4-Ethoxybenzo[*h*]quinoline,[14] yield 98%, showed mp 116–117° (from ethanol) (lit.[5] mp 119–120°).

Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.82; H, 5.92; N, 6.35.

N-Ethyl-4-quinolone.—A 4.0-g sample of 4-ethoxyquinoline was heated to 250–270° (bath temperature) until it ceased to boil. Distillation gave 3.0 g (75%) of crude N-ethyl-4-quinolone, bp 210–220° (1.3 mm). The solidified product was redistilled, bp 210–212° (1.3 mm), and recrystallized from toluene, mp 100–101°.

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.29; H, 6.46; N, 8.14.

The **picrate** of this compound was prepared in the usual manner, mp 212–214° (from ethanol).

Anal. Calcd for $C_{11}H_{11}NO \cdot C_6H_3N_3O_7$: N, 13.93. Found: N, 13.95.

N-Ethyl-4-quinolone hydrochloride was obtained by treatment of the quinolone with alcoholic HCl, mp 204–205°[15] (from acetonitrile).

Anal. Calcd for $C_{11}H_{11}NO \cdot HCl$: Cl, 16.91; N, 6.68. Found: Cl, 16.88; N, 6.74.

N-Ethylbenzo[*f*]-1-quinolone.—A 2.0-g sample of 1-ethoxybenzo[*f*]quinoline was heated to 360° (bath temperature) until the effervescence ceased. Any unchanged ether was removed by keeping the material at 100° and 0.8 mm. The crude product was obtained by sublimation at 250–300° (0.8 mm) and purified by recrystallization from toluene and aqueous alcohol and by final resublimation, mp 185–187°.

Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.56; H, 5.96; N, 6.36.

When a 1-g sample of 4-ethoxybenzo[*h*]quinoline was treated similarly, 0.8 g of unchanged ether was recovered. The only contaminant was an unidentified tar and no N-ethylbenzo[*h*]-4-quinolone was detected.

N-Ethyl-3-bromo-4-quinolone.—A solution of 1.6 g of bromine in 12.5 ml of acetic acid was added to a solution of 1.7 g of N-ethyl-4-quinolone in 10 ml of the same solvent. Brief heating on the steam bath produced an orange solution. The crystalline material which separated on cooling was filtered and suspended in water. This mixture was made alkaline with 1 *M* Na_2CO_3, and the new precipitate (1.7 g, 68%) was collected, dried, and recrystallized from ethanol, mp 204–207°.

Anal. Calcd for $C_{11}H_{10}BrNO$: C, 52.40; H, 3.99; Br, 31.70. Found: C, 52.34; H, 4.04; Br, 32.22.

Reaction of N-Ethyl-3-bromo-4-quinolone with PBr_3.—A mixture of 2.0 g of the substituted quinolone and 5 ml of PBr_3 was refluxed for 1 hr. The liquid parts were decanted and decomposed with water. The resulting solution was made alkaline with dilute NaOH and the crude product was extracted with ether. The ethereal solution was washed with water and dried (Na_2SO_4), the solvent was removed, and the remaining 3,4-dibromoquinoline was recrystallized from alcohol, mp 77° (lit.[16] mp 77–79°).

Anal. Calcd for $C_9H_5Br_2N$: C, 37.66; H, 1.75; Br, 55.69. Found: C, 37.57; H, 2.02; Br, 55.59.

Hydrolyses of Ethyl 4-Ethoxyquinoline-3-carboxylate. Method A (NaOH).—A 1-g sample of the ester was refluxed for 4 hr with 10 ml of 5% NaOH. The clear, yellow solution was acidified and 0.3 g of 4-quinolone-3-carboxylic acid was filtered, mp 245° dec[17] (from aqueous alcohol) (lit.[4] mp 269–270°).

Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33; neut equiv, 191. Found: C, 62.64; H, 4.55; N, 7.24; neut equiv, 192.

Method B (HCl).—A 1-g sample of the ester was refluxed with 20 ml of 5% HCl. After a few minutes a solid precipitate began to form and was filtered after 0.75 hr. The crude yield was 0.7 g (90%), mp 245° dec[17] (from aqueous alcohol) (lit.[4] mp 269–270°).

The infrared spectra of both samples were identical with that of authentic 4-quinolone-3-carboxylic acid.[4]

(14) This compound is reported in the literature[6] but no preparative method is given.

(15) Sample dried at 78° (0.8 mm), sealed capillary.

