A Convenient Synthesis of Substituted Piperazines *via* Aminomercuration-Demercuration of Diallylamines

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cis and *trans*-2,6-*Bis*[bromomercuriomethyl]piperazines II which bear equal or different substituents at each nitrogen are obtained in the reaction of *N*-substituted diallylamines with mercury(II) acetate and arylamines followed by a double decomposition process with potassium bromide. Their reduction with sodium borohydride lead to the corresponding 1,4-disubstituted *cis*- and *trans*-2,6-dimethylpiperazines III. Steric factors account for the remarkable stereoselectivity observed in the preparation of compounds IIIi-IIIn in which a 3:1 *cis* to *trans* isomer ratio is found.

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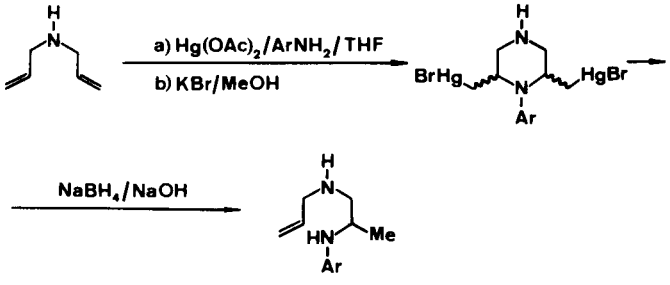
The addition of mercury(II) salts to appropriate unsaturated systems in the presence of aromatic amines has been successfully used in the preparation of saturated nitrogen-containing heterocycles (1). The reaction proceeds *via* an aminomercuration-demercuration process which involves an intermolecular cyclization. For stereochemical reasons, one of the most relevant applications of this method has been the stereoselective synthesis of diaryl substituted *trans*-2,5-dimethylpiperazines from allylamines (2).

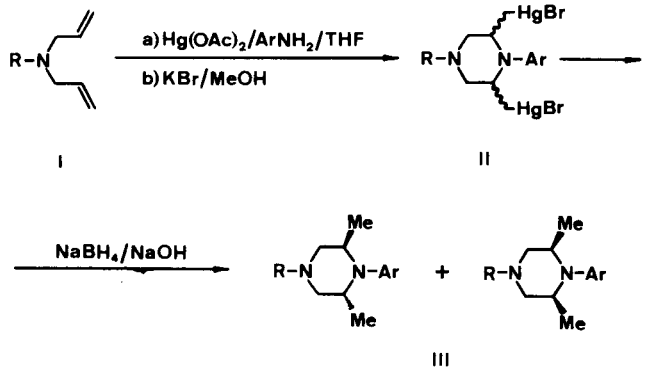
Mercurated 2,6-disubstituted piperazines can also be obtained from diallylamine, but the corresponding heterocycles free of mercury have never been obtained by reduction. Instead, unsaturated 1,2-propanediamines are generated as the result of a single deaminomercuration process (1) (Equation 1) which cannot be avoided.



(Eq.1)

We now wish to report the mercuration-reduction of *N*-substituted diallylamines. Surprisingly, in this instance, the heterocyclic backbone is sustained and consequently the overall process is adequate for the synthesis of 2,6-dimethylpiperazines.

When *N*-substituted diallylamines are allowed to react with mercury(II) acetate in the presence of primary aromatic amines at room temperature in tetrahydrofuran followed by anionic exchange with potassium bromide, the expected mixture of 1,4-disubstituted *cis*- and *trans*-2,6-*bis*[bromomercuriomethyl]piperazines II are obtained (Equation 2).



$$\left[\begin{array}{l} R = CH_3, n\text{-}C_3H_7, C_6H_5\text{-}CH_2, CH_3\text{-}CO, C_6H_5, 4\text{-}Cl\text{-}C_6H_4 \\ Ar = C_6H_5, 4\text{-}CH_3\text{-}C_6H_4, 4\text{-}CH_3O\text{-}C_6H_4, 4\text{-}Cl\text{-}C_6H_4 \end{array}\right]$$

(Eq.2)

The aminomercuration rate strongly depends on the substitution at the nitrogen site in the starting diallylamine I. The lower rate is observed for *N*-arylsubstituted amines (table 1). However the yields obtained do not depend on the substituents on the starting amines. Substituents at the *ortho*-position in the primary arenamine inhibit the mercuration reaction.

