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Liquid crystal properties of some substituted pyrazines

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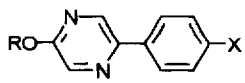
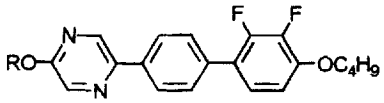
A number of biphenyl, terphenyl analogues and ethynes which contain a pyrazine ring have been made and their liquid crystal transition temperatures, together with examples of birefringence measurements, are reported. All the 2,5-disubstituted pyrazine systems are liquid crystalline showing high birefringence values for the biphenyl and terphenyl analogues, whereas the 1,5-disubstituted systems are not liquid crystalline. The pyrazine ethyne systems exhibit very high birefringence values. X-ray diffraction has been used to identify the liquid crystal phases of 2-*n*-nonyloxy-5-(4′-propylbiphenyl-4-yl)pyrazine.

1. Introduction

Although not studied extensively, pyrazine containing liquid crystals have been previously reported. For example, biphenyl, terphenyl and ester type molecules have been prepared which contain a pyrazine ring and their liquid crystal properties evaluated [1–4]. We have synthesized a range of novel pyrazine containing liquid crystal systems (see **I, II, III, IV, V** and **VI**) by the routes shown in the synthetic schemes. The liquid crystal transition temperatures for forty members of these series, together with examples of estimates of birefringence for each system are reported here. This work was carried out as part of a programme to investigate the potential of different pyrazine systems for high birefringence applications such as polymer dispersed liquid crystals.



I(X = Cl) **II**(X = Br)



V

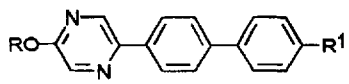
R = H or C_nH_{2n+1}

An interesting range of liquid crystal behaviours is shown by these compounds. Transition temperatures for members of the different series (**I–VI**) are listed in the tables 1–6, and are shown plotted against the number of carbon atoms (n) in the terminal alkyl chain (for series **I–V**) in the corresponding figures 1–5. Estimates of birefringence for each type of compound are given in table 7. Liquid crystal phase types were identified from optical textures observed during thermal microscopy and in one case the phase type was confirmed by X-ray diffraction.

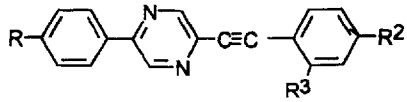
2. Results and discussion

2.1. *Systems of type* **I** *and* **II**

The liquid crystal transition temperatures (see table 1) of the 2-*n*-alkoxy-5-(4-chlorophenyl)pyrazines (**I**) are



III($R^1 = C_3H_7$) **IV**(R^1 = F)



VI($R^2 = C_5H_{11}$ or Cl when R^3 = F or H)

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Table 1. Transition tempertures (°C) of the 2-*n*-alkoxy-5-(4-chlorophenyl)pyrazines (**I**).

n	Cr–I	Cr–S_A	S_A–I	S_A–Cr
4	64·2	—	(61·8)	60·2
5	73·9	—	(63·9)	61·5
6	65·9	—	(65·2)	62·5
7	—	64·5	65·9	61·2
8	—	59·7	66·0	57·4
9	65·9	—	(64·9)	51·5
10	65·1	—	(63·9)	46·0
12	71·6	—	(61·0)	59·5

( ) indicate a monotropic transition.

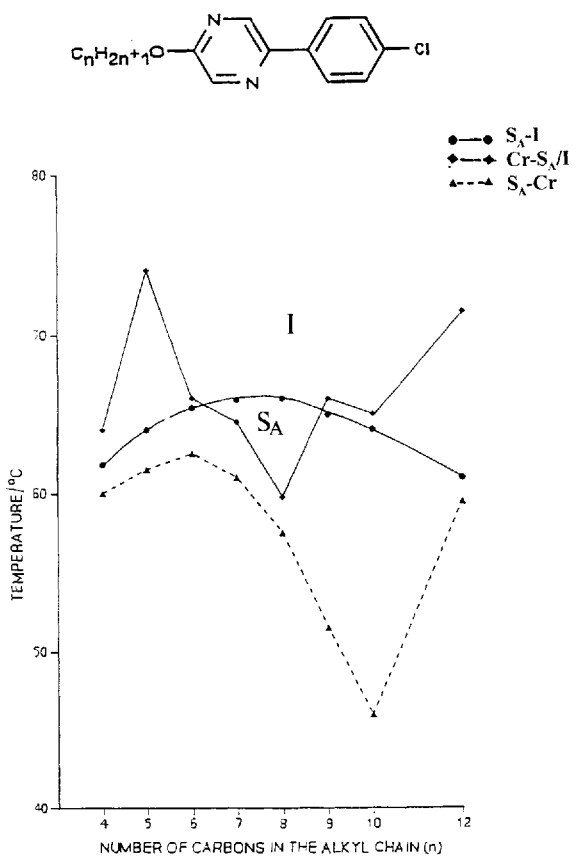


Figure 1. The transition temperatures (°C) against the alkyl chain length (*n*) for the 2-*n*-alkoxy-5-(4-chlorophenyl)pyrazines (**I**).

plotted against *n*, the number of carbon atoms in the alkoxy chain in figure 1. For the homologues made, the series exhibits only a smectic A phase with the S_A–I temperatures lying on a smooth curve rising to $n = 8$ and then falling to $n = 12$.

For the 2-*n*-alkoxy-5-(4-bromophenyl)pyrazines (**II**) (see figure 2 and the table 2) the plot of smectic A to isotropic transition temperatures against *n* shows similar characteristics to series **I**, except that the smoothly rising curve reaches a maximum at $n = 7$. At the time of preparation, there was no reference to the synthesis of any members of this series in the literature. Subsequent to their preparation some compounds of this series were reported which were prepared by a different procedure [5]. The

Table 2. Transition temperatures (°C) of the 2-*n*-alkoxy-5-(4-bromophenyl)pyrazines (**II**).

n	Cr–I	Cr—S_A	S_A–I	S_A–Cr
4	72·0	—	(67·2)	66·0
5	75·2	—	(69·0)	62·0
	75·0		(*67·0*)	
6	77·0	—	(71·0)	55·0
7	—	69·5	72·0	67·0
8	75·0	—	(71·7)	58·9
	75·0		(*71·0*)	
9	73·9	—	(71·0)	59·0
10	74·3	—	(69·7)	51·3
	77·0		(*74·0*)	
12	81·0	—	(65·7)	64·0
	80·0		(*78·0*)	

( ) indicate a monotropic transition.

