stant boiling point or constant molecular weight were obtained. With methanol, (CF$_3$)$_2$NCOCl gave an ester identical with that obtained from (CF$_3$)$_2$NCOF.

EXPERIMENTAL

Conditions for the electrochemical fluorinations were similar to those described elsewhere.[2] If additions of starting material were made in accordance with the number of Faradays passed or with the amount of hydrogen liberated, it was observed that the amount of (CF$_3$)$_2$NCOCl increased; on the other hand, when the concentration of starting material was kept to the minimum required for conductance purposes, the product was almost exclusively (CF$_3$)$_2$NCOF.

(CF$_3$)$_2$NCOCl was obtained as a colorless liquid, b.p. 38.5°. The infrared spectrum showed a well defined doublet at 5.32, 5.48 microns, and other peaks at 6.96, 7.40, 7.72, 8.10, 8.72, 9.92, 11.70, 13.05, and 13.85 microns. The NMR spectrum showed a single peak, δ-value (relative to CF$_3$COOH) 20.6 cps.

Anal. Calcd. for C$_3$ClF$_6$NO: C, 16.7; Cl, 16.5; F, 52.8; mol. wt. 215. Found: C, 17.9; Cl, 16.4; F, 52.7; mol. wt. 214.

Pyrolysis. Thirty grams (0.14 mole) (CF$_3$)$_2$NCOCl was heated in a stainless steel vessel for 6 hr. at 380–400°. Fractionation under a Dry Ice head gave 5 g. overhead, mol. wt. 65-65 (COF$_2$ mol. wt. 66, b.p. -90°); no other fractions of constant mol. wt. were obtained, and no distillation flats at $-42°$ (COClF), or $-30°$ to $-33°$ (CF$_3$N=CF$_2$).

Esterification. Reaction with methanol and distillation of the washed and dried product gave a 61% yield of (CF$_3$)$_2$NCOOCH$_3$, b.p. 73-77°, n_D^{25} 1.2990, mol. wt. 211. Known values[3] are b.p. 76°, n_D^{25} 1.2997, mol. wt. 211. Infrared spectra of the two products were identical.

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Aliphatic Reserpine Analogs[1]

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Received May 2, 1958

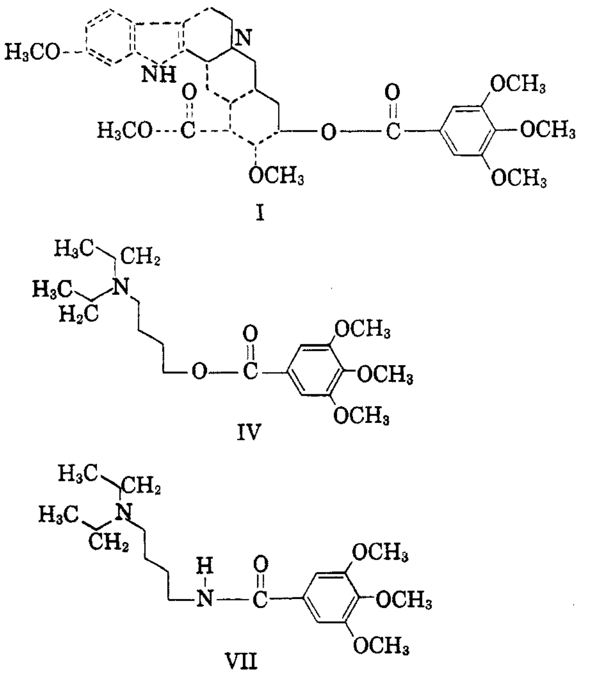
Miller and Weinberg[3] reported recently that 3-(*N*-*N*-diethylamino)propyl 3,4,5-trimethoxybenzoate has significant reserpine-like activity (equivalent to one third of the potency of reserpine); they added that the corresponding diethylaminoethyl ester did not exhibit the same properties. In view of these statements, one would anticipate that the incorporation of four instead of three carbon atoms between the tertiary nitrogen and the ether oxygen of the ester linkage would yield a moiety (IV) resembling reserpine (I) more closely in its properties. In order to evaluate this conception we have prepared 4-(*N*,*N*-diethylamino)-butyl 3,4,5-trimethoxybenzoate (IV). Since the duration of pharmacological effectiveness may be occasionally extended by replacing an ester linkage with the corresponding amide coupling, we have also prepared the *N*-[4-(*N'*,*N'*-diethylamino)butyl]-3,4,5-trimethoxybenzamide (VII). The pharmacological evaluation of these compounds is in progress.

EXPERIMENTAL[4]

4-(N,N-Diethylamino)butyl acetate (II) was obtained (66% yield) from a condensation of 4-bromobutyl acetate and diethylamine; it distilled at 110–113°/22 mm., $n_D^{26.5}$ 1.4306, in accordance with the literature.[5]

4-(N,N-Diethylamino)butanol (III). Lithium aluminum hydride reduction of II yielded 76% III; it distilled at 110–112°/22 mm., $n_D^{27.5}$ 1.4459, in accordance with the literature.[6,7]

4-(N,N-Diethylamino)butyl 3,4,5-trimethoxybenzoate hydrochloride (IV). The acid chloride of 3,4,5-trimethoxybenzoic acid (10.6 g., 0.050 mole) was prepared as described by Lasslo and Jordan.[8] The acid chloride was dissolved in 300 ml. of dry benzene, and a solution of 7.3 g. (0.050 mole) of III in 100 ml. of dry benzene was added dropwise with continuous stirring; the temperature of the reaction mixture was maintained at 29–34°. The reaction mixture was agitated for 2 additional hr. at room temperature and, subsequently, refluxed for 2 hr. (steam bath). The hydrochloride of the ester crystallized out upon cooling; it was filtered off and



I

IV

VII

Fig. I

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(1) This investigation is supported by a grant from the Geschickter Fund for Medical Research.

