12 hr, the mixture was poured into ice–water and a yellow solid was collected. A small quantity of this solid was recrystallized from ethanol, mp 198°, and was shown to be a borate ester. *Anal.* ($C_{20}H_{21}BFeN_2O_5$) H, N; C: calcd, 55.08; found, 55.57.

The yellow solid and extracts from the filtrate were combined and dissolved in a minimum of glacial acetic acid. This solution was diluted with water and a cold 20% solution of sodium hydroxide was slowly added. The basic solution was extracted with chloroform and the washed (H_2O) and dried ($MgSO_4$) extracts were concentrated *in vacuo* to give 7.29 g (66%) of I, mp 122–124° from benzene–heptane. *Anal.* ($C_{20}H_{22}FeN_2O_4$) C, H, N.

Treatment of III in benzene with dry HCl gave a hydrochloride, mp 175–180° from ethanol. *Anal.* ($C_{20}H_{23}ClFeN_2O_4$) Cl.

Preparation of II.—A mixture of 1.15 g (0.005 mole) of ferrocenecarboxaldehyde thiosemicarbazone,[5] 0.71 g of chloroacetic acid, 0.41 g of anhydrous sodium acetate, and 15 ml of glacial acetic acid was heated[7] on the steam bath for 45 min. The mixture was allowed to cool to room temperature and was filtered to give 0.66 g (38%) of II; mp 234–236° from ethanol; ir (KBr) 3300 (sh), 3100 (wk), 2940, 2750, 1785 (wk), 1725, 1640, 1110, 1005 cm^{-1}, mass spectrum 327 (100%), 262 (16%), 220 (8%), 212 (16%), 211 (18%), 185 (25)%, 162 (10%), 146 (11%), 129 (18%), 121 (42%), 56 (27%). *Anal.* ($C_{14}H_{13}FeN_3OS$) C, H, Fe, N, S.

Preparation of III.—A mixture of 1.15 g (0.005 mole) of ferrocenecarboxaldehyde thiosemicarbazone and 10 ml of acetic anhydride was heated on a steam bath for 25 min. The mixture was allowed to cool and filtered to give 1.14 g (61%) of III; mp > 215° (decomposition began at this temperature but no clearly defined melting or decomposition point could be determined) from EtOH; ir (KBr) 3220 (sh), 3160, 3050 (wk), 2940, 1720, 1640, 1610, 1110, 1010 cm^{-1}; nmr (DMSO-d_6): 12.07 (1), 7.00 (1), 4.37 (9), 2.17 (6) S. *Anal.* ($C_{26}H_{17}FeN_3O_2S$) C, H, N.

The diacetyl compound III was also obtained, contaminated with a monoacetyl–monochloroacetyl compound by replacing AcOH used in the preparation of II by Ac_2O.

Adamantoylferrocene (IV).—A complex of 5.0 g (0.025 mole) of adamantanecarboxylic acid chloride and 3.35 g of anhyd $AlCl_3$ in 150 ml of CS_2 was formed under N_2 over 2.5 hr. This solution was then added dropwise to a solution of 5.0 g (0.027 mole) of ferrocene in 100 ml of CS_2 under N_2 at room temperature. The solution was stirred at room temperature for 12 hr, H_2O added, and the organic layer separated. After washing (H_2O) and drying ($CaCl_2$) the CS_2 was removed *in vacuo* to give an orange solid. Chromatography of this solid on alumina with Skellysolve B gave ferrocene and 2.45 g (29%) of IV, mp 128–129° from heptane. *Anal.* ($C_{21}H_{24}FeO$) C, H.

Condensation of Ferrocenecarboxhydrazide with Steroids.—A mixture of 0.73 g (0.003 mole) of the hydrazide and 1.18 g (0.003 mole) of androstanolone benzoate in 30 ml of abs EtOH was heated on the steam bath for 15 min and filtered hot. Upon cooling 1.53 g (84%) of V, mp 183–185° from EtOH, was obtained. *Anal.* ($C_{37}H_{44}FeN_2O_3$) Fe, N.

In a similar manner 0.015 mole of the hydrazide and 0.015 mole of testosterone benzoate in abs EtOH gave, after heating, for 3 hr the expected hydrazide. Recrystallization from EtOH gave 5.68 g (61%) of the porduct, mp 205–206°. *Anal.* ($C_{37}H_{42}FeN_2O_3$) C, H, N.

(7) N. M. Turkevich and O. F. Lymar, *Khim. Farm. Zh.*, **3**, 26 (1969); *Chem. Abstr.*, **71**, 30314 (1969).

