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Palladium-catalysed cross-coupling reactions in the synthesis of some high polarizability materials

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Palladium-catalysed cross-coupling reactions in the synthesis of some high polarizability materials

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Liquid crystal materials of high optical anisotropy consist of moieties of high electron density in conjugation with each other along the molecular length. Such structures are conducive to convergent synthesis methods. Here we report the synthesis of a range of novel materials by the strategic use of palladium-catalysed cross-coupling methods. In addition to the traditional use of bromide and iodide leaving groups, invaluable use of the triflate leaving group and the importance of selective cross-coupling methods using both arylboronic acids and alkynylzinc chloride derivatives is illustrated. This systematic methodology allows the separate synthesis of the appropriate sub-units that can be efficiently coupled together to provide high overall product yields.

1. Introduction

The commercial success of liquid crystals is, in the main, due to their suitability for use in display devices, because of their ability to switch between orientations with different optical properties. In display devices, the optical anisotropy needs to be carefully controlled for optimum operation and the actual magnitudes required depend upon the type of display. Liquid crystal displays possess attractive features and their demand is rising dramatically because of the increasing need for cheap, low power, small, clear displays for portable equipment.

However, the anisotropic and fluid nature of nematic liquid crystals is a special combination that offers many potential applications in addition to displays. Such a novel application is the reason for the work reported here and requires room temperature nematic mixtures of very high optical anisotropy ($>0{\cdot}5$). Most currently available commercial nematic mixtures have optical anisotropy values of up to $\sim 0{\cdot}2$, and so a significant improvement has to be achieved.

The optically anisotropic nature of a nematic phase is due to the orientational order of molecules which have a greater polarizability along the molecular length than across the molecules. The degree of birefringence exhibited by a nematic phase is dependent upon the degree of polarizability anisotropy and the order parameter. An excellent recent review of birefringence in liquid crystals and how it is influenced by molecular parameters is provided by Pelzl and Hauser [1].

In order to generate nematic materials with very high optical anisotropy, compounds have been synthesized according to the general formula shown in the figure; such sectionalized structures are ideal for synthesis by palladium-catalysed cross-coupling reactions [2]. The 2,6-disubstituted naphthalene unit has previously been used to produce nematogenic liquid crystals and its fused bicyclic aromatic

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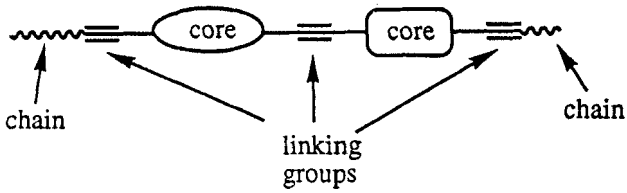


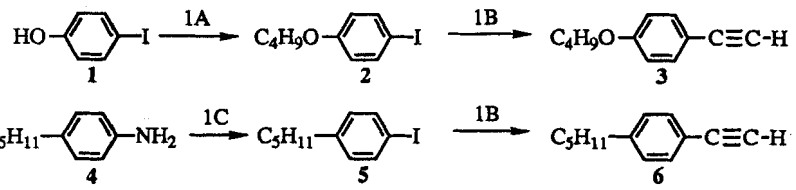
A generalized structure for high polarizability nematogens.

structure would be expected to confer a high optical anisotropy upon its derivatives. Therefore, this moiety has been used as the main core unit in the systems whose synthesis is reported here. Conjugative acetylene linking groups have been used both between two aromatic moieties and at the edge of the core between an aromatic unit and a terminal chain. In addition to the 2,6-naphthalene unit, a simple 1,4-phenyl has also been used. In order to assess the effect of hetero-atoms in the aromatic core on optical anisotropy, some 2,5-pyridine and 2,5-pyrimidine compounds have also been prepared.

2. Discussion of synthetic methods

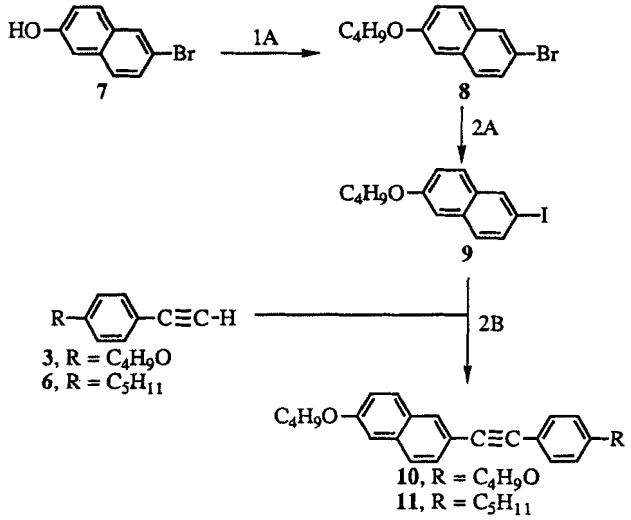
The synthesis of such a wide range of materials with functional groups in specific positions in order to produce the required physical properties needed careful consideration. The majority of the syntheses involved the use of metallation techniques [3] to prepare arylboronic acids (which can be isolated and stored indefinitely) [4] and alkynylzinc chlorides (which must be used *in situ*) followed by the use of existing [5–7], and the development of novel, palladium-catalysed cross-coupling procedures [8].

Most of the liquid crystals to be synthesized required the preparation of intermediate terminal acetylenes and some of these have also been used in the synthesis of terminal cyano-substituted liquid crystals based on 2,6-naphthalene [9]. There are several methods available for the preparation of aryl-substituted terminal acetylenes (for example, compounds **3**, **6**, **14** and **32**) and the one chosen will depend on the available starting materials; typically, methods from aryl methyl ketones (chlorination followed by dehydrochlorination) [10] or aryl aldehydes (via the debromination of a β,β-dibromostyrene derivative) [11] are used. Palladium-catalysed cross-coupling methods in the preparation of terminal acetylenes can be particularly efficient and are essential if starting from aryl halides or phenols (from which aryl triflates can be prepared). A popular and reliable method involves a palladium-catalysed cross-coupling procedure with trimethylsilylacetylene, a rather expensive reagent, which initially provides a protected terminal acetylene; deprotection is achieved in quanitative yield using potassium hydroxide in methanol at room temperature [5, 12]. This method was chosen for the preparation of the pyridine compound (**32**) because the scale of reaction was small and a good yield was essential. However, for the terminal acetylenes that were required on a larger scale, a palladium-catalysed cross-coupling reaction was used that directly provided the desired terminal acetylene [6]. This method involved the coupling, at room temperature, of the zinc chloride derivative of lithium acetylide ethylenediamine complex (see scheme 1) to an appropriate aryl iodide (**2**, **5** and **9**). Aryl bromides or triflates cannot normally be used since elevated temperatures are required in the reaction and this leads to the starting material coupling to the product as it is formed [8]. In the formation of compound **14** (see scheme 4), this would have been a problem because only the naphthyl bromides were



1A, C_4H_9Br, butanone, K_2CO_3. 1B, (i) Lithium acetylide ethylenediamine complex, $ZnCl_2$, THF; (ii) $Pd(PPh_3)_4$, THF. 1C, (i) $NaNO_2$, 36 per cent HCl; (ii) KI.

Scheme 1.



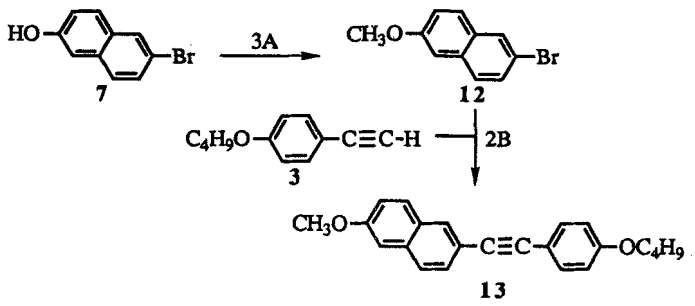
2A, KI, CuI, HMPA. 2B, (i) *n*BuLi, THF; (ii) $ZnCl_2$, THF; (iii) $Pd(PPh_3)_4$, THF.

Scheme 2.

available but, fortunately, an excellent method exists for the quantitative conversion of naphthyl bromides into naphthyl iodides [13, 14].

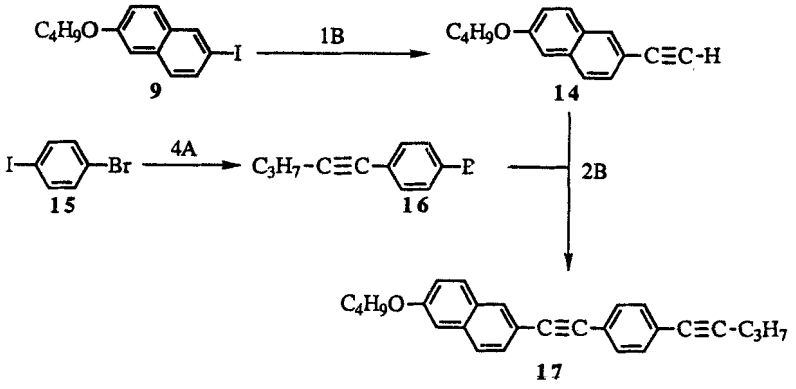
Two liquid crystal materials (compounds **10** and **11**) were prepared according to scheme 2 by the metallation of the terminal acetylene (**3** or **6**) by using *n*-butyllithium; the intermediate obtained was then converted into the zinc choloride derivative on addition of zinc chloride. The zinc chloride derivative was then coupled (*in situ*) with the appropriate naphthyl iodide, at room temperature, in the presence of a palladium catalyst [tetrakis(triphenylphosphine)palladium(0)] [6]. Scheme 3 shows that aryl bromides can similarly be used in such coupling procedures at elevated temperature and this has provided another liquid crystal material (**13**) in good yield (~60 per cent).

