Synthesis and Mesogenic Properties of *N'*-(4-Acylphenyl)-*N*-alkylpiperazines

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One synthesis of *N*-alkyl-*N'*-(4-acylphenyl)piperazines and their physical properties have been studied using calorimetric, optical, and *X*-ray crystallographic methods. The compounds exhibit only smectic phases, the higher-temperature phase being a probable smectic B. The lower-temperature smectic is uniaxial but relatively highly ordered and the measured layer spacing is equal to the calculated molecular length, indicating that the phase is orthogonal. This indicates that the phase is probably a smectic E with random orientational correlation between layers.

Liquid crystal compounds are made up of a cylindrical shaped hard core together with terminal groups. The hard core portion is usually comprised of aromatic rings such as phenyl, naphthyl and heteroatomic groups.[1] In early studies, saturated cyclic rings such as cyclohexane and bicyclo[2.2.2]octane began to be used for the hard core portion of mesogenic compounds. It has been shown that geometrically asymmetric cores composed of unequal ring units (either planar or non-planar) tend to give nematic phases.[2]

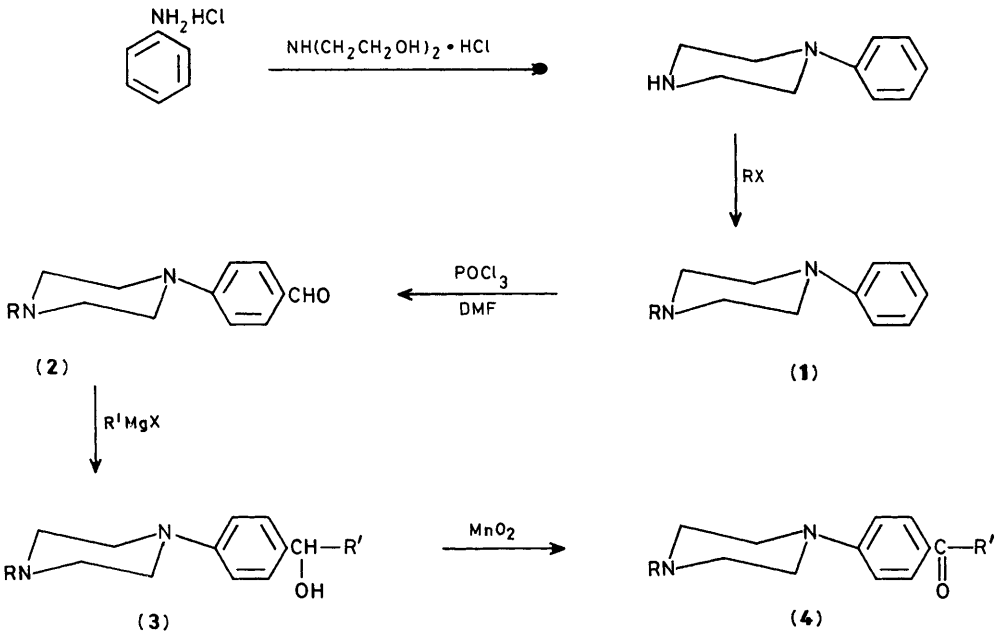
Liquid crystals of 4-(*trans*-4-n-alkylcyclohexyl)benzenecarbonitrile[3] and 4-alkyl-4-bicyclohexanecarbonitriles[4] have achieved considerable importance in display technology. In these systems only the *trans*-1,4-substituted cyclohexane ring gives mesogenic behaviour. To overcome the presence of diastereoisomerism we decided to substitute the 1,4-cyclohexane core with a piperazine ring where simultaneous nitrogen inversion and ring inversion preclude the formation of the two stereoisomers.

Synthesis

Synthesis of the mesogenic structures based on piperazine followed the strategy of Scheme 1. *N*-Phenylpiperazine prepared on a mol scale from *N*,*N*-bis-(2-hydroxyethyl)amine and aniline hydrochloride[5] was alkylated using alkyl bromides from C-4 to C-9. The *N*-alkyl-*N'*-phenylpiperazines were the starting material of a new homologous series, the *N*-alkyl-*N'*-(4-substituted aryl)piperazines. Vilsmeier–Haack formylation of *N*-alkyl-*N'*-phenylpiperazine was found to give *N*-alkyl-*N'*-(4-formylphenyl)piperazine in good yield. The aldehyde group is versatile and allows chemical modification upon treatment with n-alkylmagnesium bromide to give the corresponding secondary alcohols, followed by oxidation with active MnO_2 (freshly prepared) to give the ketones as depicted in Scheme 1.

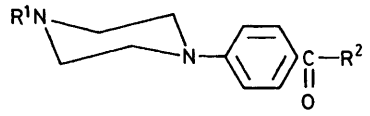
Results and Discussion

The mesogenic properties of *N'*-(4-acylphenyl)-*N*-alkylpiperazines (**4**) are shown in Table 1. These compounds exhibit smectic mesophases in contrast to the nematic phases shown by the 1-(4-alkanoylphenyl)-4-*trans*-alkylcyclohexanes.[2] Probable conjugation between the lone pair electrons of the nitrogen atom and the carbonyl group of the aromatic entity increases the dipole-dipole interaction between neighbouring molecules. This lateral dipole-dipole interaction would favour smectic



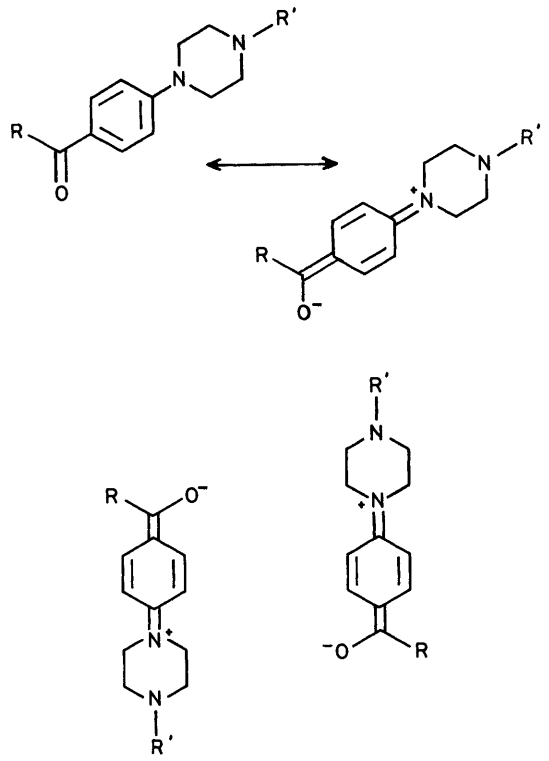
Scheme 1.

