SYNTHESES BASED ON β-PHENYLETHYLAMINES.
II. PREPARATION OF N-(2-METHOXYBENZYL)-3,4-DIMETHOXYPHENETHYLAMINE

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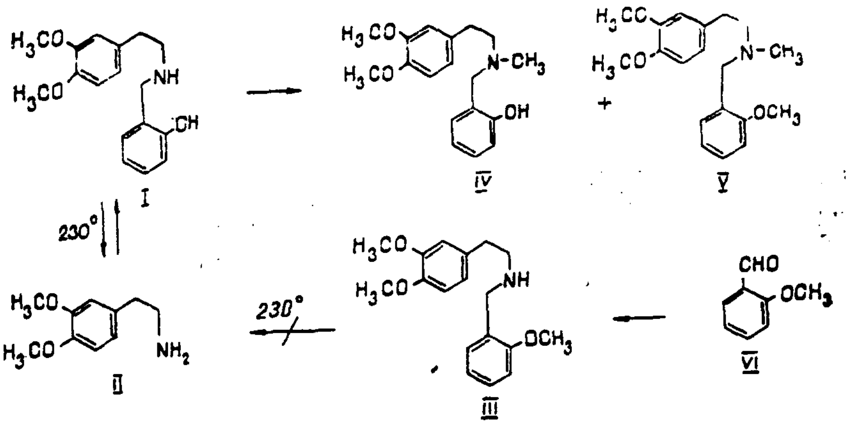
The possibility has previously been shown of using a 2-hydroxybenzyl residue for the protection of an N—H bond and the subsequent ready elimination of the protective group on thermolysis [1]. The thermal decomposition of N-(2-hydroxybenzyl)-3,4-dimethoxyphenethylamine (I) gives homovetratrylamine (II) with 80% yield. The ease of a retrodiene breakdown of a substance of the type of (I) is connected with the formation of an o-quinone methide.

It was of interest to investigate the basic possibility of the occurrence of this process in compounds with an o-methoxy group in place of a hydroxy group. With this aim, we attempted to synthesize N-(2-methoxybenzyl)-3,4-dimethoxyphenethylamine (III), starting from (I) and using Rodionov's methylating reagents — trimethylphenylammonium p-toluenesulfonate [2] and benzenesulfonate [3].

It is known that the methylation of substances containing NH and OH groups simultaneously is not a clear-cut process. In our case, the use of the above-mentioned reagents led to the formation of a complex mixture of substances, on the separation of which it was possible to isolate N-(2-hydroxybenzyl)-N-methyl-3,4-dimethoxyphenethylamine (IV, 60%), the initial amine (I), and a small amount of N-(2-methoxybenzyl)-N-methyl-3,4-dimethoxyphenethylamine (V, 10-15%). It was possible to detect only trace amounts of the desired amine (III) in the reaction products. The structure of substance (IV) was confirmed by the methylation of (I) using the method given in [4].



Thus, the given method [2, 3] proved unsuitable for the selective methylation of the OH group of compound (I). Amine (III) was therefore synthesized from o-anisaldehyde (VI) and (II) via the preparation of the imine, followed by reduction with sodium tetrahydroborate. The initial aldehyde (VI) was obtained by the methylation of salicylaldehyde with methyl iodide in 80% yield. The use for methylation of dimethyl sulfate in aqueous alkali or in acetone with the addition of potassium carbonate did not give good results.

As was expected, the amine obtained (III) proved to be stable and did not decompose in a similar way to the amine (I) at 230°C.

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ALKALOIDS OF Rauwolfia littoralis

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It has been reported previously that 3.5-3.8% of total alkaloids and 0.03% of reserpine accumulate in the roots of Rauwolfia littoralis Pierre ex Pitard (R. indochinensis M. Pichon, R. macrocarpa Standl) [1, 2]. Continuing a chemical study of this plant, we have investigated the bark of the roots and have isolated six alkaloids.

The dried and comminuted root bark was wetted with 10% ammonia solution, and the alkaloids were extracted with 96% C_2H_5OH. The extract was 2/3-evaporated in vacuum, acidified with 10% HCl, and filtered. The residue was heated with 20% CH_3COOH, and the mixture was cooled and filtered. The acetic acid solution was washed with petroleum ether to eliminate fats. The ether was driven off from the acetic acid solution by heating in the water bath. After this, the alkaloids were extracted from the acetic acid solution with C_6H_6. The solvent was distilled off in vacuum to a dry residue, which was dissolved in $CHCl_3$, and the solution was neutralized with 10% ammonia to pH 7. Then it was stirred with a small amount of Al_2O_3, and the $CHCl_3$ was driven off by blowing with air. The mixture was transferred to a chromatographic column of Al_2O_3 and chromatographed. This led to the isolation of substance (I) – yellowish (30 mg/500 g; 0.006%), $C_{33}H_{40}N_2O_9$, mp 260-262°C; UV spectrum : $\lambda_{max}^{C_2H_5OH}$ (nm): 223, 268, 295; λ_{min} 247. IR spectrum: $\lambda_{max}^{\text{paraffin oil}}$ (cm^{-1}): 3435, 1735, 1715, 1500, 1590, 1125. Substance (I) was identified as reserpine [3].

The filtrate was treated with $CHCl_3$; the chloroform fraction (A) contained a mixture of weak bases. The acid solution was made alkaline to pH 8 and was filtered and extracted with $CHCl_3$ (fraction B). The mother solution was alkalinized to pH 10-11 and was extracted with ethyl acetate, giving fraction C of strong bases. The chromatography of fraction A on a column of Al_2O_3 with elution of the alkaloids by ethyl acetate and ethyl acetate–ethanol yielded substances (II), (III), (IV), and (V).

Substance (II) with the composition $C_{42}H_{44}N_4O_6$, mp 260-265°C, $\lambda_{max}^{C_2H_5OH}$ (nm): 225, 258, 292, 307, 370, was serpentinine [4, 5]. Yield: 200 mg/500 g; 0.04%.

Substance (III) with the composition $C_{21}H_{20}N_2O_3$, mp 203-205°C, $\lambda_{max}^{C_2H_5OH}$ (nm): 252, 307, 370; λ_{min} 282, 327, was identified as alstonine [5]. Yield 25 mg/500 g; 0.005%.

Substance (IV) (yield: 10 mg/500 g; 0.002%), mp 323-325°C; $\lambda_{max}^{C_2H_5OH}$ (nm): 224, 257, 307; was not identified.

Substance (V) consisted of an oily liquid (1 ml/0.5 g; 0.1%). $\lambda_{max}^{C_2H_5OH}$ (nm): 241. It was not identified.

Substance (VI), isolated from fraction C, was yellow. Yield: 100 mg/500 g; 0.02%, mp 170-175°C. $\lambda_{max}^{C_2H_5OH}$ (nm): 253, 307, 368; λ_{min} 281 was serpentine [5, 6].

The structures of all the compounds isolated were confirmed by the results of UV and IR spectroscopies. Ajmaline was detected chromatographically in fraction B. This is the first time that any of these alkaloids have been isolated from R. littoralis.

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