PERKIN 1

Double intramolecular hetero Diels–Alder reactions of α,β-unsaturated hydrazones as 1-azadienes: a new route to 2,2′-bipyridines

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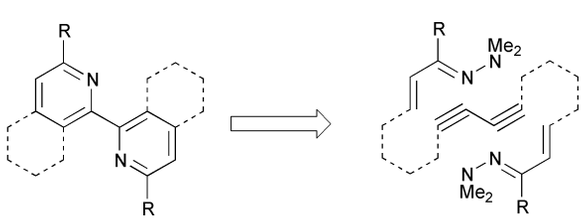
Salicylaldehyde was converted into the *O*-propynyl- and *O*-butynyl α,β-unsaturated aldehydes **4** and ketones **6**, subsequent reaction of which with *N*,*N*-dimethylhydrazine and alkyne homocoupling gave the 1,3-diyne bis-(hydrazones) **8**, substrates for a double intramolecular hetero Diels–Alder reaction. Similar substrates **11**, **15a/15c** and **15b/15d** were prepared from 2-(*N*-benzoylamino)cinnamaldehyde, hex-5-ynol and hept-6-ynol respectively. Heating the 1,3-diynyl bis(α,β-unsaturated hydrazones) **8a**, **8c**, **11** and **15a** resulted in double intramolecular Diels–Alder reaction to give, after aromatisation by loss of dimethylamine, 2,2′-bipyridines **21**–**24**.

Introduction

2,2′-Bipyridine was first synthesised by Fritz Blau in 1888 by distilling a salt of picolinic acid (pyridine-2-carboxylic acid).[1] Its ability to form complexes with metal salts was recognised immediately, and in the intervening 110 years it has been extensively used as a chelating ligand in organometallic chemistry.[2] In fact, 2,2′-bipyridine is one of the best known and most effective bidentate ligands for a range of metals, and with the recent emphasis on the use of metal catalysts in asymmetric synthesis, it is not surprising that chiral 2,2′-bipyridine ligands have found wide application. Thus, for example, chiral 2,2′-bipyridines have found use in the asymmetric addition of diethylzinc to aldehydes,[3] asymmetric cyclopropanation reactions,[4] and asymmetric allylic alkylation.[5] However, the methods used to prepare functionalised bipyridines often rely on the modification of existing pyridine rings followed by transition-metal catalysed heteroaryl coupling reactions. In view of our work on the preparation of substituted pyridines using ring synthesis reactions,[6] we became interested in developing a route to 2,2′-bipyridines in which both pyridine rings are constructed from an acyclic precursor in a single step. There is a previous example of this approach involving cobalt(I) catalysed [2 + 2 + 2]-cycloadditions between hex-5-ynenitrile and 1,3-diynes,[7] and we now report full details of a different approach based on the double intramolecular hetero Diels–Alder reaction of 1,3-diynyl bis(α,β-unsaturated hydrazones) (Scheme 1).[8,9]



Scheme 1 Alkynes and dienes are drawn aligned in the correct orientation for Diels–Alder cycloaddition.