Table 1. Transition temperatures and enthalpies for the *N'*-(4-acylphenyl)-*N*-n-alkylpiperazines (**4**)[a]



			T/°C Phase transition					Enthalpies kcal/mol^{-1}				
Compd.	R^1	R^2	K	S1	S2		I	K	S1	S2		I
(**4b**)	C_5H_{11}	C_5H_{11}	62.0[b]	75.5[c]	104.5			2.65	2.65	3.35		
(**4c**)	C_6H_{13}	C_5H_{11}	80.5	102.0	103.0			6.42	0.78	2.48		
(**4d**)	C_7H_{15}	C_5H_{11}	71.0	95.0	101.0			6.39	0.67	2.43		
(**4e**)	C_8H_{17}	C_5H_{11}	87.0	95.3	98.0			7.08	0.81	2.53		
(**4f**)	C_8H_{17}	C_6H_{13}	72.0	101.8	105.8			6.82	1.08	3.06		
(**4g**)	C_8H_{17}	C_7H_{15}	86.6	97.0	104.5			6.48	0.86	2.65		
(**4h**)	C_9H_{19}	C_5H_{11}	84.5	93.8	99.6			8.21	0.77	2.55		

[a] K and I represent crystal and isotropic phases, respectively. [b] = Probably a crystal-crystal transition. [c] = Probably the true melting point.



Scheme 2.

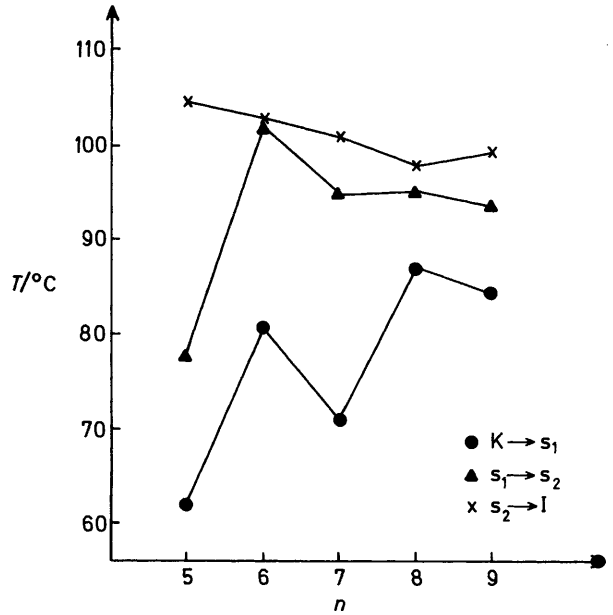


Figure 1. Plot of transition temperatures against the number of carbon atoms (*n*) in the alkyl chain (R^1) of the *N'*-(4-acylphenyl)-*N*-n-alkylpiperazines (**4**)

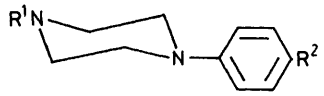
phases and increase the thermal stability of the mesophases as shown in Scheme 2.

A plot of transition temperature *versus* the number (*n*) of carbon atoms in the alkyl chain (see Figure) shows typical mesomorphic trends. The melting and smectic 1–smectic 2 (hereafter S1 and S2) transition temperatures lie on a rising curve with the even numbers having the higher temperature. The odd-even alternation is probably due to a large anisotropy of molecular polarizability arising from the increase in chain length on passing from an odd to an even number of carbons and assuming a rigid extended planar zig-zag *N*-alkylpiperazine chain.[6]

The transition temperatures and transition heats were determined with a Perkin-Elmer DSC-2 apparatus calibrated with indium. The transition temperatures, except the melting points, were checked using a Leitz Ortholux-Pol microscope with a Mettler FP-52 hot stage. The melting points could not be determined with the microscope because the texture change at the melting point is indeterminate. The compound $R^1 = R^2 = C_5H_{11}$ is an exception in that the transition heat at the S2–I transition is larger than the transition heat of the other two transitions present. The transition that is marked S1–S2 supercools by up to 13 °C on the DSC. From the DSC data and the *X*-ray and optical data to be discussed below, we consider that this compound has only one smectic phase; that is, the phase marked S1 is really a crystalline phase. For all other compounds the S2–I and S2–S1 transitions do not supercool; only the S1–K transition supercools.

Optical texture and conoscopic observations were made with the polarizing microscope and again $R^1 = R^2 = C_5H_{11}$ is an exception. For all compounds except the cited one the S2 phase separates from the isotropic in small batons and coalesces to the focal-conic fan texture. The transition S2–S1 is difficult to observe but on careful observation it can be noted that the transition is marked by a diminished number of discontinuities

