[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PRESIDENCY COLLEGE]

SYNTHESIS OF 3-METHYL ISOQUINOLINES

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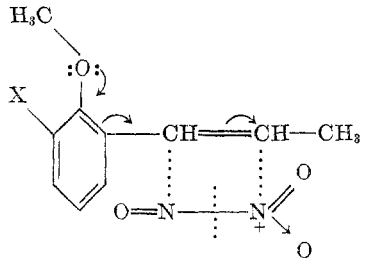
This paper is concerned with a study of the limitations and usefulness of a novel method developed by Bruckner and co-workers (1) for the synthesis of 3-methyl isoquinolines. Bruckner and co-workers have applied the method only to propenylbenzenes derived from safrole and eugenol. The scheme of work in the present study is shown in Chart I. In the group of compounds employed, poor yields were obtained in the conversion of allylphenols to propenylphenols from which, in turn, pseudonitrosites were formed only in low yields. The study was therefore conducted with the O-methyl ethers (IV) of the allylphenols, which could be transformed in high yield to propenylanisoles (V) by treatment with alkali.

All the propenyl compounds used in this study have a methoxy group *ortho* to the propenyl side chain. There were marked variations in the yield of pseudonitrosites (Table I), depending on the position of the third substituent on the benzene ring. Thus 2-methoxy-3-methyl-, 2-methoxy-3-chloro-, and 2,3-dimethoxy-propenylbenzenes gave low yields of the pseudonitrosites in comparison with the excellent yields obtained with 2-methoxy-, 2-methoxy-5-methyl-, 2-methoxy-5-chloro-, and 2,5-dimethoxy-propenylbenzenes. The mechanism of addition of dinitrogen tetroxide to olefins has been clearly elucidated by the recent work of Levy and co-workers (2). It has been suggested that the additions are polar and involve the initial attack of the electrophilic nitrogen of the nitro group to the activated double bond. If the mechanism of addition of nitrogen trioxide is formulated as shown below, the formation of the pseudonitrosites should be facilitated by electron release to the β-carbon atom.



It is possible that steric interference of the third substituent [X] with the methoxyl group inhibits electron release from the latter, slowing down the addition of nitrogen trioxide, with the result that alternate reactions like polymerization predominate.

The pseudonitrosites were smoothly transformed to the acetoxy nitro compounds (VII) by acetic anhydride and sulfuric acid. Except for α-(2-methoxy-5-chlorophenyl)-α-acetoxy-β-nitropropane (VIIc) and α-2-(1-methoxynaphthyl)-

