solvent was crystallized from EtOAc or EtOAc–petr ether (bp 40–70°) a mixture. The yields were between 45–65%.

***N*-*n*-Propyl-*N'*-aryl-*N'*-(*p*-chloro)benzoylglycinamides [I, R_4 = $NH(CH_2)_2CH_3$]. General Procedure.**—The preparation of these compounds was carried out analogously to the Et esters of *N*-aryl-*N*-aroylamino acids, by allowing equimolar amounts of the appropriate *N*-*n*-propyl-*N'*-aryl glycinamide, Et_3N, and *p*-chlorobenzoyl chloride to react in dry PhH.

Acknowledgment.—We thank Drs. L. Coscia and P. Causa for the pharmacological screening and Dr. A. DeLeonibus for the microanalyses.

Ferrocene Studies. V. Potential Medicinal Agents[1]

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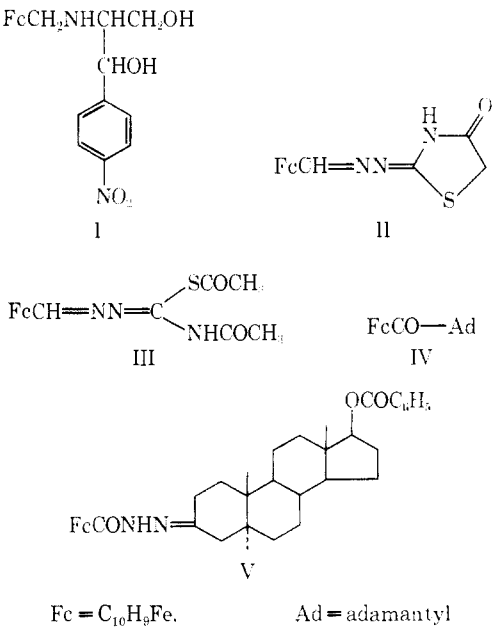
Despite the wide interest in ferrocene chemistry relatively few ferrocene derivatives have been tested for biological activities.[1a,2-5] This paper reports the preparation (see Experimental Section) of a number of new ferrocene derivatives which had no significant antibacterial, antifungal, or antiparasitic activity.



Fc = $C_{10}H_9Fe$. Ad = adamantyl

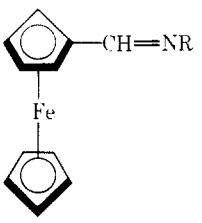
following manner. Equimolar quantities of ferrocenecarboxaldehyde and the reactants shown in Table I were dissolved in a minimum of abs EtOH and heated on a steam bath for a maximum of 30 min. After cooling to room temperature, the products shown in Table I were collected by filtration.

Condensation with D-Cycloserine.—A mixture of 5.0 g (0.05 mole) of D-cycloserine and 10.6 g (0.05 mole) of ferrocenecarboxaldehyde in 1200 ml of EtOH and 100 ml of MeOH was stirred at room temperature until all of the cycloserine dissolved. The solution was filtered and concentrated *in vacuo* to give the product indicated in Table I.

Condensation with D-(−)-*threo*-2-Amino-1-(*p*-nitrophenyl)-1,3-propanediol.—A mixture of 14.0 g (0.07 mole) of the amine, 15.0 g (0.07 mole) of ferrocenecarboxaldehyde, 0.05 g of *p*-toluenesulfonic acid, and 1200 ml of C_6H_6 was refluxed for 2 hr in a system containing a Dean–Stark trap. The solution was filtered hot and concentrated *in vacuo* to give the product indicated in Table I.

Preparation of I.—To a solution of 11.0 g of the above Schiff base in 500 ml of a 4:1 mixture of abs EtOH and dioxane was added 3.3 g of $NaBH_4$. After stirring at room temperature for

TABLE I



RNH2	Mp, °C[a,b]	Yield, %[c]	Formula	Analyses[c,d]
Sulfanilamide	170–172[e]	73	$C_{17}H_{16}FeN_2O_2S$	C, H
Sulfaguanidine	245–246[e]	76	$C_{18}H_{18}FeN_4O_2S$	N, S
p-Sulfobenzoic acid *p*-hydrazide	196–198[e]	84	$C_{18}H_{16}FeN_2O_6S$	C, H
p-Toluenesulfonhydrazide	155–157	86	$C_{18}H_{18}FeN_2O_2S$	C, H
p-Toluenesulfonhydrazide[f]	185–186	93	$C_{19}H_{20}FeN_2O_2S$[f]	C, H
1-Hydrazinophthalazine·HCl	188–190	88	$C_{15}H_{19}ClFeN_4O$[g]	C, H, Cl, Fe, N
D-Cycloserine[h]	146–147	99	$C_{14}H_{14}FeN_2O_2$	C, H, N
D-(−)-*threo*-2-Amino-1-(*p*-nitrophenyl)-1,3-propanediol[h]	143–144	79	$C_{20}H_{20}FeN_2O_3$	C, H, N

[a] Recrystallized from EtOH unless otherwise noted. [b] Decomposition points, in most cases considerable darkening occurs before decomposition. [c] Within 0.3%. [d] Ir of all compounds were as expected. [e] Compound was not recrystallized. [f] Acetylferrocene used in place of ferrocenecarboxaldehyde. [g] Monohydrate of HCl salt. [h] Not prepared by the general procedure, see Experimental section for details.

Experimental Section[6]

Condensations with Ferrocenecarboxaldehyde.—Except as otherwise noted the compounds in Table I were prepared in the

(1) (a) Part IV, F. D. Popp and E. B. Moynahan, *J. Heterocycl. Chem.*, **7**, 351 (1970); (b) This work was supported in part by a research grant from The Norwich Pharmacal Co.

(2) J. L. Madinaveitia, *Brit. J. Pharmacol.*, **24**, 352 (1965).

(3) B. Loev and M. Flores, *J. Org. Chem.*, **26**, 3595 (1961).

(4) F. D. Popp, S. Roth, and J. Kirby, *J. Med. Chem.*, **6**, 83 (1963).

(5) D. M. Wiles and T. Suprunchuk, *Can. J. Chem.*, **46**, 1865 (1968).

(6) Analyses [by Spang Microanalytical Laboratory, Ann Arbor, Mich.] are within 0.3% unless otherwise noted. Mass spectra was by Morgan and Schaffer, Montreal, Canada. All melting points are taken in capillaries and are corrected. The infrared spectra of all compounds were as expected;

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

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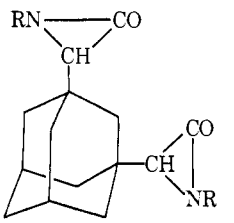
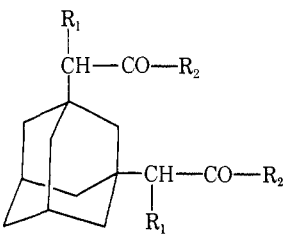
Compounds containing two or more aziridine rings, such as triethylenemelamine or 2,5-bis(1-aziridinyl)-3,6-di-*n*-propoxy-1,4-benzoquinone, have been of interest as antitumor agents for many years.[2] However, compounds having more than one aziridinone function have not been isolated. We report here 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-

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(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.