determinations in the ultraviolet region and corex cells of the same thickness were used in the visible region. The solvent used for the samples and blank was 95% ethanol. All samples were dissolved in the solvent to a concentration of 10 mg. per l. at 20 to 25°. The results in the measurement of the absorption spectra of the azlactones are expressed as the molar extinction ϵ which was obtained from the optical density readings D and the molecular weights m by the relations $k = D/cl$ and $\epsilon = km$, where c is the concentration of the solution in mg. per ml. and l is the length of the cell.

Preparation of Materials.—The crotonolactones were prepared by the following general procedure: A mixture of 0.05 mole of benzaldehyde, 0.05 mole of the corresponding β-aroylpropionic acid, 0.05 mole of freshly fused sodium acetate and 16 ml. of acetic anhydride was heated in a beaker on a hot-plate until a complete solution was obtained. The beaker was then transferred to a steam-bath and heating was continued until crystals separated. The reaction was next poured into water, the solid product filtered with suction, washed with water and finally recrystallized repeatedly from 95% ethanol until a constant melting point was obtained. The yield, in general, ranged from 50–70%. The crotonolactones No. 6–12 of Table I are relatively insoluble in 95% ethanol (10 mg./100 ml.) and were recrystallized from chloroform.

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1-Nitrofluorenone

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Recently the first synthesis of 1-nitrofluorenone has been described by Chase and Hey[2] who used the sequence: chloride of 2-methyl hydrogen 3-nitrophthalate → peroxide of this acid → methyl 3-nitrobiphenyl-2-carboxylate → 3-nitrobiphenyl-2-carboxylic acid → 1-nitrofluorenone (m.p. 188.5–189.5°). The substance was obtained later in very small amounts by the action of heat on diazotized 2-amino-6-nitrobenzophenone.[3] The structure of the substance was proved[2] by reduction to the known 1-aminofluorenone.[4]

The purpose of this Note is to describe our synthesis of 1-nitrofluorenone by three routes, two of which involve an intermediate used by Chase and Hey. These syntheses are of interest as practical preparative methods and involve several compounds described here for the first time.

(A).[5]—1-Aminofluorenone was diazotized and converted to the nitro compound by the action of sodium nitrite and mixed copper sulfites.[6]

(B).[5]—2-Aminobiphenyl → 2-acetaminobiphenyl → 3-nitro-2-acetaminobiphenyl → 3-nitro-2-aminobiphenyl → 3-nitro-2-cyanobiphenyl → 3-nitrobiphenyl-2-carboxylic acid → 1-nitrofluorenone.

(C).[7]—3-Nitrophthalimide → 6-nitrophthalamic acid → 6-nitro-2-aminobenzoic acid → methyl 6-nitro-2-aminobenzoate → methyl 3-nitrobiphenyl-2-carboxylate → 1-nitrofluorenone. The last step in this synthesis was carried out directly and avoided the isolation of 3-nitrobiphenyl-2-carboxylic acid.[2]

Experimental Part

All melting points are uncorrected.

1-Nitrofluorenone.—1-Aminofluorenone[4] was diazotized and treated with sodium nitrite and mixed copper sulfites.[6] There was obtained a 34% yield of bright yellow needles, m.p. 190.5–191.5° after recrystallization from glacial acetic acid. Mixed melting points of this product with those from our other syntheses were not depressed.

Anal. Calcd. for $C_{13}H_7O_3N$: C, 69.3; H, 3.14; N, 6.22. Found: C, 69.4; H, 3.37; N, 6.28.

Attempts to replace the diazo group by the cobaltinitrite method[8] or by the action of sodium nitrite on the diazonium fluoborate[9] were unsuccessful.

1-Nitrofluorenone Oxime.—0.91 g. of 1-nitrofluorenone and 1 g. of hydroxylamine hydrochloride were heated at 100° for five hours in 10 cc. of pyridine and 10 cc. of absolute alcohol. The reaction mixture was diluted with 200 cc. of ice-water and the oxime obtained in 97% yield, m.p. 198–199° dec.

Anal. Calcd. for $C_{13}H_8O_3N_2$: C, 65.0; H, 3.36; N, 11.7. Found: C, 65.0; H, 3.48; N, 11.4.

The infrared absorption spectrum of this compound is available.[5] The oxime was soluble in 2 *N* sodium hydroxide. It was hydrolyzed to the parent ketone by heating in 65% sulfuric acid at 125° for two hours.