In schemes 2 and 3, compounds with one acetylene linking group have been provided by two overall coupling procedures (one to provide the terminal acetylene and the other to provide the final product). In order to go one stage further and synthesize liquid crystals with two acetylene linking groups (see scheme 4), a total of three cross-coupling procedures has been used. For an efficient route to such compounds, selective couplings needed to be developed. 1-Bromo-4-iodobenzene (**15**) has two leaving groups of different reactivity. A coupling at room temperature with



3A, Dimethyl sulphate, KOH, water.

Scheme 3.

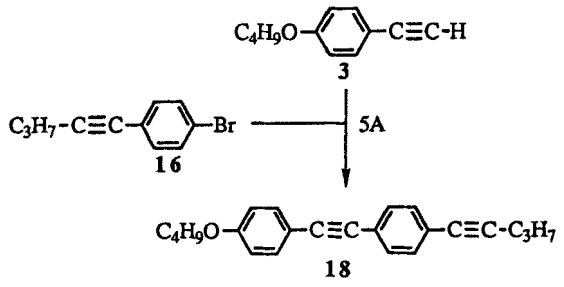


4A, (i) Pent-1-yne, *n*BuLi, THF; (ii) $ZnCl_2$, THF; (iii) $Pd(PPh_3)_4$, THF.

Scheme 4.

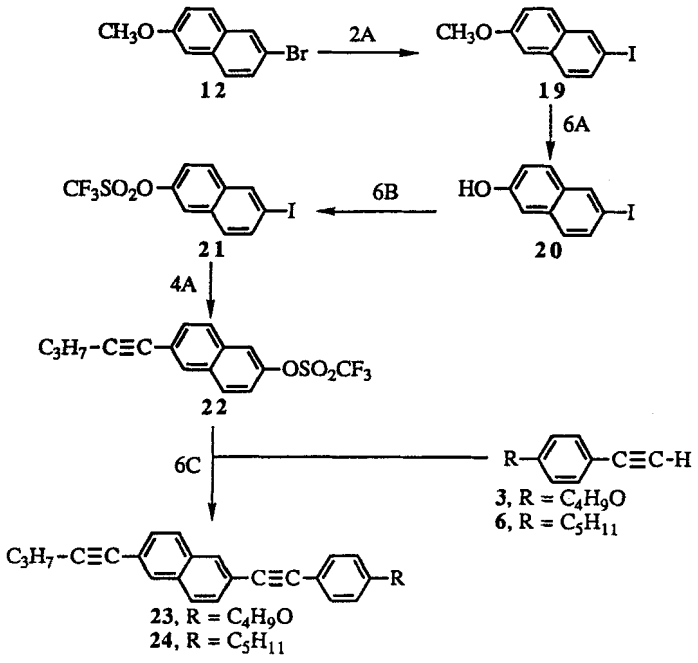
pentynylzinc chloride gives 100 per cent selectivity at the more reactive iodo site with an isolated product yield of 82 per cent. The less reactive bromo-substituent (compound **16**) has been utilized in a subsequent coupling with the zinc derivative of terminal acetylene **14** (also itself prepared by a coupling procedure) to provide compound **17** (a naphthyl-acetylene-phenyl-acetylene system) in excellent yield (77 per cent). Compound **16** has also been used (as shown in scheme 5) to provide a simple phenyl-acetylene-phenyl-acetylene system (compound **18**). However, a different coupling method [5, 12] has been used here (also see further example below) that directly couples the terminal acetylene with the aryl bromide (compound **16**) in the presence of both copper(I) iodide and tetrakis(triphenylphosphine)palladium(0) catalysts. This method is operationally much easier than the zinc chloride method [6], but the resulting product was much more difficult to purify and gave a lower yield for compound **18** (46 per cent). Also, selective coupling reactions involving this direct coupling procedure are inferior to the more involved zinc chloride coupling procedure.

Selective couplings on 2,6-naphthalene units (see schemes 6 and 7) are more demanding because of the restriction to 6-bromo-2-naphthol as the starting material. The bromo site is fine in cross-couplings, but the naphthol site has to be converted into the triflate derivative [15, 16] (compounds **21** and **25**) to provide an excellent leaving group which can be exploited in palladium-catalysed cross-couplings. The first



5A, $Pd(PPh_3)_4$, CuI, Et_3N.

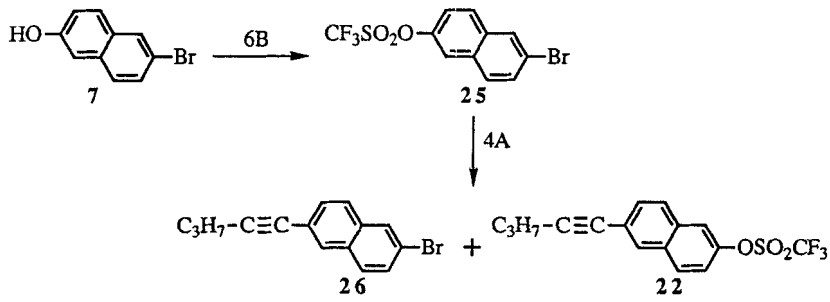
Scheme 5.



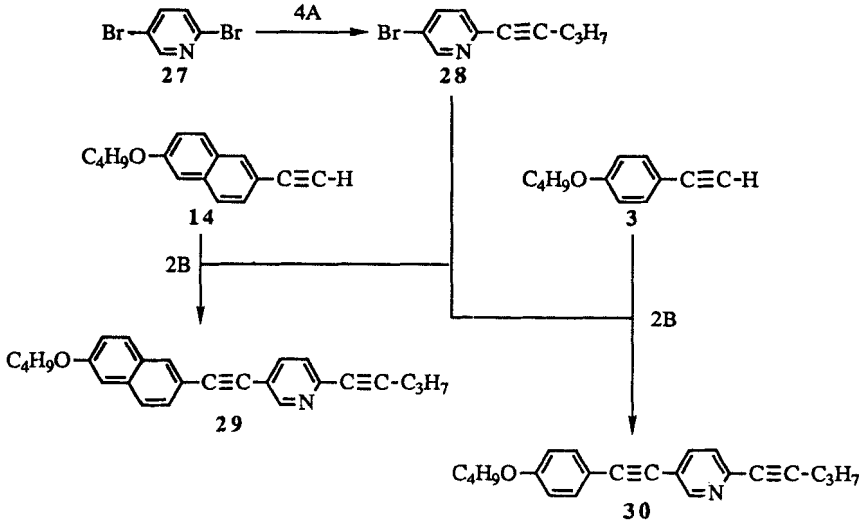
6A, BBr_3, CH_2Cl_2. 6B, *N*-Phenyltriflamide, Et_3N, CH_2Cl_2. 6C, (i) *n*BuLi, THF; (ii) $ZnCl_2$, THF; (*iii*) $Pd(PPh_3)_4$, LiCl, THF.

Scheme 6.

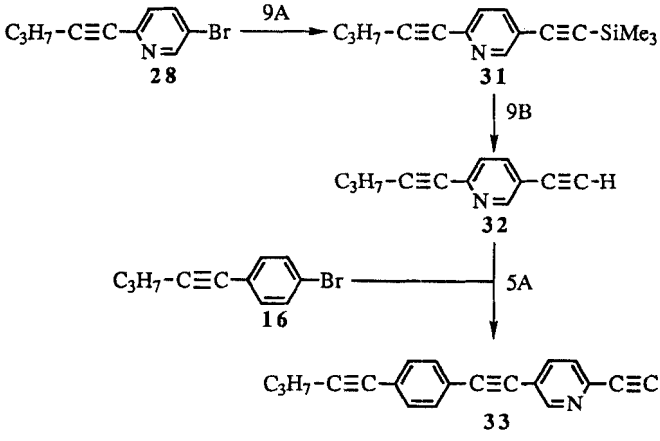
approach was to ensure optimum selectivity and so the iodo-triflate naphthalene unit (**21**) was prepared (in excellent overall yield) and, as expected, the coupling reaction with pentynylzinc chloride at room temperature gave 100 per cent selectivity at the iodo site with an excellent yield of product. Subsequent couplings with terminal acetylenes **3** and **6** provided an efficient route to liquid crystals **23** and **24**. The next approach (see scheme 7) represents an investigation into the selectivity of the bromo-triflate naphthalene compound (**25**). This compound was more easily prepared in a similarly excellent yield, but the selectivity of this unit in a coupling with pentynylzinc chloride was not 100 per cent. However, no double coupling was detected (presumably because the introduction of the acetylene group deactivates both systems **22** and **26** towards further coupling) and the two mono-coupled products were both isolated. In this case, selectivity is not



Scheme 7.



Scheme 8.



9A, Trimethylsilylacetylene, $Pd(PPh_3)_4$, CuI, Et_3N. 9B, KOH, methanol.

