

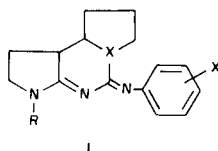
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N-(1,2,3,7,8,9,9a,9b-Octahydro-3-(phenylmethyl)-5*H*-dipyrrolo[1,2-*c*,3,2-*e*]pyrimidine-5-ylidene)benzenamines were prepared in moderate yields from the novel intermediate 1'-(phenylmethyl)-(2,3'-bipyrrolidin)-2-one **4**.

J. Heterocyclic Chem., **22**, 1381 (1985).

In our search for novel heterocyclic compounds with biological activity, we needed a synthetic route to compounds of general structure **1**. Our retrosynthetic analysis for **1** is shown in Scheme I, in which the key intermediate,



pyrrolidinylpyrrolidinone **4**, is required. A convenient synthetic procedure to the 3-pyrrolidino-2-pyrrolidinone **5** has been reported by Birchel *et al.* [1] (see Scheme II). Selective deprotection of **5** with 20% Pd(OH)₂/C (Pearlman's catalyst [2]) gave **4** in 96% yield [3]. Reaction of **4** with aryl *S*-methylisothiuronium salts **3** [4] in *N,N*-dimethylformamide with triethylamine gave the substituted guanidines **2**. Compounds of general structure **6** were cyclized, under conditions of acid-catalysis, to give the novel

N-(1,2,3,7,8,9,9a,9b-octahydro-3-(phenylmethyl)-5*H*-dipyrrolo[1,2-*c*,3,2-*e*]pyrimidine-5-ylidene)benzenamines **1** in moderate yields (See Table I).

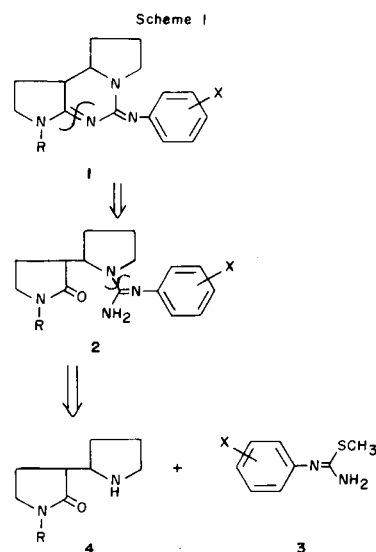
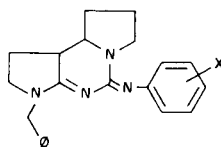
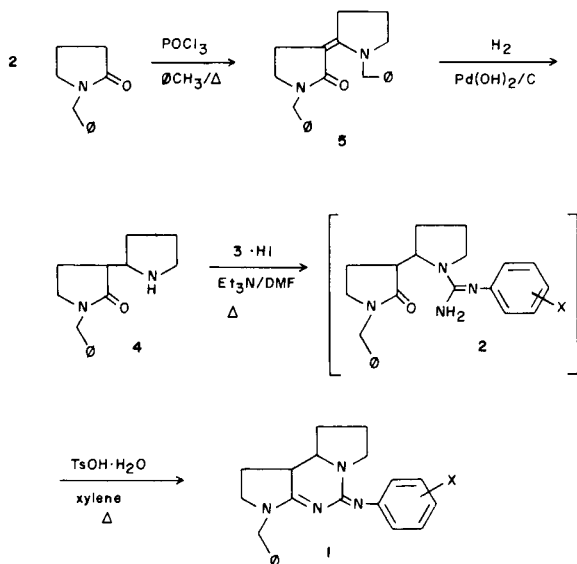


Table I



Compound Number	X	Melting Point °C	Recrystallization Solvent	Analysis Calculated	Found	% Yield
1a	-H	192-195	Methanol	C 76.71	C 76.70	53
				H 7.02	H 7.12	
				N 16.27	N 16.32	
1b	4-CH ₃	194-195	2-Propanol	C 77.06	C 77.21	20
				H 7.31	H 7.28	
				N 15.63	N 15.85	
1c	4-Cl	154-155	2-Propanol	C 69.74	C 69.93	38
				H 6.12	H 6.18	
				N 14.79	N 15.16	
1d	4-F	179-181	2-Propanol	C 72.90	C 72.82	25
				H 6.40	H 6.46	
				N 15.46	N 15.46	