(16) B. Riegel, G. R. Lappin, C. J. Albisetti, Jr., B. H. Adelson, R. M. Dodson, L. G. Ginger, and R. H. Baker, *J. Am. Chem. Soc.*, **68**, 1229 (1946).

(17) Lit.[4] mp 269–270°. The melting point of this acid depends on the rate of heating. The one reported in this paper is observed if the sample is heated slowly.

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Heterocyclic Steroids. IX. 2-Oxa-A-nor Steroids[1,2]

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Upon inspection of acetyl acid[4,5] **1a** it was noted that this secosteroid has the salient features of a disubstituted levulinic[6] acid (2). We have already prepared steroidal pyridazinones[4,7] and pyrrolinones[1] by reactions analogous to those reported[6] with levulinic acid (2). To further evaluate the levulinic acid features of **1a**, the characteristic transformation to angelica lactone analogs was undertaken.

Both forms of angelica lactone, the α and the β, can be obtained under conditions frequently associated with enol lactone formation.[6] Indeed, upon refluxing acid **1a** in acetyl chloride and acetic anhydride, both **3** and **4a** were produced. The 3(5)-ene lactone (the α analog) **3** was readily separated from the 5(10)-ene lactone (the β analog) by thin layer chromatography. The structure of **3** follows from its elemental analysis, infrared spectrum, and nmr spectrum. Infrared bands at 1770 cm^{-1} for the five-membered enol lactone and at 1725 cm^{-1} for the 17-acetate were observed. The nmr spectrum had sharp singlets at 51.5 and 122.5 cps for the 18-methyl and 17-acetate, respectively. The C-3 vinylic methyl appeared as a multiplet centered at 115.5 cps (W_H = 4.5 cps). The splitting of this methyl is the result of homoallylic coupling with the C-6 and C-10 axial protons. Coupling of this type has been reported[8] in α-angelica lactone and other compounds with similar structures.

The 5(10)-lactone **4a** was characterized by its infrared peaks at 1735 for the carbonyls and at 1655 cm^{-1} for the conjugated double bond, as well as its ultraviolet maximum at 219 mμ. In the absence of a proton α to the carbonyl, the usual splitting of the carbonyl bands in the infrared did not occur. Its nmr spectrum

(1) Part VIII: D. M. Piatak and E. Caspi, *J. Org. Chem.*, **31**, 3935 (1966).

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(3) Department of Chemistry, Northern Illinois University, DeKalb, Ill.

(4) E. Caspi, P. K. Grover, and D. M. Piatak, *Chem. Ind.* (London), 1495 (1963).

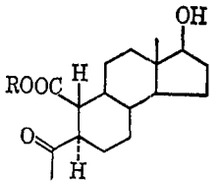
(5) E. Caspi, P. K. Grover, D. M. Piatak, and Y. Shimizu, *J. Chem. Soc.*, 3052 (1965).

(6) Various reactions of levulinic acid have been reviewed by R. H. Leonard, *Ind. Eng. Chem.*, **48**, 1331 (1956).

(7) D. M. Piatak, R. I. Dorfman, D. Tibbetts, and E. Caspi, *J. Med. Chem.*, **7**, 590 (1964).

(8) D. Gagnaire and E. Payo-Subiza, *Bull. Soc. Chim. France*, 2623 (1963); N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, p 111.

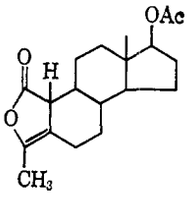
exhibited signals at 51 for the 18-methyl, 82.5 (doublet, J = 7.0 cps) for the C-3 methyl, and at 122.5 cps for the 17-acetate. The migration of the double bond is not limited to the case of lactones. A similar shift was noted in the lactam formation[1] when **1a** was treated with benzylamine.



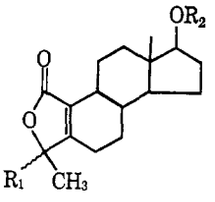
1a, R = H
b, R = CH_3

$CH_3CO\,CH_2CH_2\,COOH$

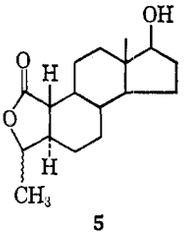
2



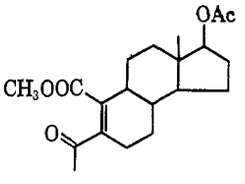
3



4a, R_1 = H; R_2 = Ac
b, R_1 = R_2 = H
c, R_1 = OH; R_2 = H
d, R_1 = OCH_3; R_2 = Ac
e, R_1 = OAc; R_2 = Ac



