

ture of 1.00 g (1.92 mmoles) of **2d**, 200 ml of dry Et₂O, and 0.539 g (4.80 mmoles) of KO-*t*-Bu (K & K Laboratories) was stirred at room temperature for 30 min (progress of reaction followed by ir spectroscopy). The reaction mixture was filtered with suction and the filtrate was evaporated under reduced pressure at 35°. The solid residue was recrystallized from heptane to afford 0.441 g (64%) of **1a**: mp 100.5–102.0°; ir, 1832 cm⁻¹; nmr τ 7.47 (2 H, s), 7.67–8.60 (14 H, m), 8.75 (18 H, s). *Anal.* (C₂₂H₃₄N₂O₂) C, H, N.

1,3-Bis[1-(1-adamantyl)-2-oxo-3-aziridinyl]adamantane (1b).—A mixture of 1.00 g (1.48 mmoles) of **2e**, 200 ml of dry Et₂O, and 0.414 g (3.70 mmoles) of KO-*t*-Bu (K & K Laboratories) was stirred at room temperature for 30 min, and worked up as described above to furnish, after recrystallization from heptane, 0.456 g (60%) of **1b**: mp ~180–190° dec; ir, 1832 cm⁻¹; nmr τ 7.40 (2 H, s), 7.41–8.79 (44 H, m). *Anal.* (C₃₄H₄₆N₂O₂) C, H, N.

Derivatives of

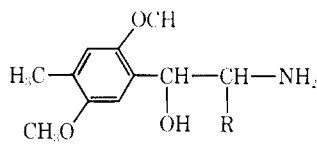
2,5-Dimethoxy-4-methylamphetamine (DOM)¹

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During the course of our investigation on psychotomimetic compounds,^{2,3} 2,5-dimethoxy-4-methylphenethanolamine (I) and 2,5-dimethoxy-4, α -dimethylphenethanolamine (II) were synthesized. These two compounds might possess hallucinogenic and/or sympathomimetic properties.



- I. R = H
II. R = CH₃

Experimental Section⁴

1-(2,5-Dimethoxy-4-methylphenyl)-2-nitroethanol.—To a stirred mixture of 3.6 g (20 mmoles) of 2,5-dimethoxy-*p*-tolualdehyde and 2.4 g (40 mmoles) of MeNO₂ in 200 ml of EtOH was added a solution of 0.8 g (20 mmoles) of NaOH in 10 ml of H₂O. A precipitation occurred within a few seconds. The mixture was stirred at room temperature for 15 min and then poured into 4 ml of AcOH and 300 g of crushed ice. The resulting mixture was stirred for 1 hr and fluffy yellow crystals contaminated with a brown gummy substance were collected on a filter. The crystals were easily separated from the gummy substance to yield 0.45 g which was recrystallized from *n*-C₆H₁₄ giving 0.2 g of needles, mp 91–92°. When the brown gummy substance was washed with 100 ml of hot *n*-C₆H₁₄ and filtered, a second crop of 1.3 g of product, mp 89–90°, was obtained. Recrystallization of the second crop of crystals from benzene–C₆H₁₄ gave 1.0 g (total yield, 25%), mp 90–91°. *Anal.* (C₁₁H₁₃NO₃) C, H, N.

Evaporation of the C₆H₁₄, the mother liquor of the first crop of product, gave 1.7 g of solid (mp 70–75°) which was primarily the unreacted aldehyde.

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(2) B. T. Ho, W. M. McIsaac, R. An. L. W. Tansey, K. E. Walker, L. F. Englert, Jr., and M. B. Noel, *J. Med. Chem.*, **13**, 26 (1970).

(3) B. T. Ho, L. W. Tansey, R. L. Balster, R. An. W. M. McIsaac, and R. T. Harris, *ibid.*, **13**, 134 (1970).

(4) Melting points were taken on a Mel-Temp apparatus and are corrected. Where analyses are indicated only by symbols of the elements or functions, analytical results obtained for those elements or functions were within $\pm 0.4\%$ of the theoretical values. Ir spectra of all the compounds were compatible with the assigned structures.

2,5-Dimethoxy-4-methylphenethanolamine.—A mixture of 1.7 g (7 mmoles) of 1-(2,5-dimethoxy-4-methylphenyl)-2-nitroethanol in 25 ml of absolute EtOH and 200 mg of 5% Pd-C catalyst was shaken with H₂ at 2–3 atmosphere for 2.5 hr. The filtered solution was evaporated *in vacuo* leaving 1.4 g (94%) of product, mp 97–100°. Recrystallization from C₆H₆–Et₂O gave 700 mg (47%) of white solid, mp 111–112°. *Anal.* (C₁₁H₁₃NO₃) C, H, N.