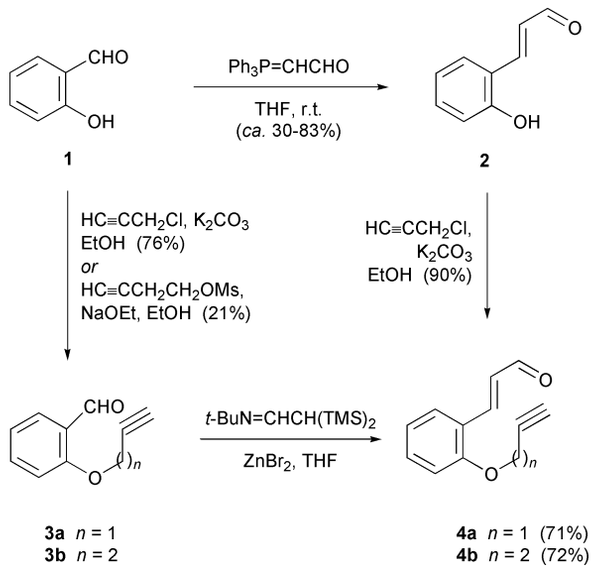
The preparation of 6-membered ring heterocyclic compounds by the hetero Diels–Alder reaction is an established tactic in organic synthesis,[10] and the use of both 1-aza- and 2-aza-dienes as components in such reactions is well known.[11] One useful route to pyridine derivatives employs α,β-unsaturated hydrazones as 1-azadienes, and since the pioneering work of Ghosez,[12] these dienes have found use in intermolecular Diels–Alder reactions to give pyridine derivatives, the reaction with quinones as dienophiles being particularly well investigated.[13] Intramolecular Diels–Alder (IMDA) reactions of α,β-unsaturated hydrazones with alkynes have also been reported,[14] and this is an attractive route to annelated pyridines since the initial Diels–Alder adduct readily aromatises by loss of dimethylamine.[15] Therefore, we decided to adapt this procedure to the direct synthesis of annelated 2,2′-bipyridines by the incorporation of an oxidative homocoupling step giving a 1,3-diyne as a bis(dienophile) capable of undergoing the desired double IMDA reaction (Scheme 1).

Results and discussion

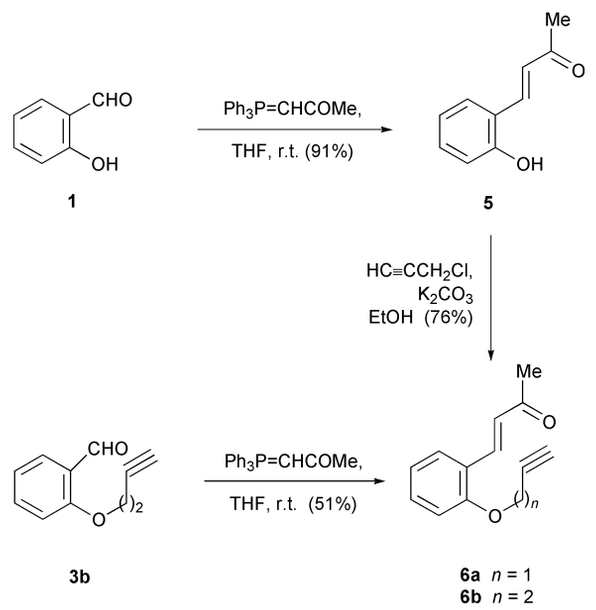
The substrates for the double IMDA reactions were prepared by a number of routes (Schemes 2–6). The first series of compounds was based on salicylaldehyde **1**; thus, reaction of the aldehyde **1** with (formylmethylene)triphenylphosphorane gave *o*-hydroxycinnamaldehyde **2** in 83% yield on a small scale. Although this aldehyde **2** could be readily converted into the required propargyl (prop-2-ynyl) derivative **4a**, its preparation proved irreproducible and low yielding on a larger scale. Therefore, the α,β-unsaturated aldehyde **4a** was prepared by carrying out the *O*-propargylation first, and reacting the aldehyde **3a** with α,α-bis(trimethylsilyl)-*N*-*tert*-butylacetaldehyde imine in the presence of zinc bromide.[16] This reagent proved superior to the Wittig reagent (formylmethylene)triphenylphosphorane. A similar sequence of reactions was used to prepare the *O*-butynyl derivative **4b** (Scheme 2). The corresponding α,β-unsaturated methyl ketones **6** were also prepared as shown in Scheme 3.

The α,β-unsaturated aldehydes **4** and methyl ketones **6** were readily converted into the corresponding *N*,*N*-dimethylhydrazones **7** and hence to the 'dimeric' 1,3-diynes **8** by Glaser–Eglinton coupling with copper(II) acetate[17] as shown on Scheme 4.