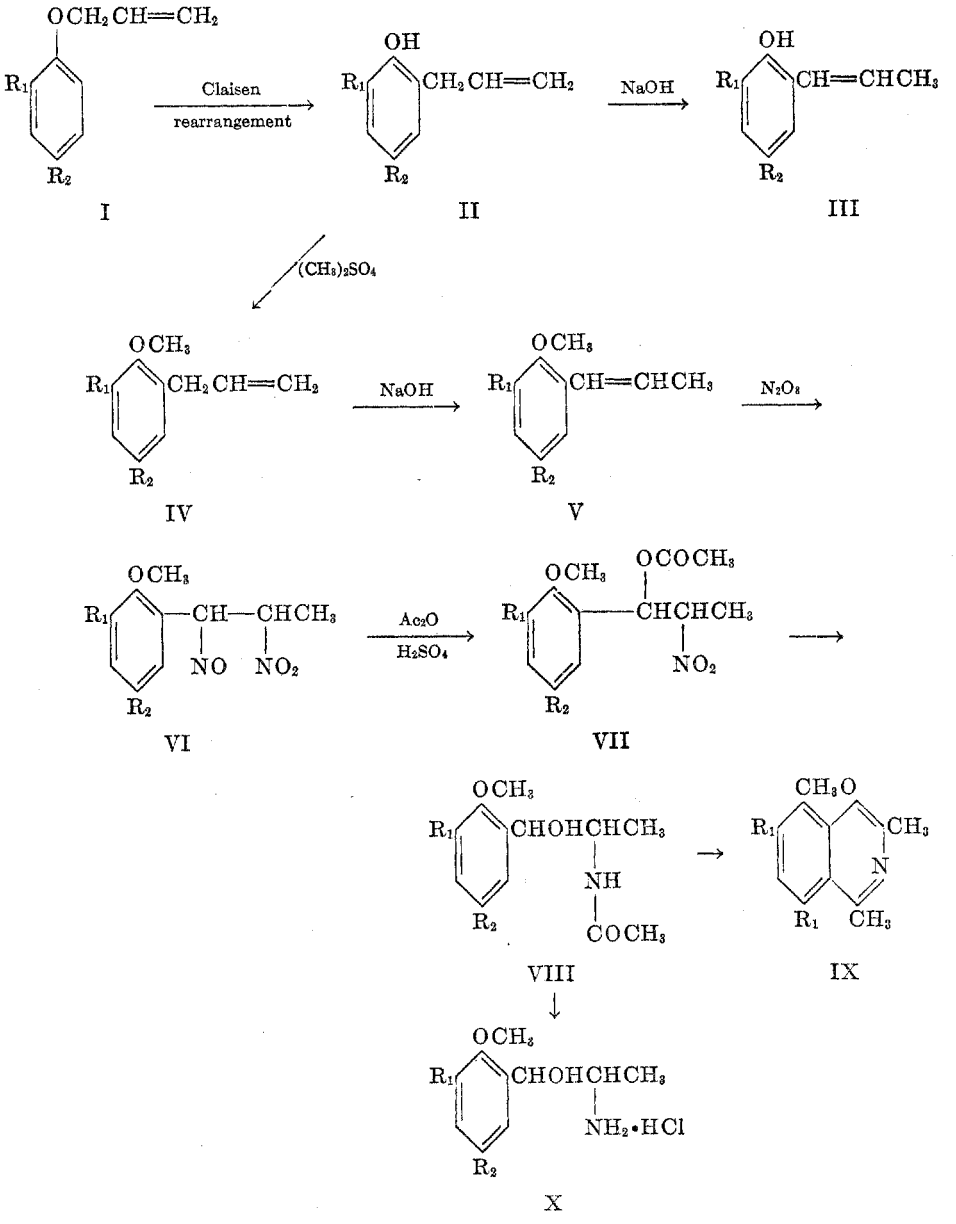


CHART I

α-acetoxy-β-nitropropane all of the acetoxy nitro compounds encountered in this series were syrupy oils which could not be induced to crystallize and were used as such for the next stage. The acetoxy nitro compounds were reduced at a mercury cathode in satisfactory yields to α-aryl-β-acetylaminopropanols (VIII)

and the latter cyclized to 1,3-dimethylisoquinolines by treatment with phosphorus oxychloride.

The product obtained by cyclization of α-(2,5-dimethoxyphenyl)-β-acetylaminopropanol (VIIId) displayed anomalous characteristics. Solutions of this substance in benzene, ether, or alcohol displayed a marked blue fluorescence when exposed to bright light. The hydrochloride was colored yellow and solutions of the base in mineral acid were deeply fluorescent. An independent synthesis according to the scheme shown below proved however that the product was indeed