Diallylamines I are prepared by *N*-alkylation of the corresponding primary amines with allyl bromide (4) or by methylation or acetylation of diallylamine (see Experimental).

The reduction of mercurated piperazines II with sodium borohydride in alkaline media leads in good yields to a mixture of *cis*- and *trans*-2,6-dimethylpiperazines III which bear equal or different substituents at each nitrogen (Equation 2). The single or double deaminomercuration process predominates in the reduction of IIa or IIb and IIf, respectively (Table 2).

The hydrolysis of *N*-acetylpiperazines IIIg and IIIh can allow the preparation of piperazines where R = H which are not accesible by direct mercuration-demercuration of diallylamine (1).

^{1}H-nmr and glc analyses of the isolated heterocycles III show these are obtained as mixture of *cis* and *trans* diastereomers. The assignments were made on the basis of

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Table 1

1,4-Disubstituted *cis*- and *trans*-2,6-*Bis*[bromomercuriomethyl]piperazines II

Compound No.	R	Ar	Time	Yield % (a)
IIa	CH_3	C_6H_5	30 minutes	99
IIb	CH_3	4-CH_3-C_6H_4	3 hours	97
IIc	*n*-C_3H_7	C_6H_5	75 minutes	99
IId	*n*-C_3H_7	4-CH_3-C_6H_4	7 hours	88
IIe	C_6H_5-CH_2	C_6H_5	30 minutes	100
IIf	C_6H_5-CH_2	4-Cl-C_6H_4	40 minutes	84
IIg	CH_3-CO	C_6H_5	5 minutes	85
IIh	CH_3-CO	4-CH_3O-C_6H_4	2 hours	89
IIi	C_6H_5	C_6H_5	9 hours	97
IIj	C_6H_5	4-Cl-C_6H_4	8 hours	90
IIk	4-Cl-C_6H_4	C_6H_5	16 hours	84
IIl	4-Cl-C_6H_4	4-CH_3-C_6H_4	10 hours	75
IIm	4-Cl-C_6H_4	4-CH_3O-C_6H_4	8 hours	79
IIn	4-Cl-C_6H_4	4-Cl-C_6H_4	5 hours	75

(a) Based on starting diallylamines I (crude).

Table 2

1,4-Disubstituted *cis*- and *trans*-2,6-Dimethylpiperazines III

Compound No.	R	Ar	Time	Yield %		Isomer Ratio
				Hg° (a)	III (b)	*cis/trans*
IIIa	CH_3	C_6H_5	20 minutes	63	36	42/58
IIIb	CH_3	4-CH_3-C_6H_4	4 days	60	— (c)	—
IIIc	*n*-C_3H_7	C_6H_5	30 minutes	79	52	40/60
IIId	*n*-C_3H_7	4-CH_3-C_6H_4	30 minutes	70	68	42/58
IIIe	$C_6H_5CH_2$	C_6H_5	2 days	58	97	21/79
IIIf	C_6H_5-CH_2	4-Cl-C_6H_4	2 days	55	— (c)	—
IIIg	CH_3-CO	C_6H_5	2 days	63	65	50/50
IIIh	CH_3-CO	4-$CH_3OC_6H_4$	2 days	75	75	6/94
IIIi	C_6H_5	C_6H_5	2 days	67	55	63/27
IIIj	C_6H_5	4-Cl-C_6H_4	30 hours	70	61	77/23
IIIk	4-Cl-C_6H_4	C_6H_5	3 days	66	80	75/25
IIIl	4-Cl-C_6H_4	4-CH_3-C_6H_4	1 day	64	93	72/28
IIIm	4-Cl-C_6H_4	4-$CH_3OC_6H_4$	3 days	75	78	76/24
IIIn	4-Cl-C_6H_4	4-Cl-C_6H_4	5 days	63	90	78/22

