, *Org. Reactions*, **3**, 108 (1946).

(2) Diphenyl- and dimethylketene react with dihydropyran to give cycloaddition products in high yields. See C. D. Hurd and R. D. Kimbrough, *J. Am. Chem. Soc.*, **82**, 1373 (1960); R. H. Hasek, P. G. Gott, and J. C. Martin, *J. Org. Chem.*, **29**, 1239 (1964).

(3) Since tertiary amines catalyze the polymerization of ketenes (see ref 1), it is important to remove excess amine prior to solvolysis of the salt.

(4) While not essential, the use of sodium iodide shortened the reaction time and afforded somewhat higher yields of V.

(5) In a 3-day period, a 43:57 mixture of VI to VII had, by quantitative nmr analysis, changed to a 17:83 mixture.