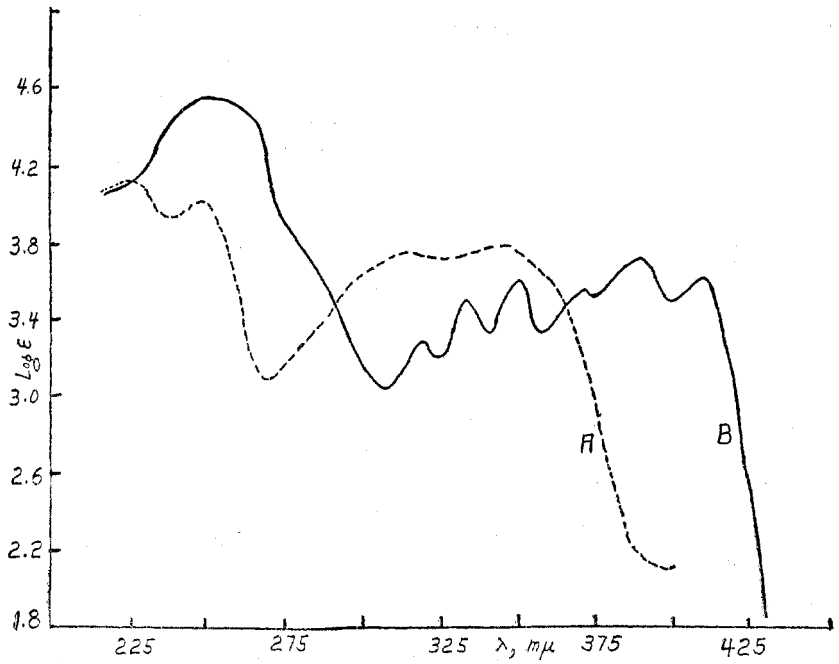
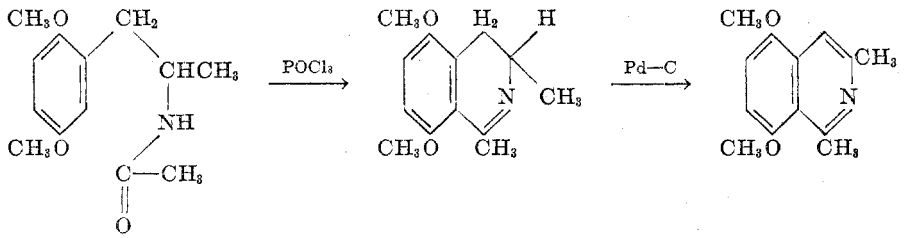


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA. A. 1,3-Dimethyl-5,8-dimethoxyisoquinoline; B. 1,3-Dimethyl-5-methoxybenz[*g*]isoquinoline.

1,3-dimethyl-5,8-dimethoxyisoquinoline. This isoquinoline is an oil which takes up water on exposure to air with remarkable facility, forming a crystalline monohydrate, m.p. 70°. The ultraviolet absorption spectrum of 1,3-dimethyl-5,8-dimethoxyisoquinoline is recorded in Fig. 1.



The cyclization of α-2-(1-methoxynaphthyl)-β-acetylaminopropanol yielded only 1,3-dimethyl-5-methoxybenz[*g*]isoquinoline. The structure assigned to this product is confirmed by the absorption spectrum which, as is to be expected (3), shows a striking similarity to that of anthracene (4). All the absorption maxima however occur at longer wave lengths than in the case of anthracene. In the absence of absorption data on the parent member of the series, benz[*g*]isoquinoline, it is not possible to say whether the shift of absorption maxima to longer wave lengths is caused merely by the substitution of an azomethine linkage for an ethylenic group in anthracene or by the further presence of methoxy and methyl groups in the compound under study.

The α-aryl-β-acetylaminopropanols (VIII) were converted by hydrolysis with methanolic hydrochloric acid to the amine hydrochlorides of general formula X. These amines may be considered to be nuclear substituted derivatives of the therapeutically useful sympathomimetic amine Propadrine (5). One of these

TABLE I

ALLYLANISOLES (IV), PROPENYLANISOLES (V), AND PSEUDONITROSITES OF THE LATTER (VI)

	ALLYLANISOLES				PROPENYLANISOLES			PSEUDONITROSITES			
IV	R_1	R_2	B.P., °C./MM.	n_D^{30}	YIELD, %	B.P., °C./MM.	n_D^{30}	YIELD, %	M.P., °C.	N	
										Calc'd	Found
a[a]	H	H	85/11	1.525		104/13	1.56	53	130	12.5	12.42
b	H	CH_3	106/14	1.525	80	118/16	1.547	58	132	11.76	11.89
c	H	Cl	135/25	1.543	72	135/19	1.566	64	116	10.83	10.92
e	CH_3	H	98/16	1.518	80	95/14	1.533	20	124	11.76	11.87
f	Cl	H	95/16	1.536	78	108/11	1.552	21	120	10.83	10.88
g	OCH_3	H	120/13	1.525	80	130/13	1.552	21	126	11.03	10.78

[a] Previously reported (12).

amines, α-(2,5-dimethoxyphenyl)-β-aminopropanol has been prepared earlier by an alternate route (6). The hydrochloride and the diacetate of this compound have been reported to melt at 215° and 119–120° respectively. The amino propanol prepared by us yields a hydrochloride and a diacetate melting at 176° and 98–100° respectively. The differences are evidently due to the fact that the amino propanols prepared by different routes differ in configuration.

