that the aldehyde condensations are misleading, and that the alkaloid actually corresponds to Ic.[2]

Reduction of dehydrocassine (IIa) under Wolff–Kishner conditions produces a compound of the constitution $C_{18}H_{31}NO$. Spectral properties of this material show that the 3-hydroxy-2, 6-dialkylpyridine system is retained, as anticipated. The unbranched character of the 6-alkyl group was shown by oxidation by nitric acid to a small quantity of acidic material, which was converted to a mixture of methyl esters by treatment with diazomethane. Gas chromatography showed that the main component corresponds in retention time to methyl laurate. Isolation of this main component by gas chromatography provided material with a mass spectrum identical with that of known methyl laurate. As both gas chromatographic retention times[3] and mass spectral fragmentation patterns[4] of branched-chain esters are known to differ from the straight-chain isomers, these results require that the Wolff–Kishner product be 2-methyl-3-hydroxy-6-dodecylpyridine (IIb), and that cassine be regarded as Ic.

Characterization of cassine included base-catalyzed exchange in deuteriomethanol to a material characterized by combustion analysis as a tetradeuterio derivative.[1] However, the mass spectrum of this material reveals the presence of variously deuterated derivatives, with the heaviest ion corresponding to a pentadeuterated material (Id). These studies are therefore consistent with the correct structure for cassine (Ic).

Experimental Section[5]

2-Methyl-3-hydroxy-6-dodecylpyridine (IIb).—Dehydrocassine[1] (IIa, 61 mg) was heated on a steam bath in 3 ml of ethylene glycol with 172 mg of potassium hydroxide and 0.7 ml of hydrazine hydrate for 0.5 hr. The flask was equipped with a downward condenser and plunged into a wax bath heated to 210°. Distillation was continued until the distillate temperature reached 180°. After 3-hr reflux the solution was cooled, acidified with hydrochloric acid, then made weakly basic with ammonium hydroxide, and extracted twice with chloroform. The organic phase was concentrated to dryness to leave 68 mg of colorless low-melting solid. Crystallization from acetone provided 38 mg, mp 90–96°, shown by gas chromatography to retain 3% of starting material. Recrystallization provided material of mp 101–103.5°; nmr,[5] δ = 7.12 (d, J = 9 cps, 1 H), 6.87 (d, J = 9 cps, 1 H), 2.70 (m, 2 H), 2.53 (s, 3 H), 1.25 (broad methylene absorption), and 0.97 ppm (m, 3 H); λ_{max}^{EtOH} 224 mμ (ε 8240), 288 mμ (ε 5850); addition of potassium hydroxide shifted the ultraviolet maxima to 245 mμ (ε 11,500) and 310 mμ (ε 6200); addition of acid shifted the maxima to 231 mμ (ε 5750) and 301 mμ (ε 9500); infrared (KBr pellet), ν_{max} 3500, 2700–2400, 1582, 1290, 830 cm^{-1}.

Anal. Calcd for $C_{18}H_{31}NO$: mol wt, 277.236. Found: mol wt, 277.236.

Oxidation.—A 29-mg sample of the above pyridine was heated on a steam bath for 10 min with 0.03 ml of nitric acid. The solution was diluted with methanol and extracted three times by hexane; the upper phase was extracted with 1 *N* sodium hydroxide in 95% methanol; the basic extract was washed with hexane, acidified by hydrochloric acid, and extracted twice with hexane. The hexane solution was treated with ethereal diazomethane. Gas chromatography (4% SE-30 on Gas-Chrom P, 0.3 × 365 cm, 130°, 1400 g/cm²) showed a mixture of which the major component had the retention time (16.0 min) of authentic methyl laurate.

The collected raffinates of the above sequence were made basic by sodium hydroxide and concentrated to dryness under reduced pressure. A single partition between methanolic hydrochloric acid and hexane provided a hexane extract which was treated with diazomethane. Gas chromatography showed this to be a mixture containing a similar amount of methyl laurate.