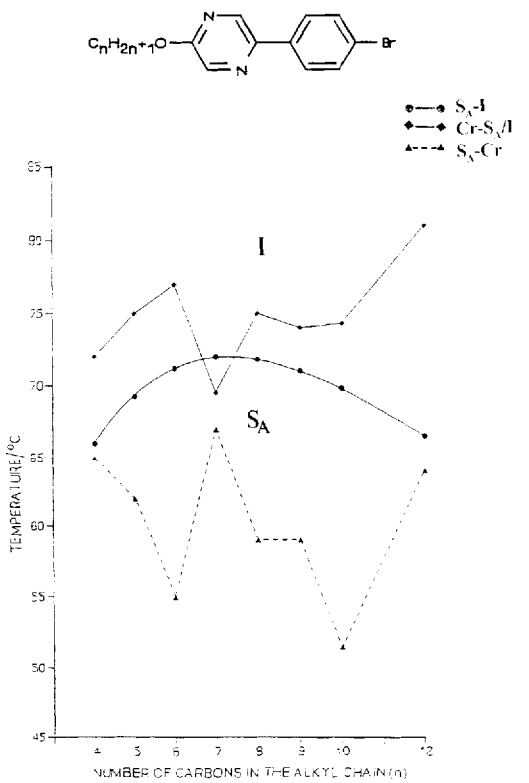


Figure 2. The transition temperatures (°C) against the alkyl chain length (*n*) for the 2-*n*-alkoxy-5-(4-bromophenyl)pyrazines (**II**).

Table 3. Transition temperatures (°C) of the 2-*n*-alkoxy-5-(4′-propylbiphenyl-4-yl)pyrazines (**III**).

n	Cr–CrE	CrE–$S_{B(HEX)}$	$S_{B(HEX)}$–S_A	S_A–N	N–I	S_A–I	CrE–Cr
4	92·5	149·4	161·0	198·7	201·8	—	75·5
5	93·2	143·0	155·5	192·8	195·0	—	80·5
6	92·6	136·5	150·0	191·0	192·1	—	74·9
7	77·3	132·6	147·0	—	—	187·9	70·6
8	84·8	128·0	141·0	—	—	185·0	67·0
9	91·8	121·9	138·3	—	—	182·5	73·5
10	94·3	118·0	134·5	—	—	180·5	79·0
12	107·2	108·0	128·4	—	—	173·0	89·4

values for the transition temperatures generally agreed with our values except for the homologues where $n = 10$ and 12. As our compounds gave satisfactory spectroscopic data with purities estimated by HPLC at greater than 99·9 per cent, and all our values of the transition temperatures fit a typical curve for these types of compound, we are confident of their identity and purity. The previously reported values are also given in table 2 in italics.

The synthetic route which we have used also produced the *N*-alkylated isomers some of which were isolated by column chromatography, namely the 1-*n*-alkyl-5-(4-chlorophenyl)pyrazin-2-ones and 1-*n*-alkyl-5-(4-bromophenyl)pyrazin-2-ones which do not exhibit liquid crystal properties. It should be noted that there was tlc evidence of conversion of the *O* to the *N*-alkylated isomers as the reaction proceeded under the basic reaction conditions. This phenomenon has been observed before, particularly with pyrimidine systems [6] and indicates that the *N*-alkyl isomers are the more thermodynamically stable products.

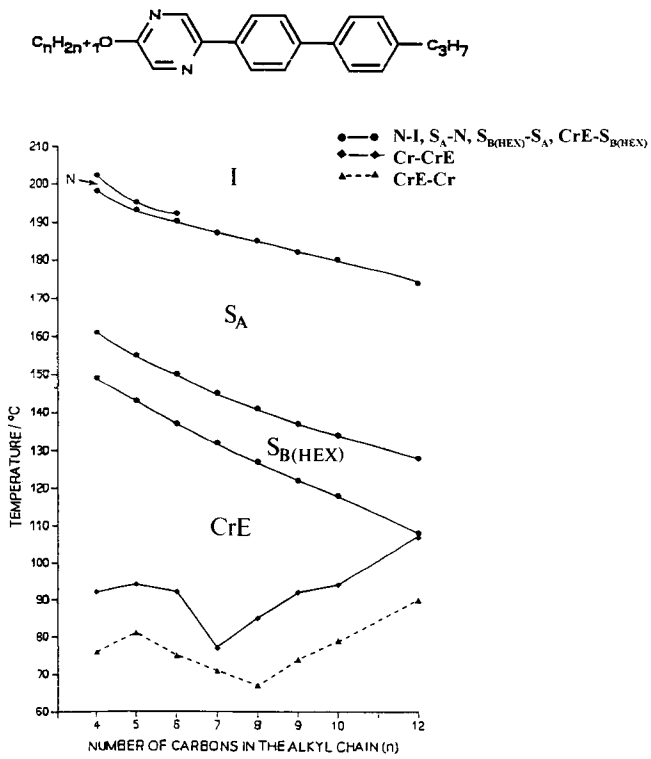


Figure 3. The transition temperatures (°C) against the alkyl chain length (*n*) for the 2-*n*-alkoxy-5-(4′-propylbiphenyl-4-yl)pyrazines (**III**).