Table 2. Elemental analysis of *N*-n-alkyl-*N'*-arylpiperazines derivatives



Compd.	R^1	R^2	Empirical formula	C Found	C (Calc.)	H Found	H (Calc.)	N Found	N (Calc.)
(1a)	C_4H_9	H	$C_{14}H_{22}N_2$	77.23	(77.06)	10.24	(10.09)	12.76	(12.84)
(1b)	C_5H_{11}	H	$C_{15}H_{24}N_2$	78.32	(77.58)	10.31	(10.34)	12.18	(12.07)
(1c)	C_6H_{13}	H	$C_{16}H_{26}N_2$	78.29	(78.05)	11.01	(10.57)	11.21	(11.38)
(1d)	C_7H_{15}	H	$C_{17}H_{28}N_2$	78.29	(78.46)	10.85	(10.77)	10.41	(10.77)
(1e)	C_8H_{17}	H	$C_{18}H_{30}N_2$	79.65	(78.83)	11.10	(10.95)	10.12	(10.22)
(1f)	C_9H_{19}	H	$C_{19}H_{32}N_2$	78.69	(79.17)	11.09	(11.11)	9.66	(9.72)
(2a)	C_4H_9	CHO(oxime)	$C_{15}H_{23}N_3O$	68.46	(68.97)	8.74	(8.81)		
(2b)	C_5H_{11}	CHO(oxime)	$C_{16}H_{25}N_3O$	70.14	(69.82)	8.98	(9.09)		
(2c)	C_6H_{13}	CHO(phenylhydrazone)	$C_{23}H_{32}N_4$	76.32	(75.82)	9.01	(8.79)		
(2d)	C_7H_{15}	CHO(phenylhydrazone)	$C_{24}H_{34}N_4$	76.56	(76.19)	9.16	(8.99)		
(2e)	C_8H_{17}	CHO(phenylhydrazone)	$C_{25}H_{36}N_4$	76.65	(76.53)	8.74	(9.18)		
(2f)	C_9H_{19}	CHO(oxime)	$C_{20}H_{33}N_3O$	71.97	(72.51)	9.91	(9.97)		
(3a)	C_4H_9	n-CH(OH)C_5H_{11}	$C_{20}H_{34}N_2O$	75.18	(75.47)	10.57	(10.69)	8.81	(8.81)
(3b)	C_5H_{11}	n-CH(OH)C_5H_{11}	$C_{21}H_{36}N_2O$	75.25	(75.90)	10.60	(10.84)	7.68	(8.43)
(3c)	C_6H_{13}	n-CH(OH)C_5H_{11}	$C_{22}H_{38}N_2O$	76.49	(76.30)	11.04	(10.98)	8.00	(8.09)
(3d)	C_7H_{15}	n-CH(OH)C_5H_{11}	$C_{23}H_{40}N_2O$	76.31	(76.66)	10.74	(11.11)	7.73	(7.78)
(3e)	C_8H_{17}	n-CH(OH)C_5H_{11}	$C_{24}H_{42}N_2O$	77.52	(77.01)	11.49	(11.23)	7.49	(7.49)
(3f)	C_8H_{17}	n-CH(OH)C_6H_{13}	$C_{25}H_{44}N_2O$	77.50	(77.32)	10.57	(11.34)	7.86	(7.22)
(3g)	C_8H_{17}	n-CH(OH)C_7H_{15}	$C_{26}H_{46}N_2O$	77.29	(77.61)	11.40	(11.44)	6.82	(6.96)
(3h)	C_9H_{19}	n-CH(OH)C_5H_{11}	$C_{25}H_{44}N_2O$	76.97	(77.32)	11.05	(11.34)	7.18	(7.22)

in the fans on transition to the lower-temperature phase. It is possible to shear the cover slip in both phases and this generally produces a homeotropic texture. Conoscopic observations on the homeotropic texture of the S2 and S1 phases show both to be uniaxial positive. The S2 phase of the compound $R^1 = R^2 = C_5H_{11}$ separates from the isotropic phase in needle or lancet-like forms (not the small batons of the other compounds) that coalesce to form a mosaic texture and it is not possible to shear the cover slip. At the temperature marked in Table 1 at the S2–S1 transition the mosaic becomes striated or broken as in a crystalline texture. It was not possible to obtain a uniformly oriented sample for conoscopic observation in either phase.

X-Ray diffraction patterns were recorded on a flat plate camera using 1 mm Lindemann capillaries in a temperature-controlled oven. A pure sample of the compound $R^1 = C_8H_{17}$, $R^2 = C_7H_{15}$ at room temperature gave a sharp low-angle ring at a distance (using Bragg's law) corresponding to 28.6 ± 2.0 Å and five or more sharp rings with large angles. In the S1 phase at 95 °C there were three sharp rings corresponding to distances of 28.2 ± 2.0, 4.6 ± 0.1, and 4.0 ± 0.1 Å. In the S2 phase at 100 °C there were two sharp rings corresponding to distances of 28.9 ± 2.0 and 4.6 ± 0.1 Å. It is important to note that the high-angle reflection is sharp and not diffuse as would be the case if S2 were a smectic A phase.

For compound $R^1 = R^2 = C_5H_{11}$ data were taken on a pure crystal at room temperature, at 69 °C, and on the once heated sample at room temperature again; these samples all gave six sharp rings (one at small angles) and all angles are within experimental error. In the S2 phase at 95 °C there are two sharp rings corresponding to distances of 22.8 ± 2.0 and 4.6 ± 0.1 Å.

From the *X*-ray, optical, and calorimetric [7] data we conclude that for compound $R^1 = R^2 = C_5H_{11}$ the phase marked S1 is really a crystalline phase and the phase S2 is a true smectic phase and probably smectic B. For all other compounds we believe that the S2 phase should also be a smectic B. The phase S1 is relatively well-ordered from the *X*-ray measurements but the cover slip can be sheared and it is uniaxial positive and these properties are contradictory. It is possible that S1 could be very weakly biaxial such that its interference figure only appears to be uniaxial; if this was the case then S1 would be identified as smectic E. Of course, S1 could be any of the ordered smectic phases with random orientational correlation between layers which would give apparent uniaxial phases. However, the calculated length for $R^1 = C_8H_{17}$, $R^2 = C_7H_{15}$ is 28.5 Å and the layer spacing from *X*-rays is 28.2 ± 2.0 Å which implies that S1 is an orthogonal phase.

Experimental

Structural analysis of the compounds was confirmed by i.r. (Perkin-Elmer 237 and 577), ^{1}H n.m.r. (Varian T-60 A), and ^{13}C n.m.r. (Varian CFT-20) (using tetramethylsilane as the standard) spectra, and elemental analysis (Tables 2 and 3).

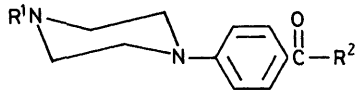
Preparation of N-*alkyl*-N'-*phenylpiperazines* (**1**).—A mixture of phenylpiperazine [5] (0.2 mol), n-alkyl bromide (0.22 mol), potassium carbonate (0.20 mol), and benzene (250 ml) was stirred and heated under reflux for 16 h. The solid was separated and the solution evaporated. The product was purified by vacuum distillation. Yield 80—90%.