To provide a sample for mass spectrometric examination, the first hexane extract was chromatographed in the vapor phase over a column 1.6 cm in diameter, 273 cm long, 30% SE-30 on Gas-Chrom P, at 175°, 1400 g/cm². Fractions were collected by condensation in a trap chilled by liquid nitrogen, and the major component was obtained pure. This material was introduced into a mass spectrometer (Associated Electrical Industries, Ltd., MS-9) by direct inlet, and produced a spectrum identical in every respect with that from known methyl laurate.

Deuteriocassine,[1] introduced into the mass spectrometer as above, produced peaks corresponding to the following *m/e:* 302 (relative height 1.0), 301 (0.94), and 300 (0.56). The molecular ion of cassine, so introduced, corresponded to *m/e* 297.

(3) A. Littlewood, "Gas Chromatography," Academic Press Inc., New York, N. Y., 1962, p 424; A. T. James and A. J. P. Martin, *Biochem. J.*, **63**, 144 (1956).

(4) R. Ryhage and E. Stenhagen in "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press Inc., New York, N. Y., 1963, p 408.

(5) All melting points were observed on a Kofler microscope hot stage and are corrected. The authors are indebted to Mrs. K. S. Warren for spectrophotometric data. Ultraviolet spectra were recorded on a Cary Model 11 MS recording spectrophotometer. Infrared spectra were observed on a Perkin-Elmer Model 21 double-beam spectrophotometer. Molecular weights were determined on an Associated Electrical Industries MS-9 double-focusing mass spectrometer by comparison to an ion of slightly less weight from perfluorotributylamine. Mass spectra were obtained at 70-ev ionizing radiation. Nmr spectra were determined on a Varian Associates A-60 nmr spectrometer in deuteriochloroform solution, using tetramethylsilane as a reference (δ = 0.0 ppm). The following abbreviations are used: s, singlet; q, quartet; m, multiplet. The figures entered after the chemical shifts represent relative proton content determined by electronic integration.

The Furanoquinoline Alkaloids. III.[1] An Attempted Synthesis of *dl*-Lunacrine and Correction of the Structure of "Demethoxylunacrine"

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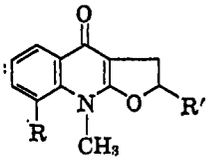
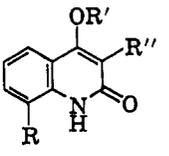
In an effort to explore the synthetic approach to furoquinoline alkaloids developed recently in these laboratories,[1] an attempt has been made to apply this synthesis to a total synthesis of *dl*-lunacrine (Ia).



Ia, R = OCH_3; R′ = $CH(CH_3)_2$
b, R = H; R′ = $CH(CH_3)_2$
c, R = OCH_3; R′ = $CH_2CH(CH_3)_2$
d, R = H; R′ = $CH_2CH(CH_3)_2$



IIa, R = OCH_3; R′ = H; R″ = $COCH_2CH(CH_3)_2$
b, R = OCH_3; R′ = CH_3; R″ = $COCH_2CH(CH_3)_2$
c, R = H; R′ = CH_3; R″ = $COCH_2CH(CH_3)_2$
d, R = OCH_3; R′ = CH_3; R″ = $CHOHCH_2CH(CH_3)_2$
e, R = OCH_3; R′ = CH_3; R″ = $CH_2COCH_2CH(CH_3)_2$

By analogy with the published synthesis of demethoxylunacrine (Ib),[1] the starting material of choice appeared to be 4-hydroxy-8-methoxy-2-quinolone,[2] which should be readily available from the cyclization of

(1) Part II: J. W. Huffman and L. E. Browder, *J. Org. Chem.*, **29**, 2598 (1964).