3-Nitro-2-cyanobiphenyl.—This was prepared from 3-nitro-2-aminobiphenyl[10] by a procedure similar to that used for the isomeric 5-nitro compound.[11] We obtained a 32% yield of crude material, m.p. 124–130°, which was sublimed to give colorless needles, m.p. 131.5–132.0°.

Anal. Calcd. for $C_{13}H_8O_2N_2$: C, 69.6; H, 3.60; N, 12.5. Found: C, 69.4; H, 3.73; N, 12.6.

3-Nitrobiphenyl-2-carboxylic Acid.—Hydrolysis of the hindered nitrile by the procedure used for the 5-nitro isomer[11] was difficult. The procedure of Sudborough[12] was used to obtain 35% yields of colorless needles, m.p. 200–205°; Chase and Hey[2] record m.p. 200.5–201.5°. The acid was cyclized by heating in concentrated sulfuric acid for ten minutes at 115° and a 93% yield of 1-nitrofluorenone obtained.

Methyl 6-Nitro-2-aminobenzoate.—6-Nitro-2-aminobenzoic acid was prepared from Eastman Kodak Co. 3-nitrophthalimide by way of 6-nitrophthalamic acid.[13,14] 2.4 g. (0.0134 mole) of the acid was dissolved in the minimum amount of dry ether and esterified with diazomethane in ether by the conventional procedure. 2.45 g. (95% yield) of crude product was washed with dilute bicarbonate solution and then recrystallized from methyl alcohol–water to give orange crystals, m.p. 105–108°.

Anal. Calcd. for $C_8H_8O_4N_2$: N, 14.3. Found: N, 14.5, 14.6.

Satisfactory values for the saponification equivalent in aqueous solution were not obtained but the acid was recovered from the partially hydrolyzed samples. We were unable to prepare the methyl ester by the conventional procedure used with isomeric nitroaminobenzoic acids,[15] by the use of methyl alcohol and ethylene dichloride,[16] by the method of Newman[17] or by the use of boron trifluoride.[18] The latter method resulted in decarboxylation.

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Methyl 3-Nitrobiphenyl-2-carboxylate.—Methyl 6-nitro-2-aminobenzoate was diazotized and subjected to the Gomberg reaction with benzene as described previously for the analogous case of methyl 5-nitro-2-aminobenzoate.[19] A 7% yield of colorless crystals, m.p. 121°, was obtained; Chase and Hey[2] record m.p. 121.5–122.5°. 0.3 g. of this substance was converted directly to yield 50 mg. of 1-nitrofluorenone by heating in 5 cc. of concentrated sulfuric acid for one hour at 100°.

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A Novel N-Alkylation Reaction

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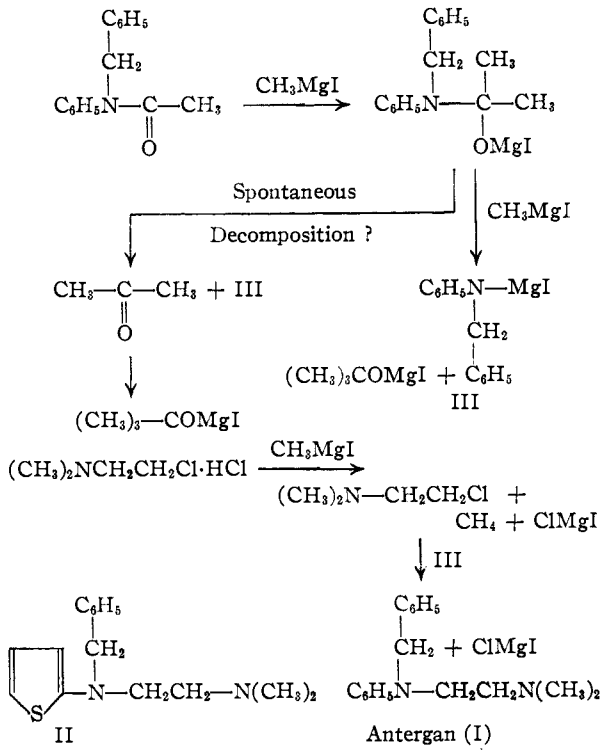
Attempts to prepare the thiophene analog (II) of Antergan (I)[1] by methods which have been successfully employed in the synthesis of its thiazole[2] and pyridine[3] isosteres have not been found practical due to the low reactivity of the halogen in 2-bromothiophene[4] and the extreme air-sensitivity of 2-thienylamines.[5] Stability of the latter in air is enhanced considerably by acetylation and the amides, in the form of N-sodio derivatives, can be alkylated.[5] Since N-benzyl-N-(2-thienyl)-acetamide, obtained in good yield by heating 2-acetamidothiophene and benzyl chloride in toluene solution in the presence of lithium amide, was on hand, a method was sought whereby this amide could be converted directly to the tertiary amine (II) without isolation of the presumably unstable 2-benzylaminothiophene. It appeared possible to accomplish this by interaction of the amide with a Grignard reagent, a method available for the preparation of ketones[6] which yields the corresponding halomagnesium amide (RR'N–MgX) as a by-product. Treatment of the reaction mixture with an alkyl halide should form the desired tertiary amine.