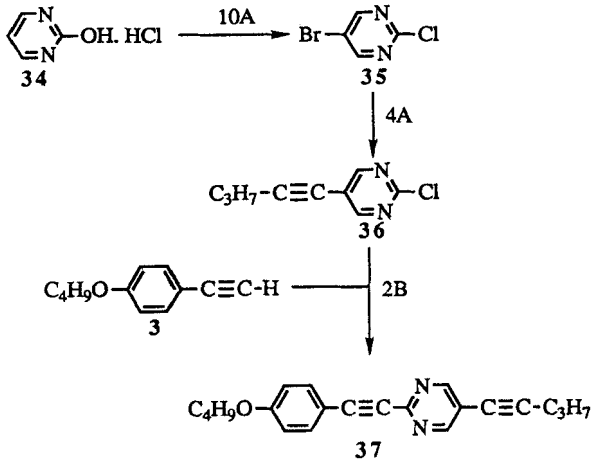
Scheme 9.

an important issue since any subsequent coupling involving either intermediate **22** or **26** would give the same product. However, in certain applications the bromo-substituted material (compound **26**) would be more useful and fortunately this was the major product (57 per cent isolated yield); the other product (compound **22**) was identical to that prepared as in scheme 6.

Selective couplings have also been used in the preparation of some heterocyclic liquid crystal materials. Scheme 8 shows that pentynylzinc chloride selectively couples at the site next to the electron withdrawing nitrogen of 2,5-dibromopyridine (compound **27**) to provide compound **28** in excellent yield (77 per cent). This compound was then involved in separate coupling reactions with the zinc chloride derivatives of terminal acetylenes **3** and **14** to provide two liquid crystal compounds (**29** and **30**) in moderate yields. It is interesting to note that the preparation of compound **28** by the direct coupling method [5, 12] gave an isolated yield of only 43 per cent.

Scheme 9 outlines the route to a liquid crystal material consisting of three acetylene linkages. This involves the overall use of four palladium-catalysed cross coupling reactions. The first provides compound **28** (see scheme 8) and the second involves trimethylsilylacetylene (as described earlier) in the direct coupling method [5, 12] described above which gave a moderate yield (54 per cent) of the protected acetylene. The quantitative removal of the protecting group efficiently provided the pyridine terminal alkyne (compound **32**). This was then coupled, again using the direct method described above, to compound **16** (itself the product of a coupling reaction) to provide the desired liquid crystal compound (**33**) in 34 per cent yield. The direct method of acetylene coupling (as used in schemes 5 and 9) is quite effective, but provides materials which are difficult to purify by column chromatography. However, purification is more straightforward if the material is relatively volatile and can be distilled (for example, compound **31**). Certainly, better isolated yields of pure materials have been obtained when the longer zinc chloride coupling method has been used.

Selective couplings have also been used to synthesize some pyrimidine liquid crystals (see scheme 10). However, this entailed the prior preparation of a pyrimidine

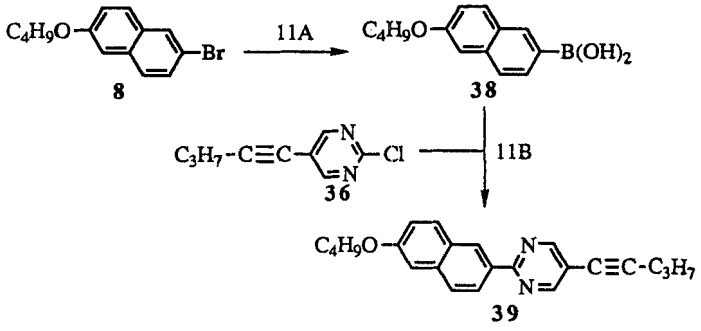


10A, (i) Br_2, water, (ii) $POCl_3$, *N*,*N*-dimethylaniline.

Scheme 10.

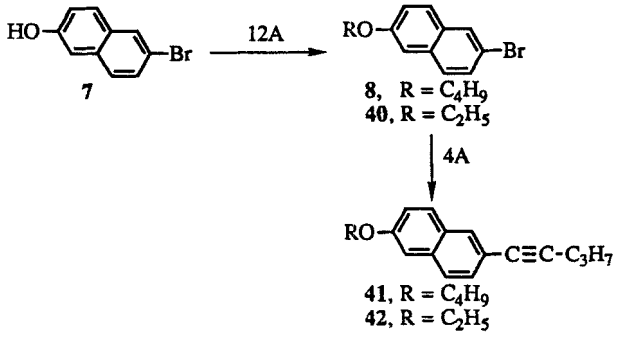
unit with two suitable leaving groups. 2-Hydroxypyrimidine hydrochloride (compound **34**) was brominated (bromine water) [17] and then, without purification, the hydroxyl group was replaced with a chloro-substituent using phosphorus oxychloride [18]. This provided a bromo-chloro-substituted pyrimidine and the selectivity towards pentynylzinc chloride was not easy to predict because normally chloro-substiutents are inert to these coupling reactions, and yet the two heterocyclic nitrogens would be expected to activate this leaving group and perhaps confer similar reactivity to that of the bromo-substituent. In the event, selectivity was 100 per cent at the bromo site at room temperature, but the reaction was rather slow and only a moderate yield of compound **36** was isolated (34 per cent). However, a repeat procedure at 50°C also gave 100 per cent selectivity at the bromo site, but this time the reaction was complete in 2·25 h and an isolated yield of 85 per cent was obtained for compound **36**. A subsequent coupling of compound **36** to the zinc chloride derivative of terminal acetylene **3** at elevated temperature occurred at the activated chloro site to give the pyrimidine based liquid crystal (compound **37**). Although GLC analysis indicated a complete reaction, the isolated yield of pure material was unexpectedly low (27 per cent).

Scheme 11 shows how both alkynylzinc chloride coupling and arylboronic acid coupling can be combined in an appropriate manner to produce a liquid crystal



11A, (i) *n*BuLi, THF; (ii) $(^{i}PrO)_3B$, THF; (iii) 10 per cent HCl. 11B, $Pd(PPh_3)_4$, DME, 2 M Na_2CO_3.

Scheme 11.



12A, RBr, butanone, K_2CO_3.

Scheme 12.

compound [2]. Compound **36** was produced from a zinc chloride coupling and the activated chloro site of this compound was then coupled to an arylboronic acid in the usual way [4] to provide another pyrimidine based liquid crystal (compound **39**) in excellent yield (74 per cent).

Scheme 12 shows the synthesis of naphthyl acetylenes (compounds **41** and **42**) by the use of just one coupling reaction. The simple alkylated bromonaphthol units were involved in zinc chloride coupling reactions, as previously described, with pentynylzinc chloride to provide good yields.

3. Discussion of transition temperatures

All of the compounds shown in table 1 are based on the 2,6-naphthyl core with a central acetylene linkage to a 1,4-phenyl core. Compound **10** has a very high melting point (149·0°C) in keeping with the expectation for such a dialkoxy-substituted system where both substituents are identical. The pentyl-substituted analogue (compound **11**)

Table 1. Transition temperatures for terminal alkoxy-, alkyl- and alkynyl-substituted 2,6-naphthyl-1,4-phenylethynes (**10**, **11**, **13** and **17**).

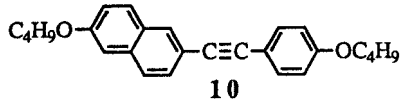
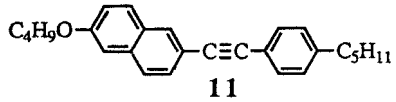
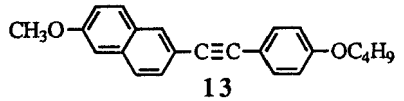
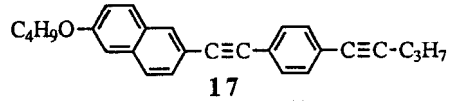
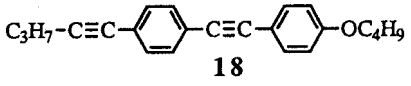
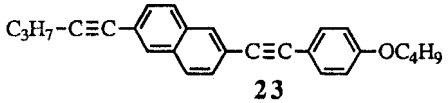
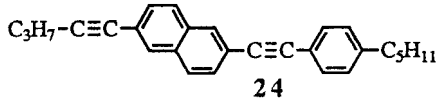
Compound	Transition temperatures/°C
 **10**	C 149·0 N 178·5 I
 **11**	C 82·0 N 143·0 I
 **13**	C 131·0 N 185·0 I
 **17**	C 126·5 N 171·0 I

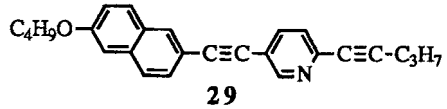
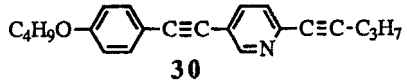
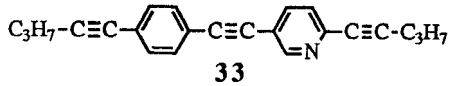
Table 2. Transition temperatures for some alkoxy-, alkyl- and alkynyl-substituted 2,6-naphthyl-1,4-phenylethynes (**18**, **23** and **24**).

Compound	Transition temperatures/°C
 **18**	C 120 (N 115·0) I
 **23**	C 124·0 N 172·0 I
 **24**	C 106·5 N 129·0 I

has a much lower melting point, with the large difference (67°C) arising because the end groups are no longer identical. The T_{NI} values of both of these compounds are high and, typically, the T_{NI} value is 35·5°C lower for the alkyl-substituted compound **11**. Compounds with terminal methoxy-substituents are renowned for their high melting points, but the melting point of compound **13** is actually lower than that for the longer butoxy-substituted system (compound **10**) because the end groups in **13** are different and give a less symmetrical molecular shape. As expected, the T_{NI} value of the methoxy-substituted system (compound **13**) is slightly higher than that for the butoxy-substituted homologue (compound **10**). In compound **17** the butoxy-substituent in the naphthyl core is retained but the other terminal substituent was changed to a pentynyl moiety. This substituent extends the conjugated core when compared with an alkyl system of equivalent length, as for compound **11**. In such a comparison the melting point has, not surprisingly, increased (by 44·5°C), but also the T_{NI} value has increased significantly (28°C). The values for compound **23** (see table 2) show that reversing the substituents in the core structure, when compared to compound **17**, has had very little effect on either melting point or clearing point.

