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The Synthesis and Liquid Crystal Properties of Some 2,5-Disubstituted Pyridines

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The synthesis and liquid crystal properties of some 2,5-disubstituted pyridines

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The synthesis is reported of fifteen three-ring 2,5-disubstituted pyridines and two pyridine-*N*-oxides where the pyridine rings carry a variety of alkyl, aryl, cyclohexyl, cyclohexylethyl and fluorinated-aryl substituents. The mesomorphic transition temperatures for these compounds have been measured; all the compounds show enantiotropic phases. The different substituent effects are discussed and comparisons are made with previous work on analogous systems where the hetero-function is replaced by C–F.

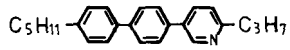
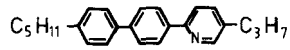
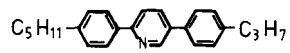
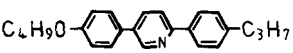
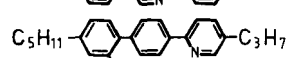
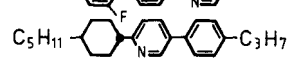
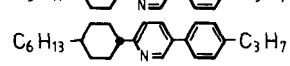
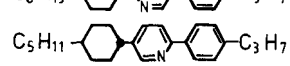
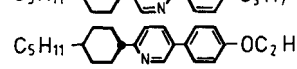
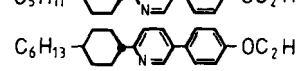
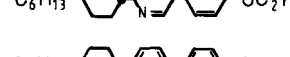
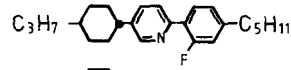
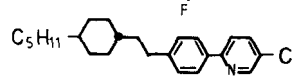
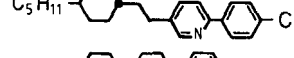
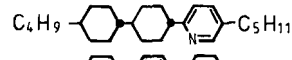
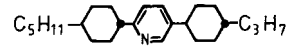
1. Introduction

We recently reported our results on the synthesis and liquid crystal properties of some 3,6-disubstituted-pyridazines [1]. The object of that work was to produce liquid crystals of negative dielectric anisotropy ($-\Delta\varepsilon$) which are required for electro-optic devices operating on a cholesteric-nematic phase change or guest-host principle to give displays of positive contrast. Pyridazine systems were chosen because the lateral dipole is produced by the lone pairs of electrons on the two nitrogen atoms which are part of the core of the molecule; consequently, these systems have similar molecular dimensions to those of benzene-containing molecules and the disadvantages of molecular broadening caused by lateral fluoro- or cyano-groups are avoided; $\Delta\varepsilon$ values of about $-9{\cdot}3$ have been reported for such systems [2]. Because some pyridazine derivatives may not be photochemically stable [3], ten different series of pyridazines were prepared with various combinations of alkyl, aryl, alkoxy, cyclohexyl, cyclohexylethyl groups etc. as the 3,6-substituents in order to determine whether or not the nature of the substituents affected the stability of the compounds. However, the photochemical stabilities and the resistivities of all of these compounds were found to be unsatisfactory. Pyridines are known to be more thermally and photochemically stable than pyridazines, and although the lone pair of electrons on a single nitrogen atom would not be expected to give as large values of $-\Delta\varepsilon$, it may still be possible, either by appropriate, additional fluoro-substitution or by formation of the *N*-oxides, to devise 2,5-disubstituted pyridines of moderate $-\Delta\varepsilon$ value and possibly with other desirable physical properties. With this objective we have prepared a range of 2,5-disubstituted pyridines, or pyridine *N*-oxides containing three ring systems; in this paper we report their preparation and transition temperatures, and make some comparisons of the liquid crystal behaviour of these and related systems.

2. Results and discussion

The transition temperatures for the seventeen compounds prepared are given in the table; all show enantiotropic phases. Detailed comparisons of trends within an

Transition temperatures (°C) for 2,5-disubstituted-pyridines and -pyridine-*N*-oxides.

		C	Sx†	S_H	S_E	S_G	S_B	S_A	N	I
(1)			●	163	●	178	●	211	●	222 ●
(2)		●							171 ●	198 ●
(3)‡		●	86 ●			91	●	164 ●	201 ●	203 ●
(4)		●	136	●		151	●	192 ●	233 ●	237 ●
(5)		●							50 ●	138 ●
(6)		●				58	●	124 ●	134 ●	156 ●
(7)		●				94	●	127 ●	134 ●	147 ●
(8)		●				48	●	163 ●	184 ●	185 ●
(9)		●						114 ●	134 ●	194 ●
(10)		●				91	●	100 ●	147 ●	190 ●
(11)		●							47 ●	149 ●
(12)		●			36	● 53	●		100 ●	150 ●
(13)		●				52	●	133 ●		150 ●
(14)		●				< 20	●			164 ●
(15)		●				< −15	●			157 ●
(16)		●						194 ●		225 ●
(17)		●						120 ●		213 ●

† Smectic phase not yet identified.