When the mother liquor was treated with Et₂O–HCl, 300 mg of HCl salt, mp 167–168° was obtained. Recrystallization from EtOH–Et₂O gave 200 mg, mp 171–172°.

2,5-Dimethoxy-4-methylpropiofenone.—To a solution of 15.2 g (0.1 mole) of 2,5-dimethoxytoluene and 9.2 g (0.1 moles) of *n*-C₃H₇COCl in 125 ml of CS₂ was added portionwise 13.4 g (0.1 mole) of AlCl₃ at such a rate that the temperature of the reaction mixture remained between 0 and 10°. (The addition required about 30 min.) After stirring at room temperature for 3 hr, the dark green mixture was decomposed by pouring into 80 ml of crushed ice and 5 ml of concentrated HCl and then filtered to yield 3.1 g of solid, mp 76–77°. The filtrate was extracted twice with 50 ml of CHCl₃. The CHCl₃ extracts were combined, dried (Na₂SO₄), and evaporated *in vacuo* leaving 15.6 g, mp 74–76°, which was recrystallized from 95% EtOH to give 8.4 g, mp 76–77°. Concentration of the mother liquor gave a third crop of 5.6 g, mp 76–77°. The total yield of the reaction was 17.1 g (82%). ir (CCl₄) 5.68 and 5.76 μ (aromatic 1,2,4-substitution); nmr (CCl₄) τ 2.8 (singlet, C₆-H), 3.3 (singlet, C₃-H). *Anal.* (C₁₂H₁₆O₃) C, H.

2,5-Dimethoxy-4-methyl- α -isonitrosopropiofenone.—MeONO (prepared from 5.5 g (80 mmoles) of NaNO₂ and 4.2 g (100 mmoles) of MeOH by the dropwise addition of 4.0 g (40 mmoles) of H₂SO₄ in 10 ml of H₂O) and HCl gas were bubbled for 1 hr into a solution of 10.4 g (50 mmoles) of 2,5-dimethoxy-4-methylpropiofenone in 200 ml of Et₂O. The addition of HCl was continued for an additional 0.5 hr. During the addition the solution turned red and gradually a precipitation occurred. After stirring overnight at room temperature the precipitate was filtered; yield, 7.5 g of yellow solid, mp 124–128°. The filtrate was extracted 3 times with 25-ml portions of 2 *N* NaOH and the aqueous solution reextracted with 50 ml of Et₂O. The Et₂O extract was dried (Na₂SO₄), and evaporated *in vacuo* giving 3.9 g, mp 130–132°. Both crops of product were combined and recrystallized from benzene to yield 8.9 g (75%) of bright yellow solid, mp 132–134°. *Anal.* (C₁₂H₁₆NO₃) C, H, N.

2,5-Dimethoxy-4, α -dimethylphenethanolamine.—A mixture of 4.7 g (20 mmoles) of 2,5-dimethoxy-4-methyl- α -isonitrosopropiofenone, 75 ml of EtOH, 5 ml of concentrated HCl, and 0.5 g of 5% Pd-C catalyst was shaken with H₂ at 2–3 atm until the consumption of H₂ ceased. The filtered solution was evaporated *in vacuo* and the oily residue washed with Et₂O to yield 4.0 g (89%) of solid, mp 233–234°. Recrystallization from EtOH gave 1.4 g, mp 237–238°. Addition of Et₂O to the mother liquor afforded additional 0.6 g of product, mp 236–238°, thereby increasing the yield to 44%. When the first 1.4 g of product was recrystallized once more from EtOH, 0.7 g of solid, mp 247–248°, was yielded. *Anal.* (C₁₂H₁₆NO₃·HCl) C, H, N.

A small amount of the HCl salt was converted into the free amine and recrystallized from CCl₄ to give a solid, mp 130–133°.

1-Substituted 2,5-Dimethylpyrroles

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Surprisingly few examples appear in the literature of pyrroles substituted in the 1 position with a heterocyclic nucleus. We wish to report the synthesis of 21 1-heterocyclic substituted 2,5-dimethylpyrroles (Table I). These compounds were tested for chemotherapeutic activity in the following screening programs: *in vitro* and *in vivo* antibacterial, *in vivo* anticoccidial,