Bis(α-lactams) Derived from Adamantane

Erach R. Talaty[1a] and Aubry E. Dupuy, Jr.[1b]

Departments of Chemistry of Wichita State University, Wichita, Kansas 67208, and Louisiana State University in New Orleans, New Orleans, Louisiana 70122

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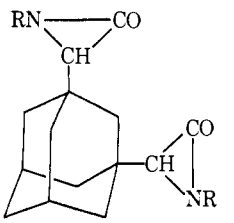
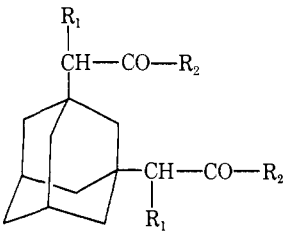
Compounds containing two or more aziridine rings, such as triethylenemelamine or 2,5-bis(1-aziridinyl)-3,6-di-*n*-propoxy-1,4-benzoquinone, have been of interest as antitumor agents for many years.[2] However, compounds having more than one aziridinone function have not been isolated. We report here the first examples of such compounds, namely, bis(α-lactams) (**1a**, **1b**) derived from adamantane-1,3-diacetic acid (**2a**).



1a, R = *t*-Bu
b, R = 1-adamantyl ($C_{10}H_{15}$)



2a, R_1 = H; R_2 = OH
b, R_1 = H; R_2 = Cl
c, R_1 = Br; R_2 = Cl
d, R_1 = Br; R_2 = NH-*t*-Bu
e, R_1 = Br; R_2 = NH-1-adamantyl

Experimental Section[3]

Adamantane-1,3-bis(*N*-*t*-butyl-2-bromoacetamide) (2d).—A mixture of 1.00 g (3.96 mmoles) of adamantane-1,3-diacetic acid (**2a**) (Aldrich Chemical Co.) and 5 ml of $SOCl_2$ (Matheson Coleman and Bell) was refluxed for 60 min and the excess $SOCl_2$ was removed under reduced pressure at 50°. Anhydrous C_6H_6 (2 ml) was added to the residue and then removed under reduced pressure to ensure complete removal of $SOCl_2$. The acid chloride **2b** was dissolved in 6 ml of CCl_4 and refluxed with Br_2 (1.44 g, 9.00 mmoles) for 5 hr. The resulting bromoacid chloride **2c** was added gradually to an ice-cold solution of 1.35 g (18.2 mmol) of *t*-butylamine in 100 ml of CH_2Cl_2. The reaction mixture was then treated with H_2O, extracted with CH_2Cl_2, and the combined CH_2Cl_2 layers were washed (5% HCl, 5% NaOH, H_2O, satd NaCl solution) and dried ($MgSO_4$). The solvent was removed *in vacuo* to give crude **2d**, which was recrystallized from $CHCl_3$–heptane to furnish 1.89 g (91% overall) of crystals: mp 261–262° dec; ir ($CHCl_3$) 3395, 1660 cm^{-1}; nmr ($CDCl_3$) τ 4.01–4.31 (2 H, broad s), 6.12 (2 H, s), 7.75–8.51 (14 H, m), 8.64 (18 H, s). *Anal.* ($C_{22}H_{36}Br_2N_2O_2$) C, H, N.

Adamantane-1,3-bis[*N*-(1-adamantyl)-2-bromoacetamide] (2e).—The crude bromoacid chloride **2c** prepared, as described above, from 1.00 g (3.96 mmoles) of **2a** was added gradually to an ice-cold solution of 1.20 g (7.92 mmoles) of 1-aminoadamantane and 1.04 g (10.28 mmol) of Et_3N in 100 ml of CH_2Cl_2. The reaction mixture was worked up as described above to afford, after recrystallization from $CHCl_3$–heptane, 2.43 g (91% overall) of **2e**: mp 299–302° dec; ir ($CHCl_3$) 3390, 1660 cm^{-1}; nmr ($CDCl_3$) τ 4.15–4.48 (2 H, broad s), 6.12 (2 H, s) 7.60–8.52 (44 H, m). *Anal.* ($C_{34}H_{48}Br_2N_2O_2$) C, H, N.

1,3-Bis(1-*t*-butyl-2-oxo-3-aziridinyl)adamantane (1a).—A mix-

(1) (a) Address inquiries to this author at the Wichita, Kansas address; (b) recipient of a Graduate Traineeship from the National Science Foundation.

(2) See, for example, D. F. Gamble, H. W. Bond, and A. Burger, "Medicinal Chemistry," A. Burger, Ed., Interscience, New York, N. Y., 1960, p 1083.

(3) Melting points were taken in sealed capillary tubes on a Mel-Temp apparatus and are uncorrected. Nmr spectra were recorded on a Varian A-60 instrument (TMS as internal standard). Unless otherwise mentioned, the solvent used for ir and nmr measurements was CCl_4.

ture of 1.00 g (1.92 mmoles) of **2d**, 200 ml of dry Et_2O, 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.* ($C_{27}H_{34}N_2O_2$) 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 Et_2O, 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.* ($C_{34}H_{46}N_2O_2$) C, H, N.