‡ The transition temperatures of some pyridines similar to this have been reported in: *Flüssige Kristalle in Tabellen*, 1974, edited by D. Demus, H. Demus and H. Zaschke (VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1974), nos. 4000–4008; see K.-D. Münzner Dissertation, Halle 1969.

The mesophases were identified by optical microscopy and have not been confirmed by miscibility or X-ray studies.

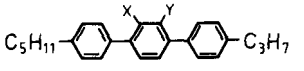
homologous series are not possible from this selection of compounds as the object of the selection was to provide a wide variety of structural types. However, some marked changes in mesophase types and transition temperatures have been noted and these are now discussed.

Compounds 1, 2 and 3 illustrate the effect produced by placing the nitrogen atom at different positions in the terphenyl core when the terminal groups are kept constant. With the nitrogen atom *ortho-* to the terminal alkyl chain (compound 1), the compound shows strong S_A character along with a pronounced tendency for more ordered phases. With the nitrogen atom at an internal position, a high melting point (possibly

concealing smectic properties) and solely nematic compound (2) or a much lower melting point nematogen 3, also with S_A and S_B phases is produced; the clearing points for the latter two compounds are closely similar. This difference between isomers in the multiplicity and thermal stabilities of mesophases is reminiscent of the marked differences caused by the different locations of a fluoro-substituent in terphenyl systems [4].

The effect of fluoro-substitution is illustrated by a comparison of the values for compounds 2 and 5; the former compound is solely nematogenic, and so the expected ability of fluorine to depress smectic phases is not seen but, as is the case with terphenyls [4], fluoro-substitution gives a marked depression of melting point (121°C) and a significant (60°C) depression of the clearing point; the corresponding depressions in lateral fluoro-substituted terphenyls are approximately 136°C and 55°C, respectively [4]. The fluoro-substituted compound 11 is also solely nematogenic and, although the values for the parent compound are not available for direct comparison, the smectic phases shown by compound 8 up to 184°C almost certainly indicate that the lateral fluoro-substituent in compound 11 has caused a substantial depression in S_A and probably S_B thermal stability.

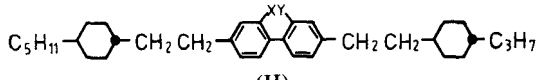
The alkoxy compound 4 cannot be compared directly with any alkyl compound listed to give a direct indication of the influence of an alkoxy group, but the approximate comparison with compound 3 indicates a high melting point and enhanced thermal stability for all the mesophases, so that this compound has the highest clearing point of all the compounds prepared; such a comparison must however be regarded with caution because of the uncertainty of the effect caused by the different position of the nitrogen atom (see later for the comparison of the transition temperatures of compounds 6 and 8). We might have anticipated that the location of the nitrogen atom at either position in the central ring would have only a minor effect, and yet the similar transposition of a fluoro-substituent in terphenyls has given a marked change in mesophase types and stabilities. For example, compounds I *a*



(I)

a, $X = F$, $Y = H$ C 50·0°C N 140·6°C I
b, $X = H$, $Y = F$ C 61·0°C S_A 99·5°C N 141·5°C I

and I *b* have similar nematic thermal stabilities but I *a* is significantly less smectogenic [4]. In a slightly different context, similar variations have also been noted in the transition temperatures for compounds such as II *a* and *b*. Here, also, the T_{N-I} values are



(II)

a, $X = H$, $Y = F$ C 76·4°C S_B 103·5°C S_A 123·3°C N 207·1°C I
b, $X = F$, $Y = H$ S_J 81·3°C S_B 110·1°C S_A 139·0°C N 206·0°C I

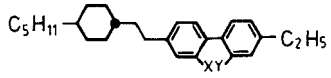
closely similar, but the higher S_A and S_B thermal stabilities are shown for the compound (II *b*) in which the C–F bond points towards the shorter terminal alkyl chain [5]. A third example of the subtle effects of fluoro-substitution on transition temperatures and its similarity to the effect caused by the position of the nitrogen atom in analogous pyridines is discussed later (see compounds III *a* and *b*).

All the other pyridines contain at least one cyclohexane ring and for the dialkyl systems 6, 7 and 8 show an S_B, S_A, N sequence of phases. The introduction of a

cyclohexyl ring (compare compounds 3 and 6) causes a reduction in the thermal stability of all mesophases of between about 30 and 67°C. Frequently cyclohexane is notable for its ability to increase the thermal stability of a mesophase [6], but when the parent system is flat and consists predominantly of π-electron regions, the introduction of a non-planar cyclohexane unit can be a disadvantage [6–8]. The alkoxy compounds 9 and 10 have higher clearing points than their alkyl analogues 6 and 7, respectively (cf. the less reliable comparison of compounds 4 and 3).