EXPERIMENTAL

Procedures for the preparation of 1,3-dimethyl-5,8-dimethoxyisoquinoline and 1,3-dimethyl-5-methoxybenz[*g*]isoquinoline are described. In other cases employing the same route similar procedures were followed and physical constants and analytical data for the intermediates and final products are recorded in the Tables.

1,3-Dimethyl-5,8-dimethoxyisoquinoline (IXd). *2,5-Dimethoxypropenylbenzene* (Vd). This substance was obtained by treatment of 2,5-dimethoxyallylbenzene (7) with a solution of potassium hydroxide in ethylene glycol at 170–175°, until the product attained a constant refractive index. Three hours of heating was adequate for the purpose, b.p. 126°/13 mm.; n_D^{30} 1.556; yield, 85%.

2,5-Dimethoxypropenylbenzene pseudonitrosite (VId). Erratic results were obtained by following the Bruckner procedure (1) in the addition of nitrogen trioxide, when working with propenyl compounds in amounts of about 20 g. Consistent and reproducible results were obtained by conducting the experiments in several 1-g. batches.

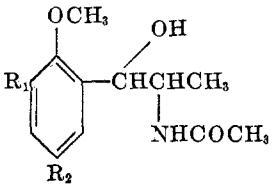
A solution of 1 g. of the freshly distilled 2,5-dimethoxypropenylbenzene in 10 ml. of ether was treated with a solution of sodium nitrite (21 g.) in 8 ml. of water. Then 10 ml. of 4 *N* sulfuric acid was added dropwise during 20 minutes. The solution turned green and then yellow and a white crystalline solid separated. After leaving in the ice chest overnight, the precipitate was filtered, washed with ether, then water, and dried in air. Twenty such experiments run simultaneously yielded 18 g. of the pseudonitrosite, m.p. 130° (decomp.).

Anal. Calc'd for $C_{11}H_{14}N_2O_5$: N, 11.03. Found: N, 10.91.

α-(2,5-Dimethoxyphenyl)-β-nitropropanol acetate (VIId). A suspension (7 g.) of the finely powdered pseudonitrosite in 20 ml. of acetic anhydride was cooled in ice and treated gradually with good stirring with 2 ml. of acetic anhydride containing a drop of concentrated sulfuric acid. The pseudonitrosite dissolved with evolution of nitrous fumes. After two

TABLE II

α-ARYL-β-ACETYLAMINOPROPANOLS (VIII)



VIII	R_1	R_2	M.P., °C.	RECRYSTALLIZED FROM	YIELD, %	N	
						Calc'd	Found
a	H	H	174	Toluene	76	6.28	6.21
b	H	CH_3	135	Benzene	41	5.91	5.95
c	H	Cl	204	Alcohol	56	5.44	5.28
e	CH_3	H	84	Benzene	49	5.91	5.87
f	Cl	H	95	Benzene	43	5.44	5.45
g	OCH_3	H	Oil	—	63	—	—

hours, the solution was poured on to ice water, the acetic anhydride was decomposed, and the emulsion was extracted with ether. The ether extract after drying and removal of ether yielded 7 g. of a colorless syrupy oil, which could not be induced to crystallize. Attempts at purification by distillation *in vacuo* led to extensive decomposition.

α-(2,5-Dimethoxyphenyl)-β-acetylaminopropanol (VIIId). A solution of 7 g. of the nitropropanol acetate (VIId) in 100 ml. of alcohol, 50 ml. of glacial acetic acid, and 3 ml. of concentrated hydrochloric acid was reduced at a mercury cathode keeping the temperature below 60°. At the end of the reduction, the solution was made neutral to Congo Red by addition of sufficient sodium acetate and evaporated to dryness *in vacuo* at 50°. The residue was dissolved in water (50 ml.) and saturated with sodium bicarbonate. On standing in the ice chest overnight the acetylamino compound separated. It was filtered, washed with a little water, and dried. Recrystallization from alcohol yielded 3.1 g., m.p. 156°.

Anal. Calc'd for $C_{13}H_{19}NO_4$: N, 5.53. Found: N, 5.73.