Derivatives of 2,5-Dimethoxy-4-methylamphetamine (DOM)[1]

Beng T. Ho, L. Wayne Tansey, and William M. McIsaac

Texas Research Institute of Mental Sciences, Houston, Texas 77025

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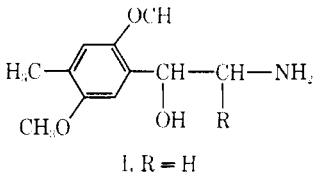
During the course of our investigation on psychotomimetic compounds,[2,3] 2,5-dimethoxy-4-methylphenethanolamine (I) and 2,5-dimethoxy-4,α-dimethylphenethanolamine (II) were synthesized. These two compounds might possess hallucinogenic and/or sympathomimetic properties.



I, R = H
II, R = CH

Experimental Section[4]

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 $MeNO_2$ in 200 ml of EtOH was added a solution of 0.8 g (20 mmoles) of NaOH in 10 ml of H_2O. 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*-C_6H_{14} giving 0.2 g of needles, mp 91–92°. When the brown gummy substance was washed with 100 ml of hot *n*-C_6H_{14} 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–C_6H_{14} gave 1.0 g (total yield, 25%), mp 90–91°. *Anal.* ($C_{11}H_{15}NO_5$) C, H, N.

Evaporation of the C_6H_{14}, the mother liquor of the first crop of product, gave 1.7 g of solid (mp 70–75°) which was primarily the unreacted aldehyde.

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 H_2 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 C_6H_6–Et_2O gave 700 mg (47%) of white solid, mp 111–112°. *Anal.* ($C_{11}H_{17}NO_3$) C, H, N.

When the mother liquor was treated with Et_2O–HCl, 300 mg of HCl salt, mp 167–168° was obtained. Recrystallization from EtOH–Et_2O gave 200 mg, mp 171–172°.

2,5-Dimethoxy-4-methylpropiophenone.—To a solution of 15.2 g (0.1 mole) of 2,5-dimethoxytoluene and 9.2 g (0.1 mole) of *n*-C_2H_5COCl in 125 ml of CS_2 was added portionwise 13.4 g (0.1 mole) of $AlCl_3$ 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 $CHCl_3$. The $CHCl_3$ extracts were combined, dried (Na_2SO_4), 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 (CCl_4) 5.68 and 5.76 μ (aromatic 1,2,4-substitution); nmr (CCl_4) τ 2.8 (singlet, C_6-H), 3.3 (singlet, C_3-H). *Anal.* ($C_{12}H_{16}O_3$) C, H.

2,5-Dimethoxy-4-methyl-α-isonitrosopropiophenone.—MeONO [prepared from 5.5 g (80 mmoles) of $NaNO_2$ and 4.2 g (100 mmoles) of MeOH by the dropwise addition of 4.0 g (40 mmoles) of H_2SO_4 in 10 ml of H_2O] and HCl gas were bubbled for 1 hr into a solution of 10.4 g (50 mmoles) of 2,5-dimethoxy-4-methylpropiophenone in 200 ml of Et_2O. 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 Et_2O. The Et_2O extract was dried (Na_2SO_4), 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.* ($C_{12}H_{15}NO_4$) C, H, N.

2,5-Dimethoxy-4,α-dimethylphenethanolamine.—A mixture of 4.7 g (20 mmoles) of 2,5-dimethoxy-4-methyl-α-isonitrosopropiophenone, 75 ml of EtOH, 5 ml of concentrated HCl, and 0.5 g of 5% Pd–C catalyst was shaken with H_2 at 2–3 atm until the consumption of H_2 ceased. The filtered solution was evaporated *in vacuo* and the oily residue washed with Et_2O to yield 4.0 g (89%) of solid, mp 233–234°. Recrystallization from EtOH gave 1.4 g, mp 237–238°. Addition of Et_2O 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.* ($C_{12}H_{19}NO_2$·HCl) C, H, N.

A small amount of the HCl salt was converted into the free amine and recrystallized from CCl_4 to give a solid, mp 130–133°.

1-Substituted 2,5-Dimethylpyrroles

Laird F. Miller and Ronald E. Bambury

Hess & Clark, Division of Richardson-Merrell, Inc., Ashland, Ohio 44805

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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,

(1) This work was partially supported by Grants MH-12959 and MH-11168, U. S. Public Health Service, Bethesda, Md.

(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 ±0.4% of the theoretical values. Ir spectra of all the compounds were compatible with the assigned structures.