Compound **18** is a simple acetylene-phenyl-acetylene-phenyl system and it was anticipated that its melting point would be significantly lower than that for the naphthyl-substituted analogue (compound **23**). However, the melting point is only slightly lower, and this, combined with the expected much reduced T_{NI} value, renders compound **18** non-mesomorphic (a virtual measurement extrapolated from mixtures in E7 revealed a T_{NI} value of 115°C). Typical reductions in melting point (17·5°C) and T_{NI} value (43°C) are seen on going from the butoxy compound **23** to the alkyl system (compound **24**) but the effect on melting point is much smaller than was seen for compounds **10** and **11** (see previous discussion). Table 3 shows a range of acetylene systems with a pyridine unit. The heterocyclic nitrogen of compound **29** has led to an increase in melting point (11·5°C) when compared to the parent system (compound **17**), and a similar increase in T_{NI} value is found (12·5°C). However, a similar comparison of the non-naphthalene system (compound **30**) with its parent compound (**18**) shows a significant reduction in melting point (27·5°C) which has provided a nematogenic compound with a T_{NI} value similar to the virtual value of the parent system. The reduced melting point of compound **30** is probably due to the symmetry-breaking effect of the heterocyclic nitrogen. However, in compound **29**, the naphthalene unit is likely to dominate the symmetry-breaking effect of the heterocyclic nitrogen and so the full

Table 3. Transition temperatures for some alkoxy- and alkynyl-substituted 2,6-naphthyl- and 1,4-phenyl-2,5-pyridinyl ethynes (**29**, **30** and **33**).

Compound	Transition temperatures/°C
 **29**	C 138·0 N 183·5 I
 **30**	C 92·5 N 115·0 I
 **33**	C 119·0 (N 100·5) I

effects of the increased polarizability are seen in terms of increased melting point and increased T_{NI} value. The replacement of the terminal butoxy-substituent of compound **30** with a pentynyl moiety (compound **33**) has led to an increase in melting point (by 26·5°C) because of the resulting identical terminal groups. A corresponding reduction in T_{NI} value has left compound **33** with a monotropic nematic phase.

The pyrimidine compound (**37**) shown in table 4 is best compared with both its parent system (compound **18**) and its pyridine analogue (compound **30**, although this is not a valid comparison for the sequential introduction of nitrogen, because the positions of the nitrogen atoms are different). It can be seen that the pyrimidine compound (**37**) has a melting point which is intermediate between that for the parent system and the pyridine compound. The T_{NI} value, however, is 16°C higher than that of either the parent system or the pyridine compound. The higher melting point and clearing point values when compared to the pyridine analogue (**30**) are due to the second heterocylic nitrogen providing increased polarizability. The directly linked phenylpyrimidine system (compound **39**) has a compact structure which will pack efficiently and this is responsible for the high melting point. However, in comparison with the naphthyl-acetylene-pyridine unit (compound **29**), the melting point is very similar. In terms of overall structure, the naphthalene unit of compound **39** has formally replaced the phenyl-acetylene moiety of compound **37**. The result of this structural change is a significant increase in melting point (30·5°C) and only a slight increase (15·5°C) in the T_{NI} value; these changes are not beneficial when the principal requirement is a lower melting point.

The compact naphthyl-acetylene compounds (**41** and **42**), shown in table 5, were synthesized to produce dopants of high optical anisotropy for small molecules with low melting points. It turns out that the melting points of such compounds are not

Table 4. Transition temperatures for 1-(4-butoxyphenyl)-2-(5-pent-1-ynyl-pyrimidin-2-yl-) ethyne (**37**) and 2-Butoxy-6-(5-pent-1-ynyl-pyrimidin-2-yl)naphthalene (**39**).

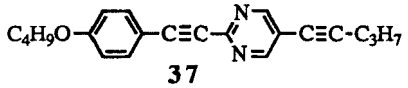
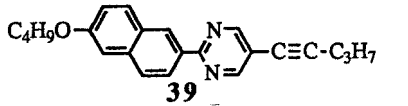
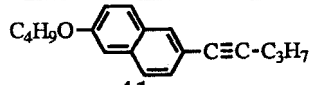
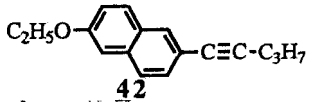
Compound	Transition temperatures/°C
 **37**	C 106·0 N 131·5 I
 **39**	C 136·5 N 146·5 I

Table 5. Transition temperature for 2-butoxy- and 2-Ethoxy-6-pent-1-ynylnaphthalenes (**41** and **42**).

Compound	Transition temperatures/°C
 **41**	C 51·0 (N −23) I
 **42**	C 65·0 (N −30) I

particularly low but the virtual T_{NI} values, as determined from extrapolated mixtures in E7, were both below −20°C.

4. Experimental

Confirmation of the structures of intermediates and products was obtained by ^{1}H NMR spectroscopy (JEOL JNM-GX270 spectrometer), infrared spectroscopy (Perkin–Elmer 457 grating spectrophotometer) and mass spectrometry (Finnigan-MAT 1020 GC/MS spectrometer). The progress of reactions was frequently monitored using a Perkin–Elmer 8320 capillary gas chromatograph fitted with a 12 m QC2/BPI-1·0 SGE column. Transition temperatures were measured using a Mettler FP 5 hot stage and control unit in conjunction with an Olympus BH2 polarizing microscope and these were confirmed using differential scanning calorimetry (Perkin–Elmer DSC-7 and IBM data station). The purity of each of the compounds shown in tables 1–5 was checked by GLC analysis (see above) and by HPLC analysis (Microsorb C18 80-215-C5 RP column) and all compounds were >99 per cent pure except where indicated otherwise.

Pent-1-yne and compounds **1, 4, 7, 15, 27** and **34** were purchased form Aldrich Chemical Co. Ltd. Tetrakis(triphenylphosphine)palladium(0) [19] was prepared according to the literature procedure.

4.1. *1-Butoxy-4-iodobenzene* (**2**)

Quantities: compound **1** (44·0 g, 0·20 mol), 1-bromobutane (45·0 g, 0·33 mol), potassium carbonate (56·0 g, 0·41 mol). The experimental procedure was as described in a previous publication [4] and the crude product was distilled. Yield 51·81 g (94 per cent); bp 108–110°C at 0·1 mmHg; ^{1}H NMR ($CDCl_3$) δ, 0·95(3 H, t), 1·45 (2 H, sext.), 1·75 (2 H, quint.), 3·90 (2 H, t), 6·65 (2 H, d), 7·60 p.p.m. (2 H, d); IR (film) ν_{max}, 2960, 2940, 2860, 1590, 1575, 1485, 1475, 1285, 1245, 1175, 1000, 820 cm^{-1}; MS *m/z* 276 (M^+), 220, 143.

4.2. *4-Butoxyphenylethyne* (**3**)

A solution of zinc chloride (31·1 g, 0·23 mol) in dry THF (200 ml) was added dropwise to a stirred, cooled (−5 to 0°C) solution of lithium acetylide ethylenediamine complex (21·00 g, 0·228 mol) in dry THF (170 ml) under dry nitrogen. The mixture was stirred at 10°C for 30 min and a solution of compound **2** (24·00 g, 0·087 mol) in dry THF (50 ml) was added dropwise at −5 to 0°C followed by the addition of tetrakis(triphenylphosphine)palladium(0) (3·17 g, 2·74 mmol). The mixture was stirred at room temperature overnight (GLC analysis revealed a complete reaction). The mixture was poured into 10 per cent hydrochloric acid and the product was extracted into ether (×2). The combined ethereal extracts were washed with aqueous sodium hydrogen carbonate and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was filtered through a short alumina column to remove some of the catalyst and then distilled. Yield 7·60 g (50 per cent); bp 80–82° at 0·1 mm Hg; ^{1}H NMR ($CDCl_3$) δ, 0·95 (3 H, t), 1·45 (2 H, sext.), 1·75 (2 H, quint.), 3·00 (1 H, s), 3·95 (2 H, t), 6·80 (2 H, d), 7·40 p.p.m. (2 H, d); IR (film) ν_{max}, 3300, 2960, 2940, 2880, 2120, 1610, 1510, 1475, 1295, 1250, 1175, 835 cm^{-1}; MS *m/z* 174 (M^+), 118, 89.

4.3. *1-Iodo-4-pentylbenzene* (**5**)

Quantities: compound **4** (20·0 g, 0·12 mol), 36 per cent hydrochloric acid (100 ml), sodium nitrite (10·50 g, 0·15 mol), potassium iodide (43·5 g, 0·26 mol). The experimental

procedure was as described in a previous publication [20] and the crude product was distilled. Yield 29·0 g (88 per cent); bp 90–95°C at 0·1 mm Hg; ^{1}H NMR ($CDCl_3$) δ, 0·90 (3 H, t), 1·25 (4 H, m), 1·55 (2 H, quint.), 2·50 (2 H, t), 6·90 (2 H, d), 7·55 p.p.m. (2H, d); IR (film) ν_{max}, 2960, 2940, 2860, 1490, 1405, 1065, 1010, 795 cm^{-1}; MS *m/z* 274 (M^+), 217.