(a) Based on mercurial II. (b) Based on mercury (0) precipitated. (c) Only starting amines detected.

the different chemical shift of the methyl groups, assuming that these appear upfield when occupying the equatorial position (7). The isomeric ratio is more accurately fixed by glc than by ^{1}H-nmr analyses, the *cis*-(e,e) isomer displaying shorter retention times than the *trans*-(e,a) isomer. The *cis* isomer predominates in 1,4-diarylsubstituted piperazines (IIIi-IIIn), probably for steric reasons (Table 2).

EXPERIMENTAL

All melting points were taken on a Büchi-Tottoli capillary melting point apparatus and are uncorrected. Glc analyses were performed in a Varian Aerograph 2800 instrument equipped with a OV-101 Chromosorb column. Infrared spectra were determined with a Pye-Unicam SP-1000 spectrometer, ^{1}H-nmr spectra were obtained with a Varian EM-390 spectrometer (TMS as internal reference) and the proton assignment was supported by a dnmr experiment. Elemental analyses of I and III were carried out with a Perkin-Elmer 240-Elemental Analyzer. Nitrogen in II was determined by Kjeldahl's method (8) and mercury was determined by gravimetric analysis (8).

Diallylamines I were synthesized according to the following methods.

(A)

To an ethereal solution of 200 mmoles of the arylamine under argon, a 0.75*N* ethereal solution of phenyllithium (270 ml., 200 mmoles) was added dropwise over a period of 30 minutes. Allyl bromide (17.0 ml., 200 mmoles) was then added dropwise in 30 minutes. After 5-6 hours the process was repeated under similar conditions. After 5 hours the reaction was hydrolyzed with water; the ethereal layer was dried over anhydrous sodium sulfate and then evaporated *in vacuo*. The residue was distilled at reduced pressure with a 25 cm Vigreux column to give the product.

(B)

The primary amine was treated with allyl bromide in water at 60-80° following the described method (4).

(C)

Diallylamine was treated with methyl iodide or acetyl chloride in ether. The reaction was hydrolyzed with 3*N* aqueous potassium hydroxide and the ethereal layer dried over anhydrous sodium sulfate. The ether was evaporated *in vacuo* and the residue distilled.

Diallylmethylamine (Ia).

Compound Ia was synthesized according to Method C in 20% yield (based on the starting amine), b.p. 111-113°, lit. (5) b.p. 112°; purity (by glc): 99%; ir (carbon tetrachloride): ν 3100, 1660, 1020, 940 (C=CH), 2950, 1460, 1380 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 2.1 (s, CH_2-N, 3H), 2.9 (d, J = 6 Hz, CH_2-C, total 4H), 5.15 (m, CH_2=C, total 4H), 5.85 (m, CH=C, total 2H) ppm.

Anal. Calcd. for $C_7H_{13}N$: C, 75.61; H, 11.78; N, 12.60. Found: C, 75.50; H, 11.72; N, 12.62.

Diallylpropylamine (Ib).

This compound was synthesized according to Method B in 54% yield (based on allyl bromide), b.p. 76-78° (15 torr); purity (by glc): 98%; ir (film): ν 3050, 1630, 990, 910 (C=CH), 2900, 1460, 1370 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 0.9 (t, J = 6 Hz, CH_3-C, 3H), 1.45 (m, CH_2-C, 2H), 2.35 (t, J = 8 Hz, CH_2-N, 2H), 3.05 (d, J = 9 Hz, CH_2-C=, total 4H), 5.1 (m, CH_2=C, total 4H), 5.8 (m, CH=C, total 2H) ppm.

Anal. Calcd. for $C_9H_{17}N$: C, 77.66; H, 12.31; N, 10.06. Found: C, 77.49; H, 12.28; N, 9.99.

Diallylbenzylamine (Ic).