Comparison of the values for compounds 6 and 8 illustrates the effect of a different location of a nitrogen atom in the cyclohexylbiphenyl system; for compound 8 all the mesophases have significantly higher thermal stabilities of between 29 and 50°C and these differences are similar to those noted for 2′-fluoro- and 3′-fluoro-substituted 4-pentyl-4″-propylterphenyls [4] and emphasize the uncertainty referred to earlier in the comparison of compounds 4 and 3. One difference, however, between the fluoroterphenyls and compounds 6 and 8 is that the former compounds have almost identical nematic thermal stability (to within 1 or 2°C) whereas the corresponding stabilities for compounds 6 and 8 differ by 29°C; this difference may result from the cyclohexane ring present in compounds 6 and 8.

The pair of compounds 12 and 13 make an interesting comparison with each other and with the related fluoro-substituted cyclohexylethylbiphenyls III *a* and *b* [9, 10]. As with the fluoro-substituted terphenyls,



(III)

a $X = H$, $Y = F$ C 24°C (S 14°C) N 103°C I
b, $X = F$, $Y = H$ C 23°C S 27°C S 56°C N 105°C I

so also for fluoro-substituted cyclohexylbiphenyls such as III *a* and *b*, it has been noted that there is a pronounced difference in mesophase thermal stabilities for the compounds with the fluorine at the different positions *ortho*- to the interannular bond, but these compounds have almost the same clearing point. So far, the reasons for these differences are not understood, but compounds 12 and 13 provide another example of this unusual effect. The clearing points of compounds 12 and 13 are the same but compound 13 is significantly more smectic in character, being S_B up to 133°C and then S_A until it clears at 150°C. On the other hand, the isomeric compound 12 is S_B up to 100°C and is then nematic; i.e. the thermal stability of its S_B phase is lower by 33°C and its S_A character is lower by at least 50°C. Each of these compounds has a low melting point, as for compounds III *a* and *b*. For compounds 14 and 15 with two cyclohexyl rings, the strong S_B tendencies of a cyclohexyl ring now predominate and the compounds are of low melting point and are solely S_B in character. Comparison of compounds 3, 6 and 15 shows that after the initial depression of clearing point (and all mesophase stabilities; see the previous discussion) caused by introducing one cyclohexyl ring, the second cyclohexyl ring has a negligible effect on the clearing point but significantly increases the S_B thermal stability. This situation can be rationalised as resulting from a cancellation of opposing effects, namely the tendency of cyclohexane *vis-a-vis* benzene to enhance mesophase stability in conflict with an inhomogeneous molecular structure with saturated (zig-zag)/unsaturated (planar) regions which would depress mesophase thermal stability. Two pyridine *N*-oxides were prepared and both show qualitatively similar changes in liquid crystal behaviour. Compound 16 (from 3) shows a much higher melting point and enhanced S_A character and compound 17 (from 7) has a higher melting point and a much higher

clearing point, and both oxides are solely S_A. The strong S_A character of pyridine *N*-oxides has been noted previously [11, 12].

3. Experimental

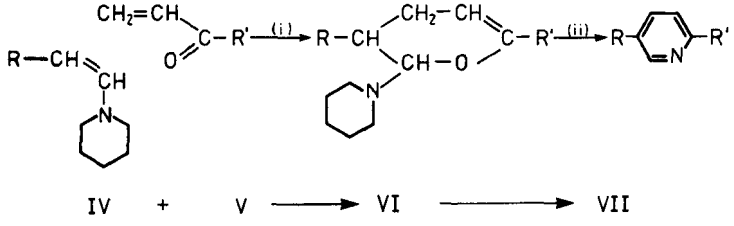
All final products were shown to be pure by tlc, glc or hplc analysis. Structural confirmation of final products and intermediates was obtained by ^1H N.M.R. spectroscopy (Jeol JNMPM × 60 spectrometer), infrared spectroscopy (Perkin-Elmer 457 grating spectrometer) and mass spectrometry (AEI MS 902 mass spectrometer).

Transition temperatures were measured using a Mettler FP5 hot stage and control unit in conjunction with an Olympus BDSP 753 polarising microscope. Sometimes calorimetry was used to confirm transition temperatures (Perkin–Elmer DSC-2C with data station).

The following compounds were provided by BDH Ltd (Poole, Dorset) under MOD Contract DCVD AT/2119/013; *trans*-4-propyl- and pentyl-cyclohexylacetic acids, *trans*-4-pentyl- and hexyl-cyclohexanecarboxylic acids, 4-pentylbiphenyl, 2-fluoro-4-pentylbiphenyl, and 4′-pentylbiphenyl-4-carboxylic acid. *trans*-4-(*trans*-4-Butyl-cyclohexyl)cyclohexanecarboxylic acid was supplied by E. Merck (Darmstadt, F.R. Germany).