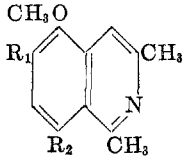
Acetylation of the above compound with acetic anhydride in pyridine at room temperature yielded α-(2,5-dimethoxyphenyl)-α-acetoxy-β-acetylaminopropane, melting at 98-100° after recrystallization from benzene.

Anal. Calc'd for $C_{15}H_{21}NO_5$: N, 4.75: Found N, 4.75.

1,3-Dimethyl-5,8-dimethoxyisoquinoline (IXd). A solution of 1 g. of the acetylamino compound in 10 ml. of dry toluene was treated with 3 ml. of phosphorus oxychloride and refluxed for 75 minutes, with exclusion of moisture. The solution was then poured into ice water and the excess phosphorus oxychloride was decomposed by gentle warming on a water-bath. A fluorescent, orange-yellow solution was obtained, which was cooled strongly in ice and basified with sodium hydroxide solution. The isoquinoline was extracted with ether and the ether extract was dried over potassium carbonate. Removal of the ether yielded 0.75 g. of a thick oil, which was dissolved in dry benzene and passed through a column of alumina (30 g.). On washing the column with benzene a yellow zone moved rapidly into the filtrate. This fraction of the eluate on removal of benzene yielded 0.65 g. of a pale yellow

TABLE III

1,3-DIMETHYLISOQUINOLINES (IX)



IX	R_1	R_2	YIELD, %[b]	HYDROCHLORIDE[c]			PICROLONATE[d]		
				M.P., °C.	N		M.P., °C.	N	
					Calc'd	Found		Calc'd	Found
a[a]	H	H	70	[e]	—	—	221	15.52	15.43
b	H	CH_3	49	174	5.9	5.65	266	15.05	15.40
c	H	Cl	41	217	5.43	5.58	230	14.43	14.74
e	CH_3	H	53	220	5.9	6.27	242	15.05	15.36
f	Cl	H	50	180	5.43	5.49	—	—	—
g	OCH_3	H	57	212	5.52	5.74	238	14.55	14.38

[a] The free base crystallized from dilute alcohol melted at 124°. Calc'd for $C_{12}H_{13}NO$: N, 7.48. Found: N, 7.37. Other isoquinolines listed in this table were oils. [b] Yield based on hydrochlorides. [c] The hydrochlorides were all crystallized from an absolute alcohol-ether mixture. [d] The picrolonates were crystallized from alcohol. [e] The hydrochloride was extremely hygroscopic.

oil, which solidified on rubbing. Recrystallization from petroleum ether yielded pale yellow silky needles melting at 70°.

Anal. Calc'd for $C_{13}H_{15}NO_2 \cdot H_2O$: C, 66.37; H, 7.23; N, 5.96.
Found: C, 66.03; H, 7.23; N, 6.04.

The *hydrochloride* obtained by passing dry hydrogen chloride through an ether solution of the base was deep yellow and was crystallized from absolute alcohol, m.p. 234°.

Anal. Calc'd for $C_{13}H_{15}NO_2 \cdot HCl \cdot H_2O$: C, 57.49; H, 6.63; N, 5.16.
Found: C, 57.42; H, 6.95; N, 5.45.

The *picrolonate*, prepared in alcoholic solution, was recrystallized from alcohol, m.p. 230°.

Anal. Calc'd for $C_{13}H_{15}NO_2 \cdot C_{10}H_8N_4O_5 \cdot H_2O$: N, 14.03. Found: N, 13.83.

Alternate synthesis of 1,3-dimethyl-5,8-dimethoxyisoquinoline. β-2,5-dimethoxyphenylisopropylamine was prepared by a different route than that reported by Baltzly and Buck (8) in better over-all yield, starting from 2,5-dimethoxybenzaldehyde (9).

α-Methyl-β-2,5-dimethoxyphenylacrylic acid. A mixture of 25 g. of 2,5-dimethoxybenzaldehyde, 20 g. of propionic anhydride, and 15 g. of freshly fused sodium propionate was heated for 48 hours at 140–150°. The mixture after cooling was treated with 300 ml. of 4 *N* sodium hydroxide solution, heated to boiling, cooled, and extracted with benzene to remove unchanged 2,5-dimethoxybenzaldehyde, and the stilbene. Neutralization of the alkaline solution yielded 20 g. of the acid which melted at 114° after one crystallization from dilute alcohol.