A comparison of the S_A–I thermal stability shows that the average S_A–I transition ($n = 5$–10) for series **I** is 65·0°C, whereas comparable data ($n = 5$–10) for series **II** give 70·7°C. This is in agreement with the generally accepted smectic end group efficiency order for halogens. Some pyridazine analogues of our pyrazine series **I** and **II** have been prepared by other workers [7]. Comparing the average values for $n = 5$ and 6 homologues of the 3-*n*-alkoxy-6-(4-bromophenyl)pyridazines and the 3-*n*-alkoxy-6-(4-chlorophenyl)pyridazines with the pyrazine analogues ($n = 5$ and 6) see table 8, it can be observed that the thermal stability of the S_A phase is decreased by 62·0°C and 58·5°C for the pyrazine compounds. This loss of S_A thermal stability may be attributed to a decrease in lateral dipole arising from the nitrogen atoms no longer being adjacent, and on the same side of the heterocyclic ring in the pyrazine system.

2.2. *Series of type* III, IV, V and VI

Series **III**, **IV**, and **V** appear to be the first examples of pyrazine terphenyl analogues reported to date which have the pyrazine ring in the terminal position. For the 2-*n*-alkoxy-5-(4′-*n*-propylbiphenyl-4-yl)pyrazines (**III**) (see figure 3 and table 3) all members of the series which have been made exhibit a smectic A phase, a smectic B (hexatic) and a crystal E phase with associated transition temperatures which all lie on descending lines and do not exhibit any significant odd–even alternation. The identities of the phases were confirmed by X-ray diffraction on the nonyloxy homologue because of the great similiarity of the textures for the smectic B phase and the E phase crystal. Homologues where $n = 4$, 5, and 6 also exhibit a short range nematic phase.

Table 4. Transition temperatures (°C) of the 2-*n*-alkoxy-5-(4′-fluorobiphenyl-4-yl)pyrazines (**IV**).

n	Cr–S_A	S_A–I	S_A–Cr_E	CrE–C	S_A–Cr
4	119·0	202·3	(96·2)	94·0	—
5	120·0	198·0	—	—	100·0
6	110·5	195·5	—	—	86·0
7	117·6	190·6	—	—	98·8
8	115·2	187·5	—	—	105·2
9	119·4	182·0	—	—	102·7
10	116·5	178·9	—	—	100·9
12	118·5	170·5	—	—	109·2

( ) indicate a monotropic transition.

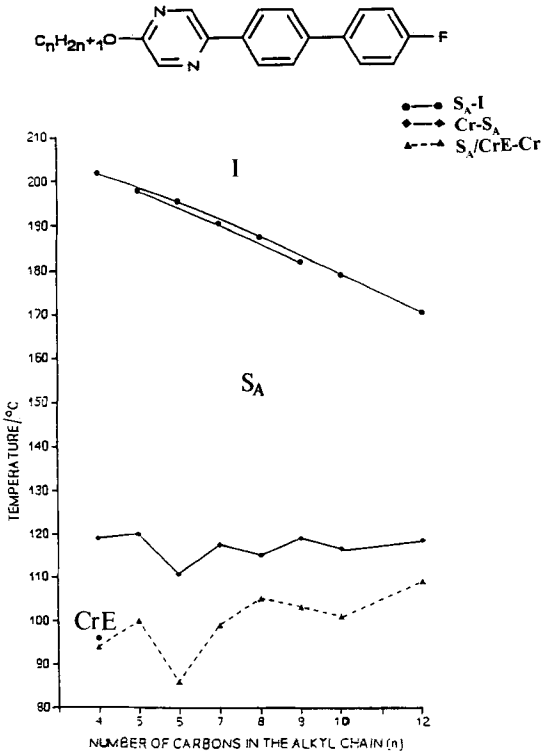


Figure 4. The transition temperatures (°C) against the alkyl chain length (*n*) for the 2-*n*-alkoxy-5-(4′-fluorobiphenyl-4-yl)pyrazines (**IV**).

The 2-*n*-alkoxy-5-(4′-fluorobiphenyl-4-yl)pyrazines (**IV**) (see figure 4 and table 4) exhibit a smectic A phase with S_A–I temperatures which lie on a falling line with some evidence of weak odd–even alternation. This series exhibits a crystal E phase when $n = 4$.

In series **V**, the 2-*n*-alkoxy-5-(4′-*n*-butoxy-2′,3′-difluorobiphenyl-4-yl)pyrazines (see figure 5 and table 5) the T_{N-I} values lie on a smoothly falling curve situated above a smectic C curve whose S_C–N values initially rise to $n = 7$ and then gradually fall.

A comparison of liquid crystal thermal stabilities is given in table 9 and shows that series **III** and **IV** have very similar smectic phase stabilities with little or no tendency to form nematic phases. Series **V** exhibits smectic and a strong nematic phases; these phases have less stability than those of series **III** and **IV** and this is clearly a result of the lateral substitution. As expected the presence of the lateral fluorine atoms in the terminal phenyl ring in series **V** has produced smectic C type materials. Exact terphenyl and other heterocyclic analogues of these pyrazine compounds are not currently in the literature so that meaningful comparisons of thermal stability cannot be made, but generally it seems that they exhibit similar phases to those

Table 5. Transition temperatures (°C) of the 2-*n*-alkoxy-5-(4′-butoxy-2′,3′-difluorobiphenyl-4-yl)pyrazines (**V**).

n	Cr–S_C	S_C–N	N–I	S_C–Cr
5	104·2	140·4	169·5	86·3
6	88·9	142·5	168·5	71·9
7	100·5	145·0	166·5	79·0
8	95·2	144·5	163·0	74·9
9	102·0	143·6	159·0	86·4
10	88·7	139·0	152·3	76·7

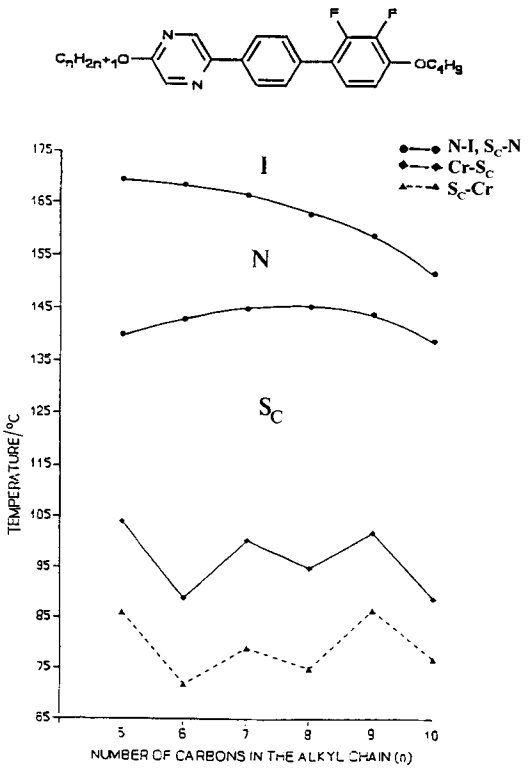


Figure 5. The transition temperatures (°C) against the alkyl chain length (*n*) for the 2-*n*-alkoxy-5-(4′-butoxy-2′,3′-difluorobiphenyl-4-yl)pyrazines (**V**).