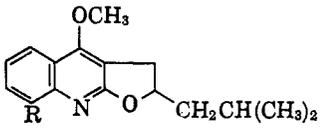
(2) B. Berinzaghi, A. Muruzabal, R. Labriola, and V. Deulofeu [*ibid.*, **10**, 181 (1945)] have prepared this compound in several steps from 2-nitro-3-methoxybenzoic acid.

ethyl *o*-methoxymalonanilate. Although ethyl malonanilate has been reported to afford 4-hydroxy-2-quinolone on treatment with polyphosphoric acid,[3] the *o*-methoxy ester failed to cyclize. The corresponding acid did, however, afford the desired quinolone in good yield. Acylation of 4-hydroxy-8-methoxy-2-quinolone with isovaleryl chloride gave the 3-isovaleryl compound IIa, which could also be obtained from the direct reaction of *o*-anisidine and diethyl isovalerylmalonate. The structure of this compound was confirmed by reduction to 3-isoamyl-4-hydroxy-8-methoxy-2-quinolone.

Reaction of the isovalerylquinolone with diazomethane gave a compound thought to be the methyl ether IIb on the basis of the similarity of the infrared spectrum to that of the compound prepared in the earlier work (IIc)[1] and analytical data. Reduction with sodium borohydride gave an alcohol to which was assigned structure IId. Cyclization with phosphorus oxychloride, followed by treatment with methyl iodide and cleavage of the 4-methyl ether, gave a compound which by analogy with the demethoxylunacrine work[1] should have been lunacrine (Ia). This material, although very similar to lunacrine, was not identical with it, nor did the melting point of the compound agree with that reported for *dl*-lunacrine.[4]

Although the synthesis of demethoxylunacrine (Ib) had appeared straightforward,[1] it appeared that either this sequence was incorrect, or that the structure of lunacrine was not as assigned.[4a] Since the structure of lunacrine has been confirmed by an unequivocal total synthesis,[4b] it seemed probable that our synthetic sequence was incorrect. This was confirmed by the nmr spectra of the various intermediates in the synthesis. In particular, the nmr spectrum of the methyl ether obtained from IIa on treatment with diazomethane did not show the two-proton doublet at δ 3.13 which was present in IIa. There was instead a singlet at δ 3.74 and a three-proton ABC pattern with the AB portion centered at δ 2.52. The only structure consistent with these data is that of 3-(2-oxo-4-methylpentyl)-4,8-dimethoxy-2-quinolone (IIe), the result of not only methylation, but diazomethane homologation as well.[5] The nmr spectrum of the alcohol obtained by borohydride reduction confirmed this assignment. It showed a one-proton multiplet at δ 4.62, and a two-proton multiplet at δ 2.87 as well as an envelope (three protons) between δ 1.2 and 2.16. The low-field proton must be that on the carbinol carbon, those at δ 2.87 the benzyl protons, and the high-field envelope must be the methylene and methine protons. The ultraviolet spectra of the ketone and the reduction product were identical, indicating that the carbinol group was probably not conjugated with the aromatic system.

Cyclization of this alcohol with phosphorus oxychloride will give the isobutyl furoquinoline (IIIa), which will then in turn give a homolog of lunacrine



IIIa, R=OCH_3
b, R=H

(Ic). The nmr spectrum of IIIa was quite similar to that reported for the precursor of "demethoxylunacrine," with the methylene protons adjacent to the furan appearing as a broad multiplet superimposed on the tertiary proton of the isopropyl group.[6] The nmr spectrum of the lunacrine homolog clearly shows the presence of these methylene protons as an envelope between δ 1.3 and 2.2.[7]

Since the proposed synthesis of lunacrine was based on the synthesis of "demethoxylunacrine,"[1] the compounds in the earlier series were reexamined, and based on their nmr and ultraviolet spectra it is apparent that "demethoxylunacrine" is in fact the isobutyl homolog Id. The compounds in the demethoxy series were resubmitted for analysis, which confirmed the conclusions reached from a study of their nmr and ultraviolet spectra.[8]

Experimental Section[9]

4-Hydroxy-8-methoxy-2-quinolone.—A suspension of 2.0 g of *o*-methoxymalonanilic acid[10] in 10 g of polyphosphoric acid was

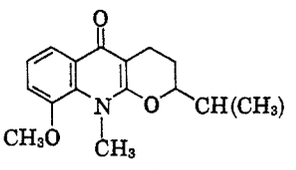
(3) J. A. Bosson, M. Rasmussen, E. Ritchie, and W. C. Taylor, *Australian J. Chem.*, **16**, 488 (1963).

