pressure.[13] The pressure was reduced to 20–25 mm., and the temperature was raised rapidly to 350° and maintained there for 0.5 hr. Extraction of the neutral fraction with ether and chromatography over basic alumina (elution with 9:1 petroleum ether–benzene) gave a colorless oil whose infrared and ultraviolet spectra very closely resembled those of anthrasteroids: $\lambda_{max}^{CS_2}$ 12.3 μ; λ_{max}^{EtOH} 222, 228, 268, and 308 mμ (absorption in the ratio 12:12:8:1, as for anthrasteroids[1]).

For dehydrogenation, 35 mg. of this oil was mixed with an equal weight of 10% Pd–C and heated in a sealed tube at 320° for 3 hr. Elution of the product from basic alumina with petroleum ether–benzene (8:1) furnished *ca.* 5 mg. of a nearly colorless fraction of Va which exhibited strong blue fluorescence in ultraviolet light: λ_{max}^{EtOH} 261, 333, 355, 374, and 394 mμ. Owing to lack of material, further work was deferred on this product.

B.—Similar dehydrogenation of 40 mg. (0.15 mmole) of the hydrocarbon IIe afforded *ca.* 10 mg. of Va as a colorless fraction by elution from basic alumina with petroleum ether–benzene (8:1). This also exhibited strong blue fluorescence in ultraviolet light: λ_{max}^{EtOH} 261, 336, 354, 374, and 394 mμ.[4] The picrate crystallized as reddish brown needles, m.p. 126–128° (lit.[4] for the picrate of *dl*-Va m.p. 128–128.5°). Chromatography of this derivative on alumina, elution with petroleum ether–benzene (3:1), and crystallization from methanol furnished the free hydrocarbon Va, m.p. 79–81°.[4]

15-Bromo-5,7,8,14-anthracholestatetraene (VIb).—To a stirred solution of 1.0 g. (2.82 mmoles) of 5,7,9,14-anthracholestatetraene (VIa)[9] in 20 ml. of carbon tetrachloride, a solution of 0.45 g. (2.82 mmoles) of bromine in 20 ml. of carbon tetrachloride was added dropwise over the course of 4 min. During the addition, hydrogen bromide was evolved, and after 20 min. water was added, and the organic product was recovered by extraction with carbon tetrachloride. The organic layer was washed with water, 5% sodium bisulfite solution, and again with water. It was then dried over anhydrous magnesium sulfate and evaporated *in vacuo*. Crystallization of the residue from ethyl acetate–ethanol gave 0.8 g. (64% yield) of colorless needles of VIb, m.p. 93–97°. Twice recrystallized from this same solvent pair, these melted at 99–100°, gave a positive Beilstein halogen test, and had $\lambda_{max}^{CS_2}$ 12.33 μ; $\lambda_{max}^{isooctane}$, m$\mu$ (ϵ), 222 (21,500), 227 (21,700), 270 (19,900), and 306 (1640). The n.m.r. spectrum had a single sharp benzenoid proton peak at τ 2.12 (determined in CCl_4 on a Varian Associates A-60 spectrometer with tetramethylsilane as an internal reference).

Anal. Calcd. for $C_{27}H_{39}Br$ (443.5): C, 73.12; H, 8.86; Br, 18.02. Found: C, 73.25; H, 8.98; Br, 18.12.

1,10-Dimethyl-*s*-octahydro-1-anthrol.—To a refluxing solution of excess methyllithium in diethyl ether [prepared from 555 mg. (80 mg.-atoms) of lithium shot and 5.68 g. (40 mmoles) of methyl iodide], 1.61 g. (7.5 mmoles) of 1-oxo-10-methyl-*s*-octahydroanthracene[8] in diethyl ether was added, with stirring, under nitrogen. The reaction was allowed to proceed for 10 hr. before ice-cold water was cautiously added and the organic product was recovered by ether extraction. The organic layer was washed with water, dried over anhydrous magnesium sulfate, and evaporated *in vacuo*. Crystallization of the residue from methanol gave 1.07 g. (62% yield) of colorless needles of 1,10-dimethyl-*s*-octahydro-1-anthrol, m.p. 116–118°. Recrystallized from the same solvent, these melted at 117–119° and had $\lambda_{max}^{CHCl_3}$ 2.7 and 2.9 μ.

