and the solution was made strongly acid with 10% sulfuric acid. After boiling the solution for 30 minutes, an excess of cold water was added, and the resulting white suspension was extracted with ether. The ether solution was washed with water, dried over sodium sulfate and evaporated to dryness, leaving 4-pregnene-3,5-dimethoxy-2-nitropropane (yellowish crystalline powder, m.p. 185-188\(^\circ\)). Recrystallization from aqueous methanol gave colorless needles, m.p. 185-188\(^\circ\). The mixed melting point with an authentic sample, m.p. 180-189\(^\circ\), was 186-189\(^\circ\). During the course of this reaction the 3-acetoxy group was hydrolyzed.

The synthesis of these phenethylamines from syringaldehyde proceeds readily and in good yield. In the case of 4,4-trimethoxybenzaldehyde, which can be obtained readily by either methylation of syringaldehyde with methyl sulfate and sodium hydroxide or from trimethylgallic acid,\(^8\) the methylamine-catalyzed reaction gave a high-melting polymeric product instead of the desired 3,4,5-trimethoxy-2-nitrostyrene, while catalysis with ammonium acetate gave the desired product in good yield. The amine-catalyzed condensation of these benzaldehydes with nitromethane is preferred when a free phenolic hydroxyl is present; the acetic acid-ammonium acetate method is superior for the condensation of 3,4,5-trialkoxynitrornethanes with nitromethane.

In distinct contrast to results obtained with tyramine hydrochloride and 4-hydroxy-3-methoxy-2-phenethylaniline hydrochloride, 4-hydroxy-3,5-dimethoxy-2-phenethylamine hydrochloride and 4-hydroxy-3-methoxy-2-phenethylamine hydrochloride, in ethanolic solution, failed to undergo ring hydrogenation in the presence of Adams catalyst. In this respect, its behavior is more like the alkylated trihydroxyphenethylamines. Alternate methods for hydrogenating this class of compounds are currently being examined.

**Experimental**

4-Ethoxy-3,5-dimethoxybenzaldehyde. —Syringaldehyde was obtained in 50% yield from 2,6-dimethoxynaphthalene by the procedure of Pearl.\(^4\) The action of ethyl iodide and anhydrous potassium carbonate on syringaldehyde, in accordance with the procedure of Head and Robertson,\(^9\) failed to give 4-ethoxy-3,5-dimethoxybenzaldehyde. In an alternate scheme, a mixture of 21.9 g. of syringaldehyde and 45 ml. of water was heated to boiling and 30 ml. of aqueous sodium hydroxide (15 g. of NaOH in 75 ml. of solution) was then added to the boiling suspension. The sodium salt of syringaldehyde which separated was redissolved and sulfuric acid was added to the mixture on further heating and stirring. Diethyl sulfate (23 g.) was then added to the boiling solution over a period of 10 minutes, and refluxing was continued for an additional hour. The boiling mixture was treated alternately with four 5.0-g. portions of diethyl sulfate and four 6-ml. portions of aqueous alkali. The oily product, which separated, was discarded. The residue, yield 21.8 g. (86%), m.p. 51-52\(^\circ\), recrystallized from ether gave light yellow plates melting at 52-53\(^\circ\).

*Anal. Caled. for C\(_{12}\)H\(_8\)O\(_4\): C, 62.7; H, 6.5. Found: C, 62.9; H, 6.7.*

3,4,5-Trimethoxybenzaldehyde. —Syringaldehyde was methylated by means of methyl sulfate and alkali by the procedure of Buck\(^10\); 21.9 g. of syringaldehyde afforded 26 g. of 3,4,5-trimethoxybenzaldehyde, m.p. 72-74\(^\circ\) (lit.\(^7\) 75-76\(^\circ\)).

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**Notes**

(1) This research is supported by Battelle Memorial Institute and in part by Public Health Service Grant No. M-600 (R).
(2) Battelle Memorial Institute.
(3) The Fels Research Institute.
(7) F. A. Ramirez and A. Burger, ibid., 72, 2781 (1950).
(9) K. H. Slotta and H. Hailer, Ber., 52, 3020 (1919).
(10) All melting points are uncorrected.
4-Hydroxy-3,5-dimethoxy-3-nitrostyrene.—A mixture of 26.2 g. of syringaldehyde, 10 ml. of redistilled nitromethane, 100 ml. of methanol and 10 ml. of 5% methanolic methylamine was warmed to stand in the dark at room temperature for 8 hours. The yellow crystalline mass was collected on a filter, washed with both methanol and ether and dried in a vacuum oven at room temperature; yield 31.6 g. (97%), m.p. 108-109° dec. Recrystallization from methanol gave yellow prisms, m.p. 118° dec.\\n*Anal.* Calcd. for C_{18}H_{18}O_8: N, 6.4. Found: N, 6.2.

The crude picrate (40 g.) was converted to the hydrochloride by treatment with a boiling mixture of 250 ml. of hydrochloric acid and 100 ml. of water. After cooling, the precipitated picric acid was extracted successively with one 75-ml. portion of nitrobenzene, two 50-ml. portions of nitrobenzene, and then with two 50-ml. portions of benzene. After treatment with Norite, the nearly colorless solution was concentrated under reduced pressure to give a total of 16.4 g. (78%) of 4-hydroxy-3,5-dimethoxy-3-nitrostyrene hydrochloride, m.p. 231-231.5°, after recrystallization from acetic acid.

\*Anal.* Calcd. for C_{18}H_{18}O_8.N.HCl: C, 45.2; H, 4.2. Found: C, 45.5; H, 4.3.

The anhydride was allowed to stand in the dark at room temperature, the product crystallized in large, stout yellow needles melting at 100-102°; yield 11.5 g. (65%), m.p. 108-109° after recrystallization from methanol-ethyl acetate. Jensch reported a m.p. of 105°.\\n
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**Purification and Physical Properties of 2,6-Lutidine and 2,4,6-Collidine**

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2,6-Lutidine and 2,4,6-collidine are presently commercially available, presumably in a state of relatively high purity. Accordingly, when we decided to include these two compounds in a study we had been making of the base strengths of substituted pyridine bases, it appeared convenient to utilize the commercial products, purified in the conventional manner by fractionation.

The materials thus obtained appeared to be of satisfactory homogeneity by the usual criteria. However, we observed certain anomalies in the data led us to question this explanation and to examine instead the homogeneity of our purified samples. We therefore undertook a study of the isolation and properties of pure 2,6-lutidine and 2,4,6-collidine. The results revealed that the purity of the commercial samples available to us were much lower than had been expected—based on an Eastman Kodak and Matheson samples of 2,4,6-collidine exhibiting purities of but 55-65%

Commercial 2,6-lutidine is generally contaminated with 3- and 4-picoline, all of which possess boiling points within 1°. It has been purified by azotropic distillation with phenol and by selective reaction of the impurities with ethyl tosylate.

We had previously observed that the heat of reaction of boron trifluoride with 2,6-lutidine is far less than that of the corresponding reactions with 3- and 4-picoline. Consequently this reaction appeared to offer a simple and convenient procedure for the selective removal of these contaminants. A sample of commercial 2,6-lutidine (Reilly Tar and Chemical Corp.) was therefore treated with