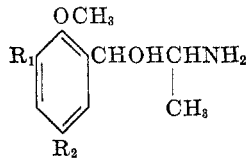
Anal. Calc'd for $C_{12}H_{14}O_4$: C, 64.86; H, 6.34.
Found: C, 64.52; H, 5.88.

α-Methyl-β-2,5-dimethoxyphenylpropionic acid. This was obtained by reduction of the above acrylic acid with sodium amalgam in nearly quantitative yield. The product melted at 61–62°. (*Cf.* Ref. 8, m.p. 59.5°).

α-Methyl-β-2,5-dimethoxyphenylpropionamide. Baltzly and Buck (8) have made this by passing dry ammonia gas into the molten acid. The following procedure gives better results.

TABLE IV

α-ARYL-β-AMINOPROPANOLS



R_1	R_2	HYDROCHLORIDE[a]			PICRATE[b]		
		M.P., °C.	N		M.P., °C.	N	
			Calc'd	Found		Calc'd	Found
H	H	156	6.45	6.77	122	13.66	13.54
H	CH_3	182	6.05	5.72	166	13.2	13.02
H	Cl	186	5.56	5.25	208	12.60	12.37
H	OCH_3	174	5.66	5.44	177	12.73	12.83
CH_3	H	167	6.05	5.71	—	—	—
Cl	H	176	5.56	5.25	122	12.60	12.47
OCH_3	H	194	5.66	5.43	196	12.73	12.68

[a] Crystallized from an absolute alcohol-ether mixture. [b] Crystallized from alcohol.

A solution of 20 g. of the pure dry acid in 20 ml. of absolute benzene was treated with 15 ml. of purified thionyl chloride. The mixture was left for 12 hours and warmed briefly on the water-bath to complete the reaction. It was then added dropwise with good stirring to 275 ml. of ammonia liquor and 10 ml. of 50% sodium hydroxide solution well cooled in ice. After 30 minutes, the precipitated amide was filtered, well washed with water, and recrystallized from hot water, m.p. 101.5° (*Cf.* Ref. 8, m.p. 99°); yield, 15 g.

β-2,5-Dimethoxyphenylisopropylamine was prepared after Baltzly and Buck (8) by the action of sodium hypochlorite on the amide in dioxane solution (sodium hypobromite caused halogenation of the ring), b.p. 140°/3 mm. Hydrochloride, m.p. 118°; yield, 80%.

The *acetyl* derivative prepared in the usual way melted at 111° after recrystallization from dilute alcohol.

Anal. Calc'd for $C_{13}H_{19}NO_3$: N, 5.91. Found: N, 6.27.

1,3-Dimethyl-5,8-dimethoxy-3,4-dihydroisoquinoline. From 1 g. of the acetyl derivative on cyclization with phosphorus oxychloride, there formed 0.6 g. of the dihydroisoquinoline which was an oil. The *picrolonate* recrystallized from alcohol melted at 185–186°.

Anal. Calc'd for $C_{13}H_{17}NO_2 \cdot C_{10}H_8N_4O_5$: N, 14.5. Found: N, 14.8.

The *hydrochloride*, recrystallized from absolute alcohol, melted at 177°.

1,3-Dimethyl-5,8-dimethoxyisoquinoline. A solution of 0.5 g. of the dihydroisoquinoline in 10 ml. of freshly distilled decalin was heated with 50 mg. of palladized charcoal (5% Pd) in a stream of dry carbon dioxide under reflux for 8 hours. After filtering from the catalyst, the decalin solution was extracted with two 25-ml. portions of 4 *N* HCl. The acid extract was freed from decalin by extraction with ether, cooled well, and basified. The isoquinoline was obtained by extraction with ether. Yield, 0.4 g. after purification by chromatography as previously, m.p. 70°. The hydrochloride and the picrolonates melted at the same temperatures as reported for the derivatives from the base prepared by the other method. Mixture melting points showed that the bases prepared by the different routes and their derivatives were identical.

2,4-DIMETHYL-5-(2′,5′-DIMETHOXYPHENYL)OXAZOLE[1]

2,5-Dimethoxypropiophenone was made according to Bruckner, *et al.* (10).