This compound was synthesized according to Method B in 56% yield (based on allyl bromide), b.p. 65-67° (0.1 torr); purity (by glc): 98%; ir (film): ν 3100, 1650, 1000, 920, (C=CH), 3040, 1600, 1500, 750, 710 (aromatic), 2900, 1460, 1380 (aliphat.) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 3.0 (d, J = 6 Hz, CH_2-N, total 4H), 3.5 (s, CH_2-Ar, 2H), 5.1 (m, CH_2=C, total 4H), 5.8 (m, CH=C, total 2H), 7.2 (m, Ar, 5H) ppm.

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48. Found: C, 83.28; H, 9.10; N, 7.52.

N,N-Diallylacetamide (Id).

This compound was synthesized according to Method C in 30% yield (based on the starting amine), b.p. 63-64° (0.1 torr); purity (by glc): 99%; ir (film): ν 3070, 990, 930 (C=CH), 1650 (C=O, C=C), 2950, 1470, 1380 (aliphat.) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 2.0 (s, CH_3-CO, 3H), 3.9 (d, J = 5 Hz, CH_2-C=, total 4H), 5.1 (m, CH_2=C, total 4H), 5.8 (m, CH=C, total 2H) ppm.

Anal. Calcd. for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 68.89; H, 9.37; N, 10.10.

N,N-Diallylaniline (Ie).

This compound was synthesized according to Method A in 81% yield (based on allyl bromide), b.p. 120-123° (15 torr), lit (6) b.p. 123° (18 torr); purity (by glc): 99%; ir (film): ν 3090, 1650, 1000, 930 (C=CH), 1600, 1510, 760, 700 (aromatic), 2900, 1460, 1390 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 3.8 (m, CH_2-N, total 4H), 5.1 (m, CH_2=C, total 4H), 5.75 (m, CH=C, total 2H), 6.55, 7.0 (2m, Ar, 5H) ppm.

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.17; H, 8.72; N, 8.08. Found: C, 83.03; H, 8.68; N, 8.12.

N,N-Diallyl-4-chloroaniline (If).

This compound was synthesized according to Method A in 75% yield (based on allyl bromide), b.p. 95-97° (0.1 torr); purity (by glc): 99%; ir (film): ν 3100, 1650, 1000, 930 (C=CH), 3010, 1600, 1570, 1520, 820 (aromatic), 2900, 1460, 1380 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 3.8 (m, CH_2-N, total 4H), 5.1 (m, CH_2=C, total 4H), 5.7 (m, CH=C, total 2H), 6.5, 7.0 (2m, Ar, 4H) ppm.

Anal. Calcd. for $C_{12}H_{14}ClN$: C, 69.39; H, 6.79; N, 6.74. Found: C, 69.24; H, 6.74; N, 6.69.

Mercuration of Diallylamines I. 1,4-Disubstituted *cis*- and *trans*-2,6-*Bis*-[bromomercuriomethyl]piperazines II. A Typical Procedure.

To a solution of diallylamine I (20 mmoles) and arylamine (150 mmoles) in tetrahydrofuran (100 ml.) mercury (II) acetate (12.75 g., 40 mmoles) was added with good stirring. Reactions were continued until no yellow precipitate of mercury (II) oxide was observed when a sample was treated with 3*N* potassium hydroxide. The solvent was removed under reduced pressure and the residue was stirred with methanol (200 ml.) and a solution of potassium bromide (5.9 g., 50 mmoles) in water (50 ml.). The solid precipitated was washed with water, methanol and ether, dried and recrystallized.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-4-methyl-1-phenylpiperazine (IIa).

This compound was obtained as a white powder, m.p. 93-95° dec (methanol/THF); ir (nujol): ν 3060, 1600, 1560, 1500, 760, 710 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{13}H_{18}Br_2Hg_2N_2$: N, 3.67; Hg, 52.56. Found: N, 3.69; Hg, 52.47.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-4-methyl-1-(4-methylphenyl)-piperazine (IIb).

