oxidized with alkaline potassium permanganate without purification. Its spectral properties were $\lambda_{max}^{CCl_4}$ 3400, 2950, 1650, and 1050 cm^{-1}; $\lambda_{max}^{CH_3OH}$ 235 mμ (log ε 4.9); nmr (CCl_4), τ 9.1–9.2 (9 H, s), 8.75 (1 H, d), 8.05 (3 H, s), 7.85 (2 H, d), 6.4 (1 H, s), 6.1 (1 H, s), and 4.35 (1 H, s).

Permanganate Oxidation of 6a to 9a.—The bromo ketone **6a** (0.35 g) was added to 3 ml of 6% NaOH and the mixture was cooled to 10° with an ice water bath. To the cooled solution was added 10 ml of 0.17 *M* $KMnO_4$, the suspension was stirred overnight and filtered, and the filtrate was acidified with dilute HCl and then continuously extracted with ether. The ether layer was dried over $MgSO_4$, filtered, and concentrated. The crude solid product was sublimed at 110° (0.8 mm) to give 150 mg of **9a**. Recrystallization from 95% ethanol gave material melting at 128–130°: $[\alpha]^{24}D$ +15° (*c* 0.8, in ethanol); $[\alpha]_{290}$ +358°, $[\alpha]_{260}$ +345°, $[\alpha]_{248}$ +276°, $[\alpha]_{232}$ +131°, $[\alpha]_{225}$ +508° (*c* 0.16, CH_3OH); CD, $[\theta]_{275}$ +6730, $[\theta]_{217}$ +2977, $[\theta]_{200}$ +4140 (*c* 0.16, CH_3OH). The infrared spectrum of **9a** showed bands at λ_{max}^{KBr} 3000, 1758, 1710, 1440, and 1370 cm^{-1}. The melting point of **9a** was not lowered when it was mixed with an authentic sample.[9] The mass spectrum of **9a** showed an intense peak at *m/e* 69 (18.6%), 41 (16.0%), 84 (9.0%), 39 (8.2%), 27 (6.6%), 43 (5.0%), and 114 (1.8%).

The dimethyl ester **9b**, prepared by treating **9a** with diazomethane, was distilled at bath temperature 128° (2.3 mm): $[\alpha]^{24}D$ +30° (*c* 0.83, $CHCl_3$); ORD as a positive plain curve $[\alpha]_{393}$ +24°, $[\alpha]_{345}$ +78°, $[\alpha]_{290}$ +208° (*c* 0.50, CH_3OH); $\lambda_{max}^{CCl_4}$ 2920, 1743, 1550, 1440, 1360, and 1220 cm^{-1}; nmr (CCl_4), τ 8.7–9.2 (9 H, s), 7.9 [1 H, d (*J* = 3 cps)], 7.45 (2 H, s), and 6.3 (6 H, d). The mass spectrum of **9b** showed prominent peaks at *m/e* 15 (4.4%), 26 (2.7%), 27 (7.5%), 28 (2.6%), 29 (7.6%), 31 (26%), 43 (6.7%), 45 (9.9%), and 46 (4.0%). The molecular ion at *m/e* 202 was not detected.

Permanganate Oxidation of 7.—The oxidation procedure previously described was applied to 150 mg of **7** in 2 ml of 6% NaOH to which was added 5 ml of 0.17 *M* potassium permanganate solution. The reaction gave 70 mg of **9a**, mp 128–130°.

(+)-2-Isopropyl-2-methyl-5-oxocaproic Acid (10a).—The following mass spectral, infrared, and circular dichroism data were obtained for **10a**: *m/e* 43 (9.3%), 55 (8.0%), 27 (6.8%), 83 (6.7%), 41 (6.6%), and 39 (4.5%); $\lambda_{max}^{CCl_4}$ 3050, 1710, 1430, and 1380 cm^{-1}; $[\theta]_{299}$ +231, $[\theta]_{285}$ +297, $[\theta]_{232}$ −264, $[\theta]_{223}$ −99 (*c* 0.31, CH_3OH).