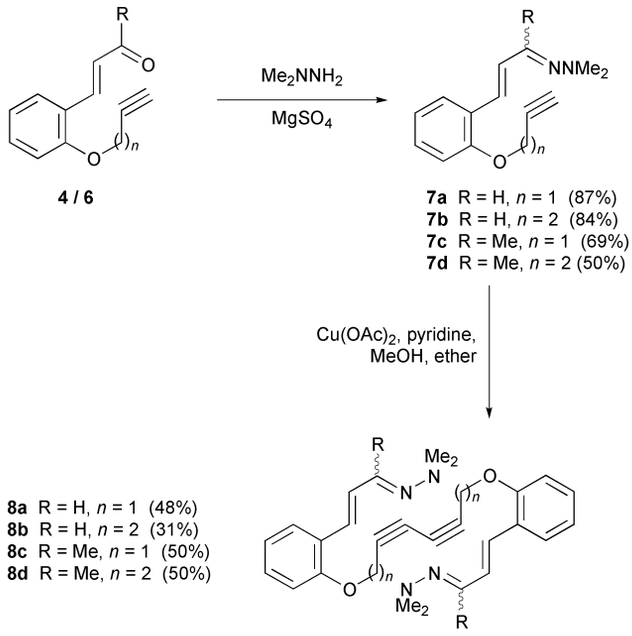
The IMDA substrate **11** was prepared from the known hydrazone **9**,[18] obtained from quinoline and benzoyl chloride



