Macroscopic Expression of Molecular Recognition. Supramolecular Liquid Crystalline Phases induced by Association of Complementary Heterocyclic Components

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Whereas the pure compounds are non-mesogenic, equimolar mixtures of the complementary components (**5**)—(**7**) and (**11**) present a liquid crystalline phase that may be attributed to the formation of the mesogenic supramolecular species (**12**).

Molecular processes occurring in a material may induce marked changes in its properties. For instance, the interaction between molecular components that by themselves would not be mesogenic, could lead to the formation of a supramolecular species presenting liquid crystalline behaviour. If so, it might be possible to make use of selective interactions so that the mesogenic supermolecule would form only from complementary components. Thus, recognition processes operating at the molecular level would be expressed at the macroscopic level of the material by the induction of a mesomorphic phase that may be termed supramolecular and 'informed' since it is conditioned by the molecular information present in its components.

The most common type of molecular species that form thermotropic liquid crystals possess an axial rigid core fitted with flexible chains at each end.[1] One may then imagine splitting the central core into two complementary halves, C and $\overline{C}$, whose association would generate the mesogenic supermolecule, as schematically represented in Figure 1. Indications to this end may already be found in the formation of mesomorphic phases by *p*-alkoxybenzoic acids[2] and 2-oxopyridine-5-carboxylic esters,[3] which was attributed to dimerisation *via* hydrogen bonding.[4] In view of the great variety of molecules that lead to liquid crystals, numerous structures may be envisaged to test the process shown in Figure 1. In particular, the rigid elements may be chosen to be complementary heterocyclic units bearing long chains and capable of associating *via* hydrogen bonding into base-pairs similar to those found in nucleic acid chemistry.[5]

We now report some results obtained along those lines. In order to take advantage of potential triple hydrogen bonding, 2,6-diacylaminopyridine and uracil were chosen as core components to which long aliphatic chains were grafted, leading to the complementary compounds C = (**5**)—(**7**) and $\overline{C}$ = (**11a**—**g**).

A series of derivatives bearing different chains (**5a,b**), (**6b**), (**7b**), and (**11a**—**g**), were synthesized in a straightforward fashion (Schemes 1 and 2), starting from 4-allyloxy-2,6-diaminopyridine[6] and from 6-formyluracil[7] or 6-chloro-methyluracil.[8] All new compounds had NMR and mass spectral, and microanalytical properties in agreement with their structure.

The formation of an array of three parallel hydrogen bonds between groups of the uracil and 2,6-diaminopyridine type as represented in (**12**) is well documented structurally, spectroscopically, and thermodynamically[9—11] and has been used for the design of acyclic[10] and macrocyclic[11] receptor units for heterocyclic bases.

Addition of (**5b**) (1 equiv.) to a $CDCl_3$ solution of (**11f**) induced marked downfield shifts of the NH ^{1}H NMR signals from δ 7.80 (**5b**) and 8.15, 9.40 (**11f**) to δ 9.60, 9.90, and 11.50. Such changes are characteristic of the formation of a triple hydrogen-bonded complex (**12**).[10,11] The temperatures and

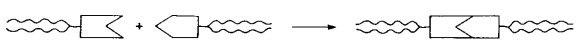
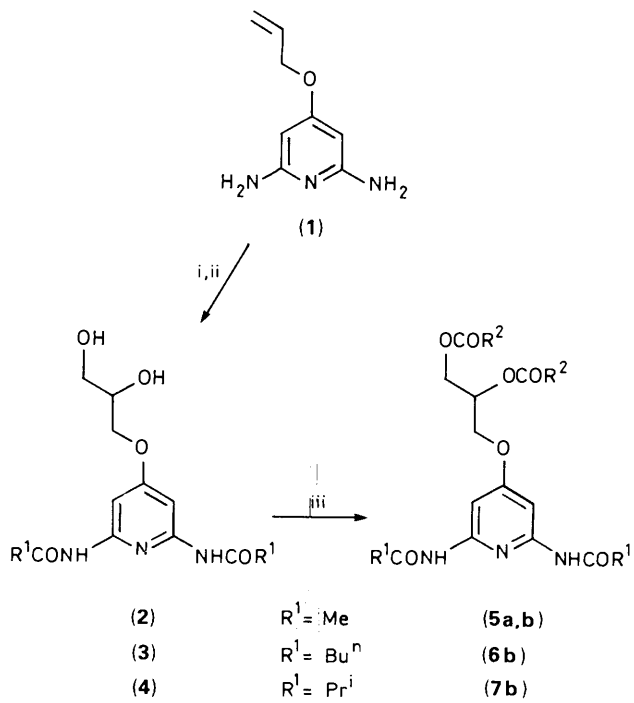
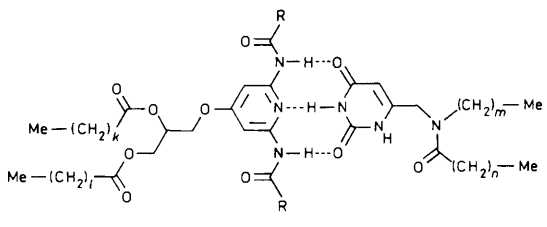