This compound was obtained as a white powder, m.p. 70-72° dec (methanol/THF); ir (nujol): ν 3040, 1610, 1560, 1510, 820 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{14}H_{20}Br_2Hg_2N_2$: N, 3.60; Hg, 51.61. Found: N, 3.61; Hg, 51.49.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-1-phenyl-4-propylpiperazine (IIc).

This compound was obtained as white crystals, m.p. 135-137° dec (methanol/THF); ir (nujol): ν 3050, 1600, 1500, 770, 710 (aromatic) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.95 (t, J = 6 Hz, CH_3-C, 3H), 1.4-2.1 (m, CH_2-Hg, CH_2-C, total 6H), 2.3-3.1 (m, CH_2-N, total 6H), 4.5 (m, CH-N, total 2H), 6.9-7.4 (m, Ar, 5H) ppm.

Anal. Calcd. for $C_{15}H_{22}Br_2Hg_2N_2$: N, 3.54; Hg, 50.70. Found: N, 3.55; Hg, 50.77.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-1-(4-methylphenyl)-4-propyl-piperazine (IId).

This compound was obtained as white crystals, m.p. 113-115° dec (acetone); ir (nujol): ν 3040, 1610, 1520, 830 (aromatic) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.95 (t, J = 6 Hz, CH_3-C, 3H), 1.4-2.1 (m, CH_2Hg, CH_2-C, total 6H), 2.3-3.1 (m with s at 2.35, CH_3-Ar, CH_2-N, total 9H), 4.45 (m, CH-N, total 2H), 7.1 (m, Ar, 4H) ppm.

Anal. Calcd. for $C_{16}H_{24}Br_2Hg_2N_2$: N, 3.48; Hg, 49.81. Found: N, 3.50; Hg, 49.70.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-4-benzyl-1-phenylpiperazine (IIe).

This compound was obtained as yellow crystals, m.p. 67-69° dec (methanol/THF); ir (nujol): ν 3060, 1600, 1500, 760, 710 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{19}H_{22}Br_2Hg_2N_2$: N, 3.34; Hg, 47.79; Found: N, 3.35; Hg, 47.65.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-4-benzyl-1-(4-chlorophenyl)-piperazine (IIf).

This compound was obtained as a white powder, m.p. 90-92° dec (THF); ir (nujol): ν 3040, 1600, 1560, 1500, 840, 760, 750, 710 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{19}H_{21}Br_2ClHg_2N_2$: N, 3.21; Hg, 45.91. Found: N, 3.23; Hg, 45.80.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-4-acetyl-1-phenylpiperazine (IIg).

This compound was obtained as a white powder, m.p. 139-140° dec; ir (nujol): ν 3040, 1540, 1500, 760, 700 (aromatic), 1600 (C=O) cm^{-1}.

Anal. Calcd. for $C_{14}H_{18}Br_2Hg_2N_2O$: N, 3.54; Hg, 50.70. Found: N, 3.58; Hg, 50.58.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-4-acetyl-1-(4-methoxyphenyl)piperazine (IIh).

This compound was obtained as a grey powder, m.p. 56-58° dec; ir (nujol): ν 3050, 1560, 1520, 840 (aromatic), 1630 (C=O) cm^{-1}.

Anal. Calcd. for $C_{15}H_{20}Br_2Hg_2N_2O_2$: N, 3.41; Hg, 48.85. Found: N, 3.42; Hg, 48.72.

cis and *trans*-2,6-*Bis*[bromomercuriomethyl]-1,4-diphenylpiperazine (IIi).

This compound was obtained as a yellow powder, m.p. 131-133° dec (chloroform/methanol); ir (nujol): ν 3050, 1600, 1520, 760, 710 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{16}H_{20}Br_2Hg_2N_2$: N, 3.39; Hg, 48.61. Found: N, 3.38; Hg, 48.47.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-1-(4-chlorophenyl-4-phenylpiperazine (IIj).

This compound was obtained as a yellow powder, m.p. 157-159° dec (chloroform/acetone); ir (nujol): ν 3050, 1600, 1520, 820, 760, 710 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{16}H_{19}Br_2ClHg_2N_2$: N, 3.26; Hg, 46.66. Found: N, 3.28; Hg, 46.51.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-4-(4-chlorophenyl)-1-phenylpiperazine (IIk).