The preparation of Antergan by this method was undertaken as a model experiment. N-Benzyl-N-phenylacetamide was treated with an excess of methylmagnesium iodide followed by dimethylaminoethyl chloride hydrochloride. The quantity of the Grignard reagent employed was sufficient to liberate the aminoalkyl halide from its salt. The product, Antergan (I), was obtained in 53.5% yield. Its picrate was identical with that obtained from a product prepared by the alkylation of N-benzylaniline with dimethylaminoethyl chloride hydrochloride in the presence of lithium amide.

When the reaction was repeated with N-benzyl-N-(2-thienyl)-acetamide in a nitrogen atmosphere, a pale yellow oil was obtained which remained unchanged for weeks when kept at room temperature in an inert atmosphere but which decomposed rapidly when exposed to air. Its elementary analysis revealed that it was not the desired diamine (II) and attempts to establish its structure have been unsuccessful thus far.

The procedure is illustrated as



Experimental[7]

N,N-Dimethyl-N'-benzyl-N'-phenylethylenediamine (I). **Alkylation of N-Benzylaniline.**—A mixture of 9.2 g. (0.05 mole) of N-benzylaniline, 8.7 g. (0.06 mole) of dimethylaminoethyl chloride hydrochloride, 2.8 g. (0.12 mole) of lithium amide (98% purity) and 100 ml. of dry benzene was refluxed for 25 hours. The reaction mixture was then filtered and the residue washed with benzene. The solvent was removed from the filtrate by distillation and the residue distilled *in vacuo*. There was obtained 11.8 g. (92%) of a pale yellow oil distilling at 159–163° (2 mm.). The picrate prepared in ether and recrystallized once from isopropyl alcohol, melted at 149–150°. Huttrer[8] reported a boiling point of 195–196° (0.03 mm.) and a melting point of 149–154° (dec.) for the picrate; Carrara[9] found that his product distilled at 157–158° (1 mm.).

From N-Benzyl-N-phenylacetamide.—To 200 ml. of an ether solution of methylmagnesium iodide, prepared from 8.5 g. (0.35 mole) of magnesium turnings and 49.7 g. (0.35 mole) of methyl iodide, 21.3 g. of N-benzyl-N-phenylacet-

(1) Antergen is the trade mark for N,N-dimethyl-N'-benzyl-N'-phenylethylenediamine, Rhône-Poulenc.

(2) C. W. Sondern and P. J. Breivogel, U. S. Patent 2,440,703 (May 4, 1948), prepared N,N-dimethyl-N'-benzyl-N'-(2-thiazolyl)-ethylenediamine by heating 2-bromothiazole with N,N-dimethyl-N'-benzylethylenediamine.

(3) C. P. Huttrer, C. Djerassi, W. L. Beears, R. L. Mayer and C. R. Scholz, THIS JOURNAL, **68**, 1999 (1946), prepared Pyribenzamine [N,N-dimethyl-N'-benzyl-N'-(2-pyridyl)-ethylenediamine] and other 2-pyridyl tertiary, as well as secondary, amines by alkylating a 2-pyridylamine with an alkyl halide in the presence of either sodamide or lithium amide.

(4) Employing the same conditions which were used successfully in condensing 2-bromopyridine [N. Weiner and I. A. Kaye, *J. Org. Chem.*, **14**, 868 (1949)] with ethanolamine, no product could be isolated from a mixture of 2-bromothiophene and the aminoalcohol. The reactants were recovered even after prolonged heating at 250° in the presence of copper powder.

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(6) W. J. Hickinbottom, "Reactions of Organic Compounds," Longmans, Green and Co., New York, N. Y., 1948, p. 276.

(7) Melting points are corrected, boiling points are not.

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