4.4. *4-Pentylphenylethyne* (**6**)

Quantities: lithium acetylide ethylenediamine complex (20·25 g, 0·22 mol), zinc chloride (30·0 g, 0·22 mol), compound **5** (24·0 g, 0·088 mol), tetrakis(triphenylphosphine)palladium(0) (3·12 g, 2·70 mmol). The experimental procedure was as described for the preparation of compound **3**. Yield 7·80 g (52 per cent); bp 122–123°C at 15 mmHg; ^{1}H NMR ($CDCl_3$) δ, 0·90 (3 H, t), 1·30 (4 H, m), 1·55 (2 H, quint.), 2·55 (2 H, t), 3·00 (1 H, s), 7·10 (2 H, d), 7·40 p.p.m. (2 H, d); IR (film) ν_{max}, 3320, 2960, 2880, 2130, 1620, 1520, 1480, 1125, 1030, 850, 830, 660, 655, 620, 565 cm^{-1}; MS *m/z* 172 (M^+), 115.

4.5. *2-Bromo-6-butoxynaphthalene* (**8**)

Quantities: compound **7** (40·0 g, 0·18 mol), 1-bromobutane (50·0 g, 0·36 mol), potassium carbonate (51·0 g, 0·37 mol). The experimental procedure was as described in a previous publication [4]. The crude product was recrystallized from ethanol to yield an off-white powder. Yield 32·2 g (64 per cent); mp 52–53°C; ^{1}H NMR ($CDCl_3$) δ, 1·00 (3 H, t), 1·55 (2 H, sext.), 2·85 (2 H, quint.), 4·05 (2 H, t), 7·08 (1 H, d), 7·15 (1 H, q), 7·48 (1 H, q), 7·58 (1 H, d), 7·63 (1 H, d), 7·90 p.p.m. (1 H, q); IR (KCl) ν_{max}, 2960, 2950, 2880, 1630, 1590, 1500, 1390, 1260, 1210, 1175, 1070, 920, 890, 850, 830 cm^{-1}; MS *m/z* 280 (M^+), 278 (M^+), 224, 222, 195, 193.

4.6. *2-Butoxy-6-iodonaphthalene* (**9**)

A mixture of compound **3** (20·0 g, 0·072 mol), potassium iodide (180·0 g, 1·08 mol), copper(I) iodide (68·6 g, 0·36 mol), in hexamethylphosphoramide (HMPA) (200 ml) was stirred at 160°C under dry nitrogen for 18 h (GLC analysis revealed a complete reaction). The cooled mixture was poured into 10 per cent hydrochloric acid (300 ml) and the product was extracted into ether, and left at room temperature overnight. The insoluble copper salts were filtered off and washed well with ether as was the separated aqueous layer. The combined ethereal extracts were washed with water, aqueous sodium sulphite, and dried ($MgSO_4$). The solvent was removed *in vacuo* to yield a pale yellow solid. Yield 22·75 g (97 per cent); mp 66–67°C; ^{1}H NMR ($CDCl_3$) δ, 1·00 (3 H, t), 1·50 (2 H, sext.), 1·80 (2 H, quint.), 4·05 (2 H, t), 7·05 (1 H, d), 7·13 (1 H, q), 7·45 (1 H, d), 7·60 (1 H, d), 7·64 (1 H, q), 8·12 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2860, 1625, 1585, 1500, 1460, 1390, 1260, 1215, 1170, 915, 890, 855, 825 cm^{-1}; MS *m/z* 326 (M^+), 270, 200, 143.

4.7. *1-(6-Butoxynaphth-2-yl)-2-(4-butoxyphenyl)ethyne* (**10**)

A solution of *n*-butyllithium (2·60 ml, 2·5 M in hexane, 6·50 mmol) was added dropwise to a stirred, cooled (−5 to 0°C) solution of compound **3** (1·10 g, 6·32 mmol) in dry THF (50 ml) under dry nitrogen. This mixture was stirred for 10 min and a solution of zinc chloride (0·90 g, 6·62 mmol) in dry THF (50 ml) was added dropwise at −5 to 0°C. The mixture was then stirred at room temperature for 15 min and a solution of compound **9** (2·00 g, 6·13 mmol) in dry THF (30 ml) was added dropwise at −5 to 0°C followed by the addition of tetrakis(triphenylphosphine)palladium(0) (0·3721 g, 0·32 mmol). The mixture was stirred at room temperature overnight (GLC analysis

revealed almost complete reaction) and poured into 10 per cent hydrochloric acid. The product was extracted into ether (× 2), and the combined ethereal extracts were washed with aqueous sodium hydrogen carbonate and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 4 : 1) to give a colourless solid which was recrystallized from ethanol–ethyl acetate (20 : 1) to yield colourless crystals. Note: GLC analysis revealed the presence of some starting material (compound **9**) which was isolated during purification as a colourless solid (0·33 g). Yield 0·22 g (22 per cent); transitions (°C) C 149·0 N 178·5 I; ^{1}H NMR ($CDCl_3$) δ, 1·00 (6 H, 2 × t), 1·55 (4 H, m), 1·80 (4 H, m), 3·95 (2 H, t), 4·05 (2 H, t), 6·87 (2 H, d), 7·10 (1 H, d), 7·14 (1 H, q), 7·47 (2 H, d), 7·53 (1 H, q), 7·66 (1 H, d), 7·70 (1 H, d), 7·94 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2860, 1620, 1600, 1515, 1470, 1395, 1390, 1250, 1210, 1175, 900, 865, 835 cm^{-1}; MS *m/z* 372 (M^+), 316, 260.

4.8. *1-(6-Butoxynaphth-2-yl)-2-(4-pentylphenyl)ethyne* (**11**)

Quantities: compound **6** (1·35 g, 7·85 mmol), *n*-butyllithium (3·20 ml, 2·5 M in hexane, 8·00 mmol), zinc chloride (1·15 g, 8·45 mmol), compound **9** (2·35 mmol), tetrakis(triphenylphosphine)palladium(0) (0·3101 g, 0·27 mmol). The experimental procedure was as described for the preparation of compound **10**. The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 12 : 1) to give a colourless solid which was recrystallized from ethanol–ethyl acetate (20 : 1) to yield colourless crystals. Yield 1·70 g (64 per cent); transitions (°C) C 82·0 N 143·0 I; ^{1}H NMR ($CDCl_3$) δ, 0·90 (3 H, t), 1·05 (3 H, t), 1·35 (4 H, m), 1·65 (4 H, m), 1·85 (2 H, quint.), 2·65 (2 H, t), 4·10 (2 H, t), 7·10 (1 H, d), 7·14 (1 H, q), 7·18 (2 H, d), 7·47 (2 H, d), 7·54 (1 H, q), 7·67 (1 H, d), 7·71 (1 H, d), 7·96 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2980, 2940, 2860, 1630, 1605, 1470, 1390, 1260, 1210, 1175, 1140, 1070, 1025, 980, 965, 865, 850, 820 cm^{-1}; MS *m/s* 370 (M^+), 355, 314, 257.

4.9. *2-Bromo-6-methoxynaphthalene* (**12**)

Dimethyl sulphate (33·80 g, 0·268 mol) was added to a stirred solution of compound **7** (50·00 g, 0·224 mol) and potassium hydroxide (15·00 g, 0·268 mol) in water (220 ml) at room temperature. The stirred mixture was heated at 70°C for 1 h and stirred at room temperature overnight (TLC and GLC analysis revealed a complete reaction). The product was filtered off, washed with 10 per cent sodium hydroxide, water and dried well and then extracted into dichloromethane. The organic extract was washed with 10 per cent sodium hydroxide, water and dried ($MgSO_4$). The solvent was removed *in vacuo* to give a colourless solid. Yield 50·9 g (96 per cent); mp 108–110°C; ^{1}H NMR ($CDCl_3$) δ, 3·90 (3 H, s), 7·09 (1 H, d), 7·16 (1 H, q), 7·49 (1 H, q), 7·60 (1 H, d), 7·64 (1 H, d), 7·91 p.p.m. (1 H, d); IR (KCl) ν_{max}, 1630, 1595, 1500, 1390, 1265, 1215, 1170, 1070, 1035, 905, 855, 820 cm^{-1}; MS *m/z* 238 (M^+), 236 (M^+), 223, 221, 208, 206, 195, 193.

4.10. *1-(4-Butoxyphenyl)-2-(6-methoxynaphth-2-yl)ethyne* (**13**)

Quantities: compound **3** (2·50 g, 0·014 mol), *n*-butyllithium (5·75 ml, 2·5 M in hexane, 0·014 mol), zinc chloride (2·00 g, 0·015 mol), compound **12** (2·80 g, 0·012 mol), tetrakis(triphenylphosphine)palladium(0) (0·6939 g, 0·60 mmol). The experimental procedure was similar to that described for the preparation of compound **10** except that the mixture was heated under reflux for 22 h (overnight for convenience; GLC and TLC analysis revealed a complete reaction). The crude mixture was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 4 : 1) to give a colourless solid which was recrystallized from ethanol-ethyl acetate (1 : 1) to yield

colourless crystals. Yield 2·55 g (64 per cent); transitions (°C) C 131·0 N 185·0 I; ^{1}H NMR ($CDCl_3$) δ, 1·00 (3 H, t), 1·50 (2 H, sext.), 1·80 (2 H, quint.), 3·90 (3 H, s), 4·00 (2 H, t), 6·88 (2 H, d), 7·10 (1 H, d), 7·15 (1 H, q), 7·48 (2 H, d), 7·53 (1 H, q), 7·68 (1 H, d), 7·70 (1 H, d), 7·95 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2880, 1600, 1515, 1485, 1390, 1260, 1250, 1215, 1170, 1035, 900, 860, 825 cm^{-1}; MS *m/z* 330 (M^+), 315, 274, 259.

