colorless oil: bp 92–94° (0.01 mm); $n^{20}D$ 1.549. *Anal.* ($C_{12}H_{14}O_2$) C, H.

Amino Alcohols I and II.—The appropriate epoxide[17] (0.075 mole) and amine (0.1 mole) were dissolved in 70 ml of *i*-PrOH and heated in a sealed vessel at 80° for 4 hr. The solvent was removed under reduced pressure and the oily residue was distilled. Results are summarized in Tables I and II.

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(17) 1-(*p*-Cyclopropylphenoxy)-2,3-epoxypropane was prepared in a similar manner as for the *ortho* derivative and was used without distillation.

2,3,6-Trimethoxynitrostyrene and Its β-Phenethylamine

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In a report of a general synthesis of a number of β-phenethylamines, Merchant and Mountwala[1] condensed 2,3,6-trimethoxybenzaldehyde (2,4-DNP, mp 223°)[2] with $MeNO_2$ and obtained an oil. This was not further purified, and was reduced to yield an amine whose picrate melted at 166–167°. Clark, *et al.*,[3] following the above procedure, obtained a β-phenethylamine as a hydrochloride, mp 122–123°. In contrast to the other trimethoxy derivatives evaluated, these authors reported that this compound had no activity in the presence of soluble amine oxidase from rabbit liver.

We now doubt that the 2,3,6-trimethoxyphenethylamine reported in the previous two communications was the correct compound. Using a method different from that in ref 2, 2,3,6-trimethoxybenzaldehyde was prepared; its 2,4-dinitrophenylhydrazone melted at 207° which compares with that reported by Shulgin.[4]

Condensing the substituted aldehyde with $MeNO_2$ resulted in a *crystalline* substituted nitrostyrene which melted at 99–100°. The nmr signals at δ 8.60 and 8.96 were due to the ethylenic protons and a coupling constant of J = 21 Hz indicated[5] a *trans* configuration for this compound. The melting points of the picrate and hydrochloride of the corresponding β-phenethylamine are now given as 176 and 135°, respectively.

Biological Activity.—The compound produced hypomotility in 20-g Swiss-albino mice when administered ip as a saline solution at 16 mg/kg. At 31 mg/kg the compound induced fatal convulsions.

Following a modified monomine oxidase procedure of Wurtman and Axelrod[6] using homogenized mouse brain, the amine at a concentration of 2.5×10^{-4} M inhibited by 43% the production of indole-^{14}C acetic acid from tryptamine-2-^{14}C. This compound is either a competitive substrate for the monoamine oxidase or an inhibitor of that enzyme.

Experimental Section[7]

2,3,6-Trimethoxy-β-nitrostyrene.—A mixture of 4.5 g (0.025 mole) of 2,3,6-trimethoxybenzaldehyde, 1.3 g of NH_4OAc, 1.7 ml of $MeNO_2$, and 15 ml of AcOH was refluxed for 1.5 hr. On cooling, yellow crystals were separated. Recrystallization from EtOH gave 3.2 g (54%) of mp 99–100°; nmr ($CHCl_3$) δ 4.12, 4.16, 4.20 (s, 9, OCH_3), 7.08, 7.48 (AB pattern, 2, aromatic), 8.60, 8.96 (AB pattern, 2, J = 21 Hz, HC=CH); ir spectra as expected. *Anal.* ($C_{11}H_{13}NO_5$) C, H, N.

2,3,6-Trimethoxy-β-phenethylamine.—To a stirred suspension of 2.0 g of LAH in 120 ml of anhyd Et_2O was added slowly a soln of 2.9 (0.012 mole) of the nitrostyrene in 100 ml of Et_2O–C_6H_6. The mixture was refluxed 2 hr, excess of LAH was decomposed (wet Et_2O), and 6 *N* HCl was added until pH 6. Then it was treated with 29 g of potassium sodium tartrate followed by 25% NaOH soln until pH 9. The mixture was extracted with CH_2Cl_2 upon evaporation the free amine was obtained as a faintly yellow syrup.

Two drops of the free amine were added to a boiling solution of picric acid in EtOH, after 48 hr large, yellow crystals, mp 176° (sharp) were obtained. Merchant and Mountwala[1] reported mp 166–167°.

The rest of the syrup was dissolved in Et_2O and HCl gas was bubbled through the solution until saturation. On evaporation, a syrup was obtained which was crystallized from *i*-PrOH–EtOAc (1:3); 1.35 g (47%) of white needles, mp 130–133° were obtained.

Recrystallization from the same solvent gave mp 134–135°; tlc (on silica gel IB-F, developed with 1-BuOH–AcOH–H_2O, 4:1:1, and visualized by spraying with ninhydrin) R_f 0.65; nmr (D_2O) δ 3.05–3.22 (m, 4, aliphatic H), 3.82, 3.88 (s, 9, OCH_3), 9.90, 7.14 (AB pattern, 2, aromatic H); ir spectra as expected. *Anal.* ($C_{11}H_{18}ClNO_3$) C, H, N.

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(7) Melting points were taken on a Nalge-Axelrod micro hot stage and are corrected. Analytical results where indicated by symbols of the elements were within ±0.2 of theoretical values. The ir spectra were measured with a Perkin-Elmer Model 337 spectrophotometer, and nmr spectra with a Varian A-60 spectrometer.

Synthesis of B/C *trans*-Fused Morphine Structures. V.[1] Pharmacological Summary of *trans*-Morphine Derivatives and an Improved Synthesis of *trans*-Codeine

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Preceding papers[1,4,5] from this laboratory presented the synthesis of B/C *trans*-morphine and related compounds. The present paper concerns the evaluation of the analgetic activities of these compounds and

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