5



6

The 5(10)-ene lactone **4a** could be prepared alternatively from the pseudo-γ-ketone[5] (lactol) **4c**. The lactol was dissolved in aqueous methanolic sodium hydroxide and reduced with sodium borohydride to the 17-hydroxy lactone **4b**, which was acetylated to **4a**. The frequently observed 1,4-hydride ion addition to conjugated ketones also occurred as evidenced by the isolation of the saturated lactone **5**. The same product was isolated from the borohydride reduction of keto acid **1a**. In view of the fact that the 5α,10β stereochemistry of **1a** has been established, it follows that the 1,4-addition product has structure **5**.

When the β-angelica lactone **4a** was saponified in methanol with aqueous sodium hydroxide and subsequently treated with diazomethane, ester **1b** was isolated in good yield. Apparently the double bond isomerized from the 5(10) to the 3(5) position prior to opening of the lactone ring. Isomerization of the double bond in angelica lactone by base has been inferred from the isolation of various dimers.[6] In the present case dimerization presumably did not take place due to the bulkiness of the molecules involved.

Previously,[5] we had described ester **6** obtained by treating lactol **4c** first with diazomethane, then acetic anhydride. In the mother liquor a minor amount of lactol ether **4d** has now been found. The product was identified by its ultraviolet maximum at 218 mμ and its infrared bands at 1735 for the carbonyl and at 1670 cm^{-1} for the double bond. Nmr singlets for methyls were observed at 50.5 for the 18-methyl and at 121.5 cps for the acetate methyl. Signals for the methoxyl appeared at 186 and 189 cps, revealing the presence of C-3 isomers. The total area was equal to three protons and the ratio was about 9:10, respectively. Confirmation of the existence of isomers was provided by the signal for the C-3 methyl which appeared as a narrow doublet at 93 with a coupling of about 1 cps.

Of incidental interest is that acetylation of lactol **4c** with acetic anhydride–pyridine at room temperature yielded diacetoxy lactol **4e**. The diacetate had infrared peaks at 1760, 1730, and 1670 cm^{-1}, as might be expected. In contrast to lactols **4a–d** which showed ultraviolet maxima at 218–219 mμ, the maximum in **4e** was shifted to 225 mμ. Again, the product isolated is found to be a mixture of isomers. Besides the nmr signals at 50.5 for the 18-methyl and at 121.5 for the two acetates, the C-3 methyl was observed as two signals at 100 and 102 cps.

Experimental Section[9]

17β-Acetoxy-3-methyl-2-oxa-1-oxo-A-norestr-3(5)-ene (3).—A solution of acetyl acid **1a** in acetic anhydride (3.0 ml) and acetyl chloride (2.0 ml) was refluxed for 16 hr. The mixture was cooled and decomposed with ice. The steroids were dissolved in ethyl acetate and washed with a sodium bicarbonate solution and water. The neutral fraction was chromatographed on a tlc plate (benzene–ethyl acetate, 4:1) into two zones. The more mobile zone was eluted to yield 50 mg of α-lactone **3**, while the other zone gave 40 mg of β-lactone **4a**.

Repeated recrystallization of the 3(5)-ene lactone **3** from ethyl acetate–pentane gave colorless crystals: mp 136–141°, sinters; ν_{max} 1770 and 1725 cm^{-1}; λ_{max} 232 mμ (ε 2800); nmr 51.5 (18-methyl), 115.5 (W_H = 4.5 cps, C-3-methyl), 122.5 (17-acetate), 277 cps (triplet, J = 7.5 cps, 17α-proton).

Anal. Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.60; H, 8.35.

17β-Acetoxy-3ξ-methyl-2-oxa-1-oxo-A-norestr-5(10)-ene (4a). A.—The 5(10)-ene lactone **4a** isolated from the less mobile zone in the above experiment, was recrystallized from ethyl acetate–pentane to mp 92–100°; ν_{max} 1735 and 1655 cm^{-1}; λ_{max} 219 mμ (ε 9700); nmr 51 (18-methyl), 82.5 (doublet, J = 7.0 cps, C-3-methyl), 122.5 cps (17-acetate).

B.—The lactone **4a** was formed by acetylation of the 17-hydroxy analog **4b** prepared below. It was found to be identical with the product isolated in part A.