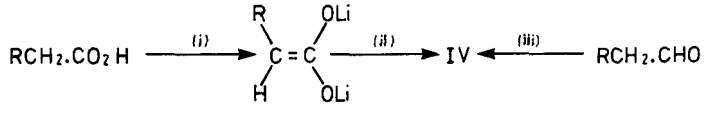
4-Propylphenylacetic acid, 4-ethoxyphenylacetic acid and 4′-pentylbiphenyl-4-ylacetic acid were prepared by Friedel-Crafts acetylation of the appropriate aromatic system followed by a Willgerodt reaction on the methyl ketone.

The synthesis of the pyridines, outlined in Scheme 1 and based on the method reported by Botteghi *et al.* [13], involves the reaction of an enamine (IV) with an appropriate vinyl ketone (V) to give a dihydropyran (VI). The reaction of (VI) with hydroxylamine hydrochloride gives a pyridine (VII).



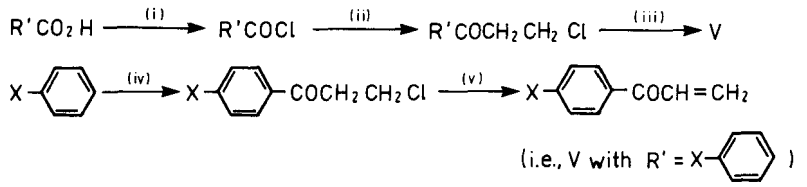
Scheme 1. (i) THF, room temperature. (ii) H_2O/EtOH, $NH_2OH.HCl$, heat.

Two methods (see Scheme 2) were used to produce the required enamines; in simple cases, e.g. for 1-piperidinopent-1-ene, the enamine was prepared from the aldehyde and piperidine, but in other cases it was more convenient to prepare the enamine from the carboxylic acid by using the method of Knorr *et al.* [14].



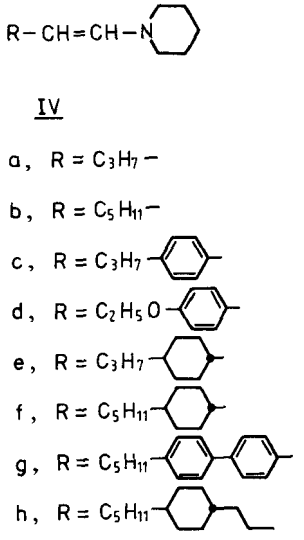
Scheme 2. (i) iPr_2NLi, THF, < 10°C. (ii) *N*-(Methoxymethylene)piperidinium methyl sulphate, −70°C. (iii) piperidine, K_2CO_3.

The vinyl ketones were prepared by one of two methods shown in Scheme 3. For non-aromatic systems an acid chloride was reacted with ethene and aluminium



Scheme 3. (i) $SOCl_2$. (ii) $CH_2{=}CH_2$, $AlCl_3$, CH_2Cl_2. (iii) Et_3N, THF. (iv) $ClCH_2CH_2COCl$, $AlCl_3$, CH_2Cl_2. (v) Et_3N, THF (*in situ*).

trichloride to give a 1-substituted-3-chloropropan-1-one which was reacted with triethylamine to give the vinyl ketone either separately or in the presence of the enamine. For aromatic systems, a Friedel–Crafts reaction with 3-chloropropanoyl chloride to give the 1-substituted-3-chloropropan-1-one was the preferred method. Representative procedures are given later. The enamines IV *a–h* and vinyl ketones V *a–j* were required for the preparation of the pyridines 1–15.



Enamines (IV *a–h*)

1-(N-Piperidinyl)pent-1-ene (IV *a*) (b.p. 101–104°C/18 mm Hg; yield 70 per cent) was prepared by a conventional procedure from pentanal and piperidine as described in [15] and [16]. *1-(N-Piperidinyl)hept-1-ene* (IV *b*) (b.p. 123–124°C/18 mm Hg; yield 73 per cent) was prepared following the same procedure.

1-(N-Piperidinyl)-2-(4-propylphenyl)ethene (IV *c*). A solution of *n*-butyllithium in hexane (9·5 M, 30·9 ml, 0·294 mole) was added to di-isopropylamine (29·68 g, 0·293 mole) in tetrahydrofuran (25 ml) at −20°C under nitrogen. The solution was allowed to warm to room temperature and then the stirred solution was cooled in ice-water whilst a solution of 4-propylphenylacetic acid (26·11 g, 0·147 mole) in dry tetrahydrofuran (150 ml) was added dropwise keeping the temperature below 10°C. The mixture was stirred at room temperature for 1 h, and volatile material was removed by rotary evaporation using an oil pump. The orange, glassy residue was dissolved in tetrahydrofuran (300 ml) and cooled to −70°C, and *N*-(methoxymethylene)piperidinium methyl sulphate [17] was added dropwise with stirring. The sulphate

remained as a semi-solid suspension which slowly dissolved, with an exothermic reaction, when the solution was warmed above −30°C. The solution was allowed to warm to room temperature and then stirred for 1 h.