Anal. Calcd. for $C_{16}H_{22}O$ (230.4): C, 83.43; H, 9.63. Found: C, 83.73, H, 9.66.

1,10-Dimethylanthracene.—A portion of the above alcohol (575 mg., 2.5 mmoles) was mixed with an equal weight of 30% Pd–C and heated in a sealed tube at 320° for 3 hr. The product was taken up in petroleum ether and purified by elution from basic alumina. A nearly colorless fraction, which exhibited a strong blue fluorescence in ultraviolet light, was eluted slowly with petroleum ether and crystallized readily from ethanol to give 150 mg. (29% yield) of very pale green needles of 1,10-dimethylanthracene, m.p. 86–89°. Crystallized from the same solvent, these melted at 88–89° and showed λ_{max}^{EtOH}, mμ (log ϵ), 257 (3.4) (shoulder), 350 (3.7), 268 (3.9), and 389 (3.8).

Anal. Calcd. for $C_{16}H_{14}$ (206.3): C, 93.16; H, 6.84. Found: C, 93.03; H, 6.95.

The picrate crystallized from ethanol as deep purple needles, m.p. 127.5–128°.

Anal. Calcd. for $C_{22}H_{17}N_3O_7$ (435.4): C, 60.70; H, 3.94; N, 9.65. Found: C, 60.67; H, 4.01; N, 9.78.

5-Isodehydroabietic Lactones[1]

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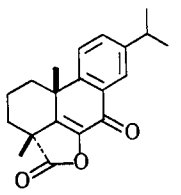
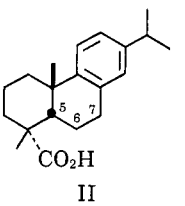
Received April 22, 1965

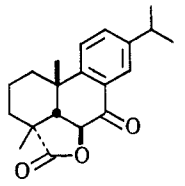
In a recent study of the chemistry of dehydroabietic acid, formation of the enol lactone I was reported.[2] Its several reduction products were assumed to possess A–B *trans* stereochemistry. However, since the product of its catalytic hydrogenation has recently been shown to be 5-isodehydroabietic acid (II),[3] an investigation of the structure of the hydroxylactone obtained on sodium borohydride reduction of I and its oxidation product, a 7-ketolactone, was undertaken. Two facts showed rapidly that the reduced lactones also belonged to the 5-iso series. Clemmensen reduction of the 7-ketolactone yielded 5-isodehydroabietic acid (II).[4] Analysis of the p.m.r. spectrum of the lactone revealed its 5β-H (doublet at 2.32 p.p.m.) strongly coupled (J = 13.0 c.p.s.) with its C-6 hydrogen (doublet at 5.04 p.p.m.) indicating a *trans*, diaxial relationship between them.[5] Hence the compound possessed structure III.



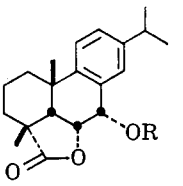
I



II



III



IVa, R = H
b, R = Ac

Despite attempts to repeat the preparation of the hydroxylactone and thereupon ketolactone III,[2] sodium borohydride reduction of I has led recently consistently to a new hydroxylactone. Jones oxidation of this compound yielded a new ketolactone whose sodium borohydride reduction reyielded the hydroxylactone while calcium–ammonia reduction, followed by hydrogenation, gave 5-isodehydroabietic acid (II). The p.m.r. spectrum of the ketolactone showed its 5β-hydrogen (doublet at 2.70 p.p.m.) coupled (J = 8.0 c.p.s.) with the C-6 hydrogen (doublet at 5.05 p.p.m.). These data are consistent only with struc-

(1) This research was supported by the National Science Foundation.

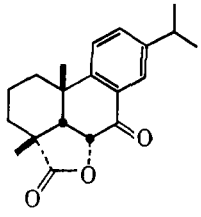
(2) E. Wenkert, R. W. J. Carney, and C. Kaneko, *J. Am. Chem. Soc.*, **83**, 4440 (1961).