17β-Hydroxy-3ξ-methyl-2-oxa-1-oxo-A-norestr-5(10)-ene (4b).—A solution of lactol **4c** (200 mg) in methanol (15 ml) was titrated to a phenolphthalein end point with 1 N aqueous sodium hydroxide. Sodium borohydride (400 mg) was added, and the mixture was stored at room temperature overnight. The methanol was removed *in vacuo*, and the solution was acidified with 2 N hydrochloric acid. The steroids were recovered with ethyl acetate and washed with water. The residue was chromatographed on a tlc silica plate (ethyl acetate–benzene, 1:1). The most mobile zone was the saturated lactone **5** (see below). The next zone was eluted to give 70 mg of the α,β-unsaturated lactone **4b**.

An analytical sample of **4b** was prepared by recrystallization from ethyl acetate to mp 152–157°, sinters; ν_{max} 3500, 1735, 1665 cm^{-1}; λ_{max} 219 mμ (ε 10,000).

Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.95; H, 8.78.

17β-Hydroxy-3ξ-methyl-2-oxa-1-oxo-A-nor-5α-estrane (5). A.—The most mobile tlc zone from the reduction of **4c** (see above)

(9) All melting points were taken on a micro hot stage and are corrected. Infrared spectra were taken on solids in KBr blotters. Nmr spectra were recorded in deuteriochloroform solutions on a Varian Associates HA-60 spectrometer. Ultraviolet spectra were taken in methanol. Thin layer chromatography (tlc) was done on silica gel HF_{254} from Merck, A. G.

was eluted to give 30 mg of **5**: mp 143–148°; ν_{max} 3290 and 1770 cm^{-1}; nmr 47.5 (18-methyl), 83.5 cps (doublet, J = 6.0 cps, C-3-methyl).

Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 72.98; H, 9.34.

B.—Acetyl acid **1a** (110 mg) was dissolved in methanol (7 ml) and titrated with 1 N sodium hydroxide until a phenolphthalein end point was reached. After the addition of sodium borohydride (150 mg) the mixture was stored overnight. The solvent was removed, the solution was acidified, and the steroids were recovered with ethyl acetate. Removal of the solvent gave 110 mg of crude product, which was separated on a silica tlc plate. Elution of the mobile zone gave 60 mg of lactone **5** identical with the sample obtained in part A.

17β-Acetoxy-3ξ-methoxy-3ξ-methyl-2-oxa-1-oxo-A-norestr-5(10)-ene (4d).—The mother liquors (150 mg) from the methylation and acetylation of lactol **4c** (525 mg) were chromatographed on tlc silica plates. The lactol ether **4d** (80 mg) was eluted and recrystallized from methanol to give colorless crystals: mp 145–147°; ν_{max} 1735 and 1670 cm^{-1}; λ_{max} 218 mμ (ε 7000); nmr 50.5 (18-methyl), 93 (doublet, *ca.* J = 1.0 cps, C-3-methyl), 121.5 (17-acetate), 186 and 189 (total equivalent to three protons, C-3-methoxyl), 279 cps (triplet, J = 7.5 cps, 17α-hydrogen).

Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 69.24; H, 8.40.

3ξ,17β-Diacetoxy-3ξ-methyl-2-oxa-1-oxo-A-norestr-5(10)-ene (4e).—The lactol **4c** was acetylated[10] as usual to yield the diacetate **4e**. Repeated recrystallizations from ethyl acetate gave an analytical sample: mp 131–134°; ν_{max} 1760, 1730, 1670 cm^{-1}; λ_{max} 225 mμ (ε 7400); nmr 50.5 (18-methyl), 100 and 102 (total equivalent three protons, C-3-methyl), 121.5 cps (3- and 17-acetates).

Anal. Calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 66.70; H, 7.46.

Methyl 17β-Hydroxy-4-methyl-4-oxo-1,4-seco-2,3-bisnor-5α-estran-1-oate (1b).—The acetoxy lactol **4a** (60 mg) was dissolved in methanol (5 ml) and 1 N sodium hydroxide (1 ml) and the mixture was refluxed for 2 hr under nitrogen. Upon a conventional work-up, 45 mg of acid **1a** was obtained, which was treated with diazomethane to yield the ester **1b** identical with the previously described sample.[5]

(10) We wish to thank Dr. P. K. Grover for this experiment.