The two-phase mixture was poured into ice-cold 2 M-sodium hydroxide (500 ml) and the resultant mixture was washed with ether (3 × 400 ml). The combined ether washings were washed with water (300 ml), dried ($MgSO_4$) and finally concentrated to give compound (X *c*) as an orange, viscous oil which was used without further purification; yield 29·3 g, 85 per cent; $^1H(CDCl_3)\delta$ 0·7–2·0 (11H, m), 2·1–3·2 (6H, m), 5·2–5·4 (1H, d), 6·5–6·7 (1H, d), 6·8–7·2 (4H, m). The following compounds were prepared by using the procedure described for compound (IV *c*).

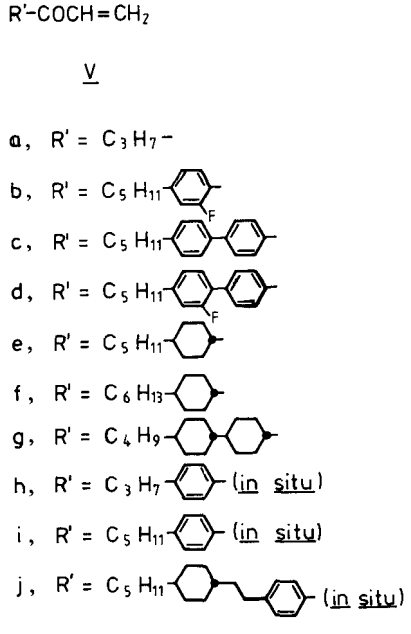
1-(4-Ethoxyphenyl)-2-(N-*piperidinyl)ethene* (IV *d*) (from 4-ethoxyphenylacetic acid). M.p. 70–74°C; $^1H(CDCl_3)\delta$ 1·1–1·9 (9H, m), 2·2–3·2 (4H, m), 3·7–4·3 (2H, q), 5·2–5·5 (1H, d) 6·4–6·7 (1H, d), 6·6–7·3 (4H, m).

1-(N-*Piperidinyl)-2-*(trans-*4-propylcyclohexyl)ethene* (IV *e*) (from *trans*-4-propylcyclohexylacetic acid). Crude yield 35 per cent; $^1H(CDCl_3)\delta$ 0·8–2·0 (22H, m), 2·5–2·9 (5H, m), 4·2–4·7 (1H, dd), 5·8–6·1 (1H, d).

1-(trans-*4-Pentylcyclohexyl)-2-*(N-*piperidinyl)ethene* (IV *f*) (from *trans*-4-pentylcyclohexylacetic acid). Yield 29 per cent; $^1H(CDCl_3)\delta$ 0·8–2·0 (26H, m), 2·5–2·9 (5H, m), 4·2–4·7 (1H, dd), 5·8–6·1 (1H, d).

1-(4'-Pentylbiphenyl-4-yl)-2-(N-*piperidinyl)ethene*) (IV *g*) (from 4'-pentylbiphenyl-4-ylacetic acid). Crude yield 95 per cent; $^1H(CDCl_3)\delta$ 0·5–2·3 (15H, m), 2·3–4·0 (6H, m), 5·2–5·3 (1H, d), 6·9–8·1 (9H, m).

1-(trans-*4-Pentylcyclohexylethyl)-2-*(N-*piperidinyl)ethene* (IV *h*) (from 4-(*trans*-4-pentylcyclohexyl)butanoic acid [18]). Crude yield 90 per cent; $^1H(CDCl_3)\delta$ 0·8–2·0 (29H, m), 2·5–2·9 (6H, m), 4·2–4·7 (1H, m), 5·8–6·1 (1H, d).



Vinyl ketones (V *a–j*)

The following compounds were prepared by using the procedure described for compound V *f*.

Hex-1-en-3-one (V *a*) (from butanoyl chloride); b.p. 32°C/20 mm Hg, yield 54 per cent; ^{1}H($CDCl_3$)δ 0·7–1·2 (3H, t), 1·2–2·0 (2H, m), 2·4–2·7 (2H, t), 5·6–6·4 (3H, m).

1-(2-Fluoro-4-pentylphenyl)prop-2-en-1-one (V *b*) (from 2-fluoro-4-pentylbenzoic acid [18]) was generated *in situ* from the chloropropanone.

1-(4′-Pentylbiphenyl-4-yl)prop-2-en-1-one (V *c*) (from 4′-pentylbiphenyl-4-carboxylic acid) was generated *in situ* from the chloropropanone which had m.p. 66–68°C (72 per cent yield); ^{1}H($CDCl_3$)δ 0·7–2·2 (9H, m), 2·4–2·7 (2H, t), 3·1–3·6 (2H, t), 3·6–4·1 (2H, t), 6·8–8·1 (8H, m).