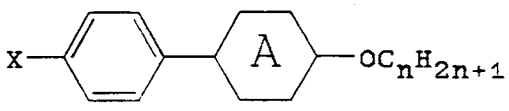
Table 6. Transition temperatures (°C) of the phenylpyrazinyl ethynes (VI).

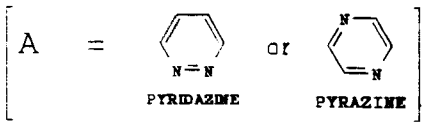
R	R^2	R^3	Cr–N/S_A	S_A–N	N–I
H	C_5H_{11}	F	80·0	—	95·0
C_3H_7	Cl	H	143·2	152·5	221·0

Table 7. Birefringence values, Δn, for representative members of pyrazine based liquid crystal series I–VI.

Series	R	R^2	R^3	Δn
I	C_6H_{13}	—	—	0·18
II	C_6H_{13}	—	—	0·19
III	C_6H_{13}	—	—	0·33
IV	C_6H_{13}	—	—	0·17
V	C_6H_{13}	—	—	0·30
VI	C_3H_7	Cl	—	0·44
VI	H	C_5H_{11}	F	0·38

Table 8. Comparison of the average transition temperatures for pyrazine series I and II with the analogous pyridazine compounds ($n = 5$ and 6)





X	A	Average S_A–I/°C
Cl	Pyrazine	64·6
Cl	Pyridazine	123·0
Br	Pyrazine	70·0
Br	Pyridazine	132·0

Table 9. Average transition temperatures for series III, IV and V.

Series	Homologues averaged	Average S–N†/I/°C	Average N–I/°C
III	7–10	184·0	—
IV	7–10	184·8	—
V	7–10	143·3†	160·3

that might be expected for analogous terphenyl systems. Two examples of ethyne based compounds (VI) were made and the results are given in table 6; both compounds exhibit liquid crystal properties.

Values of birefringence are given in table 7 for at least one member of each of the series prepared. From these data it may be concluded that for the two ring series I and II, which are directly comparable, the replacement of a terminal chlorine with a bromine has resulted in a small increase in birefringence. Of the three ring terphenyl type systems, series III and V have the highest birefringence values whereas series IV only seems to have values comparable with the two ring systems. The three ring systems with an acetylene linkage appear to have by far the highest birefringence values. The birefringence values seem reasonably good for the various types of compounds that have been made. However, studies [8] on model compounds have indicated that some pyrazine containing systems may not have a high light stability and this could limit their potential for commercial applications.

3. Experimental

3.1. *Analysis*

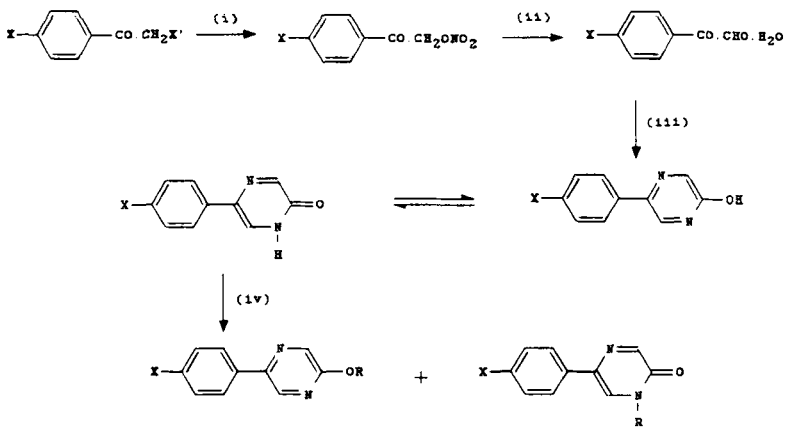
Thermal optical microscopy was carried out using a Nikon Optiphot-2 polarizing microscope in conjunction with a Linkam THMS 600 hot stage and TMS 91 control unit. IR spectra were recorded (KBr discs) using a Perkin–Elmer 782 infrared spectrophotometer, and ^{1}H NMR spectra were measured with tetramethylsilane as internal standard using a Perkin–Elmer R32 90 MHz spectrometer. Mass spectra determined using a VG Trio-2 quadrupole mass spectrometer. The purity of all liquid crystal materials was confirmed as satisfactory by HPLC (> 99·5 per cent) using a C_{18} reverse phase column, a Perkin–Elmer LC235 diode array and acetonitrile or methanol as eluents. In some cases elemental analysis was also used in addition to HPLC as a further confirmation of purity. Birefringence measurements were obtained by extrapolation at 20°C using 5–10 wt % solutions of the novel compounds in I_{eu} or E7, using an Abbé refractometer at 589 nm. X-ray diffraction studies were carried out on powder samples contained in 0·3 mm Lindemann glass tubes. Filtered CuK_α radiation was used.

3.2. *Synthesis*

3.2.1. *2-Alkoxy-5-(4-halogenophenyl)pyrazines* (I, II) *and 1-alkyl-5-(4-halogenophenyl)-2-pyrazinones (see scheme 1)*

3.2.1.1. *4-Bromophenylglyoxal monohydrate*

Powdered silver nitrate (8·6 g, 0·041 mol) was added to a solution of 4-bromophenacyl bromide (11·5 g,



(i) = $AgNO_3/CH_3CN$
(ii) = $CH_3CO_2Na.3H_2O$
(iii) = $NH_2CH_2CONH_2.HCl/CH_3OH/NaOH$
(iv) = n-$RBr/K_2CO_3/(CH_3)_2NCHO$
Where R = C_nH_{2n+1}, and X = Br or Cl

Scheme 1.

