1-(1-Aryl-3-ethylthiocarbamido)-4-arylaminothiocarbonyl)-piperazines as Possible Anticonvulsants

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Several 1-(1-aryl-3-ethylthiocarbamido)-4-(arylaminothiocarbonyl)piperazines were synthesized as possible anticonvulsants. These 1,4-disubstituted piperazines were characterized by their sharp melting points and elemental and spectral analyses.

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The various diverse pharmacological properties have been reported to be associated with piperazine derivatives. These include central nervous system depressant activity (1,2), anticonvulsant activity (3-5) and anti-inflammatory activity (6-10). These observations prompted the synthesis of some 1,4-disubstituted piperazines. Some of these substituted piperazines have been reported earlier to possess anticonvulsant activity and exhibit selective inhibition of nicotinamide adenine dinucleotide dependent oxidations by rat brain homogenates (5).

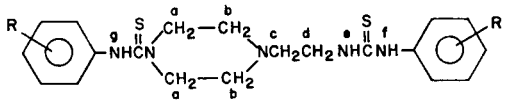
Table I

Physical Constants of 1-(1-Aryl-3-ethylthiocarbamido)-4-(arylaminothiocarbonyl)piperazines

Compound No.	R	M.p. °C	Yield %	Molecular Formula	Analyses % Calculated C	H	N	Found C	H	N
1	4-I	224	98	$C_{20}H_{23}I_2N_5S_2$	38.86	3.53	10.75	36.82	3.45	10.78
2	2,4-Cl_2	194	95	$C_{20}H_{21}Cl_4N_5S_2$	44.70	3.91	13.03	44.62	3.85	13.12
3	3,4-Cl_2	232	92	$C_{20}H_{21}Cl_4N_5S_2$	44.70	3.91	13.03	44.81	3.92	13.00
4	αC_4H_2	200	80	$C_{28}H_{29}N_5S_2$	67.33	5.81	14.03	67.14	5.88	14.15
5	β-C_4H_2	194	87	$C_{28}H_{29}N_5S_2$	67.33	5.81	14.03	67.30	5.71	13.81

Table II

Spectral data of 1-(1-Aryl-3-ethylthiocarbamido)-4-(arylaminothiocarbonyl)piperazines (a)



Compound No.	R	Characteristic Bands in Infrared Spectra (cm^{-1}) -NH	C=C	C=S	Chemical Shifts in Nuclear Magnetic Resonance Spectra (b) b, c	a, d	e and aromatic protons	g	f	R
1	4-I	3300	1600	1140	2.53 (b)	3.43-4.16 (m)	7.00-7.90 (m)	9.30 (s)	9.70 (s)	---
2	2,4-Cl_2	3240	1580	1140	2.46 (b)	3.40-4.13 (m)	7.20-8.10 (m)	9.30 (b)	9.30 (b)	---
3	3,4-Cl_2	3240	1590	1140	2.46 (b)	3.40-4.10 (m)	7.00-8.00 (m)	9.40 (s)	9.80 (s)	---
4	α-C_4H_2	3260	1600	1130	2.40 (b)	3.43-4.23 (m)	7.13-8.13 (m)	9.40 (s)	9.80 (s)	---
5	β-C_4H_2	3280	1590	1140	2.46 (b)	3.43-4.20 (m)	7.20-8.00 (m)	9.50 (s)	9.86 (s)	---
6	H	3300	1600	1140	2.50 (b)	3.46-4.10 (m)	6.73-7.80 (m)	9.30 (s)	9.66 (s)	---
7	2-CH_3	3320	1570	1120	2.43 (b)	3.40-4.10 (m)	6.90-7.40 (m)	9.00 (s)	9.20 (s)	2.30 (s)
8	4-CH_3	3280	1600	1140	2.43 (b)	3.36-4.00 (m)	6.80-7.60 (m)	9.10 (s)	9.46 (s)	2.33 (s)
9	2,4-$(CH_3)_2$	3260	1590	1140	2.46 (b)	3.36-4.00 (m)	6.80-7.30 (m)	8.90 (s)	9.10 (s)	2.10 (s), 2.23 (s)
10	4-OCH_3	3300	1610	1140	2.46 (b)	3.40-4.00 (m)	6.70-7.46 (m)	9.10 (s)	9.40 (s)	3.70 (s)
11	4-Cl	3300	1600	1140	2.50 (b)	3.50-4.13 (m)	7.10-7.60 (m)	9.50 (b)	9.50 (b)	---
12	4-Br	3310	1600	1140	2.43 (b)	3.33-4.06 (m)	7.06-7.73 (m)	9.23 (s)	9.60 (s)	---

(a) Compound **6-12** have been reported earlier (5). (b) a, b, c, d, e, f and g represent the protons of the corresponding groups. Signal multiplicity in nmr is represented by b, s or m in parenthesis where b = broad, s = singlet and m = multiplate.

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The reaction of *N*-(2-aminoethyl)piperazine with suitable arylisothiocyanate resulted in the formation of 1-(1-aryl-3-ethylthiocarbamido)-4-(arylaminothiocarbonyl)-piperazines.

EXPERIMENTAL

All compounds were analyzed for their carbon, hydrogen, and nitrogen contents. Melting points were taken in an open capillary tube with an immersion thermometer and are corrected. Infrared spectra of these compounds were recorded as suspension in nujol mull on Beckman IR-12 spectrophotometer. The nuclear magnetic resonance spectra of these compounds were obtained on Varian EM-390 spectrometer using deuterated dimethylsulfoxide as a solvent and tetramethylsilane as a reference.

1-(1-Aryl-3-ethylthiocarbamido)-4-(arylaminothiocarbonyl)piperazines (**1-12**).

N-(2-Aminoethyl)piperazine (0.01 mole) and appropriate arylisothiocyanate (0.02 mole) were placed in a round bottom flask containing 50 ml. of absolute ethanol. The reaction mixture was refluxed on a steam bath for 4 hours. The solvent was removed by distillation under reduced pressure. The solid mass thus obtained was washed with diethylether, dilute hydrochloric acid, and finally with cold water. The crude disubstituted piperazines were recrystallized from dimethylformamide-water. These piperazines were characterized by their sharp melting points and spectral and elemental analyses.

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