(4) (a) S. Goodwin and E. C. Horning, *J. Am. Chem. Soc.*, **81**, 1908 (1959); (b) E. A. Clarke and M. F. Grundon, *J. Chem. Soc.*, 438 (1964).

(5) There was also obtained from the diazomethane reaction a small quantity of an isomer of IIe. Based primarily on ultraviolet and nmr data this compound is almost certainly 3-(1-oxo-4-methylpentyl)-4,8-dimethoxy-2-quinolone. It is interesting to note the carbonyl region in both this compound and IIe are almost identical.

(6) Although implicit faith in the electronic integration of the nmr spectrum originally run on compound IIIb would have given the correct structural formula, the analytical results in the whole series seemed to preclude any structure other than that of an isopropyl furoquinoline.[1]

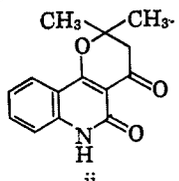
(7) Although the possibility that this compound is the pyranoquinoline i cannot be completely excluded, the ultraviolet spectrum appears to be that of a furoquinoline [see H. Rapoport and K. G. Holden, *J. Am. Chem. Soc.*,



i

82, 4395 (1960)]. Also the splitting pattern in the nmr of the benzyl protons appears identical with that of the equivalent protons in lunacrine.

(8) We have no good explanation for the consistently low carbon analyses given by compounds in both series. This same problem has been encountered with the angular furoquinolines in the methoxy series, where it has not been found possible to obtain satisfactory (or reproducible) analytical data. The structures originally assigned to the compounds in both series were based on infrared and analytical data. For reasons which are not at all apparent, the carbonyl absorption of the nonconjugated ketones IIe and its demethoxy analog appears at the same place (5.90 μ) as that of the conjugated ketone ii employed in the total synthesis of flindersine [F. F. C. Brown, G. K.



ii

Hughes, and E. Ritchie, *Australian J. Chem.*, **9**, 277 (1956)]. A search of the notebooks describing our earlier work indicates that for reasons which are unclear the ultraviolet spectrum of the demethoxy analog of IIe was not recorded.

(9) All melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were taken either as liquid films on sodium chloride plates or as potassium bromide disks employing a Perkin-Elmer Model 137 spectrophotometer. Ultraviolet spectra were taken on a Perkin-Elmer Model 202 spectrophotometer using methanol as a solvent. The nmr spectra were taken on a Varian A-60 nmr spectrometer, using deuteriochloroform as the solvent and tetramethylsilane as an internal standard. Microanalyses were determined by Galbraith Laboratories, Knoxville, Tenn., or Schwarzkopf Laboratory, Woodside, N. Y.

(10) P. A. Petyunin and N. G. Panferova, *Zh. Obshch. Khim.*, **21**, 1533 (1951); *Chem. Abstr.*, **46**, 2531a (1952).

TABLE I

Compd	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
3-(2-Oxo-4-methylpentyl)-4-methoxy-2-quinolone	$C_{16}H_{19}NO_3$	70.31	7.01	5.12	70.10	7.01	5.34
3-(2-Hydroxy-4-methylpentyl)-4-methoxy-2-quinoline	$C_{16}H_{21}NO_3$	69.79	7.69	5.09	74.99	7.91	5.21
2-Isobutyl-4-methoxy-2,3-dihydrofuro[2,3-*b*]quinoline	$C_{16}H_{19}NO_2$	74.68	7.44	5.44	74.99	7.68	5.69
1-Methyl-2-isobutyl-2,3-dihydrofuro[2,3-*b*]-4-quinolone ("demethyoxylunacrine")	$C_{16}H_{19}NO_2$	74.68	7.44	5.44	74.48	7.34	5.47

heated at 150° for 30 min. The reaction mixture was cooled and diluted with water, and the precipitated solid was collected. The solid material was washed with water, dissolved in 10% sodium hydroxide, filtered, and acidified with 10% hydrochloric acid. The solid precipitate was collected, washed with water, and recrystallized from acetone–methanol to give 1.2 g (68%) of quinolone, mp 170°, followed by resolidification and melting with sublimation at 250° (lit.[4] mp 246°).