2,5-Dimethoxy-α-isonitrosopropiophenone. This has been reported in a patent (11), but only one form is reported whereas two forms are obtained by the following procedure:

A solution of 13 g. of 2,5-dimethoxypropiophenone in 100 ml. of dry ether was cooled in an ice-salt bath and treated with 9 g. of freshly distilled butyl nitrite while passing in a stream of dry hydrogen chloride. A white solid separated towards the end of the addition of butyl nitrite and HCl was passed for a further 20 minutes. The mixture was left overnight, filtered, and the yellow residue repeatedly washed with water. Recrystallization from alcohol gave 2 g. of crystals, m.p. 106°.

Anal. Calc'd for $C_{11}H_{13}NO_4$: N, 6.28. Found: N, 6.48.

The filtrate and washings were repeatedly extracted with ether. The ether extract was shaken with dilute (2 *N*) sodium hydroxide in several portions. The alkali extract on cooling and acidification with hydrochloric acid gave a sticky solid, purified by crystallization from dilute alcohol, m.p. 98°; yield, 5.48 g.

Anal. Calc'd for $C_{11}H_{13}NO_4$: N, 6.28. Found: N, 6.52.

These two compounds are evidently stereoisomers and were reduced to the same α-amino-2,5-dimethoxypropiophenone.

α-Amino-2,5-dimethoxypropiophenone hydrochloride (11). A solution of 1 g. of either of the forms of α-isonitroso-2,5-dimethoxypropiophenone in 30 ml. of absolute alcohol containing 1 g. of hydrogen chloride was added to a previously reduced suspension of 0.1 g. of Adam's catalyst in 10 ml. of absolute alcohol. During eight hours 203 ml. of hydrogen was absorbed at N.T.P. (2 moles). The alcohol was removed *in vacuo* and the residue was taken up in absolute alcohol, when an infusible material separated (0.25 g.). The filtrate was evaporated to dryness and the residue recrystallized from absolute alcohol-ether, m.p. 176°; yield, 0.65 g.

Anal. Calc'd for $C_{11}H_{15}NO_3 \cdot HCl$: N, 5.70. Found: N, 5.82.

The *acetyl* derivative was formed by dissolving 0.5 g. of the above hydrochloride in 2 ml. of water and 2 ml. of acetic anhydride and then adding a concentrated sodium hydroxide solution dropwise with good shaking. The precipitated derivative was filtered and recrystallized from dilute alcohol, m.p. 114°.

Anal. Calc'd for $C_{13}H_{17}NO_4$: N, 5.58. Found: N, 5.67.

2,4-Dimethyl-5-(2′,5′-dimethoxyphenyl)oxazole. A solution of 1 g. of the acetylamino compound in 10 ml. of toluene was refluxed with 3 ml. of phosphorus oxychoride for 70 minutes. After cooling, the solution was poured into water, the excess oxychloride was decomposed, and the oxazole was removed by extraction with chloroform. After removal of chloroform 0.4 g. of a pale brown oil was obtained. A solution of this oil in alcohol, ether, or

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[1] This compound was prepared for comparison with 1,3-dimethyl-5,8-dimethoxyisoquinoline.

benzene displayed only a feeble fluorescence. A colorless hydrochloride, m.p. 132°, was obtained by passing dry HCl gas through an ethereal solution of the oxazole, but this was too hygroscopic to be analyzed. The picrolonate melted at 162° after recrystallization from alcohol.

Anal. Calc'd for $C_{23}H_{23}N_5O_8$: N, 14.08. Found: N, 14.25.

1,3-DIMETHYL-5-METHOXYBENZ[*g*]ISOQUINOLINE

2-Allyl-α-naphthol methyl ether was made by methylation of 2-allyl-α-naphthol (12), b.p. 150°/11 mm., n_D^{30} 1.595.

2-Propenyl-1-naphthol methyl ether, b.p. 160–162°/11 mm., n_D^{30} 1.625.

2-Propenyl-1-naphthol methyl ether pseudonitrosite. From 1 g. of the propenyl compound 0.4 g. of the pseudonitrosite was obtained, m.p. 128° (decomp.).

Anal. Calc'd for $C_{14}H_{14}N_2O_4$: N, 10.22. Found: N, 10.49.