This compound was obtained as a yellow powder, m.p. 130-131° dec (acetone/THF); ir (nujol): ν 3050, 1600, 1510, 840, 820, 760, 720 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{16}H_{19}Br_2ClHg_2N_2$: N, 3.26; Hg, 46.66. Found: N, 3.26; Hg, 46.49.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-4-(4-chlorophenyl)-1-(4-methylphenyl)piperazine (IIl).

This compound was obtained as a yellow powder, m.p. 122-123° dec (methanol/acetone); ir (nujol): ν 3060, 1630, 1610, 1530, 830 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{19}H_{21}Br_2ClHg_2N_2$: N, 3.21; Hg, 45.91. Found: N, 3.23; Hg, 45.83.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-4-(4-chlorophenyl)-1-(4-methoxyphenyl)piperazine (IIm).

This compound was obtained as a grey powder, m.p. 127-129° dec (methanol/THF); ir (nujol): ν 3040, 1630, 1540, 1500, 850 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{19}H_{21}Br_2ClHg_2N_2O$: N, 3.15; Hg, 45.09. Found: N, 3.17; Hg, 44.96.

cis- and *trans*-2,6-*Bis*[bromomercuriomethyl]-1,4-*bis*[4-chlorophenyl]piperazine (IIn).

This compound was obtained as a yellow powder, m.p. 152-153° dec (chloroform); ir (nujol): ν 3060, 1600, 1500, 820 (aromatic) cm^{-1}.

Anal. Calcd. for $C_{16}H_{18}Br_2Cl_2Hg_2N_2$: N, 3.13; Hg, 44.86. Found: N, 3.12; Hg, 44.75.

Reduction of II. 1,4-Disubstituted *cis*- and *trans*-2,6-Dimethylpiperazines III. General Procedure.

A solution of sodium borohydride (0.5 g., 13 mmoles) in 2.5*N* aqueous sodium hydroxide (10 ml.) was added to a stirred solution of II (13 mmoles) in a mixture of aniline (10 ml.), tetrahydrofuran (50 ml.) and 0.5*N* aqueous sodium hydroxide (100 ml.). The reaction was continued until no further precipitation of mercury(0) was noticeable. The resultant mixture was then extracted with ether, the organic layer washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo*. The residue was distilled at 0.001 torr to yield III. Solid products were further purified by recrystallization from hot hexane.

cis- and *trans*-2,4,6-Trimethyl-1-phenylpiperazine (IIIa).

This compound had b.p. 85-88° (0.001 torr); ir (film): ν 3060, 1600, 1580, 1500, 770, 710 (aromatic), 2900, 1470, 1380 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 0.7, 0.9 (2d, J = 6 Hz, CH_3-C, total 6H), 1.8-2.8 (m with s at 2.2, CH_2-N CH_3-Ar, total 7H), 3.1, 3.45 (2m, CH-N, total 2H), 7.1 (m, Ar, 5H) ppm.

Anal. Calcd. for $C_{13}H_{20}N_2$: C, 76.43; H, 9.87; N, 13.71. Found: C, 76.31; H, 9.83; N, 13.69.

cis- and *trans*-2,6-Dimethyl-1-phenyl-4-propylpiperazine (IIIc).

This compound had b.p. 85-89° (0.001 torr); ir (film): ν 3060, 1600, 1580, 1500, 770, 750, 710 (aromatic), 2900, 1470, 1380 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 0.75, 0.95 (2d, J = 6 Hz, CH_3-CH, total 6H), 0.95 (t, J = 6 Hz, CH_3-CH_2, 3H), 1.5 (m, CH_2-C, 2H), 1.85-2.80 (m with t at 2.25, J = 6 Hz, CH_2-N, total 6H); 3.15, 3.60 (2m, CH-N, total 2H), 7.0 (m, Ar, 5H) ppm.