N-*Butyl*-N'-*phenylpiperazine* (**1a**). B.p.$_{0.03}$ 108 °C; i.r. 1 605 (C=C), 757 (C–H), and 689 cm^{-1} (C–C); $\delta_H(C_6D_6)$ 0.90 (3 H, t, Me), 1.08—1.82 (4 H, m, CH_2), 2.33 and 3.02 (10 H, 2m, CH_2N), and 6.65—7.38 (5 H, 2m, ArH); $\delta_C(C_6D_6)$ 151.9, 128.25, 119.58, 116.28 (C-1, C-3, C-4, C-2 ArC), 58.46 (C-1), 53.59 and 49.39 (N–CH_2–CH_2–N'), 29.54 (C-2), 20.94 (C-3), and 14.31 (C-4).

N-*Pentyl*-N'-*phenylpiperazine* (**1b**). B.p.$_{0.01}$ 120 °C; i.r. 1 600 (C=C), 757 (C–H), and 690 cm^{-1} (C–C); $\delta_H(CDCl_3)$ 0.90 (3 H, t, Me), 1.08—1.82 (6 H, m, CH_2), 2.35 (2 H, t, CH_2N), 2.50 and 3.15 (8 H, 2 m, NCH_2), and 6.55—7.32 (5 H, 2m, ArH); $\delta_C(CDCl_3)$ 151.65, 128.90, 119.13, 115.90 (C-1, C-3, C-4, C-2 ArC), 58.59 (C-1), 53.33 and 49.04 (N–CH_2–CH_2–N'), 29.87 (C-3), 26.85 (C-2), 22.75 (C-4), and 14.24 (C-5).

N-*Hexyl*-N'-*phenylpiperazine* (**1c**). B.p.$_{0.01}$ 125 °C; i.r. 1 600 (C=C), 690 (C–H), and 756 cm^{-1} (C–C); δ_H 0.88 (3 H, t, Me),

Table 3. Elemental analysis of *N'*-(4-acylphenyl)-*N*-n-alkylpiperazines (**4**)



Compd.	R^1	R^2	Empirical formula	C Found (Calc.)	H Found (Calc.)	N Found (Calc.)
(**4a**)	C_4H_9	C_5H_{11}	$C_{20}H_{32}N_2O$	76.01 (75.95)	10.56 (10.13)	8.90 (8.86)
(**4b**)	C_5H_{11}	C_5H_{11}	$C_{21}H_{34}N_2O$	76.21 (76.36)	10.29 (10.30)	8.48 (8.48)
(**4c**)	C_6H_{13}	C_5H_{11}	$C_{22}H_{36}N_2O$	76.82 (76.74)	10.57 (10.46)	7.66 (8.14)
(**4d**)	C_7H_{15}	C_5H_{11}	$C_{23}H_{38}N_2O$	77.27 (77.09)	10.65 (10.61)	7.70 (7.82)
(**4e**)	C_8H_{17}	C_5H_{11}	$C_{24}H_{40}N_2O$	76.89 (77.42)	10.64 (10.75)	7.08 (7.53)
(**4f**)	C_8H_{17}	C_6H_{13}	$C_{25}H_{42}N_2O$	78.06 (77.72)	10.78 (10.82)	7.18 (7.25)
(**4g**)	C_8H_{17}	C_7H_{15}	$C_{26}H_{44}N_2O$	78.23 (78.00)	10.93 (11.00)	7.02 (7.00)
(**4h**)	C_9H_{19}	C_5H_{11}	$C_{25}H_{42}N_2O$	77.62 (77.71)	10.35 (10.88)	7.21 (7.25)

1.05—1.65 (8 H, m, CH_2), 2.40 and 3.03 (8 H, 2 m, NCH_2), and 6.55—7.32 (5 H, 2m, ArH).

N-*Heptyl*-N'-*phenylpiperazine* (**1d**). B.p.$_{0.01}$ 132 °C; i.r. 1 605 (C=C), 755 (C–H), and 689 cm^{-1} (C–C); δ_H 0.88 (3 H, t, Me), 1.05—1.80 (10 H, m, CH_2), 2.28 (2 H, t, CH_2N), 2.43 and 3.08 (8 H, 2 m, CH_2N), and 6.62 and 7.43 (5 H, 2m, ArH); δ_C 151.37, 128.90. 119.31, 115.81 (C-1, C-2, C-3, C-4 ArC), 58.69 (C-1), *53.30* and 49.02 (N–CH_2–*CH_2*–N'), 31.83 (C-5), 29.29 (C-4), 27.53 (C-3), 26.95 (C-2), 22.64 (C-6), and 14.06 (C-7).

N-*Octyl*-N'-*phenylpiperazine* (**1e**). B.p.$_{0.01}$ 146—148 °C; i.r. 1 600 (C=C), 755 (C–H), and 689 cm^{-1} (C–C); δ_H($CDCl_3$) 0.88 (3 H, t, Me), 1.05—1.68 (12 H, m, CH_2), 2.30 (2 H, t, CH_2N), 2.47 and 3.10 (8 H, 2 m, CH_2N), and 6.65—7.35 (5 H, 2 m, ArH); δ_C($CDCl_3$) 151.32, 128.90, 119.32, 115.81 (C-1, C-3, C-4, C-2 ArC), 58.69 (C-1), *53.30* and 49.02 (N–CH_2–*CH_2*–N'), 29.58 (C-5), 29.30 (C-4), 27.62 (C-3), 26.95 (C-2), 22.65 (C-7), and 14.07 (C-8).