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recrystallized from benzene. The colorless crystals (16.7 g., 89% yield) melted at 139.0–140.0° (uncorr.).

Anal. Calcd. for $C_{18}H_{30}ClNO_5$: C, 57.52; H, 8.04; Cl, 9.42; N, 3.73. Found: C, 57.39; H, 8.15; Cl, 9.45; N, 3.83.

4-(N,N-Diethylamino)butyronitrile (V). Condensation of 4-bromobutyronitrile with diethylamine yielded 89% V; it distilled at 100–102°/22 mm., $n_D^{26.5}$ 1.4334, in accordance with the literature.[9]

4-(N,N-Diethylamino)butylamine (VI). Lithium aluminum hydride reduction of V yielded 86% VI; it distilled at 86–87°/22 mm., $n_D^{27.5}$ 1.4425, in accordance with the literature.[10]

N-[4-(N′,N′-Diethylamino)butyl]-3,4,5-trimethoxybenzamide (VII). The acid chloride (*loc. cit.*) of 3,4,5-trimethoxybenzoic acid (10.6 g., 0.050 mole) was dissolved in 300 ml. of dry benzene, and a solution of 7.2 g. (0.050 mole) of VI in 100 ml. of dry benzene was added dropwise with continuous stirring; the temperature of the reaction mixture was maintained at 29–34°. Subsequently, the reaction mixture was refluxed for 3 hr. The benzene was removed under reduced pressure. The semisolid residue was treated with saturated aqueous sodium carbonate, and the base was extracted with ethyl ether. The ethereal solution was dried over anhydrous sodium sulfate, filtered; upon removal of the solvent 11.4 g. (68% yield) of the crude base remained behind. The pure compound distilled at 223.0–224.0°/0.20–0.25 mm. and melted at 68.0–69.0° (uncorr.).

Anal. Calcd. for $C_{18}H_{30}N_2O_4$: C, 63.88; H, 8.94; N, 8.28. Found: C, 63.78; H, 8.97; N, 8.33.

Attempts to prepare the crystalline hydrochloride of this compound proved unsuccessful.

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4-Pyridylhydantoins[1]

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Received May 2, 1958

Three hydantoins carrying 4-pyridyl substituents have been prepared for testing as possible anticonvulsants. This completes a series of pyridylhydantoins, the first members of which were reported previously.[2,3] The corresponding alkyl pyridyl ketones were prepared as intermediates. Methyl-4-pyridyl ketone was prepared by a Claisen condensation of ethyl isonicotinate and ethyl acetate according to the procedure of Kolloff and Hunter.[4] Ethyl 4-pyridyl ketone and *n*-hexyl 4-pyridyl ketone could only be obtained in small yield and in impure state by the action of alkyl halides on the sodium derivative of ethyl isonicotinoyl acetate, the Claisen condensation product. This agrees with the observation of Burrus and Powell.[5]

All three ketones were prepared in satisfactory yield by the action of the proper Grignard reagent on 4-cyanopyridine. The hydantoins were prepared by the method used in the previous reports.

EXPERIMENTAL[6]

4-Cyanopyridine. This was prepared from isonicotinic acid, ammonium acetate and acetic acid by the method used by Adkins[7] for the preparation of the 3-isomer, b.p. 185–190°, m.p. 76–79°.

Methyl 4-pyridyl ketone. Claisen condensation of methyl or ethyl isonicotinate with ethyl acetate gave a product which was contaminated with unreacted ester, as shown by its infrared spectrum. It was necessary to reflux the ketone for several hours with 10% HCl to obtain a pure product. The addition of an ether solution of 4-cyanopyridine to a cold solution of methyl magnesium iodide gave the ketone in 50% yield, b.p. 105–107° at 20 mm., n_D^{26} 1.5254; phenylhydrazone, m.p. 148–149° (reported[8] 150°); picrate, m.p. 129.5–130° (reported[8] 129–130°).

Ethyl 4-pyridyl ketone. No record of the preparation of this compound in a pure state could be found in the literature. It was prepared from 4-cyanopyridine and ethyl magnesium bromide. In the case of both the methyl and the ethyl ketones careful fractionation was required to remove unreacted 4-cyanopyridine. The yield of the ethyl ketone was 51%, b.p. 104–106° at 10 mm., n_D^{23} 1.5199; phenylhydrazone, m.p. 140–142; picrate, m.p. 125.5–126.5°.

Anal. Ketone, calcd. for C_8H_9ON: N, 10.37. Found: N, 10.58.

Hexyl 4-pyridyl ketone. This ketone was prepared by the same procedure, using *n*-hexylmagnesium chloride, in a yield of 44%, b.p. 124–125° at 3 mm., n_D^{25} 1.4996; phenylhydrazone, m.p. 154.0–155.5°; picrate, m.p. 106.5–107.5°.

Anal. Ketone, calcd. for $C_{12}H_{17}ON$: C, 75.35; H, 8.96. Found: C, 75.17; H, 8.82.

Hydantoins. The hydantoins were prepared by the reaction of the ketones with KCN and $(NH_4)_2CO_3$ following the procedure used previously.[2]

TABLE I
5-ALKYL-5-PYRIDYLHYDANTOINS

Alkyl Group	M.P.	%C		% H		Yield,
		Calcd.	Found	Calcd.	Found	%
Methyl	234.5–235.5	56.53	56.54	4.75	4.89	88
Ethyl	181.5–183.0	58.52	58.30	5.40	5.45	82.5
n-Hexyl	146.0–147.0	64.34	64.40	7.33	7.57	86

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