4.11. *6-Butoxynaphth-2-ylethyne* (**14**)

Quantities: lithium acetylide ethylenediamine complex (8·50 g, 0·092 mol), zinc choloride (12·60 g, 0·093 mol), compound **9** (12·00 g, 0·037 mol), tetrakis-(triphenylphosphine)palladium(0) (2·15 g, 1·86 mmol). The experimental procedure was as described for the preparation of compound **3**. The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 10 : 1) to yield a colourless solid. Yield 6·76 g (82 per cent); mp 35–36°C; ^{1}H NMR ($CDCl_3$) δ, 1·00 (3 H, t), 1·50 (2 H, sext.), 1·80 (2 H, quint.), 3·10 (1 H, s), 4·05 (2 H, t), 7·08 (1 H, d), 7·15 (1 H, q), 7·47 (1 H, q), 7·64 (1 H, d), 7·68 (1 H, d), 7·93 p.p.m. (1 H, d); IR (KCl) ν_{max}, 3320, 2960, 2940, 2880, 2120, 1635, 1605, 1505, 1470, 1395, 1270, 1230, 1175, 1125, 895, 855, 815 cm^{-1}; MS *m/z* 224 (M^+), 168, 150, 139.

4.12. *1-Bromo-4-pent-1-ynylbenzene* (**16**)

Quantities: pent-1-yne (5·28 g, 0·078 mol), *n*-butyllithium (7·80 ml, 10·0 M in hexane, 0·078 mol), zinc chloride (10·80 g, 0·079 mol), compound **15** (5·28 g, 0·078 mol), tetrakis(triphenylphosphine)palladium(0) (2·80 g, 2·40 mmol). The experimental procedure was as described for the preparation of compound **10**. Yield 14·20 g (82 per cent); bp 130–134°C at 15 mm Hg; ^{1}H NMR ($CDCl_3$) δ, 1·05 (3 H, t), 1·60 (2 H, sext.), 2·35 (2 H, t), 7·20 (2 H, d), 7·40 p.p.m. (2 H, d); IR (film) ν_{max}, 2960, 2940, 2860, 1485, 1395, 1340, 1070, 1010, 1000, 820 cm^{-1}; MS *m/z* 224 (M^+), 223, 222 (M^+), 221, 209, 207, 202, 200, 185, 183.

4.13. *1-(6-Butoxynaphth-2-yl)-2-(4-pent-1-ynylphenyl)ethyne* (**17**)

Quantities: compound **14** (1·60 g, 7·14 mmol), *n*-butyllithium (2·90 ml, 2·5 M in hexane, 7·25 mmol), zinc chloride (1·00 g, 7·35 mmol), compound **16** (1·57 g, 7·04 mmol), tetrakis(triphenylphosphine)palladium(0) (0·4129 g, 0·36 mmol). The experimental procedure was as described for the preparation of compound **13**. The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 4 : 1) to yield a colourless solid which was recrystallized from ethanol–ethyl acetate (1 : 1) to yield colourless crystals. Yield 1·77 g (77 per cent); transitions (°C) C 126·5 N 171·0 I; ^{1}H NMR ($CDCl_3$) δ, 0·95 (3 H, t), 1·05 (3 H, t), 1·50 (2 H, sext.), 1·65 (2 H, sext.), 1·85 (2 H, quint.), 2·40 (2 H, t), 4·10 (2 H, t), 7·10 (1 H, d), 7·17 (1 H, q), 7·37 (2 H, d), 7·47 (2 H, d), 7·52 (1 H, q), 7·67 (1 H, d), 7·71 (1 H, d), 7·96 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2880, 1625, 1600, 1470, 1390, 1260, 1215, 1175, 860, 840, 820 cm^{-1}; MS *m/z* 366 (M^+), 337, 323, 310, 281.

4.14 *1-(4-Butoxyphenyl)-2-(4-pent-1-ynylphenyl)ethyne* (**18**)

A stirred mixture of compound **3** (1·22 g, 7·01 mmol), compound **16** (1·55 g, 6·95 mmol), copper(I) iodide (0·10 g, 0·53 mmol) and tetrakis-(triphenylphosphine)palladium(0) (0·42 g, 0·36 mmol) in dry triethylamine (40 ml) was heated under reflux under dry nitrogen for 19 h (GLC analysis revealed almost complete reaction). Ether and water were added to the cooled reaction mixture and the aqueous layer was washed with ether and the combined ethereal extracts were washed

with brine and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)—dichloromethane, 5 : 1) to give an off-white solid which was recrystallized from hexane to yield colourless crystals. Yield 1·00 g (46 per cent); transitions (°C) C 120·0 (N 115·0) I; ^{1}H NMR ($CDCl_3$) δ, 0·95 (3 H, t), 1·05 (3 H, t), 1·45 (2 H, sext.), 1·65 (2 H, sext.), 1·80 (2 H, quint.), 2·40 (2 H, t), 3·95 (2 H, t), 6·86 (2 H, d), 7·35 (2 H, d), 7·41 (2 H, d), 7·45 p.p.m. (2 H, d); IR (KCl) ν_{max}, 2960, 2940, 2860, 2220, 1610, 1600, 1520, 1290, 1245, 1175, 845 cm^{-1}; MS *m/z* 316 (M^+), 260, 231.

4.15. *2-Iodo-6-methoxynaphthalene* (**19**)

Quantities: compound **12** (15·00 g, 0·063 mol), potassium iodide (158·0 g, 0·95 mol), copper(I) iodide (60·5 g, 0·32 mol), HMPA (180 ml). The experimental procedure was as described for the preparation of compound **9**. Yield 17·50 g (98%); mp 138–140°C. ^{1}H NMR ($CDCl_3$) δ, 3·95 (3 H, s), 7·07 (1 H, d), 7·13 (1 H, q), 7·46 (1 H, d), 7·60 (1 H, d), 7·65 (1 H, q), 8·14 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2840, 1625, 1580, 1500, 1390, 1265, 1215, 1035, 900, 855, 820 cm^{-1}; MS *m/z* 284 (M^+), 269, 241.

4.16. *6-Iodonaphth-2-ol* (**20**)

Quantities: compound **19** (10·00 g, 0·035 mol,), boron tribromide (10·0 ml, 22·00 g, 0·088 mol). The experimental procedure was as described in a previous publication [21]. Yield 9·45 g (100%); mp 129–131°C; ^{1}H NMR ($CDCl_3$) δ, 5·15 (1 H, s), 7·07 (1 H, d), 7·09 (1 H, q), 7·40 (1 H, d), 7·61 (1 H, d), 7·63 (1 H, q), 8·13 p.p.m. (1 H, d); IR (KCl) ν_{max}, 3500–3000, 1630, 1585, 1505, 1395, 1350, 1260, 1210, 905, 860, 815 cm^{-1}; MS *m/z* 270 (M^+), 182, 143.

4.17. *6-Iodonaphth-2-yl triflate* (**21**)

A solution of *N*-phenyltriflamide (8·35 g, 0·023 mol) is dry dichloromethane (50 ml) was added dropwise to a stirred, cooled (−78°C) solution of compound **20** (6·00 g, 0·022 mol) in dry dichloromethane (80 ml) and dry triethylamine (4·50 g, 0·045 mol) under dry nitrogen. The stirred mixture was allowed to warm to room temperature overnight (GLC and TLC analysis revealed a complete reaction). The mixture was washed with aqueous sodium carbonate and the separated aqueous layer was washed with dichloromethane. The combined organic extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel/dichloromethane) to give an off-white solid. Yield 8·80 g (100 per cent); mp 65–66°C; ^{1}H NMR ($CDCl_3$) δ, 7·38 (1 H, q) 7·60 (1 H, d), 7·71 (1 H, d), 7·80 (1 H, d), 7·82 (1 H, q), 8·30 p.p.m. (1 H, d); IR (KCl) ν_{max}, 1500, 1420, 1210, 1200, 1145, 1110, 960, 915, 880, 805, 720, 650, 605 cm^{-1}; MS *m/z* 402 (M^+), 269, 241.

4.18. *6-Pent-1-ynylnaphth-2-yl triflate* (**22**)

Quantities: pent-1-yne (1·60 g, 0·0235 mol), *n*-butyllithium (2·35 ml, 10·0 M in hexane, 0·0235 mol), zinc chloride (3·20 g, 0·0235 mol), compound **21** (8·20 g, 0·020 mol), tetrakis(triphenylphosphine)palladium(0) (1·20 g, 1·0 mmol). The experimental procedure was as described for the preparation of compound **10**. The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 5 : 1) to give a pale yellow oil. Yield 6·33 g (92 per cent); ^{1}H NMR ($CDCl_3$) δ, 1·10 (3 H, t), 1·70 (2 H, sext.), 2·45 (2 H, t), 7·34 (1 H, q), 7·53 (1 H, q), 7·68 (1 H, d), 7·75 (1 H, d), 7·81 (1 H, d), 7·92 p.p.m. (1 H, d); IR (film) ν_{max}, 2980, 2950, 2880, 2240, 1605, 1505, 1430, 1250, 1220, 1145, 1110, 960, 920, 890, 860, 810 cm^{-1}; MS *m/z* 342 (M^+), 313, 209.