1-(2′-Fluoro-4′-pentylbiphenyl-4-yl)prop-2-en-1-one (V *d*) (from 2′-fluoro-4′-pentylbiphenyl-4-carboxylic acid, prepared from 2-fluoro-4-pentylbiphenyl by reaction with oxalyl chloride-aluminium trichloride, followed by hydrolysis [19] was generated *in situ* from the chloropropanone (78 per cent yield) which had ^{1}H($CDCl_3$)δ 0·6–1·9 (9H, m) 2·5–2·9 (2H, t), 3·3–3·7 (2H, t), 3·7–4·2 (2H, t), 6·7–8·2 (7H, m).

1-(trans-*4-Pentylcyclohexyl)prop-2-en-1-one* (V *e*) (from *trans*-4-pentylcyclohexanecarboxylic acid); b.p. 87°C/0·07 mm Hg, yield 69 per cent; ^{1}H($CDCl_3$)δ 0·6–2·3 (20H, m), 2·2–2·8 (1H, m), 5·4–6·4 (3H, m).

1-(trans-*4-Hexylcyclohexyl)prop-2-en-1-one* (V *f*)

trans-*4-Hexylcyclohexanecarboxylic acid chloride* (VIII). *trans*-4-Hexylcyclohexanecarboxylic acid (21·2 g, 0·1 mole) was added to thionyl chloride (50 ml) and the mixture was heated under reflux for two hours. The excess of thionyl chloride was removed *in vacuo* and the residue was distilled to give compound (VIII) as a clear liquid; b.p. 151–154°C/20 mm Hg, yield 17·3 g, 75 per cent.

1-(trans-*4-Hexylcyclohexyl)-3-chloropropan-1-one* (IX). Compound (VIII) (14·0 g, 0·0607 mole) was added dropwise over 15 min to a suspension of anhydrous aluminium trichloride (8·09 g, 0·0607 mole) in dichloromethane (40 ml) under an atmosphere of nitrogen at 0–5°C. The mixture was stirred at 0°C until all the solution had dissolved ($\frac{1}{2}$–1 h). The clear solution was then cooled to -10°C in an ice-salt bath and, with vigorous stirring, ethene was bubbled into the solution at a rate that equalled the rate at which it dissolved. When no more ethene was being dissolved (6 h), the excess of ethene was driven off by blowing nitrogen through the solution. The solution was then poured slowly into a mixture of ice and 2 M-HCl. The organic layer was separated and the aqueous layer was washed (dichloromethane, 2 × 40 ml). The combined organic layers were washed with water (2 × 50 ml) and dried ($MgSO_4$). Evaporation of the solvent gave crude IX as a viscous, orange liquid which was used without further purification; yield 12·6 g, 80 per cent.

Crude IX (12·6 g, 0·0487 mole) was dissolved in dry tetrahydrofuran (50 ml) and triethylamine (10·8 g, 0·107 mole) was added dropwise over 5 min at room temperature. The mixture was heated under reflux under nitrogen for 3·5 h. The solid triethylamine hydrochloride was filtered off and washed with a small amount of dichloromethane. The solvents were removed from the filtrate and the residue was taken up in dichloromethane (50 ml), washed successively with water (50 ml) and aqueous sodium hydrogen carbonate (50 ml) and dried ($MgSO_4$). The solvent was removed and the residue was distilled to give compound V *f* as a clear liquid; b.p. 60–63°C/0·03 mm Hg; ^{1}H($CDCl_3$)δ 0·7–2·2 (22H, m), 2·2–2·8 (1H, m), 5·4–6·4 (3H, m).

1-[trans-*4-*(trans-*4-Butylcyclohexyl)cyclohexyl]*prop-2-en-1-one* (V *g*) (from *trans*-4-(*trans*-4-butylcyclohexyl)cyclohexanecarboxylic acid) was generated *in situ* from the chloropropanone (50 per cent yield) which had ^{1}H($CDCl_3$)δ 0·6–2·5 (29H, m), 2·8–3·2 (2H, t), 3·6–4·0 (2H, t).

1-(4-Propylphenyl)prop-2-en-1-one (V *h*) was generated *in situ* from 3-chloro-1-(4-propylphenyl)propan-1-one (X) which was prepared in the following way.

3-Chloro-1-(4-propylphenyl)propan-1-one (X). Propylbenzene (12·0 g, 0·1 mole) and 3-chloropropanoyl chloride (12·7 g, 0·1 mole) were added simultaneously and dropwise to a suspension of anhydrous aluminium trichloride (13·5 g, 0·1 mole) in dichloromethane (50 ml) at 0°C. The mixture was then stirred overnight at room temperature and poured into a water-ice mixture. The organic layer was separated, and the aqueous layer washed with dichloromethane (2 × 50 ml). The combined organic layers were washed with water (2 × 100 ml) and dried ($MgSO_4$). The solvents were removed to give a dark brown oil which crystallized on cooling. The solid was crystallized from light petroleum (b.p. 40–60°C) several times; yield 12·2 g, 58 per cent, m.p. 54–56°C; $^1H(CDCl_3)\delta$ 0·5–1·2 (3H, t), 1·2–2·0 (2H, m), 2·3–2·8 (2H, t), 3·1–3·7 (2H, t), 3·7–4·1 (2H, t), 7·0–8·0 (4H, m).