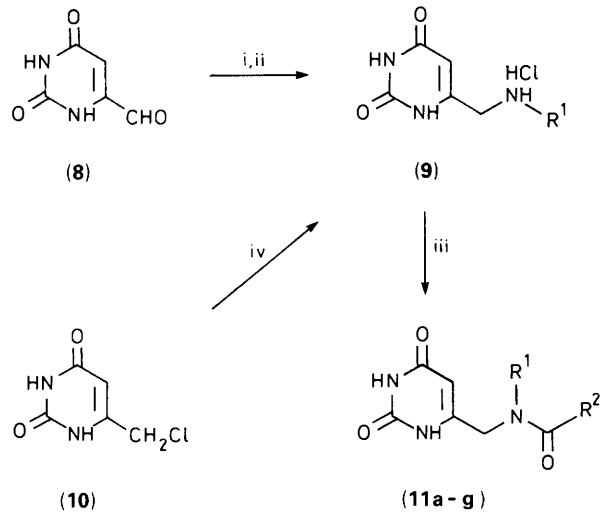
Figure 1. Schematic representation of the formation of a mesogenic supermolecule from two complementary components.



Scheme 1. *Reagents and conditions*: i, $(R^1CO)_2O$, pyridine, room temp., 14 h, 85—95%; ii, crude amide, $KMnO_4$, acetone/H_2O, 10—20 °C, 2 h, chromatography on SiO_2 (MeOH/$CHCl_3$ 10:90), 60%; iii, R^2COCl, pyridine, $CHCl_3$, room temp., 24 h, chromatography on SiO_2 (MeOH/$CHCl_3$ 5:95), 70%, recrystallisation from CH_2Cl_2/MeOH.



† ER 285 (Collège de France) and URA 422 (Université Louis Pasteur) of the C.N.R.S.



Scheme 2. *Reagents and conditions*: i, R^1NH_2, EtOH, reflux, 4 h, 70%; ii, crude imine, $NaBH_4$, EtOH/H_2O, reflux, 4 h, HCl (1 M), recrystallisation from EtOH, 85%; iii, R^2COCl, pyridine, $CHCl_3$, room temp., 24 h, chromatography on SiO_2 (MeOH/$CHCl_3$ 5:95), 70%, recrystallisation from CH_2Cl_2/MeOH; iv, R^1NH_2, Pr^iOH, reflux, 14 h, 60%.

Table 1. Physical properties of the derivatives (**5**)—(**7**) of 2,6-diaminopyridine[a] and (**11**) of uracil.[b]

Compound	R^1	R^2	Transition[c] T/°C	ΔH/kcal mol^{-1}
(**5a**)	Me	$C_{11}H_{23}$	K 30—46 I	12.9
(**5b**)	Me	$C_{17}H_{35}$	K 55—58 I	22.5
(**6b**)	Bu^n	$C_{17}H_{35}$	K 37—42 I	18.3
(**7b**)	Pr^i	$C_{17}H_{35}$	K 40—44 I	18.0
(**11a**)	C_8H_{17}	C_7H_{15}	K 77 K	9.5
			K 148 I	7.3
(**11b**)	C_8H_{17}	$C_{17}H_{35}$	K 82 K	16.4
			K 138 I	7.4
(**11c**)	$C_{12}H_{25}$	C_7H_{15}	K 43; 75; 95 K	8.1
			K 143 I	7.1
(**11d**)	$C_{12}H_{25}$	$C_{11}H_{23}$	K 73—79; 88—90 K	13.0
			K 142—144 I	7.9
(**11e**)	$C_{12}H_{25}$	$C_{17}H_{35}$	K 45; 70; 85 K	15.4
			K 135 I	8.6
(**11f**)	$C_{16}H_{33}$	$C_{17}H_{35}$	K 75—95; 98 K	12.3
			K 129 I	5.9
(**11g**)	$C_{18}H_{37}$	$C_{11}H_{23}$	K 55—59 K	3.3
			K 100—105 K	10.7
			K 132—135 I	7.1

[a] ^{1}H NMR of derivatives (**5**)—(**7**) ($R^2 = C_nH_{2n+1}$) ($CDCl_3$, 200 MHz): δ 0.87 (6H, t, 2Me), 1.25 [m, $(2n - 6)$ CH_2, 4Me, (**7**)], 1.62 (4H, m, 2 CH_2), 2.20 [6H, s, 2MeCO, (**5**)], 2.34 (4H, m, 2 CH_2CO), 2.54 [2H, m, 2 CHCO, (**7**)], 4.32 (4H, m, 2 CH_2O), 5.37 (1H, m, CHO), 7.5 (2H, s, Py), 7.7—7.9 (2H, br. s, NH). Py = pyridine. [b] ^{1}H NMR of derivatives (**11**) ($R^1 = C_mH_{2m+1}$, $R^2 = C_nH_{2n+1}$) ($CDCl_3$, 200 MHz): δ 0.88 (6H, t, 2Me), 1.30 [m, $(m + n - 6)$ CH_2], 1.6 (4H, m, 2 CH_2), 2.35 (2H, t, CH_2CO), 3.28 (2H, t, CH_2N), 4.16 (2H, s, NCH_2-C=), 5.52 (1H, s, 5-H), 8,15 (1H, s, NH), 9.40 (1H, s, NH). [c] Measured with a Perkin-Elmer microcalorimeter DSC2. K = crystalline phase, I = isotropic phase. 1 cal = 4.184 J.