N-*Nonyl*-N'-*phenylpiperazine* (**1f**). B.p.$_{0.01}$ 151 °C; i.r. 1 600 (C=C), 757 (C–H), and 689 cm^{-1} (C–C); δ_H($CDCl_3$) 0.90 (3 H, s, Me), 1.08—1.92 (14 H, m, CH_2), 2.43 (2 H, t, CH_2N), 2.60 and 3.27 (8 H, 2 m, CH_2N), 7.40—7.52 (5 H, 2 m, ArH); δ_C($CDCl_3$) 151.39, 128.93, 119.36, 115.84 (C-1, C-3, C-4, C-2 ArC), 58.72 (C-1), *53.25* and 49.05 (N–CH_2–*CH_2*–N'), 31.86 (C-7), 29.59 (C-5), 29.32 (C-4, C-6), 27.57 (C-3), 26.95 (C-2), 22.65 (C-8), and 14.07 (C-9).

Preparation of N-*Alkyl*-N'-(4-*formylphenyl*)*piperazines* (**2**).—To dimethylformamide (3.5 mol) cooled in an ice-bath, phosphoryl trichloride (1 mol) was added in small portions. After addition cooling, stirring was continued for 10 min, when *N*-alkylphenylpiperazine (0.5 mol) dissolved in dimethylformamide was added and a red precipitate began to form. The reaction mixture was heated on a steam-bath for 2 h. The mixture was then cooled and poured over a saturated solution of sodium acetate–ice with vigorous stirring. Before neutralization with NaOH the mixture was stored in the refrigerator overnight. The mixture was extracted with CH_2Cl_2 and the organic layer was washed with water, dried ($CaSO_4$), and evaporated. Yield 95% (crude product). For analysis the oxime was prepared.

Preparation of oximes. A mixture of NH_2OH·HCl (0.5 g), water (2 ml), and 10% NaOH (2 ml) was added to a solution of aldehyde (0.2 g) dissolved in ethanol (10 ml). The mixture was heated and ethanol added until dissolution. After cooling the precipitate was filtered and recrystallized from ethanol.

Preparation of phenylhydrazones. A solution of phenylhydrazine hydrochloride (0.5 g), MeCOONa (0.8 g), and water (5 ml) was added to aldehyde (0.2—0.4 g) dissolved in ethanol (10 ml). The method then proceeded as for the oximes.

N-*Butyl*-N'-(4-*formylphenyl*)*piperazine* (**2a**). M.p. Ar–CH=N–OH 172 °C, b.p.$_{0.05}$ (ArCHO) 182—184 °C; i.r. (KBr) 1 670 (C=O) and 1 595 cm^{-1} (C=C); δ_H($CDCl_3$) 0.90 (3 H, t, Me), 1.12—1.80 (4 H, m, CH_2), 2.33 (2 H, t, CH_2N), 2.50 and 3.35 (8 H, 2m, CH_2N), 6.85 and 7.72 (4 H, 2d, *J* 9 Hz, ArH), and 9.75 (1 H, s, CHO); δ_C($CDCl_3$) 189.93 (C=O), 154.37, 130.95, 126.31, 112.64 (C-1, C-3, C-4, C-2 ArC), 57.47 (C-1), *56.56* and 46.35 (N–CH_2–*CH_2*–N'), 28.29 (C-2), 19.98 (C-3), and 13.39 (C-4).

N'-(4-*Formylphenyl*)-N-*pentylpiperazine* (**2b**). M.p. Ar–CH=N–OH 162—163 °C; b.p.$_{0.5}$ (ArCHO) 174—176 °C; i.r. (KBr) 1 677 (C=O) and 1 592 cm^{-1} (C=C); δ_H($CDCl_3$) 0.87 (3 H, t, Me), 1.03—1.80 (6, H, m, CH_2), 2.40 and 3.27 (10 H, 2 m, CH_2N), 6.73 and 7.57 (4 H, 2 d, *J* 8 Hz, ArH), and 9.73 (1 H, s, CHO); δ_C($CDCl_3$) 154.99, 131.65, 127.04, 113.37 (C-1, C-3, C-4, C-2 ArC), 58.58 (C-1), *52.82* and 47.07 (N–CH_2–*CH_2*–N'), 29.68 (C-3), 26.43 (C-2), 22.55 (C-4), and 14.04 (C-5).

N'-(4-*Formylphenyl*)-N-*hexylpiperazine* (**2c**). M.p. Ar–CH=N–NH–Ph 172—173 °C; i.r. (KBr) 1 686 (C=O) and 1 592 cm^{-1} (C=C); δ_H($CDCl_3$) 0.87 (3 H, t, Me), 1.03—1.90 (8 H, m, CH_2), 2.43 and 3.30 (10 H, 2 m, CH_2N), 6.73 and 7.57 (4 H, 2 d, *J* 8 Hz, ArH), and 9.60 (1 H, s, CHO); δ_C($CDCl_3$) 189.93 (C=O), 154.99, 131.65, 127.04, 113.37 (C-1, C-3, C-4, C-2 ArC), 58.58 (C-1), *52.82* and 47.07 (N–CH_2–*CH_2*–N'), 29.68 (C-4), 26.48 (C-2 and C-3), 22.55 (C-5), and 14.04 (C-6).

N'-(4-*Formylphenyl*)-N-*heptylpiperazine* (**2d**). M.p. Ar–CH=N–NH–Ph 171 °C; i.r. (KBr) 1 685 (C=O) and 1 592 cm^{-1} (C=C); δ_H($CDCl_3$) 0.87 (3 H, t, Me), 1.03—1.80 (10 H, m, CH_2), 2.47 and 3.33 (10 H, m, CH_2N), 6.77 and 7.63 (4 H, 2 d, *J* 8 Hz, ArH), and 9.67 (1 H, s, CHO).

N'-(4-*Formylphenyl*)-*N-octylpiperazine* (**2e**). M.p. Ar–CH=N–NH–Ph 165 °C; i.r. (KBr) 1 666 (C=O) and 1 600 cm^{-1} (C=C); δ_H($CDCl_3$) 0.83 (3 H, t, Me), 1.03—1.60 (12 H, m, CH_2), 2.93 (2 H, t, CH_2N), 3.37 and 3.83 (8 H, 2 m, CH_2), 6.83 and 7.67 (4 H, 2 d, *J* 8 Hz, ArH), and 9.68 (1 H, s, CHO); δ_C($CDCl_3$) 190.09 (C=O), 153.18, 131.40, 128.18, 114.33 (C-1, C-3, C-4, C-2 ArC), 56.99 (C-1), *50.82* and 44.27 (N–CH_2–*CH_2*–N'), 31.21 (C-6), 28.57 (C-4 and C-5), 26.33 (C-3), 23.20 (C-2), 22.12 (C-7), and 13.63 (C-8).