4.19 *1-(4-Butoxyphenyl)-2-(6-pent-1-ynylnaphth-2-yl)ethyne* (**23**)

Quantities: compound **3** (1·10 g, 6·32 mmol), *n*-butyllithium (3·95 ml, 1·6 M in hexane, 6·33 mmol), zinc chloride (0·90 g, 6·61 mmol), compound **22** (2·05 g, 6·00 mmol), tetrakis(triphenylphosphine)palladium(0) (0·2414 g, 0·21 mmol), lithium chloride (0·5810 g, 0·014 mol). The experimental procedure was as described for the preparation of compound **13** except that lithium chloride was added with the tetrakis-(triphenylphosphine)palladium(0). The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 4 : 1) to give a colourless solid which was recrystallized from ethanol–ethyl acetate (1 : 1) to yield colourless crystals. Yield 1·41 g (64 per cent); transitions (°C) C 124·0 N 172·0 I; ^{1}H NMR ($CDCl_3$) δ, 0·95 (3 H, t), 1·10 (3 H, t), 1·50 (2 H, sext.), 1·65 (2 H, sext.), 1·80 (2 H, quint.), 2·45 (2 H, t), 4·00 (2 H, t), 6·88 (2 H, d), 7·45 (1 H, q), 7·48 (2 H, d), 7·54 (1 H, q), 7·71 (2 H, 2 × d), 7·86 (1 H, d), 7·96 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2860, 1610, 1520, 1475, 1290, 1250, 1180, 1110, 905, 840, 830 cm^{-1}; MS *m/z* 366 (M^+), 281.

4.20. *1-(4-Pentylphenyl)-2-(6-pent-1-ynylnaphth-2-yl)ethyne* (**24**)

Quantities: compound **6** (1·08 g, 6·28 mmol), *n*-butyllithium (3·95 ml, 1·6 M in hexane, 6·33 mmol), zinc chloride (0·90 g, 6·61 mmol), compound **22** (2·05 g, 6·00 mmol), tetrakis(triphenylphosphine)palladium(0) (0·2310 g, 0·20 mmol), lithium chloride (0·5269 g, 0·012 mol). The experimental procedure was as described for the preparation of compound **23**. The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 5 : 1) to give a pale yellow solid which was recrystallized from ethanol–ethyl acetate (2 : 1) to yield colourless crystals. Yield 1·37 g (63 per cent); transitions (°C) C 106·5 N 129·0 I; ^{1}H NMR ($CDCl_3$) δ, 0·90 (3 H, t), 1·10 (3 H, t), 1·30 (4 H, m), 1·65 (4 H, m), 2·45 (2 H, t), 2·65 (2 H, t), 7·17 (2 H, d), 7·45 (1 H, q), 7·48 (2 H, d), 7·55 (1 H, q), 7·71 (2 H, 2 × d), 7·87 (1 H, d), 7·97 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2880, 1600, 1515, 1480, 1025, 900, 830 cm^{-1}; MS *m/z* 364 (M^+), 335, 307, 278.

4.21 *6-Bromonaphth-2-yl triflate* (**25**)

Quantities: compound **7** (2·80 g, 0·0126 mol), *N*-phenyltriflamide (4·93 g, 0·0138 mol), triethylamine (2·55 g, 0·025 mol). The experimental procedure was as described for the preparation of compound **21**. The crude product was purified by column chromatography (silica gel/dichloromethane) to give an off-white solid. Yield 4·40 g (98 per cent); mp 52–53°C; ^{1}H NMR ($CDCl_3$) δ, 7·37 (1 H, q), 7·61 (1 H, q), 7·69 (1 H, d), 7·71 (1 H, d), 7·79 (1 H, d), 8·01 p.p.m. (1 H, d); IR (KCl) ν_{max}, 1595, 1505, 1420, 1250, 1210, 1200, 1145, 1110, 920, 890, 880, 805, 720, 660, 610 cm^{-1}; MS *m/z* 356 (M^+), 254 (M^+), 223, 221, 195, 193.

4.22 *2-Bromo-6-(pent-1-ynyl)naphthalene* (**26**)

Quantities: pent-1-yne (1·02 g, 0·015 mol), *n*-butyllithium (6·00 ml, 2·5 M in hexanes, 0·015 mol), zinc chloride (2·05 g, 0·015 mol), compound **25** (4·80 g, 0·0135 mol). tetrakis(triphenylphosphine(palladium(0) (0·50 g, 0·43 mmol). The experimental procedure was as described for the preparation of compound **13** except that the mixture was heated under reflux for 4 h (GLC analysis revealed a complete reaction, two product peaks were present but no double-coupled material was detected). The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C) to give a colourless solid. Yield 2·10 g (57 per cent); mp 80–81°C; ^{1}H NMR ($CDCl_3$) δ, 1·05 (3 H, t), 1·65 (2 H, sext.), 2·45 (2 H, t), 7·47 (1 H, q), 7·52 (1 H, q), 7·63 (1 H, d), 7·65 (1 H, d), 7·85 (1 H, d), 7·94 p.p.m. (1 H, d); IR (KBr) ν_{max}, 2960, 2940, 2860, 1590, 1490, 1465, 1285, 1215, 1140, 1065, 895, 825, 650 cm^{-1}; MS *m/z* 274 (M^+), 272 (M^+), 259, 257, 245, 243.

4.23 *5-Bromo-2-pent-1-ynylpyridine* (**28**)

Quantities: pent-1-yne (3·07 g, 0·045 mol), *n*-butyllithium (4·50 ml, 10·0 M in hexane, 0·045 mol), zinc chloride (6·15 g, 0·045 mol), compound **27** (10·00 g, 0·042 mol), tetrakis(triphenylphosphine)palladium(0) (1·46 g, 1·26 mmol). The experimental procedure was as described for the preparation of compound **10**. The crude product was purified by column chromatography silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 1 : 2) to give a colourless solid which was recrystallized from hexane mp 22°C; ^{1}H NMR ($CDCl_3$) δ, 1·05 (3 H, t), 1·70 (2 H, sext.), 2·40 (2 H, t), 7·26 (1 H, d), 7·74 (1 H, q), 8·59 p.p.m. (1 H, d); IR (film) ν_{max}, 2960, 2940, 2880, 2240, 1570, 1550, 1460, 1370, 1090, 1005, 835, 645 cm^{-1}; MS *m/z* 225 (M^+), 223 (M^+), 210, 208, 197, 195.

4.24. *1-(6-Butoxynaphth-2-yl)-2-(2-pent-1-ynylpyridin-5-yl)ethyne* (**29**)

Quantities: compound **14** (1·35 g, 6·03 mmol), *n*-butyllithium (2·40 ml, 2·5 M, in hexane, 6·00 mmol), zinc chloride (0·85 g, 6·25 mmol), compound **28** (1·30 g, 5·80 mmol), tetrakis(triphenylphosphine)palladium(0) (0·2176 g, 0·19 mmol). The experimental procedure was as described for the preparation of compound **13**. The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 1 : 3) to give a colourless solid which was recrystallized from hexane-1,2-dimethoxyethane (10 : 1) to yield colourless crystals. Yield 0·86 g (40 per cent); transitions (°C) C 138·0 N 183·5 I; ^{1}H NMR ($CDCl_3$) δ, 0·95 (3 H, t), 1·05 (3 H, t), 1·50 (2 H, sext.), 1·65, (2 H, sext.), 1·85 (2 H, quint.), 2·45 (2 H, t), 4·10 (2 H, t), 7·11 (1 H, d), 7·17 (1 H, q), 7·38 (1 H, d), 7·51 (1 H, q), 7·70 (1 H, d), 7·73 (1 H, d), 7·77 (1 H, q), 7·78 (1 H, d), 8·71 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2860, 2220, 1620, 1600, 1460, 1390, 1260, 1215, 1175, 905, 860, 820 cm^{-1}; MS *m/z* 367 (M^+), 311, 296, 282.

4.25 *1-(4-Butoxyphenyl)-2-(2-pent-1-ynylpyridin-5-yl)ethyne* (**30**)

Quantities: compound **3** (1·17 g, 6·72 mmol), *n*-butyllithium (2·70 ml, 2·5 M in hexane, 6·75 mmol), zinc chloride (0·92 g, 6·76 mmol), compound **28** (1·50 g, 6·70 mmol), tetrakis(triphenylphosphine)palladium(0) (0·3120 g, 0·27 mmol). The experimental procedure was as described for the preparation of compound **13**. The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 1 : 2) to give an off-white solid which was recrystallized from hexane to yield colourless crystals. Yield 1·25 g (59 per cent); transitions (°C) C 92·5 N 115·0 I; ^{1}H NMR ($CDCl_3$) δ, 0·95 (3 H, t),1·10 (3 H, t), 1·50 (2 H, sext.), 1·65 (2 H, sext.), 1·80 (2 H, quint.), 2·40 (2 H, t), 3·95 (2 H, t), 6·88 (2 H, d), 7·33 (1H, d), 7·46 (2 H, d), 7·70 (1 H, q), 8·65 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2860, 2220, 1605, 1510, 1470, 1290, 1250, 835 cm^{-1} MS *m/z* 317 (M^+), 261, 246, 233.