Diethyl Isovalerylmalonate.—A solution of 120 g of diethyl malonate in 100 ml of dry ether was added over a period of 2 hr to suspension of 26 g of 52% sodium hydride mineral oil dispersion in 1000 ml of dry ether. The resulting thick slurry of sodiomalonic ester was stirred slowly overnight at room temperature, and a solution of 25 g of isovaleryl chloride in 200 ml of dry ether was added dropwise over a 1-hr period. The reaction was stirred 5 hr at room temperature; 25 ml of acetic acid was added cautiously, followed by 200 ml of water, and 100 ml of 10% hydrochloric acid. The aqueous layer was drawn off and discarded, and the organic layer was washed thoroughly with water and 10% sodium carbonate solution and dried, and the solvent was removed *in vacuo*. The resulting pale yellow liquid was distilled through a 6-in. Vigreux column at 31-mm pressure to give 66.2 g of recovered diethyl malonate, bp 96–100°, an intermediate fraction of 8.4 g, bp 101–118°, and 24.3 g (46%) of the desired product, bp 118–120°.[11]

3-Isovaleryl-4-hydroxy-8-methoxy-2-quinolone. A.—A mixture of 11.4 g of isovaleryl malonic ester and 4.0 g of *o*-anisidine was heated under reflux for 30 min in 40 ml of phenyl ether. The reaction mixture was cooled, diluted with 40 ml of hexane, and scratched to induce crystallization. The product was collected, washed with a small portion of cold hexane, and recrystallized from cyclohexane to give 1.43 g (18%) of pale yellow crystals, mp 142–143°. Extraction of the mother liquors with 10% sodium hydroxide and acidification gave, after recrystallization, 0.43 g (5.4%) of somewhat inferior material, mp 138–141°. The analytical sample was crystallized from cyclohexane and had mp 142–143°.[12]

Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.23; N, 5.09. Found: C, 65.30; H, 6.30; N, 5.09.

B.—To 1.0 g of 4-hydroxy-8-methoxy-2-quinolone in 20 ml of *sym*-tetrachloroethane was added 2 ml of isovaleryl chloride. The mixture was allowed to stand at room temperature for 15 hr and then cooled in an ice bath, and 2.8 g of aluminum chloride was added. The reaction mixture was allowed to stand at room temperature for 3 days and then was poured into a mixture of ice and concentrated hydrochloric acid. The organic layer was drawn off and extracted with two portions of 10% sodium hydroxide. The basic solution was washed with ether and acidified. The precipitated solid was collected and recrystallized from cyclohexane–ethyl acetate to give 0.89 g (54%) of material, mp 139–140°, identical with that obtained in part A. The nmr spectrum of this material shows peaks at δ 7.58 (q, one proton), 4.0 *ca.* (m, three protons), 3.93 (s, three protons), 3.15 (d, J = 6 cps, two protons), 2.25 (m, one proton), 1.01 (d, J = 6 cps, six protons).

Reduction of 3-Isovaleryl-4-hydroxy-8-methoxy-2-quinolone.—To a solution of 0.55 g of the isovaleryl quinolone in 35 ml of isopropyl alcohol was added 0.50 g of sodium borohydride, and the reaction was heated 12 hr at reflux. The pale yellow solution was cooled, diluted with water, and cautiously acidified. After standing an hour at room temperature, the precipitated solid was collected and recrystallized from aqueous acetic acid to give 0.28 g (52%) of 3-(3-methylbutyl)-4-hydroxy-8-methoxyquinoline,[13] mp and mmp 234–236°.

(11) K. Von Auwers and H. Jacobsen [*Ann.*, **426**, 161 (1922)] reported a boiling point of 141° at 14 mm for this compound.

(12) The yield of this reaction varied from a maximum of 23% to a minimum of 7.5% for a number of runs, carried out under apparently identical conditions. The yield figures cited are for one recrystallized product, both from extraction of the mother liquors, and direct crystallization.