N'-(4-*Formylphenyl*)-N-*nonylpiperazine* (**2f**). M.p. Ar–CH=N–OH 146 °C; i.r. (KBr) 1 675 (C=O) and 1 597 cm^{-1} (C=C); δ_H($CDCl_3$) 0.80 (3 H, t, Me), 0.93—1.73 (14 H, m, CH_2), 2.40 and 3.27 (10 H, 2 m, CH_2N), 6.70 and 7.57 (4 H, 2 d, *J* 8 Hz, ArH), and 9.60 (1 H, s, CHO); δ_C($CDCl_3$) 189.75 (C=O), 154.88, 131.54, 126.95, 113.28 (C-1, C-3, C-4, C-2 ArC), *52.72* and 46.97 (N–CH_2–*CH_2*–N'), 59.49 (C-1), 31.74 (C-7), 26.30 (C-5), 29.10 (C-4 and C-6), 27.35 (C-3), 26.75 (C-2), 22.47 (C-8), and 13.96 (C-9).

Preparation of N-*Alkyl*-N'-4-(1-*hydroxyalkyl*)*phenylpiper-*

azines (**3**).—To *N*-n-alkyl-*N'*-(4-formylphenyl)piperazine (**2**) (0.1 mol) dissolved in ether was added dropwise at room temperature the Grignard reagent, which was prepared from alkyl bromide (0.1 mol) and magnesium (0.11 mol) in ether. The mixture was stirred for 2 h, then poured onto a mixture of ice–dil. HCl and extracted with CH_2Cl_2 which dissolved the piperazinium chloride. The organic layer was washed with 10% NaOH to liberate the base, then washed with water, dried, and evaporated. The residue was recrystallized from acetone. Yield 75—85%.

N-*Butyl*-N'-[4-(1-*hydroxyhexyl*)*phenyl*]*piperazine* (**3a**). M.p. 116 °C; i.r. (KBr) 3 144 (OH) and 1 615 cm^{-1} (C=C); $\delta_H(C_6D_6)$ 0.92 (6 H, t, Me), 1.08—1.95 (12 H, m, CH_2), 2.52 and 3.05 (10 H, 2 m, CH_2N), 4.52 (1 H, t, CH), 6.77 and 7.17 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(C_6D_6)$ 151.11, 137.65, 127.11, 116.25 (C-1, C-4, C-3, C-2 ArC), 74.05 (C-1'), 58.63 (C-1), *53.74* and 49.35 (N–CH_2–CH_2–N'), 39.89 (C-2'), 32.27 (C-4'), 29.29 (C-2), 26.20 (C-3'), 23.07 (C-5'), 21.03 (C-3), and 14.29 (C-4 and C-6').

N'-[4-(1-*Hydroxyhexyl*)*phenyl*]-N-*pentylpiperazine* (**3b**). M.p. 120 °C; i.r. (KBr) 3 155 (OH) and 1 615 cm^{-1} (C=C); $\delta_H(CDCl_3)$ 0.92 (6 H, t, Me), 1.06—1.80 (14 H, m, CH_2), 2.30 (2 H, t, CH_2N), 2.50 and 3.00 (8 H, 2 m, CH_2N), 3.83 (1 H, s, OH), 4.47 (1 H, t, CH), 6.74 and 7.15 (4 H, w 2 d, *J* 8 Hz, ArH); $\delta_C(CDCl_3)$ 149.61, 135.81, 125.79, 114.86 (C-1, C-4, C-3, C-2 ArC), 72.81 (C-1'), 57.80 (C-1), *52.23* and 48.04 (N–CH_2–CH_2–N'), 38.07 (C-2'), 30.85 (C-4'), 28.89 (C-3), 25.38 (C-2), 24.70 (C-3'), 21.59 (C-4 and C-5'), and 13.07 (C-5 and C-6').

N-*Hexyl*-N'-[4-(1-*hydroxyhexyl*)*phenyl*]*piperazine* (**3c**). M.p. 115 °C; i.r. (KBr) 3 155 (OH) and 1 613 (cm^{-1} (C=C); $\delta_H(CDCl_3)$ 0.90 (6 H, t, Me), 1.08—1.85 (16 H, m, CH_2), 2.37 (2 H, t, CH_2N), 2.55 and 3.22 (8 H, 2 m, CH_2N), 4.55 (1 H, t, CH), 6.87 and 7.28 (4 H, 2d, *J* 8 Hz, ArH); $\delta_C(CDCl_3)$ 150.61, 136.71, 126.82, 115.84 (C-1, C-4, C-3, C-2 ArC), 73.85 (C-1'), 58.83 (C-1), *53.21* and 49.04 (N–CH_2–CH_2–N'), 39.05 (C-2'), 31.84 (C-4 and C-4'), 27.34 (C-3), 26.61 (C-2), 25.63 (C-3'), 22.58 (C-5 and C-5'), and 14.03 (C-6 and C-6').

N-*Heptyl*-N'-[4-(1-*hydroxyhexyl*)*phenyl*]*piperazine* (**3d**). M.p. 109 °C; i.r. (KBr) 3 144 (OH) and 1 613 cm^{-1} (C=C); $\delta_H(CDCl_3)$ 0.88 (6 H, t, Me), 1.08—1.85 (18 H, m, CH_2), 2.37 (2 H, t, CH_2N), 2.58 and 3.10 (8 H, 2 m, CH_2N), 4.58 (1 H, t, CH), and 6.90 and 7.30 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(CDCl_3)$ 150.68, 136.71, 126.84, 115.90 (C-1, C-4, C-3, C-2 ArC), 73.92 (C-1'), 58.87 (C-1), *53.23* and 49.03 (N–CH_2–CH_2–N'), 39.04 (C-2'), 31.83 (C-5 and C-4'), 29.28 (C-4), 27.73 (C-3), 26.75 (C-2), 25.68 (C-3'), 22.64 (C-6 and C-5'), and 14.06 (C-7 and C-6').