Anal. Calcd. for $C_{15}H_{24}N_2$: C, 77.56; H, 10.41; N, 12.06. Found: C, 77.60; H, 10.36; N, 12.09.

cis- and *trans*-2,6-Dimethyl-1-(4-methylphenyl)-4-propylpiperazine (IIId).

This compound had b.p. 85-90° (0.001 torr); ir (film): ν 3040, 1620, 1580, 1510, 820, 810 (aromatic), 2900, 1460, 1370 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 0.7, 0.9 (2d, J = 6 Hz, CH_3-CH, total 6H), 0.9 (t, J = 6 Hz, CH_3-CH_2, 3H), 1.45 (m, CH_2-C, 2H), 1.7-2.9 (m with s at 2.2, CH_2-N, CH_3-Ar, total 9H), 3.0, 3.5 (2m, CH-N, total 2H), 6.9 (m, Ar, 4H) ppm.

Anal. Calcd. for $C_{16}H_{26}N_2$: C, 77.99; H, 10.64; N, 11.37. Found: C, 77.85; H, 10.56; N, 11.40.

cis- and *trans*-2,6-Dimethyl-4-benzyl-1-phenylpiperazine (IIIe).

This compound had b.p. 120-125° (0.001 torr); ir (film): ν 3080, 1610, 1550, 1510, 770, 720 (aromatic), 2900, 1470, 1380 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 0.75, 0.95 (2d, J = 6 Hz, CH_3-C, total 6H), 1.9-2.8 (m, CH_2-N, total 4H), 3.0-3.8 (m with s at 3.4, CH-N, CH_2-N, total 4H), 7.2 (m, Ar, 5H) ppm.

Anal. Calcd. for $C_{19}H_{24}N_2$: C, 81.39; H, 8.63; N, 9.99. Found: C, 81.27; H, 8.60; N, 10.01.

cis- and *trans*-2,6-Dimethyl-4-acetyl-1-phenylpiperazine (IIIg).

This compound had b.p. 110-115° (0.001 torr); ir (film): ν 3080, 1600, 1500, 780, 760, 710, 700 (aromatic), 1660 (C=O), 2900, 1460, 1380 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 0.75, 0.95 (2d, J = 6 Hz, CH_3-C, total 6H), 2.05 (s, CH_3-CO, 3H), 2.6-3.8 (m, CH_2-N, CH-N, total 6H), 7.1 (m, Ar, 5H) ppm.

Anal. Calcd. for $C_{14}H_{20}N_2O$: C, 72.39; H, 8.68; N, 12.06. Found: C, 72.25; H, 8.61; N, 12.13.

cis- and *trans*-2,6-Dimethyl-4-acetyl-1-(4-methoxyphenyl)piperazine (IIIh).

This compound had b.p. 115-119° (0.001 torr); ir (film): ν 3080, 1580, 1520, 830 (aromatic), 1650 (C=O), 2900, 1460, 1380 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 0.7, 0.85 (2d, J = 6 Hz, CH_3-C, total 6H), 2.0 (s, CH_3-CO, 3H), 2.2-4.0 (m with s at 3.7, CH_2-N, CH-N, CH_3-O, total 9H), 6.8 (m, Ar, 4H) ppm.

Anal. Calcd. for $C_{15}H_{22}N_2O_2$: C, 68.67; H, 8.45; N, 10.68. Found: C, 68.59; H, 8.46; N, 10.70.

cis- and *trans*-2,6-Dimethyl-1,4-diphenylpiperazine (IIIi).

This compound had b.p. 105-110° (0.001 torr); ir (film): ν 3060, 1600, 1520, 790, 760, 710 (aromatic), 2900, 1460, 1380 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 0.8, 1.05 (2d, J = 6 Hz, CH_3-C, total 6H), 2.5-3.7 (m, CH_2-N, CH-N, total 6H), 6.8 (m, Ar, total 10H) ppm.