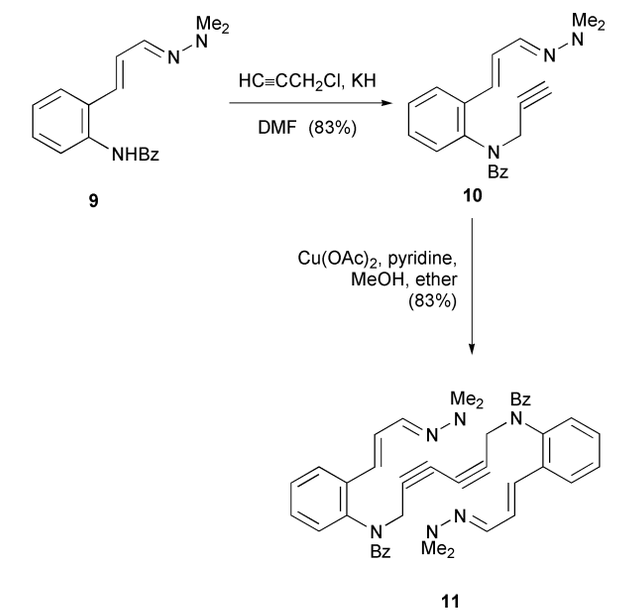
Scheme 2



Scheme 3



Scheme 4



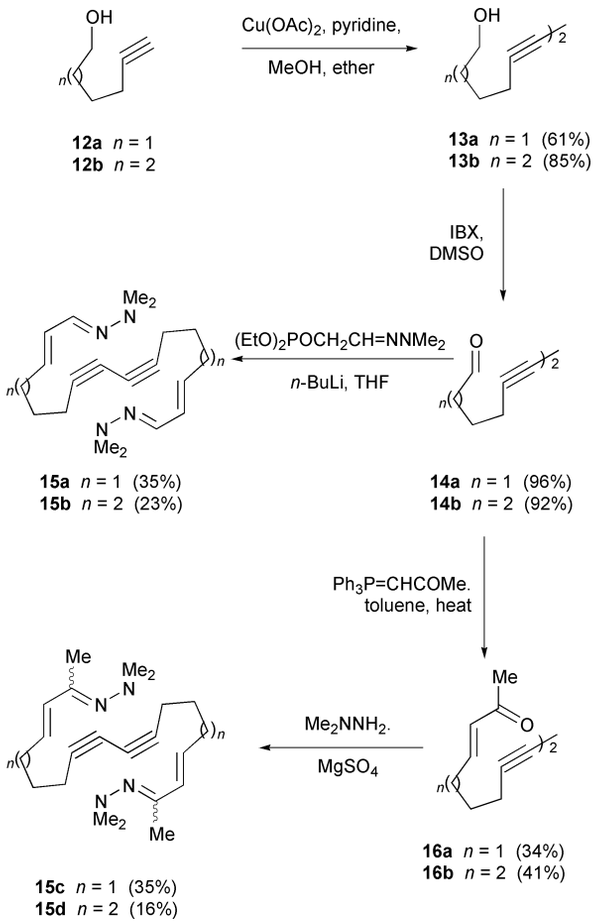
Scheme 5

in an abnormal Reissert reaction to give *o*-(*N*-benzoylamino)-cinnamaldehyde followed by hydrazone formation. The subsequent *N*-propargylation and oxidative homocoupling of the alkyne both proceeded in good yield as shown in Scheme 5.

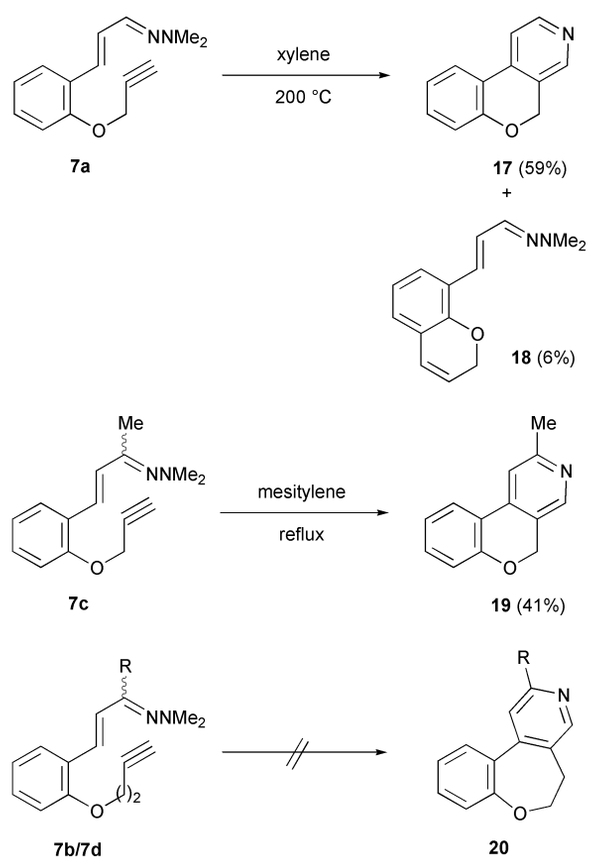
The final set of substrates were obtained from hex-5-ynol **12a** or hept-6-ynol **12b**. Although the former alkynol is commercially available, the latter was obtained by base catalysed isomerisation of hept-3-ynol.[19] Homocoupling reaction of the alkynols **12** gave the corresponding 1,3-diynes **13**, readily oxidised to the dialdehydes **14** using 1-hydroxy-3-oxo-1,3-dihydro-1,2-benziodoxole 1-oxide (2-iodylbenzoic acid, IBX) in DMSO.[20] The dialdehydes **14** were converted directly into the hydrazones **15a** and **15b** of the homologous α,β-unsaturated aldehydes by reaction with the *N*,*N*-dimethylhydrazone of diethyl formylmethylphosphonate in a Wadsworth–Emmons reaction.[15] Alternatively the α,β-unsaturated ketones **16** were prepared by Wittig reaction with aldehydes **14**, followed by reaction with *N*,*N*-dimethylhydrazine to give the hydrazones **15c** and **15d** as shown in Scheme 6.