3-(2-Oxo-4-methylpentyl)-4,8-dimethoxy-2-quinolone.—A solution of 4.0 g of 3-isovaleryl-4-hydroxy-8-methoxy-2-quinolone in 200 ml of ether containing 2 ml of methanol was added slowly to a solution of diazomethane (from 15.0 g of nitrosomethylurea) in 300 ml of ether. The pale yellow solution was allowed to stand at room temperature for 14 hr and was concentrated to dryness, and the residue was dissolved in hexane and chromatographed on 50 g of Merck alumina. Elution with 4:1 hexane–chloroform gave 2.0 g of solid material. Recrystallization from chloroform–hexane gave 1.8 g (35%) of material, mp 108–133°. Repeated recrystallization from the same solvent pair gave the analytical sample, mp 144–145°.

Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.11; H, 6.79; N, 4.54. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Reanalysis gave C, 67.62, 67.48; H, 7.10, 7.12.

The infrared spectrum shows carbonyl bands at 5.90 and 6.12 μ, and the ultraviolet spectrum shows λ_{max} 237 mμ (log ϵ 4.29), 253 (4.43), 282 (3.93), 292 (sh) (3.90), 332 (3.57), and 346 (sh) (3.47). The nmr spectrum shows peaks at δ 7.07 (m, three protons), 3.92 and 3.89 (s, three protons each), 3.73 (s, two protons), 0.94 (d, J = 7 cps, six protons), and an ABC pattern (or A_2B) with two protons at δ 2.43 and the third at *ca.* δ 2.0.

Tlc (silica gel G, benzene–acetone 5:1) of the mother liquors from the first recrystallization gave two spots, one with R_f 0.32, corresponding to the above ketone, and one with R_f 0.40. Chromatography of 0.35 g of this material and elution with 1:1 ether–methylene chloride gave 0.40 g of a second compound, mp 136–138°. Recrystallization from hexane–methylene chloride gave 0.026 g of material, mp 138–139°.

Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.46; H, 7.20; N, 4.63.

The infrared spectrum of this compound is very similar to that of the above keto methyl ether, and the ultraviolet shows λ_{max} 231 mμ (log ϵ 4.34), 254 (4.42), 288 (3.93), and 343 (3.56). The nmr spectrum shows peaks at δ 7.38 (q, one proton), 7.08 (q, two protons), 3.92 (s, six protons), 2.88 (d, J = 7 cps, two protons), 1.05 (d, J = 6 cps, six protons), and a broad multiplet (three protons) between δ 1.2 and 2.5.

3-(2-Hydroxy-4-methylpentyl)-4,8-dimethoxy-2-quinolone.—To a solution of 1.75 g of the dimethoxyquinolone in 200 ml of isopropyl alcohol was added 3.5 g of sodium borohydride. The reaction mixture was heated at reflux 12 hr and cooled, and dilute hydrochloric acid was added cautiously to decompose the excess hydride. The mixture was diluted with water and extracted with three portions of methylene chloride. The organic extracts were combined and dried, and the solvent was removed at reduced pressure. The residue was dissolved in warm methanol, diluted with water, and cooled, affording 1.0 g (55%) of crude alcohol, mp 118–122°. Repeated recrystallization from acetone–hexane gave the analytical sample as white platelets, mp 142–143°.

Anal. Calcd for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.79, 66.88; H, 7.86, 7.63; N, 4.88.

The ultraviolet spectrum of this compound shows λ_{max} 237 mμ (log ϵ 4.36), 254 (4.55), 282 (4.03), 292 (sh) (3.99), 332 (3.72), and 346 (sh) (3.55). The nmr spectrum shows peaks at δ 7.10 (m, three protons), 4.62 (m, one proton), 3.99, 3.91 (s, three protons each), 2.85 (AB portion of an ABX), 0.93 (d, J = cps, six protons), and a three-proton envelope between δ 1.1 and 2.1.