1-(4-Pentylphenyl)prop-2-en-1-one (V *i*) was generated *in situ* from 3-chloro-1-(4-pentylphenyl)propan-1-one (XI) (prepared from pentylbenzene in a similar way to that described for compound (X)).

3-Chloro-1-(4-pentylphenyl)propan-1-one (XI), yield 68 per cent, m.p. 49–51°C; $^1H(CDCl_3)\delta$ 0·5–2·0 (9H, m), 2·3–2·8 (2H, t), 3·1–3·6 (2H, t), 3·6–4·0 (2H, t), 7·0–8·0 (4H, m).

1-(4-[trans-4-Pentylcyclohexylethyl]phenyl)prop-2-en-1-one (V *j*) was generated *in situ* from 3-chloro-1-(4-[*trans*-4-pentylcyclohexylethyl]phenyl)propan-1-one (XII) (prepared from *trans*-4-pentylcyclohexylethylbenzene in a similar way to that described for compound (X)). *trans*-4-Pentylcyclohexylethylbenzene was prepared from benzene and *trans*-4-pentylcyclohexylacetyl chloride in a standard Friedel–Crafts reaction (m.p. of ketone 43–45°C; yield 83 per cent), followed by a Huang–Minlon reduction (b.p. 125°C/0·3 mm Hg; yield 70 per cent).

3-Chloro-1-(4-[trans-4-pentylcyclohexylethyl]phenyl)propan-1-one (XII), yield 73 per cent, m.p. 73–74°C; $^1H(CDCl_3)\delta$ 0·5–2·3 (23H, m), 2·4–2·9 (2H, t), 3·1–3·5 (2H, t), 3·6–4·1 (2H, t), 7·0–8·0 (4H, m).

Pyridines

Two general methods of preparation and a third procedure are now described. The preparative routes to the other pyridines are then given in an abbreviated form.

2-(trans-4-Hexylcyclohexyl)-5-(4-propylphenyl)pyridine (7). Compound (V *f*) (1·11 g, 500 mmole) and compound (IV *c*) (1·15 g, 502 mmole) were dissolved in dry tetrahydrofuran (10 ml) and stirred at room temperature for 72 h [13]. The solvent was removed and the viscous residue was suspended in water–ethanol (1 : 1, 3 ml); hydroxylamine hydrochloride (1·55 g, 0·0223 mole) was added and the mixture was heated under reflux for 24 h. The solvent was removed under reduced pressure and the residue was taken up in ether (20 ml) and the organic layer was washed with sodium hydrogen carbonate (10 per cent, 20 ml), water (20 ml) and dried ($MgSO_4$). The ether was removed and the residue was purified by column chromatography on neutral alumina with chloroform-light petroleum (b.p. 40–60°C) (1 : 2) as the eluent. The product was crystallized several times (hexane) to give compound (7) as a white solid which was shown to be pure by hplc and tlc; yield 0·42 g, 23 per cent; $^1H(CDCl_3)\delta$ 0·6–2·3 (27H, m), 2·3–3·0 (3H, m), 7·0–7·9 (6H, m), 8·7–8·9 (1H, m).

5-(trans-4-Pentylcyclohexyl)-2-(4-propylphenyl)pyridine (8). Triethylamine (2·02 g, 0·02 mole) was added dropwise to a stirred solution of compound (X) (4·16 g, 0·0198 mole) in dry tetrahydrofuran (5 ml). Large amounts of a precipitate were

formed and the suspension was stirred for 1 h at room temperature. A solution of compound (IV *f*) (5·25 g, 0·0198 mole) in tetrahydrofuran (5 ml) was added and the mixture was stirred for 72 h.

The solvent was removed to give an orange solid which was dissolved in ethanol–water (1 : 1, 10 ml) and then heated under reflux with vigorous stirring with hydroxylamine hydrochloride (4·11 g, 0·059 mole) for 72 h. The solvent was evaporated and the brown residue was treated with sodium hydroxide solution (10 per cent, 100 ml) and ether (50 ml). The ethereal layer was separated and the aqueous layer was washed with ether (2 × 50 ml). The combined ether layers were washed with water (100 ml) and dried ($MgSO_4$). After removal of solvent, the residue was purified by column chromatography [neutral alumina, light petroleum (b.p. 40–60°C)–chloroform (2 : 1)] to give a white solid which was crystallized (hexane) to give compound (8) which was shown to be pure by hplc and tlc; yield 1·93 g, 28 per cent; $^1H(CDCl_3)\delta$ 0·7–2·2 (25H, m), 2·2–2·9 (3H, m), 7·2–8·4 (6H, m), 8·6–8·9 (1H, m).

The following compounds were purified by column chromatography (neutral alumina) followed by recrystallization to give products which were pure by hplc and tlc analysis.