(3) E. Wenkert, A. Afonso, P. Beak, R. W. J. Carney, P. W. Jeffs, and J. D. McChesney, *J. Org. Chem.*, **30**, 713 (1965).

(4) This experiment was performed by R. W. J. Carney.

(5) Both 4- and 10-methyl signals appeared at 1.50 p.p.m.

ture V.[6] The p.m.r. spectrum of the 7-acetoxylactone, obtained on acetylation of the hydroxylactone, showed a C-5-H doublet at 2.43 p.p.m. (J = 7.0 c.p.s.), a C-6-H quartet at 5.15 p.p.m. (J = 7.0, 2.5 c.p.s.), and a C-7-H multiplet at 6.29 p.p.m. ($J_{6,7}$ = 2.5 c.p.s.), characteristic of structure IVb. Hence its precursor possesses structure IVa.



V

Thus, all reduction products appear to be 5-iso compounds, as might be expected from an initial methanolytic ring opening of the lactone I, followed by borohydride reduction of the resultant 5-iso-6,7-dione. The rapid formation of a yellow color in the methanolic solution of I upon borohydride addition is consistent with this view. The low yield of reduction product may be due to much enol–acid–borohydride complex formation.

Experimental Section

5-Isodehydroabietic Acid. A.—A mixture of 28 mg. of lactone III, 3 g. of amalgamated zinc, 2 ml. of acetic acid, and 6 ml. of 6 *N* hydrochloric acid was refluxed for 50 hr. The mixture was cooled, decanted, and extracted with ether. The extract was washed with 5% sodium hydroxide, the aqueous extract acidified and extracted with ether. The organic extract was dried over magnesium sulfate and evaporated. The residue (16 mg.) was crystallized from aqueous methanol yielding the acid II, m.p. 121–124° (lit.[3] m.p. 121–124°); the infrared spectrum was identical with that of an authentic specimen.

B.—Calcium (15 mg.) was added to a solution of 35 mg. of ketolactone V in 5 ml. of tetrahydrofuran and 30 ml. of liquid ammonia. Upon dissolution of the metal, 200 mg. of ammonium sulfate was added and the mixture was evaporated. Addition of 5% hydrochloric acid, extraction with chloroform, and evaporation of the extract yielded 30 mg. of solid. A mixture of the latter, 5 drops of concentrated sulfuric acid, and 45 mg. of 10% palladium–charcoal in 15 ml. of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. Upon filtration of the catalyst the solution was washed with water and evaporated. Sublimation of the residue yielded 15 mg. of II, m.p. and m.m.p. 123–124°; its spectra were identical with those of an authentic sample.

Hydroxylactone IVa.—A solution of 200 mg. of lactone I and 100 mg. of sodium borohydride in 25 ml. of methanol was left standing for 30 min. and then evaporated under reduced pressure. Water was added to the residue and the solution was extracted with ether. The extract was dried over anhydrous sodium sulfate and evaporated. Trituration of the residue with ether yielded crystals whose sublimation gave 20 mg. of lactone IVa, m.p. 238°; spectra—infrared (Nujol), OH 2.82 (m), C=O 5.67 (s) μ; p.m.r., three-proton singlets at 0.98, 1.31 (4- and 10-methyls, respectively), three-proton doublets at 1.13, 1.18 (J = 7 c.p.s.) (isopropyl methyls), one-proton doublet at 2.45 (J = 6.5 c.p.s.) [C-5-H], one-proton quartet at 5.08 (J = 6.5, 2.5 c.p.s.) [C-6-H], one-proton doublet at 5.28 p.p.m. (J = 2.5 c.p.s.) [C-7-H]. *Anal.* Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.28; H, 8.34.