0·041 mol) in acetonitrile (80 cm^3). After stirring for 24 h at ambient temperature, the precipitated silver bromide was removed by filtration and washed with ether. The filtrate and washings were combined and the solvent was removed under reduced pressure (30 mm Hg at 30°C) to leave the crude nitrate ester. This was redissolved in ether (100 cm^3), washed with water, and dried ($MgSO_4$). The solvent was removed to yield the nitrate ester (9·2 g, 86 per cent) which was used without further purification in the next step.

Sodium acetate trihydrate (7·3 g, 0·054 mol) was added to a solution of the above product (9·2 g, 0·035 mol) in dimethylsulphoxide (150 cm^3). After stirring for 30 min at ambient temperature the reaction mixture was poured on to ice (600 g) and was saturated with sodium chloride. The product was extracted into ether (3 × 100 cm^3) and the ether layer was washed with saturated sodium bicarbonate (100 cm^3), followed by water (2 × 100 cm^3), and dried ($MgSO_4$). The solvent was removed under reduced pressure at 30°C to give the crude product which was recrystallized from aqueous acetone to yield 4-bromophenylglyoxal monohydrate as white crystals (7·8 g, 82 per cent; m.p. 127–128°C; lit. [9] 125–126·5°C); *m/z* 213 [$M^+ - 18(H_2O)$].

A similiar preparation using 4-chlorophenacyl bromide gave *4-chlorophenylglyoxal monohydrate* (68 per cent; m.p. 106–133°C); *m/z* 168 [M^+-$18(H_2O)$]; IR (KBr); 3500–3300 (broad band OH), 1700 (C=O), 1600 (C=C) cm^{-1}. ^1H NMR (DMSO-d_6) 5·6 [1 H, t, aldehyde hydrate CH (s on D_2O exchange)], 5·9–6·6 [2 H, br s, $(OH)_2$ (removed on D_2O exchange)], 7·5–7·7 (2 H, d, ArH), 8·0–8·2 (2 H, d, ArH).

3.2.1.2. *5-(4-Bromophenyl)-2(1 H)-pyrazinone*

4-Bromophenylglyoxal monohydrate (6·9 g, 0·03 mol) was dissolved in methanol (20 cm^3), the solution was cooled to below −40°C (CO_2/acetone) and dry, powdered, glycinamide hydrochloride (3·2 g, 0·03 mol) was added with constant stirring. The temperature was allowed to rise slowly to −30°C and was maintained at that temperature whilst sodium hydroxide (3·0 g, 0·75 mol) in water (10 cm^3) was added, dropwise. The reaction mixture was stirred and maintained at −20 to −10°C for 1 h, for 2 h at −10 to 0°C, then at 0 to 20°C for 2 h. The reaction mixture was cooled to 0°C and the pH was adjusted to 5·0 with concentrated hydrochloric acid. A precipitate was formed which was collected, washed with water, then dried. The product was purified by dissolving the crude solid in dichloromethane (30 cm^3) and extraction into sodium hydroxide solution (50 cm^3 of 1 M). The aqueous layer was washed with dichloromethane (2 × 20 cm^3) and the pH was adjusted to 5·0 with hydrochloric acid. A further reprecitation was carried out and the solid was washed with water until the washings were neutral. After collecting and drying the product the *5-(4-bromophenyl)-2(1H)-pyrazinone* was obtained as beige crystals (4·3 g, 57 per cent; m.p. 226–228°C decomp.); *m/z* 251 (M^+); IR (KBr): 3100–2300 (NH), 1680 (C=O), 1600, 1400 (C=C aromatic) cm^{-1}. ^1H NMR (DMSO-d_6): 7·5–8·0 (4 H, m, ArH), 8·1, 8·2 (2 × 1 H, s, pyrazine-H), 12·0–13·0 (1 H, br s, NH exchanged by D_2O).

Similarily prepared was *5-(4-chlorophenyl)-2(1H)-pyrazione* (51 per cent; m.p. 222°C decomp., lit. [10] 218–220°C); *m/z* 206 (M^+).

3.2.1.3. *5-(4-Bromophenyl)-2-pentoxypyrazine and 5-(4-bromophenyl)-1-pentylpyrazin-2-one*

1-Bromopentane (4·5 g, 0·03 mol) was added to a mixture of 5-(4-bromophenyl)-2 (1*H*)-pyrazinone (5·0 g, 0·02 mol) and potassium carbonate (7·0 g, 0·050 mol) in *N*, *N*-dimethylformamide (50 cm^3). The reaction mixture was stirred and heated for about 15 min at 100°C then cooled and diluted with water (100 cm^3). The products were extracted into ethyl acetate (2 × 100 cm^3), washed with sodium hydroxide solution (2 × 80 cm^3, 1 M), water (2 × 100 cm^3), and dried ($MgSO_4$). The solvent was removed under reduced pressure to yield an oil which was subjected to chromatography [silica gel, eluent: light petroleum (b.p. 60–80°C): dichloromethane (3:2)]. Two products were isolated—the *O*- and *N*-alkylated isomers.

The alkoxypyrazine was recrystallized from methanol until the m.p. and mesomorphic transition temperatures were constant. *5-(4-bromophenyl)-2-pentoxypyrazine* was obtained as white crystals (1·5 g, 23 per cent). Found: C, 56·1; H, 5·5; N, 8·8 per cent. $C_{15}H_{17}BrN_2O$ requires: C, 56·3; H, 5·3; N, 8·8 per cent; *m/z* 320 (M^+); IR (KBr): 2950–2850 (CH, alkane), 1600, 1500 (C=C aromatic) cm^{-1}. ^1H NMR ($CDCl_3$): 0·8–1·9 [9 H, m, pentyl $Me(CH_2)_3$], 4·2–4·4 (2 H, t, CH_2O), 7·6, 7·8 (2 × 2 H, d, ArH), 8·2, 8·4 (2 × 1 H, s, pyrazine-H). The purity, as shown by HPLC, was >99·9 per cent.