(+)-Methyl 2-Isopropyl-2-methyl-5-oxocaproate (10b).—The following mass spectral, infrared, optical rotatory dispersion, and nmr data were obtained for **10b**: *m/e* 43 (14.1%), 15 (6.0%), 41 (5.9%), 83 (5.7%), and 55 (4.7%); $\lambda_{max}^{CCl_4}$ 2900, 1750, 1720, and 1250 cm^{-1}; $[\alpha]_{400}$ +32°, $[\alpha]_{375}$ +40°, $[\alpha]_{350}$ +56°, $[\alpha]_{325}$ +96°, $[\alpha]_{305}$ +152°, $[\alpha]_{265}$ −134°, and $[\alpha]_{250}$ −28° (*c* 0.60, dioxane); nmr (CCl_4), τ 9.25 (3 H, s), 9.05 (6 H, 2d), 8.30 (1 H, d), 8.20 (2 H, s), 7.95 (3 H, s), 7.80 (2 H, m), and 6.40 (3 H, s).

(+)-2-Isopropyl-2-methylglutaric Acid (11a).—The following mass spectral infrared, and optical rotatory dispersion data were obtained for **11a**: *m/e* 69 (18.6%), 41 (16.0%), 84 (9.0%), 39 (8.2%), 27 (6.5%), and *m/e* 43 (5.0%); λ_{max}^{KBr} 3000, 1758, 1710, 1440, and 1370 cm^{-1}; $[\alpha]_{340}$ +44°, $[\alpha]_{303}$ +56°, $[\alpha]_{245}$ +90° (*c* 0.51, dioxane).

(+)-Dimethyl 2-Isopropyl-2-methylglutarate (11b).—The following mass spectral, infrared, rotatory dispersion, and nmr were obtained for **11b**: *m/e* 43 (14.1%), 15 (6.0%), 41 (5.9%), 83 (5.7%), 55 (4.7%), and 27 (4.0%); $\lambda_{max}^{CCl_4}$ 3000, 1743, 1440, and 1380 cm^{-1}; $[\alpha]_{375}$ +36°, $[\alpha]_{330}$ +52°, and $[\alpha]_{240}$ +144° (*c* 0.8, CH_3OH); nmr (CCl_4), τ 9.1 (3 H, s), 9.0 (6 H, weak s), 7.8–8.4 (5 H, broad m), and 6.4 (6 H, s).

Registry No.—1, 15815-63-1; 2, 5298-65-7; 3, 15815-65-3; 4, 15815-66-4; 5, 15815-67-5; 6a, 15815-68-6; 7, 15815-69-7; 9a, 5033-83-0; 9b, 15815-71-1; 10a, 15815-75-5; 10b, 15815-72-2; 11a, 15815-73-3; 11b, 15815-74-4.

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Alternate Precursors in Biogenetic-Type Syntheses. III.[1] A Ring D Indoline Analog of the Aporphine Alkaloids. Indole as the Alkylating Agent in the Friedel–Crafts Reaction

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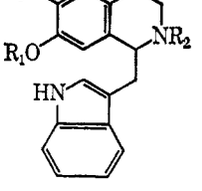
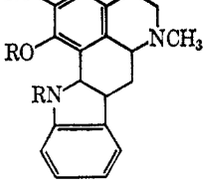
In the first[2] paper of this series we suggested the possible biogenetic conversion of an indole analog of norlaudanosoline into an indole analog of morphine. Since it is well known that norlaudanosoline also can lead to the aporphine alkaloids,[3] the logical development of this theme is the conversion of an indole analog of norlaudanosoline into an indole analog of an aporphine. Chemically, the preferred method of cyclizing the possible biogenetic intermediate **3** seemed to be the alkylation of the benzene ring by the 2,3-double bond of the indole nucleus. Although the alkylation of a benzene ring by an indolenium salt has been described by Harley-Mason and Waterfield,[4] these authors also reported that 1-methyltryptamine and catechol do not react. However, in our case the two reactive centers would be held in a more favorable steric relationship.