Acetoxylactone IVb.—A solution of 30 mg. of lactone IVa in 1 ml. of acetic anhydride and 1 ml. of pyridine was heated for 3 hr. on the steam bath. Upon evaporation of the solution under vacuum, the residue was extracted with ether. Evaporation of the extract and crystallization of the residue from petroleum ether (b.p. 30–60°) gave 32 mg. of crystalline lactone IVb, m.p. 152–153°; spectra—infrared (CCl_4), C=O 5.62 (s), 5.74 (s) μ; p.m.r., three-proton lines at 1.17, 1.18, 1.30, and 1.31 (4-, 10- and isopropropyl methyls), and three-proton singlet at 2.30 p.p.m. (acetate methyl). *Anal.* Calcd. for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 74.03; H, 7.86.

Ketolactone V.—Jones reagent (2 ml.) was added rapidly to an ice-cold solution of 61 mg. of lactone IVa in 25 ml. of acetone, and the mixture was stirred for 4 min. It was poured onto ice and extracted with chloroform. The extract was washed with water, 5% sodium bicarbonate solution, and again with water. Evaporation of the organic solution yielded 54 mg. of solid whose crystallization from ether gave long needles of lactone V: m.p. 128°; spectra—ultraviolet (95% EtOH), λ_{max} 255 mμ (log ϵ 3.92), 300 mμ (log ϵ 3.23), λ_{min} 233 mμ (log ϵ 3.45), 285 mμ (log ϵ 3.15); infrared (Nujol), C=O 5.65 (s), 5.85 (s), C=C 6.21 (m) μ; p.m.r., three-proton singlets at 1.29, 1.43 (4- and 10-methyls), six-proton doublet at 1.36 p.p.m. (J = 7.0 c.p.s.) (isopropyl methyls). *Anal.* Calcd. for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.97; H, 7.71.

Sodium borohydride, 15 mg., was added in small portions to a solution of 30 mg. of the lactone V in 5 ml. of methanol and the mixture was left standing for 30 min. at room temperature. Water and 5% hydrochloric acid were added and the mixture was extracted with chloroform. Evaporation of the solvent yielded 30 mg. of crystalline IVa, m.p. and m.m.p. 238°; the spectra were identical with those of an authentic sample.

(6) A Dreiding model of V reveals that one of the conformers of this all-*cis* bridgehead arrangement forces the 7-keto function out of coplanarity with the benzene ring without introducing undue extra strain into the ring system. This may be the stable conformation and account for the unusual spectral properties of the aromatic ketone: an infrared carbonyl stretching band of too low a wave length, an abnormally low-intensity infrared C=C stretching band, and a major ultraviolet absoption peak of anomalously low intensity (see the Experimental Section).

Penicillin Sulfoxides

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Received August 16, 1965

The sulfoxides of benzylpenicillin and phenoxymethylpenicillin have been prepared by esterification of the carboxyl function followed by oxidation with sodium metaperiodate[1] or hydrogen peroxide,[2] and subsequent removal of the protecting group by hydrogenolysis. We wish to report a general procedure for the *direct* preparation of penicillin sulfoxides. Using sodium metaperiodate in aqueous solution at pH 6.5–7.0 we have obtained the sulfoxides of phenoxymethylpenicillin, (5-methyl-3-phenyl-4-isoxazolyl)penicillin (oxacillin[3]), D-(−)-α-aminobenzylpenicillin (ampicillin[3]), 6-N-carbobenzyloxyaminopenicillanic acid, 6-phthalimidopenicillanic acid, 6-triphenylmethylaminopenicillanic acid, and 6-aminopenicillanic acid by direct oxidation of their salts or free acids. Ampicillin was also oxidized as its N-carbobenzyloxy derivative, and the protecting group was then removed by hydrogenolysis. The sulfoxides were characterized by elemental analyses and by their infrared spectra (KBr disk). A weak-to-medium intensity band due to the S→O stretching

(1) A. W. Chow, N. M. Hall, and J. R. E. Hoover, *J. Org. Chem.*, **27**, 1381 (1962).

(2) E. Guddal, P. Morch, and L. Tybring, *Tetrahedron Letters*, **No. 9**, 381 (1962).

(3) The trademarks of Bristol Laboratories, a division of Bristol-Myers Co., for oxacillin and ampicillin are, respectively, Prostaphlin and Polycillin.