2-Isobutyl-4,8-dimethoxy-2,3-dihydrofuro[2,3-*b*]quinoline.—To a solution of 2.0 g of 3-(2-hydroxy-4-methylpentyl)-4,8-dimethoxy-2-quinolone in 10 ml of dry pyridine was added 2.0 ml of phosphorus oxychloride. The solution was allowed to stand at room temperature for 15 min and then heated on the steam bath 1 hr. After cooling the reaction mixture was poured into water, and the precipitated solid was collected and dried. The solid material was taken up in a 1:1 mixture of hexane and chloroform and chromatographed on Merck alumina. Elution with

(13) J. W. Huffman, *J. Org. Chem.*, **26**, 1470 (1961).

the same solvent gave the furoquinoline as a white solid. Recrystallization from hexane–acetone gave 0.45 g (24%) of material, mp 103–104°. Recrystallization from the same solvent pair gave the analytical sample, mp 106–107°.

Anal. Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found:[14] C, 70.57; H, 7.20; N, 5.47.

1-Methyl-2-isobutyl-8-methoxy-2,3-dihydrofuro[2,3-*b*]-4-quinolone.—A solution of 0.045 g of the above quinoline in 3 ml of iodomethane was heated at reflux 10 min, cooled, and allowed to stand at room temperature for 24 hr. The precipitated solid was collected and washed with hexane to give 0.040 g of off-white solid, mp 135–136°. This material shows λ_{max} 217 mμ (log ε 4.89), 254 (4.87), 258 (sh) (4.87), 303 (4.16), and 330 (3.81). Since this material decomposed on attempted recrystallization, 0.040 g was dissolved in 1 ml of pyridine and heated on the steam bath 22 hr.[15] The solvent was evaporated, the residue was taken up in methylene chloride, washed with water, and dried, and the solvent was removed *in vacuo* leaving 18 mg (66% based on methiodide[16]) of white solid. Recrystallization from ethyl acetate–hexane gave white crystals, mp 90–91°. The infrared spectrum (solution) of this compound was very similar but not identical with that of a sample of (−)-lunacrine, the ultraviolet spectrum in both neutral and acidic solution was identical with that reported for lunacrine.[4b] This compound also has the same R_f value on tlc in two systems (benzene–acetone 4:1 and methanol–hydrochloric acid–water, both on silica gel G) as natural lunacrine. The mother liquors from the recrystallization of the supposed lunacrine gave a small quantity of a yellow picrate, mp 163–165°[17] (*dl*-lunacrine picrate is reported to melt at 211–212°).[4b]

The nmr spectrum of this "lunacrine" is very similar to that of lunacrine,[18] with the exception of a broad multiplet (three protons) between δ 1.3 and 2.0. The analytical sample, mp 92–93°, was recrystallized from hexane. (*dl*-Lunacrine is reported to melt at 146–148°.)[4]

Anal. Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37. Found: C, 70.93; H, 7.60.

Compounds Related to "Demethoxylunacrine."—The compounds originally reported[1] were recrystallized and resubmitted for analysis as summarized in Table I. This entire series of compounds originally gave analytical data for one less methylene unit. The nmr spectra of all the above are virtually identical with those reported for the 8-methoxy series, except for the aromatic regions and methoxyl group.

Acknowledgments.—This work was supported in part by Public Health Service Research Career Program Award 1-K3-GM-5433-01 from the National Institute of General Medical Sciences and in part by Grant GM-08731, also from the National Institute of General Medical Sciences. We wish to thank Dr. Sidney Goodwin for a sample of lunacrine.

(14) There was insufficient material for reanalysis. It should be noted that calcd for $C_{16}H_{19}NO_3$ is C, 70.31; H, 7.01; N, 5.12.

(15) R. A. Corral and O. O. Orazi, *Tetrahedron*, **21**, 909 (1965). Demethylation with lithium bromide–acetonitrile[4b] also gave adequate results.

(16) Tlc of the mother liquors from formation of the methiodide indicated that this material comprised the bulk of the organic soluble residues from the quaternization.

(17) There was insufficient material for analysis.

(18) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962, Spectrum 325.

