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.

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[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-

[1] Presented in part at the 153rd National Meeting of the American Chemical Society, Miami, Beach, Fla., April 1967, p O29.

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$$\underset{\text{I}}{CCl_3P(O)(OEt)_2} + KF \longrightarrow K^+ + \underset{\text{II}}{[CCl_3]^-} + \underset{\text{III}}{FP(O)(OEt)_2} \quad (1)$$

fluoridate (III) (see eq 1). In the presence of the water of hydration, the trichloromethide ion (II) would immediately be hydrolyzed to chloroform[9] (eq 2),

$$\underset{\text{II}}{[CCl_3]^-} + H_2O \longrightarrow OH^- + CHCl_3 \quad (2)$$

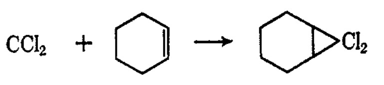
and the diethyl phosphorofluoridate (III) would be hydrolyzed with the formation of diethyl hydrogen phosphate (IV)[10] (eq 3).

$$\underset{\text{III}}{FP(O)(OEt)_2} + H_2O \longrightarrow \underset{\text{IV}}{HOP(O)(OEt)_2} + HF \quad (3)$$

The procedure was repeated using anhydrous potassium fluoride. Upon warming diethyl trichloromethylphosphonate with anhydrous potassium fluoride a good yield of diethyl phosphorofluoridate (III) was obtained. Apparently, under mild conditions, and in the absence of water, carbon–phosphorus bond scission had again occurred. It was not clear what the other product(s) of the reaction might be because, from the stoichiometry of the reaction, the other products are the potassium ion and the trichloromethide ion (II).

It has been shown that dichlorocarbene (V) is produced from the trichloromethide ion in several other reactions by the loss of chloride ion[11] (eq 4). Dichlorocarbene (V) adds readily to olefins to form cyclopropane derivatives;[11] so the reaction was repeated in the presence of cyclohexene and 7,7-dichlorobicyclo-[4.1.0]heptane (dichloronorcarane) (VI) was isolated in 40% yield (eq 5).

$$\underset{\text{II}}{[CCl_3]^-} \longrightarrow Cl^- + \underset{\text{V}}{CCl_2} \quad (4)$$


(5)

V VI

Anhydrous sodium fluoride is almost completely ineffective in promoting the cleavage. Lithium fluoride and calcium fluoride are completely ineffective. Ammonium fluoride works as well, if not better, than potassium fluoride in effecting the scission. Antimony trifluoride apparently is somewhat active and silver monofluoride produces a rather exothermic reaction with diethyl trichloromethylphosphonate resulting in carbon–phosphorus bond scission. The carbon–phosphorus bonds in diethyl dichloromethylphosphonate, diethyl chloromethylphosphonate, and diethyl methylphosphonate are unaffected by warming with anhydrous potassium fluoride.

If methanol is used as a solvent to increase the solubility of the potassium fluoride in diethyl trichloromethylphosphonate (I) the reaction proceeds quite exothermically at room temperature to give diethyl methyl phosphate (VII) (eq 6).

$$\underset{\text{I}}{CCl_3P(O)(OEt)_2} + KF + MeOH \longrightarrow \underset{\text{VII}}{MeOP(O)(OEt)_2} \quad (6)$$

The mechanism and synthetic applications of this cleavage are presently under investigation.

Experimental Section

Reaction with Potassium Fluoride Dihydrate.—After heating a mixture of 51.1 g (0.2 mol) of diethyl trichloromethylphosphonate and 46.4 g (0.49 mol) of potassium fluoride dihydrate at reflux (71°) for 30 min, 20 g (84%) of chloroform (bp 58–60 (740 mm), n^{25}D 1.4437) was distilled from the reaction mixture.

Reaction with Anhydrous Potassium Fluoride.—In a flask fitted with a reflux condenser protected by a calcium chloride tube 206 g (0.81 mol) of diethyl trichloromethylphosphonate and 188 g (3.24 mol) of anhydrous potassium fluoride were stirred over a steam bath for 60 hr. Distillation from the reaction flask gave 108.5 g (86%) of diethyl phosphorofluoridate: bp 80–80.5 (32 mm); n^{27}D 1.3710; $d^{27}{}_4$ 1.1399.

Anal. Calcd for $C_4H_{10}FO_3P$: C, 30.78; H, 6.46; F, 12.17; P, 19.85. Found: C, 30.78, 30.83; H, 6.23, 6.24; F, 12.15, 12.20; P, 19.97, 19.81.

Note: Phosphorofluoridates are known to be extremely toxic. At lower concentration their vapors have a myotic effect (pupil constriction) on the eye and at higher concentrations they can cause respiratory collapse.[12]

Reaction in Cyclohexene.—In a flask fitted with a reflux condenser protected by a calcium chloride tube 112 g (0.5 mol) of diethyl trichloromethylphosphonate, 58 g (1.0 mol) of anhydrous potassium fluoride, and 82 g (0.5 mol) of cyclohexene were stirred while heated in an oil bath at 110° for 24 hr. After filtering, the precipitate was washed with two 50-ml portions of dry ether. The filtrate and washings were combined and the ether and unreacted cyclohexene were distilled out. The residue was stirred with 100 ml of water for 4 hr at 60°. The hydrolysate was extracted with two 50-ml portions of petroleum ether. After drying over magnesium sulfate the petroleum ether was removed from the combined extracts at 20 mm on a rotary evaporator. Distillation of the residue gave 33.0 g (40.0%) of dichloronorcarane, bp 84–85° (17 mm), n^{24}D 1.5010.

Anal. Calcd for $C_7H_{10}Cl_2$: C, 50.93; H. 6.11; Cl, 42.96. Found: C, 50.83, 50.93; H, 6.11, 6.04; Cl, 43.01, 42.90.

Reaction in Methanol.—Diethyl trichloromethylphosphonate (25.6 g, 0.1 mol) was added, dropwise at first, to 11.6 g (0.2 mol) of anhydrous potassium fluoride, with stirring. When there was no apparent evidence of reaction the remainder of the ester was run into the flask. In about 2 min the temperature began to rise so rapidly that the flask had to be cooled with an ice bath to keep the methanol from refluxing at a rate that exceeded the capacity of the condenser. When the reaction had subsided heat was applied to keep the methanol refluxing for 24 hr. After cooling, 50 ml of ether was added, the solids were filtered, and distillation of the filtrate gave 13.5 g (80%) of diethyl methyl phosphate, bp 104–105° (21 mm), n^{21}D 1.4031.

Registry No.—I, 866-23-9; III, 358-74-7; V, 1605-72-7; VI, 823-69-8; VII, 867-17-4.

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3,5-Dichlorotyrosines. Preparation of D and L Forms[1]

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A number of references to 3,5-dichloro-L-tyrosine have been reported[2–4] which are based on a synthesis

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