Anal. Calcd. for $C_{18}H_{22}N_2$: C, 81.15; H, 8.32; N, 10.52. Found: C, 81.03; H, 8.28; N, 10.47.

cis- and *trans*-2,6-Dimethyl-1-(4-chlorophenyl)-4-phenylpiperazine (IIIj).

This compound was obtained as white crystals, m.p. 115-117° (isometric ratio *cis*/*trans*: 80/20); ir (deuteriochloroform): ν 3050, 1600, 1500, 820 (aromatic), 2900, 1470, 1390 (aliphatic) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.85, 1.05 (2d, J = 6 Hz, CH_3-C, total 6H), 2.6-3.9 (m, CH_2-N, CH-N, total 6H), 7.1 (m, Ar, total 9H) ppm.

Anal. Calcd. for $C_{18}H_{21}ClN_2$: C, 71.87; H, 7.04; N, 9.31. Found: C, 71.74; H, 7.01; N, 9.33.

cis- and *trans*-2,6-Dimethyl-4-(4-chlorophenyl)-1-phenylpiperazine (IIIk).

This compound had b.p. 118-123° (0.001 torr); ir (film): ν 3080, 1600, 1500, 820, 780, 760, 710, 700 (aromatic), 2900, 1470, 1390 (aliphatic) cm^{-1}; ^{1}H-nmr (carbon tetrachloride): δ 0.85, 1.05 (2d, J = 6 Hz, CH_3-C, total 6H), 2.6-3.9 (m, CH_2-N, CH-N total 6H), 6.5-7.4 (m, Ar, total 9H) ppm.

Anal. Calcd. for $C_{18}H_{21}ClN_2$: C, 71.87; H, 7.04; N, 9.31. Found: C, 71.69; H, 6.98; N, 9.33.

cis- and *trans*-2,6-Dimethyl-4-(4-chlorophenyl)-1-(4-methylphenyl)piperazine IIIl.

This compound was obtained as white crystals, m.p. 147-148° (isomeric ratio *cis/trans*: 86/14), 150-152° (93/7); ir (nujol): ν 3060, 1630, 1600, 1530, 840, 830 (aromatic) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.85, 1.05 (2d, J = 6 Hz, CH_3-C, total 6H), 2.35 (s, CH_3-Ar, 3H), 2.5-3.7 (m, CH_2-N, CH-N, total 6H), 7.1 (m, Ar, total 8H) ppm.

Anal. Calcd. for $C_{19}H_{23}ClN_2$: C, 72.47; H, 7.36; N, 8.90. Found: C, 72.38; H, 7.33; N, 8.92.

cis- and *trans*-2,6-Dimethyl-4-(4-chlorophenyl)-1-(4-methoxyphenyl)piperazine (IIIm).

This compound was obtained as white crystals, m.p. 129-130° (isomeric ratio *cis/trans*: 81/19); ir (nujol): ν 3070, 1600, 1560, 1510, 840 (aromatic) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.8, 1.0 (2d, J = 6 Hz, CH_3-C, total 6H), 2.5-3.7 (m, CH_2-N, CH-N, total 6H), 3.8 (s, CH_3-O, 3H), 7.05 (m, Ar, total 8H) ppm.

Anal. Calcd. for $C_{19}H_{23}ClN_2O$: C, 68.97; H, 7.01; N, 8.47. Found: C, 68.79; H, 6.88; N, 8.46.

cis- and *trans*-2,6-Dimethyl-1,4-*bis*[4-chlorophenyl]piperazine (IIIn).

This compound was obtained as white crystals, m.p. 154-156° (isomeric ratio *cis/trans*: 66/34); ir (nujol): ν 3080, 1600, 1510, 830 (aromatic) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.9, 1.05 (2d, J = 6 Hz, CH_3-C, total 6H), 2.6-3.8 (m, CH_2-N, CH-N, total 6H), 6.7-7.4 (m, Ar, total 8H) ppm.

Anal. Calcd. for $C_{18}H_{20}Cl_2N_2$: C, 64.48; H, 6.01; N, 8.35. Found: C, 64.39; H, 5.96; N, 8.38.

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