One-Step Synthesis of Polyalkyl-2-iodo-*p*-benzoquinones

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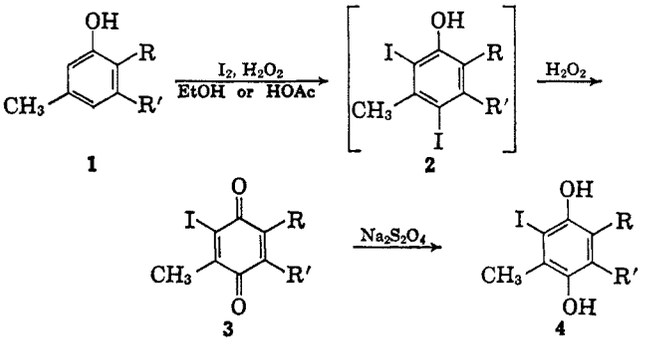
During an investigation of synthetic routes to iodopseudocumoquinone (**3**, R = R′ = CH_3) desired for other studies,[1] it was found that when the oxidative iodination procedure[2] described for the preparation of triiodophenol was applied to pseudocumenol-6 (**1**, R = R′ = CH_3) and other similarly substituted polyalkylphenols **1**, it led directly to the iodinated *p*-benzoquinones **3** (Scheme I). This combined iodination and oxidative deiodination reaction proceeded at elevated temperatures in the presence of excess 30% hydrogen peroxide, thus providing a convenient one-step method for the preparation of a variety of di- and trialkyl-2-iodo-*p*-benzoquinones. In Table I are listed a number of *p*-benzoquinones prepared in this manner, and in Table II are shown the iodohydroquinones obtained by reduction of the quinones with sodium dithionite.

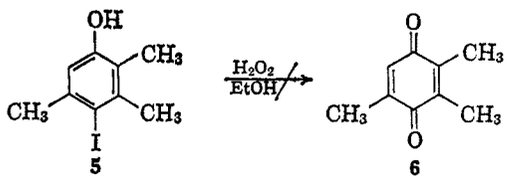
SCHEME I



R = alkyl; R′ = H, alkyl

When the iodination of pseudocumenol-6 was carried out at room temperature in the presence of the theoretical amount of oxidant,[3] the diiodophenol **2** (R = R′ = CH_3) could be isolated from the reaction mixture. On being heated in alcohol with an excess of hydrogen peroxide, **2** (R = R′ = CH_3) rapidly lost iodine and yielded the benzoquinone **3** (R = R′ = CH_3), identical with the product obtained directly from pseudocumenol-6.

Oxidative iodination of pseudocumenol-6 with 1 equiv of iodine gave a monoiodinated product whose infrared spectrum shows[4] it to be 4-iodo-2,3,5-trimethylphenol (**5**). This compound, on attempted oxidation



to the known pseudocumoquinone **6** under the conditions used for the conversion of **2** to **3**, was recovered unchanged. The relief of steric crowding in the diiodo compound **2** (R = R′ = CH_3) may be the reason for

(1) C. A. Bishop, R. F. Porter, and L. K. J. Tong, *J. Am. Chem. Soc.*, **85**, 3991 (1963).

(2) J. E. Marsh, *J. Chem. Soc.*, 3164 (1927).

(3) T. D. Aldoshin and V. S. Chalykh'yan, *J. Gen. Chem. USSR*, **9**, 748 (1939); *Chem. Abstr.*, **34**, 3972 (1940).

(4) Infrared spectra for 2,4-diiodo-5,6-dimethylphenol and 2,4-diiodo-3,5,6-trimethylphenol show sharp oxygen–hydrogen stretching absorptions at 2.95 and 2.9 μ, respectively. The monoiodinated compound has a stronger and broader absorption near 3 μ. This suggests that the hydroxyl group in the monoiodinated compound is not as sterically hindered as in those phenols with iodine in the 2-position. Therefore, we assign the iodine atom in **5** to the 4-position. The authors acknowledge with thanks the help of Miss Thelma Davis of these laboratories in the analysis of the spectrum.