α-2-(1-Methoxynaphthyl)-β-nitropropanol acetate. The pseudonitrosite (7 g.) yielded on treatment with acetic anhydride and sulfuric acid as previously, 6.5 g. of the β-nitropropanol acetate. Recrystallization from methanol gave crystals, m.p. 88°.

Anal. Calc'd for $C_{16}H_{17}NO_5$: N, 4.62. Found: N, 4.28.

α-2-(1-Methoxynaphthyl)-β-acetylaminopropanol was formed in 50% yield by electrolytic reduction of the previous compound. Recrystallization from dilute alcohol gave crystals, m.p. 115°.

Anal. Calc'd for $C_{16}H_{19}NO_3$: N, 4.98. Found: N, 5.15.

1,3-Dimethyl-5-methoxybenz[g]isoquinoline. Cyclization of 1 g. of the acetylamino compound yielded by the usual procedure 0.45 g. of a sticky brown solid. This was dissolved in 5 ml. of benzene and passed through a column of alumina (30 g.). On developing with benzene a light yellow zone rapidly moved into the filtrate.

This portion of the eluate gave 0.35 g. of an orange-yellow solid. Recrystallization from petroleum ether gave pale yellow crystals, m.p. 118°. Solutions of this solid in alcohol, ether, or benzene were intensely fluorescent.

Anal. Calc'd for $C_{16}H_{15}NO$: C, 81.02, H, 6.33.
Found: C, 80.88, H, 6.45.

The *picrolonate* recrystallized from absolute alcohol melted at 228°.

Anal. Calc'd for $C_{26}H_{23}N_5O_6$: C, 62.29; H, 4.59.
Found: C, 62.46; H, 4.59.

α-(2-Methoxy-5-chlorophenyl)-β-nitropropanol acetate. The pseudonitrosite (IVc) (7 g.) gave on treatment with acetic anhydride and sulfuric acid and working up as previously 7.5 g. of a yellow solid. Recrystallization from methanol yielded crystals, m.p. 80°.

Anal. Calc'd for $C_{12}H_{14}ClNO_5$: N, 4.86. Found: N, 4.73.

Other compounds of this type in this series were syrupy oils.

α-2-(1-methoxynaphthyl)-β-aminopropanol. A solution of 1 g. of α-2-(1-methoxynaphthyl)-β-acetylaminopropanol in 40 ml. of 1% methanolic hydrochloric acid was refluxed for one hour. The methanol was then distilled off and the residue dissolved in water (20 ml.), cooled well, and basified with sodium hydroxide solution. The base was extracted with ether, the ether extract shaken with small portions of dilute hydrochloric acid (2 *N*), and the base reprecipitated from the acid extract by addition of sodium hydroxide solution. The base so purified was extracted with ether and the ether was removed after drying over potassium carbonate. After removal of ether, the residual base was dried over sodium hydroxide *in vacuo* and converted to the hydrochloride by passing dry hydrogen chloride through a solution in absolute ether. The hydrochloride was recrystallized from an absolute alcohol-ether mixture. Yield, 0.6 g., m.p. 240°.

Anal. Calc'd for $C_{14}H_{18}ClNO_2$: N, 5.23. Found: N, 5.38.

The *picrate* melted at 228°.

Anal. Calc'd for $C_{20}H_{20}N_4O_9$: N, 12.17. Found: N, 12.33.

The amino propanols listed in Table IV were prepared by the procedure described above.

Acknowledgment. Our grateful thanks are due to Mr. B. S. Thyagarajan for carrying out the analyses.

SUMMARY

1. Eight new 3-methyl substituted isoquinolines have been synthesized by the Bruckner method. Considerable variations in the yields of the pseudonitrosites occur dependent on the relative positions of other substituents with respect to the propenyl side chain on the aromatic ring.

2. The product of the cyclization of α-(2,5-dimethoxyphenyl)-β-acetylaminopropanol was proved to be 1,3-dimethyl-5,8-dimethoxyisoquinoline by an independent synthesis.

3. α-2-(1-methoxynaphthyl)-β-acetylaminopropanol yielded 1,3-dimethyl-5-methoxybenz[*g*]isoquinoline as the only isolable product. The absorption spectrum of this substance shows a striking similarity to that of anthracene, as is to be expected.

4. Eight α-aryl-β-aminopropanols, analogs of Propadrine, have been prepared.

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