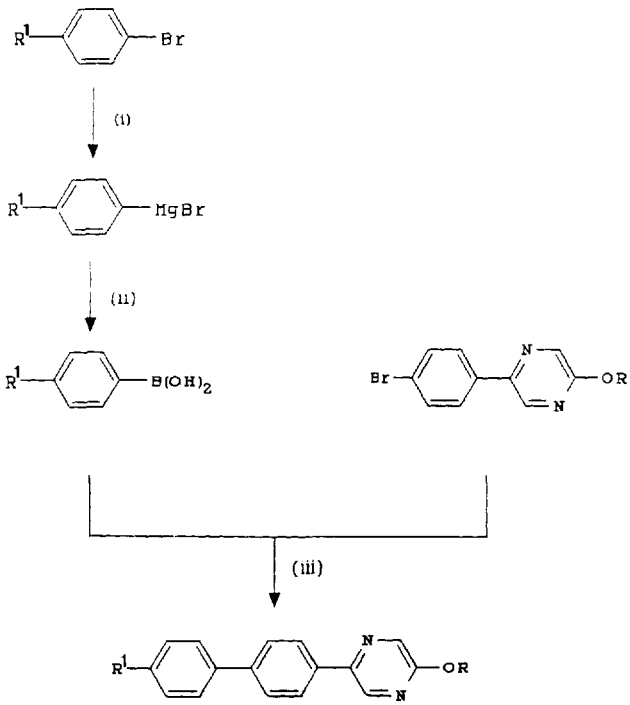
The *N*-alkylpyrazine was recrystallized from light petroleum (b.p. 60–80°C). *1-Pentyl-5-(4-bromophenyl)pyrazine-2-one* was obtained as pale yellow crystals (4·2 g, 66 per cent; m.p. 112°C); Found: C, 56·3; H, 5·4; N, 8·8 per cent. $C_{15}H_{17}BrN_2O$ requires C, 56·3: H, 5·3; N, 8·8 per cent; *m/z* 320 (M^+); IR (KBr): 3100–2700 (CH, alkane), 1650 (C=O), 1600, 1500 (C=C aromatic), 1480 (CH_2 bend) cm^{-1}. ^1H NMR ($CDCl_3$): 0·6–1·8 [9 H, m, $Me(CH_2)_3$], 3·8–4·1 (2 H, t, CH_2N), 7·5–7·9 (5 H, ArH and pyrazine-H), 8·2 (pyrazine-H).

The following 2-alkoxy-5-(4-bromophenyl)pyrazines were obtained in a similar way using the appropriate 1-bromoalkane, each giving the expected analytical data: $C_nH_{2n+1}O$, $n = 4, 6, 7, 8, 9, 10, 12$.

The 1-alkyl-5-(4-bromophenyl)pyrazin-2-ones which were isolated and characterized were: C_nH_{2n+1}, $n = 4, 6, 7, 8, 9, 10$.

Using the same procedure, the 2-alkoxy-5-(4-chlorophenyl)pyrazines with the following alkyl chain lengths were obtained: C_nH_{2n+1}, $n = 4$–10, and the 1-alkyl compounds having the following chain lengths: C_nH_{2n+1}, $n = 4, 6, 10, 12$.

3.2.2. *2-Alkoxy-5-(4'-propylbiphenyl-4-yl)pyrazines* (**III**) (*see scheme2*)



(i) = Mg/THF
(ii) = $(CH_3O)_3B$/HCl (aq)
(iii) = $Pd(PPh_3)_4/Na_2CO_3$/ (aq)/Toluene

Where $R^1 = C_3H_7$ or F
and $R = C_nH_{2n+1}$

Scheme 2.

3.2.2.1. *2-Pentyloxy-5-(4'-propylbiphenyl-4-yl)pyrazine*

4-Propylphenylboronic acid (9·0 g, 0·055 mol) was added to a mixture of 5-(4-bromophenyl)-2-pentyloxypyrazine (16·05 g, 0·05 mol), sodium carbonate solution (40 cm^3, 2 mol dm^{-3}) and tetrakis(triphenylphosphine)palladium(0) (0·2 mol %) in toluene (80 cm^3). The mixture was heated under reflux until reaction was shown (TLC) to be complete (about 16 h). The organic layer was separated, the aqueous layer was shaken with dichloromethane (2 × 80 cm^3) and the combined organic layers were dried ($MgSO_4$), concentrated, then subjected to column chromatography [silica gel: eluent, light petroleum (b.p. 60–80°C):ethyl acetate (10:1)]. The product was recrystallized from ethanol. *2-pentyloxy-5-(4'-propylbiphenyl-4-yl)pyrazine* was obtained as white crystals (1·0 g, 56 per cent). Found: C, 80·3; H, 7·7; N, 7·8 per cent. $C_{24}H_{28}N_2O$ requires C, 80·0; H, 7·8; N, 7·8 per cent; *m/z* 360 (M^+); IR (KBr): 2900 (CH, alkane), 1480 (C=C, aromatic), 1180 (CO, ether) cm^{-1}. ^1H NMR ($CDCl_3$): 0·8–1·9 (14 H, m, alkyl), 2·5 2·7 (2 H, t, CH_2), 4·3–4·4 (2 H, t, CH_2O), 7·2–8·1 (8 H, m, ArH), 8·2, 8·4 (2 × 1 H, s, pyrazine-H).

Similarly prepared, using the appropriate alkoxypyrazine, were: $C_nH_{2n+1}O$; $n = 4, 6, 7, 8, 9, 10, 12$.