N'-[4-(1-*Hydroxyhexyl*)*phenyl*]-N-*octylpiperazine* (**3e**). M.p. 108 °C; i.r. (KBr) 3 144 (OH) and 1 610 cm^{-1} (C=C); $\delta_H(CDCl_3)$ 0.90 (6 H, t, CH_2), 1.08—1.87 (20 H, m, CH_2), 2.33 (2 H, t, CH_2N), 2.65 and 3.31 (8 H, 2 m, CH_2N), 2.87 (1 H, s, OH), 4.62 (1 H, t, CH), 6.91 and 7.30 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(CDCl_3)$ 150.78, 136.24, 126.85, 115.91 (C-1, C-4, C-3, C-2 ArC), 74.27 (C-1'), 58.81 (C-1), *53.24* and 49.11 (N–CH_2–CH_2–N'), 38.88 (C-2'), 31.84 (C-6 and C-4'), 29.52 (C-5), 29.28 (C-4), 27.64 (C-3), 26.77 (C-2), 25.61 (C-3'), 22.58 (C-7 and C-5'), and 13.99 (C-8 and C-6').

N'-[4-(1-*Hydroxyheptyl*)*phenyl*]-N-*octylpiperazine* (**3f**). M.p. 123 °C; i.r. (KBr) 3 174 (OH) and 1 618 cm^{-1} (C=C); $\delta_H(CDCl_3)$ 0.93 (6 H, t, Me), 1.08—1.92 (22 H, m, CH_2), 2.33 (2 H, t, CH_2N), 2.45 and 3.03 (8 H, 2 m, CH_2N), 2.73 (1 H, s, OH), 4.60 (1 H, t, CH), 6.83 and 7.33 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(CDCl_3)$ 151.34, 137.31, 127.13, 116.29 (C-1, C-4, C-3, C-2 ArC), 74.21 (C-1'), 58.98 (C-1), *53.61* and 49.51 (N–CH_2–CH_2–N'), 39.84 (C-2'), 32.24 (C-6 and C-5'), 29.96 (C-4 and C-5), 29.77 (C-4'), 27.93 (C-3), 27.31 (C-2), 26.37 (C-3'), 23.03 (C-7 and C-6'), and 14.25 (C-7' and C-8).

N'-[4-(1-*Hydroxyoctyl*)*phenyl*]-N-*octylpiperazine* (**3g**). M.p. 105 °C; i.r. (KBr) 3 160 (OH) and 1 612 cm^{-1} (C=C); $\delta_H(CDCl_3)$ 0.93 (6 H, t, Me), 1.06—1.85 (24 H, m, CH_2), 2.40 and 3.00 (10 H, 2 m, CH_2N), 2.75 (1 H, s, OH), 4.53 (1 H, t, CH), and 6.83 and 7.30 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(CDCl_3$–$C_6D_6)$ 151.29, 136.84, 126.76, 116.21 (C-1, C-4, C-3, C-2 ArC), 74.32 (C-1'), 58.89 (C-1), *53.60* and 49.59 (N–CH_2–CH_2–N'), 39.54 (C-2'), 32.13 (C-6 and C-6'), 29.88 (C-5 and C-5'), 29.58 (C-4 and C-4'), 27.85 (C-3), 27.25 (C-2), 26.26 (C-3'), 22.86 (C-7 and C-7'), and 14.07 (C-8 and C-8').

N'-[4-(1-*Hydroxyhexyl*)*phenyl*]-N-*nonylpiperazine* (**3h**). M.p. 105 °C; i.r. (KBr) 3 174 (OH) and 1 618 cm^{-1} (C=C); $\delta_H(CDCl_3)$ 0.88 (6 H, t, CH_2), 1.05—1.78 (22 H, m, CH_2), 2.12 (2 H, t, CH_2N), 2.53 and 3.03 (8 H, 2 m, CH_2N), 3.43 (1 H, s, OH), 4.50 (1 H, t, CH), 6.79 and 7.20 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(CDCl_3)$ 150.51, 136.55, 126.61, 115.68 (C-1, C-4, C-3, C-2 ArC), 73.76 (C-1'), 58.64 (C-1), *53.06* and 48.86 (N–CH_2–CH_2–N'), 38.88 (C-2'), 31.68 (C-4' and C-7), 29.43 (C-5), 29.14 (C-4 and C-6), 27.48 (C-3), 26.52 (C-2), 25.52 (C-3'), 22.48 (C-5' and C-8), 13.89 (C-6' and C-9).

Preparation of N'-(4-*Acylphenyl*)-N-*alkylpiperazines* (**4**).—To a solution of ROH (4 g) in benzene, active MnO_2 (20 g) was added. After stirring for one week at room temperature the solution was filtered, the filtrate evaporated, and the residue recrystallized from light petroleum (b.p. 50—70 °C)–ether. Yield 90—95%.

Preparation of active MnO_2. The activity of the reagent varied with the method of preparation; material of good activity was obtained by oxidizing manganese(II) ions with an excess of permanganate under alkaline conditions.[8].

N'-(4-*Hexanoylphenyl*)-N-*pentylpiperazine* (**4b**). I.r. (KBr) 1 667 (C=O) and 1 610 cm^{-1} (C=C); $\delta_H(C_6D_6)$ 0.88 (6 H, t, Me), 1.06—1.62 (12 H, m, CH_2), 1.80 (2 H, t, CH_2C=O), 2.86 (2 H, t, CH_2N), 2.27 and 3.06 (8 H, 2 m, CH_2N), 6.74 and 7.15 (4 H, 2 d, *J* 9 Hz ArH); $\delta_C(C_6D_6)$ 197.16 (C=O), 154.31, 130.00, 128.32, 113.78 (C-1, C-3, C-4, C-2 ArC), 58.71 (C-1), *53.12* and 47.74 (N–CH_2–CH_2–N'), 38.09 (C-2'), 32.00 (C-4'), 29.93 (C-3), 26.99 (C-2), 24.96 (C-3'), 22.96 (C-4 and C-5'), and 14.18 (C-5 and C-6').