enthalpies of transition of the pure compounds (**5**)—(**7**) and (**11**) and of a series of mixtures were determined by differential scanning microcalorimetry and are given in Tables 1 and 2.

Table 2. Transition temperatures (°C) and enthalpies [ΔH] (kcal mol^{-1}) for 1:1 mixtures of the compounds (**5**)—(**7**) and (**11**).[a]

Compound mixture	
(**11a**)/(**5b**)	K 30—56; 62—82 I
(**11b**)/(**5b**)	K 27—41; 62—74 I
(**11c**)/(**5b**)	K 33—49; 72—81 I
(**11d**)/(**5b**)	K 30—59; 67—87 I
(**11e**)/(**5a**)	K 30—46; 60—73 (M 71 [0.73]) I
(**11e**)/(**5b**)	K 40—45; 62—75 (M 72 [0.64]) I
(**11e**)/(**6b**)	K 34—39; 47—78 (M 57 [1.12]) I
(**11e**)/(**7b**)	K 36—55; 62—75 I
(**11f**)/(**5b**)	K 30—67; 72—82 (M 77 [0.94]) I
(**11g**)/(**5b**)	K 20—85 (M 73 [0.60]) I

[a] K = crystalline phase, (M) = metastable mesomorphic phase, I = isotropic phase. The ranges indicated cover several solid-solid transitions.

Several of the pure compounds show solid-state polymorphism but none of them presents a mesomorphic phase (Table 1). All the 1:1 mixtures studied melt below 90 °C (with crystalline polymorphism) and five of them display a *metastable mesomorphic phase*, confirmed by observation with a polarizing microscope (equipped with a variable temperature stage) and by *X*-ray diffraction. This mesophase is only observed when the aliphatic chains of (**11**) are long enough (**11e—g**). Shortening of these chains appears to have less effect in component (**5**) than in (**11**) since the mixtures (**11e**)/(**5b**) and (**11e**)/(**5a**) behave similarly. However, the nature of *N*-acyl groups of the 2,6-diaminopyridine unit seems to be of importance since the I → M transition (I = isotropic phase, M = metastable mesomorphic phase) takes place at a much lower temperature for (**11e**)/(**6b**) (R = Bu^n) than for (**11e**)/(**5b**) (R = Me) and disappears for (**11e**)/(**7b**) (R = Pr^i).

Since a triply hydrogen-bonded 1:1 complex has been established for an analogous system both in the solid state and in solution,[9—11] one may conclude that the same structure (**12**) is maintained in the mesomorphic phase and that it is the formation of (**12**) that induces the appearance of the mesophase. *X*-Ray diffraction data on the (**11e**)/(**5a**) and (**11f**)/(**5b**) mixtures agree with the mesophases being of the columnar hexagonal type. The columns, of 37.0 and 40.4 Å diameter respectively, are formed by a stack of plates, each of which contains two supermolecules (**12**) side-by-side, with a contact distance of 3.50 Å between successive plates. Such an arrangement is somewhat reminiscent of base pair stacking in double stranded DNA.

On the basis of solution data for similar series,[10] the variation in the *N*-acyl groups in (**5b**), (**6b**), and (**7b**) should not much affect the stability of the complexes. The destabilisation of the mesophase for the (**11e**)/(**7b**) (R = Pr^i) mixture would then not be due to steric hindrance at the binding sites but perhaps rather to packing perturbation due to the presence of a branched group on the central core, which is known to destabilize certain mesophases.[12]

The present results show that molecular recognition-dependent liquid crystals may be engineered, based on mesogenic supermolecules formed by association of complementary components. This amounts to a macroscopic reading of molecular information *via* a phase change which, being a highly co-operative process, also represents an amplification

of molecular recognition and information from the microscopic to the macroscopic level.‡

Numerous extensions may be envisaged, such as the use of components bearing several recognition subunits, the introduction of various central cores, in particular those already known to yield molecular liquid crystals,[1] the introduction of light- or electro-sensitive units, and the potential use for detection devices, as well as the extension to various recognition components of biological nature.[5]

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‡ Lipophilic compounds of type (**5**)—(**7**) and (**11**) might also be incorporated into organized assemblies such as molecular films or vesicles in order to confer recognition features on these species.[13]