3.2.2.2. *2-Alkoxy-5-(4'-fluorobiphenyl-4-yl)pyrazines* (**IV**)

In an analogous manner to that described above, using 4-fluorophenylboronic acid, the corresponding fluoro compounds were obtained. For example *2-heptyloxy-5-(4'-fluorobiphenyl-4-yl)pyrazine*, white crystals (51 per cent yield). Found: C, 76·1; H, 7·0; N, 7·8 per cent. $C_{23}H_{25}FN_2O$ requires C, 75·8; H, 6·9; N, 7·7 per cent; *m/z* 364 (M^+); IR (KBr): 2900 (CH, alkane), 1480 (C=C, aromatic), 1180 (CO, ether) cm^{-1}. ^1H NMR ($CDCl_3$): 0·9 (3 H, t, Me), 1·2–1·9 (10 H, m, $(CH_2)_5$), 4·4 (2 H, t, CH_2O), 7·2 (2 H, m, ArH), 7·6–7·8 (4 H, m, ArH), 8·0 (2 H, m, ArH), 8·3, 8·6 (2 × 1 H, s, pyrazine-H).

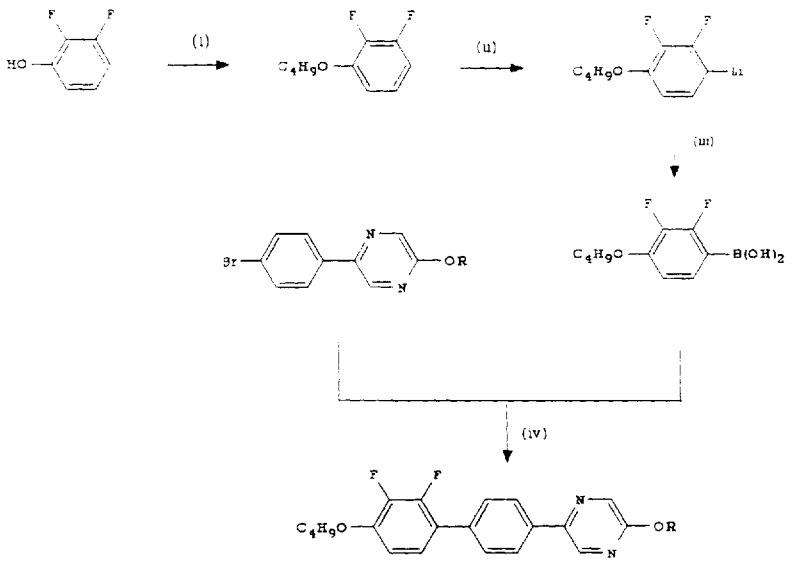
The following analogues were prepared in a similar way using the appropriate alkoxypyrazine: $C_nH_{2n+1}O$; $n = 4, 5, 6, 8, 9, 10, 12$.

3.2.3. *2-Alkoxy-5-(4'-butoxy-2',3'-difluorobiphenyl-4-yl)pyrazines* (**V**) (*see scheme 3*)

3.2.3.1. *4-Butoxy-2,3-difluorophenylboronic acid*

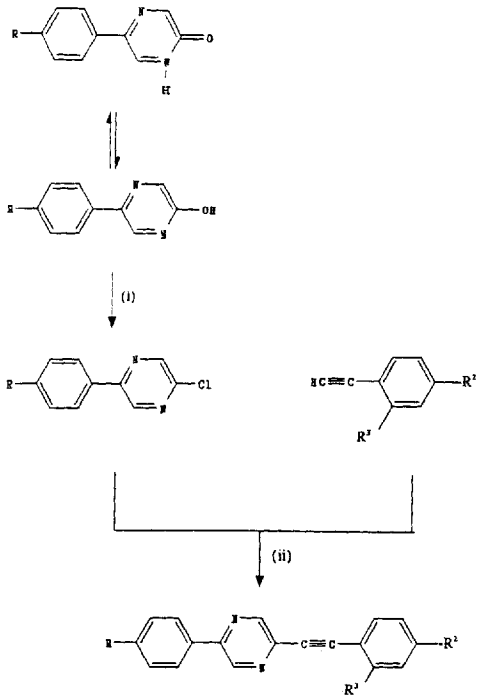
Butyl lithium [33·8 cm^3, 0·054 mol (1·6 M in hexane)] was added, dropwise, to a stirred, cooled (−78°C), solution of 2,3-difluorobutoxybenzene (10·0 g, 0·054 mol) in dry tetrahydrofuran (90 cm^3) under dry nitrogen. The reaction mixture was maintained under these conditions for 2·5 h then a previously cooled solution of triisopropyl borate (16·2 g, 0·086 mol) in dry tetrahydrofuran (60 cm^3) was added, dropwise, at −78°C. The reaction mixture was allowed to warm to room temperature overnight and was then stirred for 1 h with 10 per cent hydrochloric acid (100 cm^3). The product was extracted into ether (2 × 80 cm^3), the solution was dried ($MgSO_4$) and the solvent then removed under reduced pressure to yield a beige solid. This was washed with light petroleum (b.p. 60–80°C) to give *4-butoxy-2,3-difluorophenylboronic acid* (11·7 g, 94 per cent); *m/z* 636 (trimer anhydride); IR (KBr): 3700 (broad OH), 2900 (CH, alkalane), 1620 (C=C aromatic), 1480 (CH_2 bend), other bands at 1350, 1300, 1220, 1040 cm^{-1}. ^1H NMR (DMSO-d_6): 1·0 (3 H, t, Me), 1·5 (2 H, m, CH_2), 1·8 (2 H, m, CH_2), 4·1 (2 H, CH_2O), 6·9, 7·4 (2 × 2 H, m, ArH), 8·2 (2 H, s, OH, removed by D_2O exchange).

Using the method described above for 2-pentyloxy-5-(4'-propylbiphenyl-4-yl)pyrazine, but using 4-butoxy-2,3-difluorophenylboronic acid, allowed the synthesis of the alkoxy-butoxy-difluorobiphenylylpyrazines (**V**). For example *2-pentoxy-5-(4'-butoxy-2',3'-difluoro-biphenyl-4-yl)pyrazine* was obtained as white crystals (56 per cent); Found: C, 70·6; H, 6·7; N, 6·8 per cent. $C_{25}H_{28}F_2N_2O_2$ requires C, 70·4; H, 6·6; N, 6·6 per cent; *m/z* 426 (M^+); IR (KBr): 2900 (CH aromatic), 1640, 1500 (C=C aromatic), other bands at 1480, 1350, 1300, 1200, 1080 cm^{-1}. ^1H NMR ($CDCl_3$): 1·0 (6 H, m, $2CH_3$), 1·4–1·6 [6 H, m, $(CH_2)_3$], 1·8 [4 H, m, $(CH_2)_2$], 4·2, 4·4 (2 × 2 H, t, CH_2O), 6·8, 7·2, (2 × 1 H, m, ArH), 7·6, 8·0 (2 × 2 H, m, ArH), 8·2, 8·6 (2 × 1 H, s, pyrazine-H).