The tetrahydroisoquinoline **1** was prepared from N-(3,4-dimethoxyphenethyl)indole-3-acetamide *via* a Bischler–Napieralski cyclization and reduction. Treatment with ethyl formate followed by lithium aluminum hydride reduction converted **1** into its N-methyl derivative (**2**). Strong acid should now bring about hydrolysis of the dimethoxy groups to produce the indole analog of norlandanosoline (**3**) which might



1, $R_1 = CH_3$; $R_2 = H$
2, $R_1 = CH_3$; $R_2 = CH_3$
3, $R_1 = H$; $R = CH_3$



4, R = H
5, R = C(=O)CH_3

well cyclize under the conditions being utilized for hydrolysis. Accordingly, when **2** was refluxed in concentrated hydrobromic acid, the product isolated analyzed for a dihydroxy dihydrobromide indicative of hydrolysis followed by cyclization to **4**, a ring D indoline analog of the aporphine alkaloids. Ultraviolet absorption in acid at 261 mμ (ε 9300), 268 (1300), and 291 (3900) is also consistent[4] with the cyclized compound **4** and not **3**. For further characterization **4** was converted into its triacetyl derivative **5**, whose

(1) For Part II, see G. C. Morrison, R. O. Waite, and J. Shavel, Jr., *J. Org. Chem.*, **32**, 2555 (1967).

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nmr spectrum showed the four indoline aromatic protons at 7.2 ppm as a complex pattern and the proton of the diacetoxybenzene at 6.9 ppm as a singlet.

The cyclization of **3** to **4** appears to be the first example of participation of the 2,3-double bond of indole as the alkylating agent in the Friedel–Crafts reaction.

Experimental Section[5]

The melting points were determined using a Thomas–Hoover apparatus which had been calibrated against known standards. The infrared spectra were recorded with a Baird Model 455 instrument in chloroform solutions. The ultraviolet spectra were obtained with a Beckman DKI spectrophotometer in 95% ethanol solutions. The nmr spectra were determined with a Varian Associates A-60 spectrometer in deuterated dimethyl sulfoxide solutions unless otherwise noted.

1,2,3,4-Tetrahydro-1-(indol-3-ylmethyl)-6,7-dimethoxyisoquinoline (1).—A solution of 204 g of N-(3,4-dimethoxyphenethyl)indole-3-acetamide[6] in 450 ml of phosphorus oxychloride was allowed to stand at room temperature for 20 hr. The reaction mixture was poured into 3 l. of ether. The precipitate was rubbed up to a gummy consistency and the supernatant was decanted. The gum was then washed with an additional 1.5 l. of ether. The residue was dissolved in 3 l. of ethanol and diluted with 500 ml of water and the pH was adjusted to 3 with 10% sodium hydroxide solution. Sodium borohydride (50 g) was added portionwise while the temperature was held at 20–30°. After the addition had been completed stirring was continued for an additional 30 min. The pH was adjusted to below 2 with 20% hydrochloric acid and then above 11 with 40% sodium hydroxide solution. After the addition of 1200 ml of water, the mixture was extracted with ether. The ether layer was dried over sodium sulfate and the solvent was removed. Recrystallization of the residue from benzene gave 87 g (45%) of a solid: mp 158–159°; γ_{max} 3440 cm^{-1} (indole NH); λ_{max} mμ (ϵ) 221 (43,400), 282 (10,300), and 290 sh (9250). The nmr spectrum in deuteriochloroform showed the two aromatic protons of the dimethoxybenzene ring at 6.65 (singlet) and 6.85 (singlet) ppm. The five aromatic protons of the indole system formed a complex pattern between 7.0 and 7.8 ppm.

Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.50; H, 6.62; N, 8.44.

1,2,3,4-Tetrahydro-1-(indol-3-ylmethyl)-6,7-dimethoxy-2-methylisoquinoline (2).—A solution of 30.0 g of 1,2,3,4-tetrahydro-1-(indol-3-ylmethyl)-6,7-dimethoxyisoquinoline in 300 ml of ethyl formate was refluxed for 25 hr. On standing there was deposited 30 g of a solid which was dissolved in 1 l. of tetrahydrofuran and added to a suspension of 10.0 g of lithium aluminum hydride in 250 ml of tetrahydrofuran. After the addition had been completed stirring was continued for 6 hr. The excess hydride was destroyed by the cautious dropwise addition of water. The reaction mixture was filtered and the solvent was removed. The residue, after recrystallization from benzene–Skellysolve B, gave 25.5 g (67%) of a crystalline solid, mp 125–127°. Further recrystallization gave an analytical sample, mp 126–127°.

Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 74.88; H, 7.22; N, 8.54.

4,5,6,6a,7,7a,12,12a-Octahydroisoquino-6-methyl[8,8a,1-*a*,*b*]-carbazole-1,2-diol Dihydrobromide Monohydrate (4).—A solution of 10.0 g of 1,2,3,4-tetrahydro-1-(indol-3-ylmethyl)-6,7-dimethoxy-2-methylisoquinoline in 150 ml of hydrobromic acid was refluxed for 15 hr. The reaction mixture was concentrated *in vacuo* (100 mm) to 100 ml. On standing there was deposited 2.8 g (20%) of a crystalline solid, mp 247–257°. Concentration to 30 ml gave an additional 3.5 g (25%), mp 271–277°. Recrystallization from water gave an analytical sample: mp 260–265°; λ_{max} mμ (ϵ) 240 infl (9800) and 291 (5800).

Anal. Calcd for $C_{19}H_{20}N_2O_2 \cdot 2HBr \cdot H_2O$: C, 46.74; H, 4.95; N, 5.74; Br, 32.73. Found: C, 46.92; H, 5.08; N, 5.99; Br, 32.55.

12-Acetyl-4,5,6,6a,7,7a,12,12a-octahydro-6-methylisoquino-[8,8a,1-*a*,*b*]carbazole-1,2-diol Diacetate (5).—To a solution of 10.0 g of 4,5,6,6a,7,7a,12,12a-octahydroisoquino-6-methyl-[8,8a,1-*a*,*b*]carbazole-1,2-diol dihydrobromide monohydrate in 250 ml of pyridine was added 100 ml of acetic anhydride. After standing for 20 hr at room temperature the volatiles were removed *in vacuo* at 50°. Chromatography of the residue on neutral alumina gave an oil on elution with methylene chloride. Crystallization from benzene–Skellysolve B gave 3.0 g (30%) of a solid, mp 182–183.5°. Further recrystallization gave an analytical sample: mp 185–186°; λ_{max} mμ (ϵ) 248 (11,700), 278 (4000), and 288 sh (2800); γ_{max} 1770 (C=O, esters) and 1660 cm^{-1} (C=O, amide).

Anal. Calcd for $C_{25}H_{26}N_2O_5$: C, 69.11; H, 6.03; N, 6.45. Found: C, 69.14; H, 6.15; N, 6.57.

Registry No.—**1**, 15832-21-0; **2**, 15832-22-1; **4**, 15856-51-6; **5**, 15832-23-2.

(5) Melting points are corrected. The authors are indebted to Mr. A. Lewis and his associates, to Mr. R. Puchalski for the spectral data, and to Mrs. U. Zeek for analytical determinations.

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Fluoride-Induced Cleavage of the Carbon–Phosphorus Bond in Diethyl Trichloromethylphosphonate. A New Source of Dichlorocarbene and Dialkyl Phosphorofluoridates[1]

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Although the carbon–phosphorus bond in dialkyl trichloromethylphosphonates is cleaved by warming with aqueous alkali,[3] it has been reported that in the absence of alkali this bond is stable. Refluxing with concentrated or aqueous acids,[4] alcohols or phenols[5,6] does not affect the carbon–phosphorus bond. The reaction of these esters with primary amines was at first believed to be a case of carbon–phosphorus bond scission,[7] but this was later disproved.[8]

While attempting to prepare diethyl trifluoromethylphosphonate through halogen exchange by warming diethyl trichloromethylphosphonate (I) with potassium fluoride, it was noted that a significant quantity of chloroform was produced. It was then discovered that the potassium fluoride used was actually the dihydrate.

Although a little surprising, this was interpreted as a carbon–phosphorus bond scission, with the formation of the trichloromethide ion (II) and diethyl phosphoro-

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(2) To whom inquiries should be directed.

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