5-(4′-Pentylbiphenyl-4-yl)-2-propylpyridine (*1*), from compound (V *a*) and compound (IV *g*). Yield 21 per cent $^1H(CDCl_3)\delta$ 0·7–2·1 (14H, m), 2·5–3·0 (4H, m), 7·2–8·3 (10H, m), 8·4–8·7 (1H, m).

2-(4′-Pentylbiphenyl-4-yl)-5-propylpyridine (*2*) from compound (V *c*) and compound (IV *a*). Yield 16 per cent; $^1H(CDCl_3)\delta$ 0·6–2·0 (14H, m), 2·4–2·9 (4H, m), 7·1–8·2 (10H, m), 8·5–8·7 (1H, m).

2-(4-Pentylphenyl)-5-(4-propylphenyl)pyridine (*3*), from compound (V *i*) and compound (IV *c*). Yield 19 per cent; $^1H(CDCl_3)\delta$ 0·8–2·2 (14H, m), 2·7–3·1 (4H, t), 7·5–8·5 (10H, m), 8·3–8·5 (1H, m).

5-(4-Butoxyphenyl)-2-(4-propylphenyl)pyridine (*4*) was prepared by reaction of 4-propylphenyllithium with pyridine, followed by addition of 4-iodobutoxybenzene to the reaction intermediate (see [20]). Yield 7 per cent; $^1H(CDCl_3)\delta$ 0·7–2·1 (12H, m), 2·4–2·6 (2H, t), 3·8–4·2 (2H, t), 6·8–8·0 (10H, m), 8·7–8·9 (1H, m).

2-(2′-Fluoro-4′-pentylbiphenyl-4-yl)-5-propylpyridine (5) was prepared from compound (V *d*) and compound (IV *a*). Yield 19 per cent; $^1H(CDCl_3)\delta$ 0·7–2·1 (14H, m), 2·4–2·9 (4H, m), 6·9–8·3 (9H, m), 8·5–8·7 (1H, m).

2-(trans-*4-Pentylcyclohexyl*)*-5-(4-propylphenyl)pyridine* (6) was prepared from compound (V *e*) and compound (IV *c*). Yield 18 per cent; $^1H(CDCl_3)\delta$ 0·7–2·3 (25H, m), 2·3–3·0 (3H, m), 7·0–7·9 (6H, m), 8·8–9·0 (1H, m).

5-(4-Ethoxyphenyl)-2-(trans-*4-pentylcyclohexyl*)*pyridine* (9) was prepared from compound (V *e*) and compound (IV *d*). Yield 17 per cent; $^1H(CDCl_3)\delta$ 0·6–3·0 (24H, m), 3·8–4·4 (2H, q), 6·8–7·9 (6H, m), 8·7–8·9 (1H, m).

5-(4-Ethoxyphenyl)-2-(trans-*4-hexylcyclohexyl*)*pyridine* (10) was prepared from compound (V *f*) and compound (IV *d*). Yield 14 per cent; $^1H(CDCl_3)\delta$ 0·5–2·9 (26H, m), 3·8–4·4 (2H, q), 6·8–7·9 (6H, m), 8·7–9·0 (1H, m).

2-(2-Fluoro-4-pentylphenyl)-5-(trans-*4-propylcyclohexyl*)*pyridine* (11) was prepared from compound (V *b*) and compound (IV *e*). Yield 14 per cent.

2-(4-[trans-*4-Pentylcyclohexylethyl*]*phenyl)-5-propylpyridine* (12) was prepared from compound (V *j*) and compound (IV *a*). Yield 34 per cent; $^1H(CDCl_3)\delta$ 0·5–2·2 (28H, m), 2·2–2·9 (4H, m), 7·1–8·1 (6H, m), 8·4–8·7 (1H, m).

5-(trans-*4-Pentylcyclohexylethyl*)*-2-(4-propylphenyl)pyridine* (13) was prepared from compound (V *h*) and compound (IV *h*). Yield 11 per cent; $^1H(CDCl_3)\delta$ 0·6–2·2 (28H, m), 2·5–2·9 (4H, m), 7·2–8·3 (6H, m), 8·6–8·8 (1H, m).

2-[trans-*4*-(trans-*4*-*Butylcyclohexyl*)*cyclohexyl*]-*5*-*pentylpyridine* (14) was prepared from compound (V *g*) and compound (IV *b*). Yield 8 per cent; ^{1}H($CDCl_3$)δ 0·6–2·2 (37H, m), 2·3–2·8 (3H, m), 6·9–7·6 (2H, m), 8·2–8·4 (1H, m).

2-(trans-*4*-*Pentylcyclohexyl*)-*5*-(trans-*4*-*propylcyclohexyl*)*pyridine* (15) was prepared from compound (V *e*) and compound (IV *e*). Yield 10 per cent.

The pyridine oxides (16 and 17) were prepared by oxidation of the appropriate pyridine using *m*-chloroperbenzoic acid in dichloromethane [21].

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