(i) = n-$C_4H_9Br/K_2CO_3/C_2H_5COCH_3$
(ii) = $CH_3(CH_2)_3Li/-78°C$
(iii) = $[(CH_3)_2CHO]_3B$
(iv) = $Pd(PPh_3)_4/Na_2CO_3$ (aq)/Toluene
Where R = C_nH_{2n+1}

Scheme 3.



Where R = H, then $R^2 = C_5H_{11}$ and $R^3 = F$

(i) = $POCl_3/H_2SO_4$
(ii) = $CuI/Pd(PPh_3)_4/[(CH_3)_2CH]_2NH$

Where R = C_3H_7 then R^2 = Cl and R^3 = H

(i) = $POCl_3/(C_2H_5)_3N^+CH_3Cl^-$
(ii) = $CuI/Pd(Ph_3)_4/[(CH_3)_2CH]_2NH$

Scheme 4.

Also obtained were the 2-alkoxy analogues C_nH_{2n+1} where $n = 6–10$.

3.2.4. *Arylpyrazinyl alkynes* (**VI**) (*see scheme 4*)

3.2.4.1. *2-Chloro-5-(4-propylphenyl)pyrazine*

5-(4-Propylphenyl)-2(1*H*)-pyrazinone (5·0 g, 0·0234 mol) was dissolved in phosphorus oxychloride (50 cm^3, 0·2 mol) containing triethylmethylammonium chloride (3·6 g, 0·0234 mol). The reaction mixture was heated under reflux for 1 h, cooled to room temperature, then carefully poured on to ice (100 g), after which it was stirred for 1 h. The product was extracted into ethyl acetate (2 × 80 cm^3) then washed with 1 M sodium hydroxide solution (2 × 100 cm^3) followed by water (2 × 100 cm^3) and finally dried ($MgSO_4$). The solvent was removed under reduced pressure to leave a brown gum which was applied to a silica gel column and eluted using light petroleum (b.p. 60–80°C): ethyl acetate (5 : 1). Removal of the solvent gave a solid which was recrystallized from light petroleum (b.p. 60–80°C) as pale yellow crystals (2·3 g, 42 per cent; m.p. 67–68°C). Found: C, 66·8; H, 5·6: N, 11·9 per cent. $C_{13}H_{13}ClN_2$ requires C, 67·1; H, 5·6; N, 12·0 per cent; *m/z* 232 (M^+); IR (KBr): 2850–2950 (CH alkane), 1600 (C=C aromatic), 1460 (CH_2 bend), 1330 (CH_3 bend), 800 (CH aromatic, out of plane bend) cm^{-1}. ^1H NMR ($CDCl_3$): 1·3–1·7 (3 H, t, Me), 1·9–2·4 (2 H, m, CH_2), 3·0–3·3 (2 H, t, CH_2), 7·7–7·9, 8·3, 8·6 (2 × 2 H, d, ArH), 9·1, 9·3 (2 × 1 H, s, pyrazine-H).

Similarly prepared, but using a small quantity of concentrated sulphuric acid as catalyst instead of triethylmethylammonium chloride, was *2-chloro-5-phenylpyrazine* (54 per cent; m.p. 96°C, lit. [10] 96–98°C).

3.2.4.2. *2-(4-Chlorophenylethynyl)-5-(4-propylphenyl) pyrazine*

2-Chloro-5-(4-propylphenyl)pyrazine (1·2 g, 0·005 mol), 4-chlorophenylethyne [11] (0·7 g, 0·005 mol), tetrakis-(triphenylphosphine)palladium(0) (0·1 g, 2 mol %), copper(I) iodide (0·16 g, 2 mol %) and diisopropylamine (10 cm^3) were heated under reflux under nitrogen until reaction was complete (TLC), which was about 40 h. The reaction mixture was cooled, then diluted with water (50 cm^3) and shaken with dichloromethane (2 × 25 cm^3). The extract was dried ($MgSO_4$) and the solvent evaporated under reduced pressure to leave a brown oil. This was chromatographed [silica gel: eluent; light pertroleum (b.p. 60–80°C) and ethyl acetate increasing up to 10 per cent]. Fractions containing a fluorescent component were pooled and the solvent was removed. The solid which remained was recrystallized from light petroleum (b.p. 60–80°C) and dichloromethane (5 : 1) to yield *2-(4-chlorophenylethynyl)-5-(4-propylphenyl)pyrazine* as pale yellow solid (0·5 g, 30 per cent). Found: C, 75·7; H, 5·2; N, 8·2 per cent. $C_{21}H_{17}ClN_2$ requires C, 75·9; H, 5·1; N, 8·4 per cent; *m/z* 332 (M^+); IR (KBr): 2900 (CH alkane), 1600 (C=C), 1480 (CH_2 bend) cm^{-1}. ^1H NMR (CD_2Cl_2): 0·9–1·0 (3 H, t, Me), 1·6–1·8 (2 H, m, CH_2), 2·6–2·7 (2 H, t, CH_2), 7·3–7·44 (4 H, m, ArH), 7·6, 8·0 (2 × 2 H, d, ArH), 8·8, 9·0 (2 × 1 H, s, pyrazine-H).

A similar reaction using 2-fluoro-4-pentylphenylethyne [11] gave *2-(2'-fluoro-4'-pentylphenylethynyl)-5-phenylpyrazine* (67 per cent).

Steps (i) and (ii) in scheme 2, and step (i) in scheme 3 involve known procedures and are well documented in the literature.

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