N'-(4-*Hexanoylphenyl*)-N-*hexylpiperazine* (**4c**). I.r. (KBr) 1 666 (C=O) and 1 605 cm^{-1} (C=C); $\delta_C(C_6D_6)$ 197.14 (C=O), 154.43, 130.25, 128.79, 113.90 (C-1, C-3, C-4, C-2 ArC), 58.72 (C-1), *53.23* and 49.98 (N–CH_2–CH_2–N'), 38.09 (C-2'), 32.11 (C-4 and C-4'), 27.37 (C-2 and C-3), 24.79 (C-3'), 22.85 (C-5 and C-5'), and 14.04 (C-6 and C-6').

N'-(4-*Hexanoylphenyl*)-N-*heptylpiperazine* (**4d**). I.r. (KBr) 1 669 (C=O) and 1 602 cm^{-1} (C=C); $\delta_H(C_6D_6)$ 0.93 (6 H, t, Me), 1.08—1.57 (16 H, m, CH_2), 1.73 (2 H, t, CH_2C=O), 2.33 (2 H, t, CH_2N), 2.77 and 3.12 (8 H, 2 m, CH_2N), 6.75 and 8.02 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(C_6D_6)$ 197.14 (C=O), 154.41, 130.24, 128.65, 113.89 (C-1, C-3, C-4, C-2 ArC), 58.71 (C-1), *53.22* and 49.96 (N–CH_2–CH_2–N'), 38.09 (C-2'), 32.20 (C-5 and C-4'), 29.25 (C-4), 27.82 (C-3), 27.35 (C-2), 24.78 (C-3'), 22.94 (C-6 and C-5'), and 14.14 (C-7 and C-6').

N'-(4-*Hexanoylphenyl*)-N-*octylpiperazine* (**4e**). I.r. (KBr) 1 667 (C=O) and 1 605 cm^{-1} (C=C); $\delta_H(C_6D_6)$ 0.92 (6 H, t, CH_2), 1.06—1.60 (18 H, m, CH_2), 1.80 (2 H, t, CH_2C=O), 2.67 and 3.03 (8 H, 2 m, CH_2), 2.73 (2 H, t, CH_2N), and 6.66 and 7.98 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(C_6D_6)$ 198.46 (C=O), 154.25, 130.06, 127.88, 113.48 (C-1, C-3, C-4, C-2 ArC), 58.67 (C-1), *52.94* and 47.68 (N–CH_2–CH_2–N'), 38.04 (C-2'), 31.79 (C-6 and C-4'), 29.49 (C-5), 29.14 (C-4), 27.54 (C-3), 26.93 (C-2), 24.86 (C-3'), 22.52 (C-7 and C-5'), and 13.86 (C-8 and C-6').

N'-(4-*Heptanoylphenyl*)-N-*octylpiperazine* (**4f**). I.r. (KBr) 1 664 (C=O) and 1 608 cm^{-1} (C=C); $\delta_H(C_6D_6)$ 0.88 (6 H, t, Me), 1.12—1.60 (20 H, m, CH_2), 1.78 (2 H, t, CH_2C=O), 2.27 and 3.05 (8 H, 2 m, CH_2N), 2.75 (2 H, t, CH_2N), 6.70 and 8.03 (4 H, 2 d, *J* 9 Hz, ArH); $\delta_C(C_6D_6)$ 197.20 (C=O), 154.35, 130.19, 128.49, 113.83 (C-1, C-3, C-4, C-2 ArC), 58.77 (C-1), *53.16* and 47.77

(N–CH_2–*CH_2*–N′), 38.14 (C-2′), 32.18 (C-6 and C-5′), 29.96 (C-4′), 29.62 (C-4 and C-5), 27.88 (C-3), 27.40 (C-2), 25.07 (C-3′), 23.00 (C-7 and C-6′), and 14.32 (C-8 and C-7′).

N′-(4-*Octanoylphenyl*)-N-*octylpiperazine* (**4g**). I.r. (KBr) 1 666 (C=O) and 1 612 cm^{-1} (C=C); $\delta_H(C_6D_6)$ 0.93 (6 H, t, Me), 1.08—1.63 (22 H, m, CH_2), 1.81 (2 H, t, CH_2C=O), 2.30 and 3.07 (8 H, 2 m, CH_2N), 2.78 (2 H, t, CH_2N), and 6.69 and 8.06 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(C_6D_6)$ 197.09 (C=O), 154.37, 130.19, 128.75, 113.96 (C-1, C-3, C-4, C-2 ArC), 58.78 (C-1), *53.18* and 47.93 (N–CH_2–*CH_2*–N′), 38.16 (C-2′), 32.15 (C-6 and C-6′), 29.85 (C-4′), 29.61 (C-4 and C-5), 27.79 (C-3 and C-5), 27.40 (C-2), 25.20 (C-3′), and 22.90 (C-7 and C-7′), 14.10 (C-8 and C-8′).

N′-(4-*Hexanoylphenyl*)-N-*nonylpiperazine* (**4h**). I.r. (KBr) 1 665 (C=O) and 1 610 cm^{-1} (C=C); $\delta_H(C_6D_6)$ 0.90 (6 H, t, Me), 1.08—1.80 (20 H, m, CH_2), 2.40 (2 H, t, CH_2C=O), 2.57 and 3.37 (8 H, 2 m, CH_2N), 2.87 (2 H, t, CH_2N), and 6.89 and 7.92 (4 H, 2 d, *J* 8 Hz, ArH); $\delta_C(C_6D_6)$ 197.14 (C=O), 154.41, 130.24, 128.54, 113.88 (C-1, C-3, C-4, C-2 ArC), 58.83 (C-1), *53.22* and 47.85 (N–CH_2–*CH_2*–N′), 38.09 (C-2′), 32.32 (C-4′), 32.10 (C-7), 30.02 (C-5), 29.78 (C-4 and C-6), 27.93 (C-3), 27.45 (C-2), 24.78 (C-3′), 22.96 (C-8 and C-5′), and 14.17 (C-9 and C-6′).

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