4.26 *2-Pent-1-ynyl-5-trimethylsilylethynylpyridine* (**31**)

Quantities: trimethylsilylethyne (1·12 g, 0·011 mmol), compound **28** (2·50 g, 0·011 mol), copper(I) iodide (0·11 g, 0·58 mmol), tetrakis(triphenylphosphine)palladium(0) (0·63 g, 0·55 mmol). The experimental procedure was as described for the preparation of compound **18** (GLC analysis revealed a complete reaction). The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 1 : 2) to give a yellow/brown oil which was distilled (Kugelrohr, 150°C (maximum) at 0·1 mmHg) to yield a colourless oil. Yield 1·42 g (54 per cent); ^{1}H NMR ($CDCl_3$) δ, 0·25 (9 H, s), 1·05 (3 H, t), 1·65 (2 H, sext.), 2·45 (2 H, t), 7·30 (1 H, d), 7·65 (1 H, q), 8·60 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2880, 2860, 2220, 2160, 1585, 1470, 1365, 1250, 1020, 860, 840, 760 cm^{-1}; MS *m/z* 241 (M^+), 226.

4.27 *2-Pent-1-ynylpyridin-5-ylethyne* (**32**)

An aqueous 1·0 M solution of potassium hydroxide (7·0 ml) was added dropwise to a stirred solution of compound **31** (1·35 g, 5·60 mmol) in methanol (60 ml) at room temperature. The mixture was stirred at room temperature for 1·5 h (GLC analysis revealed a complete reaction). The product was extracted into ether and water was added; the aqueous layer was washed with ether, the combined ethereal extracts were washed with brine and dried ($MgSO_4$). The solvent was removed *in vacuo* to yield a colourless oil. Yield 0·94 g (99 per cent); ^{1}H NMR ($CDCl_3$) δ, 1·05 (3 H, t), 1·65 (2 H, sext.), 2·45 (2 H, t), 3·25 (1 H, s), 7·32 (1 H, d), 7·69 (1 H, q), 8·65 p.p.m. (1 H, d); IR (KCl) ν_{max}, 3300, 2960, 2940, 2860, 2220, 1590, 1545, 1470, 1370, 1020, 845 cm^{-1}; MS *m/z* 169 (M^+), 154, 141, 127, 113.

4.28 *1-(4-Pent-1-ynylphenyl)-2-(2-pent-1-ynylpyridin-5-yl)ethyne* (**33**)

Quantities: compound **32** (0·82 g, 4·79 mmol), compound **16** (1·07 g, 4·80 mmol), tetrakis(triphenylphosphine)palladium(0) (0·29 g, 0·25 mmol), copper(I) iodide (0·10 g, 0·53 mmol), triethylamine (40 ml). The experimental procedure was as described for the preparation of compound **18**. The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 1 : 3) to give a brown solid which was recrystallized from hexane-1,2-dimethoxyethane (10 : 1) to yield off-white crystals. Yield 0·5 g (34 per cent); transitions (°C) C 119·0 (N 100·5) I; ^{1}H NMR ($CDCl_3$) δ, 1·00 (6 H, t), 1·65 (4 H, sext.), 2·40 (4 H, t), 7·38 (2 h, d), 7·41 (1 H, d), 7·45 (2 H, d), 7·72 (1 H, q), 8·70 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2860, 2210, 1605, 1520, 1340, 1260, 1210, 895, 860, 755 cm^{-1}; MS *m/z* 311 (M^+), 296, 282, 267.

4.29. *5-Bromo-2-chloropyrimidine* (**35**)

Bromine (67·00 g, 0·419 mol) was added slowly, dropwise, to a stirred solution of compound **34** (50·00 g, 0·377 mol) in water (200 ml) at room temperature (exothermic reaction but no cooling used). The solution was stirred for 1 h (until cool) and then the water and the excess of bromine were removed *in vacuo* to give a pale yellow solid which was dried *in vacuo* (0·1 mm Hg). Phosphorus oxychloride (500 ml) and *N,N*-dimethylaniline (20 ml) were added carefully and the mixture was heated under reflux for 4 h. The cooled mixture was poured on to ice (care!) and extracted into ether (× 2). The combined ethereal extracts were washed with aqueous sodium hydrogen carbonate and dried ($MgSO_4$). The solvent was removed *in vacuo* to yield an off-white solid which was recrystallized from ethanol to yield colourless crystals. Yield 23·55 g (32 per cent); mp 77–79°C (lit. 79°C [18]); ^{1}H NMR ($CDCl_3$) δ, 8·70 p.p.m. (s); IR (KCl) ν_{max}, 1700, 1540, 1400, 1365, 1170, 1160, 1015, 765, 640 cm^{-1}; MS *m/z* 196 (M^+), 194 (M^+) 192 (M^+), 171, 169.

4.30. *2-Chloro-5-pent-1-ynylpyrimidine* (**36**)

Quantities: pent-1-yne (3·00 g, 0·044 mol), *n*-butyllithium (4·40 ml, 10·0 M in hexane, 0·044 mol), zinc chloride (6·00 g, 0·044 mol), compound **35** (8·00 g, 0·041 mol), tetrakis(triphenylphosphine)palladium(0) (1·50 g, 1·30 mmol). The experimental procedure was as described for the preparation of compound **11**. The reaction mixture was carefully monitored by GLC analysis and heated at 50°C for 2·25 h (GLC analysis revealed a complete reaction). The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 1 : 3) to give a pale orange liquid (100 per cent pure by GLC analysis). Yield 6·27 g (85 per cent); ^{1}H NMR ($CDCl_3$) δ, 1·05 (3 H, t), 1·65 (2 H, sext.), 2·40 (2 H, t), 8·60 p.p.m. (2 H, s); IR (KCl)

ν_{max}, 2960, 2940, 2860, 2250, 1575, 1420, 1400, 1170, 940, 770, 645 cm^{-1}; MS *m/z* 182 (M^+), 180 (M^+).

4.31 *1-(4-Butoxyphenyl)-2-(5-pent-1-ynylpyrimidin-2-yl)ethyne* (**37**)

Quantities: compound **3** (0·92 g, 5·29 mmol), *n*-butyllithium (2·15 ml, 2·5 M in hexane, 5·37 mmol), zinc chloride (0·75 g, 5·51 mmol), compound **36** (0·90 g, 4·99 mmol), tetrakis(triphenylphosphine)palladium(0) (0·3267 g, 0·28 mmol). The experimental procedure was as described for the preparation of compound **13**. The mixture was heated under reflux for 22 h (GLC analysis revealed a complete reaction). The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 1 : 2) to give a colourless solid which was recrystallized from hexane to yield colourless crystals. Yield 0·43 g (27 per cent); transitions (°C) C 106·0 N 131·5 I; ^{1}H NMR ($CDCl_3$) δ, 0·90 (3 H, t), 1·05 (3 H, t), 1·50 (2 H, sext.), 1·65 (2 H, sext.), 1·80 (2 H, quint.), 2·45 (2 H, t), 4·00 (2 H, t), 6·88 (2 H, d), 7·60 (2 H, d), 8·69 p.p.m. (2 H, s); IR (KCl) ν_{max}, 2960, 2940, 2860, 2220, 2200, 1605, 1515, 1430, 1295, 1250, 1170, 1040, 1010, 840, 800 cm^{-1}; MS *m/z* 318 (M^+), 303, 289, 275, 262, 233.

4.32 *6-Butoxynapth-2-ylboronic acid* (**38**)

Quantities: compound **8** (8·60 g, 0·031 mol), *n*-butyllithium (12·40 ml, 2·5 M in hexanes, 0·031 mol), tri-isopropyl borate (12·0 g, 0·064 mol). The experimental procedure was as described in a previous publication [4]. Yield 8·50 g (100 per cent) ^{1}H NMR ($CDCl_3$) δ, 1·05 (3 H, t), 1·55 (2 H, sext.), 1·85 (2 H, quint.), 4·10 (2 H, t), 7·14 (1 H, d), 7·22 (1 H, q), 7·82 (1 H, d), 7·96 (1 H, d), 8·24 (1 H, q), 8·72 p.p.m. (1 H, d) no obvious OH absorption; IR (KCl) ν_{max}, 3600–3100, 2960, 2940, 2860, 1630, 1485, 1470, 1385, 1350, 1325, 1205, 805 cm^{-1}; MS *m/z* 590, 579, 565, 552, 536, 522, 509, 496, 480, 465, 255, 200, 144.

4.33. *2-Butoxy-6-(5-pent-1-ynylpyrimidin-2-yl)naphthalene* (**39**)

Quantities: compound **36** (1·60 g, 8·86 mmol), compound **38** (2·60 g, 0·011 mol), tetrakis(triphenylphosphine)palladium(0) (0·35 g, 0·30 mmol). The experimental procedure was as described in a previous publication [4]. The crude product was purified by column chromatography (silica gel/petroleum fraction (bp 40–60°C)–dichloromethane, 1 : 2) to give a colourless solid which was recrystallized from ethyl acetate–ethanol (1 : 1) to yield colourless crystals. Yield 2·25 g (74 per cent); transitions (°C) C 136·5 N 146·5 I; ^{1}H NMR ($CDCl_3$) δ, 1·00 (3 H, t), 1·10 (3 H, t), 1·50 (2 H, sext.), 1·65 (2 H, sext.), 1·85 (2 H, quint.), 2·45 (2 H, t), 4·10 (2 H, t), 7·14 (1 H, d), 7·17 (1 H, q), 7·80 (1 H, d), 7·87 (1 H, d), 8·46 (1 H, q), 8·80 (2 H, s), 8·87 p.p.m. (1 H, d); IR (KCl) ν_{max}, 2960, 2940, 2860, 2210, 1630, 1605, 1575, 1490, 1470, 1430, 1420, 1390, 1255, 1200, 1070, 980, 910, 870, 815, 790 cm^{-1}; MS *m/z* 344 (M^+), 288, 259.

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