Scheme 11



EXPERIMENTAL

All melting points are uncorrected. The nmr spectra were recorded on a Perkin-Elmer R-32 spectrometer at 90 MHz with tetramethylsilane as an internal standard, ir spectra were recorded on a Perkin-Elmer Model 21 spectrometer and low-resolution mass spectra were recorded on a Finnigan 4023 GC/MS/DS instrument (chemical ionization, methane). Microanalyses were performed by the Analytical Laboratories of The Dow Chemical Co., Midland, Michigan. No attempt was made to optimize yields.

1-(Phenylmethyl)-3-(1-(phenylmethyl)-2-pyrrolidinylidene)-2-pyrrolidinone (5).

To a solution of 200 g (1.14 moles) of 1-benzyl-2-pyrrolidinone in 800 ml of toluene was added dropwise 112 ml (1.2 moles) of phosphorus oxychloride. The reaction was refluxed for 4 hours, then cooled. After cautiously quenching with 800 ml of water, the layers were separated and the toluene layer was discarded. The aqueous layer was carefully basified

with solid sodium hydroxide. After extraction with methylene chloride, drying (sodium sulfate) and concentration, a tan oil, which rapidly crystallized, was obtained. Recrystallization (ethyl acetate) gave 120 g (53%) of 5 as a light tan solid, mp 84.5-87° (lit [1] mp 74-75°).

1'-(Phenylmethyl)-(2,3'-bipyrrolidin)-2'-one (4).

A 1.0 g (3 mmoles) quantity of 5 was dissolved in 50 ml of ethanol and 0.5 g of 20% Pd(OH)₂/C was added. The reaction was placed on a Parr hydrogenator at an initial pressure of 50 psi. After 24 hours the catalyst was removed by filtration and the filtrate was concentrated to give 0.7 g (96%) of 4, mp 80-82° (hexane); ir (nujol): 3350 (NH), 1685 (C=O) cm⁻¹; nmr (deuteriochloroform): δ 7.40-7.08 (m, 5H), 4.42 (s, 2H), 3.30-2.55 (m, 5H), 2.25-1.35 (m, 7H); ms: 245 (M⁺ + 1), 273 (M⁺ + 29).

Anal. Calcd. for C₁₅H₂₀N₂O: C, 73.74; H, 8.25; N, 11.46. Found: C, 73.80; H, 8.31; N, 11.50.

N-(1,2,3,7,8,9,9a,9b-Octahydro-3-(phenylmethyl)-5H-dipyrrolo[1,2-c,3,2-e]-pyrimidine-5-ylidene)benzenamine (1a).

A solution of 8.9 g (0.036 mole) of 4, 10.6 g (0.036 mole) of N-(phenyl)-S-methylisothioureahydroiodide, 7 ml of triethylamine and 80 ml of N,N-dimethylformamide was heated at reflux under nitrogen. After 24 hours, the cooled reaction solution was partitioned between methylene chloride and water. The organic phase was concentrated and the residue mixed with 6.8 g (0.036 mole) of p-toluenesulfonic acid monohydrate and 100 ml of xylene. The reaction mixture was heated at reflux for 2 hours and the water formed was collected in a Dean-Stark trap. After cooling, the xylene was decanted away and the residue was treated with water, methylene chloride and triethylamine. The organic phase was dried (sodium sulfate) and concentrated to give a tan solid. Recrystallization (methanol) gave 5.7 g of 1a as buff needles. An additional 0.86 g of 1a was obtained from the mother liquors; ir (nujol): 1605 cm⁻¹ (broad); nmr (deuteriochloroform): δ 7.40-6.68 (m, 10H), AB pattern, δ_A = 4.62, δ_B = 4.24 (J = 15 Hz, 2H), 3.83-3.02 (m, 5H), 2.73-1.29 (m, 7H); ms: 345 (M⁺ + 1), 373 (M⁺ + 29).

REFERENCES AND NOTES

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