The Schmidt Reaction with Camphorquinone

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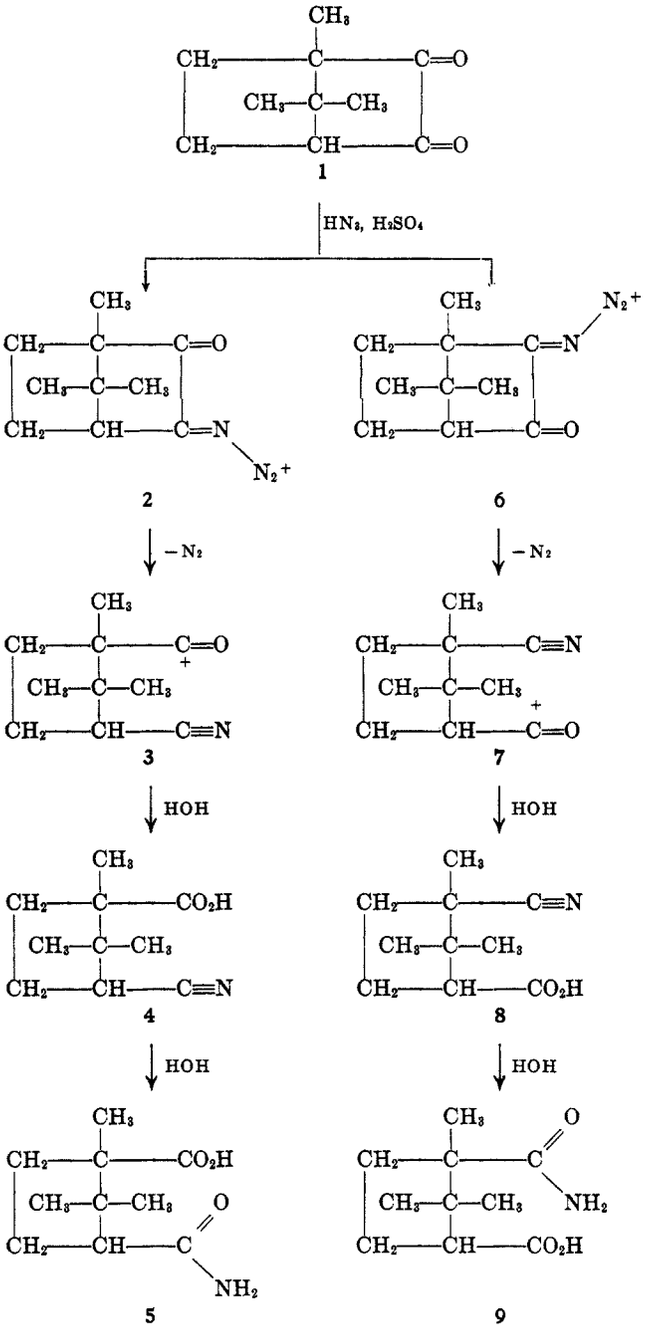
The similarity of the Beckmann rearrangement of the camphorquinone-3-oximes and the rearrangement of the camphorquinone-3-hydrazones[1] and -semicarbazones[2] led to the present study. A common product was α-camphoramic acid, having been produced by cleavage instead of the normal carbon to nitrogen rearrangement.

When subjected to Schmidt reaction conditions (sulfuric acid added to a chloroform solution of the ketone and hydrogen azide) as described in the Experimental Section, camphorquinone (**1**, Scheme I) produced α-camphoramic acid (**5**), β-camphoramic acid (**9**), and a small amount of α-camphornitrilic acid (**4**). It is considered that **4** and **5** arose from attack on the 3 position, whereas attack at the 2 position produced **9**. That the majority of the reaction product is **5** is in accord with the well-known fact that the 3 position in **1** is much more reactive than the 2 position.

SCHEME I



Smith[3] has recently reviewed the cleavage-type Schmidt reaction. He also suggests[4] that the hydrazone rearrangement and Schmidt reaction have a common iminodiazonium ion intermediate. Zook and Paviak[5] applied the Schmidt reaction to a series of *t*-butyl alkyl ketones and found that the bulkier *t*-butyl group migrated in the normal manner as expected but in very poor yields, the main reaction being cleavage to the *t*-butyl carbonium ion (which alkylated the solvent if benzene or toluene were used) and a nitrile or hydrolysis product of a nitrile. Intermediates **2**, **3**, **4**, **6**, **7**, and **8** are consistent with their mechanism

(1) K. N. Carter, *J. Org. Chem.*, **23**, 1409 (1958).
(2) K. N. Carter and G. S. Blakely, unpublished results.
(3) P. A. S. Smith in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p 517.
(4) Reference 3, p 527.
(5) H. D. Zook and S. C. Paviak, *J. Am. Chem. Soc.*, **77**, 2501 (1955).