Although the main aim was to investigate the double IMDA reaction of the 1,3-diynes (see below), the IMDA reactions of the mono-alkynes **7** were also briefly investigated. The IMDA reaction of the hydrazone **7a** occurred upon heating in xylene in a sealed tube and gave the chromeno[3,4-*c*]pyridine **17** in 59% yield as reported by Dolle and co-workers in their original paper,[15] although a minor byproduct was also isolated. This was identified as the benzopyran **18**, and presumably results from a [3,3]-sigmatropic rearrangement followed by [1,5]-hydrogen shift and cyclisation, a known reaction of aryl propargyl ethers.[21] Attempts to catalyse the IMDA reaction using $LiNTf_2$, a system employed successfully by Ghosez and co-workers with α,β-unsaturated hydrazone based azadienes,[12c] proved unsuccessful.

The α,β-unsaturated ketone hydrazone **7c** also underwent IMDA reaction to give the pyridine **19** in modest yield. α,β-Unsaturated hydrazones with a substituent at C-2 are known to be poorer 1-azadienes, since the substituent (methyl in this case) forces the dimethylamino group out of the diene plane thereby preventing the delocalisation of the nitrogen lone pair which enhances the diene reactivity.[12c] The two butynyl derivatives **7b** and **7d**, however, failed to give any of the benzoxepinopyridines **20** on heating in xylene (Scheme 7). The formation of 7-membered rings in IMDA reactions is generally less favourable than the corresponding reactions which form 6- (or 5-) membered rings.[22]

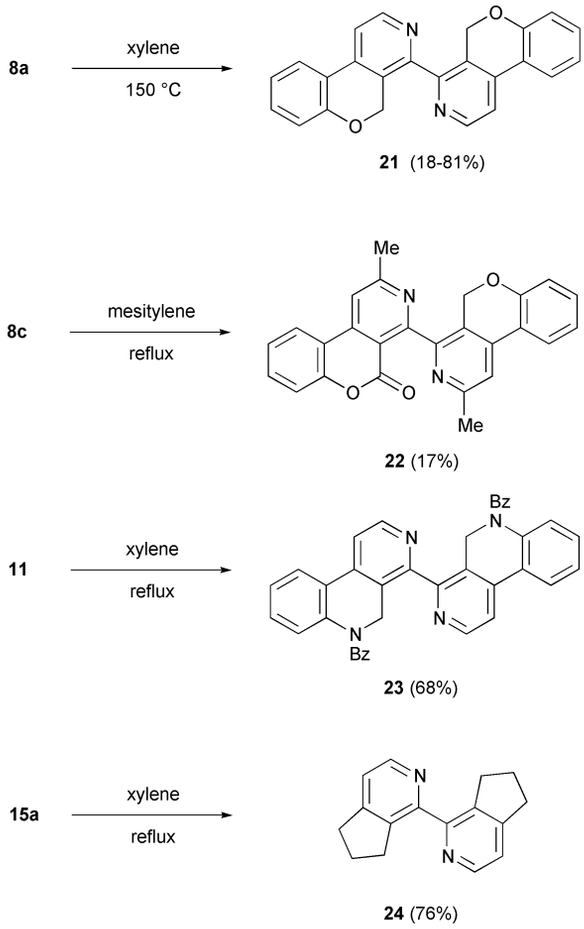


Scheme 6



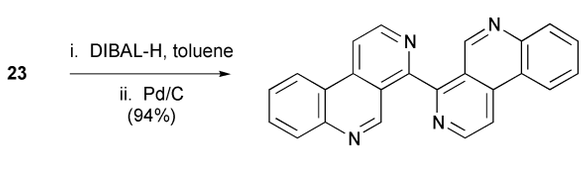
Scheme 7

The key double IMDA reactions were next investigated. Heating the 1,3-diyne bis(hydrazone) **8a** in xylene gave the desired annelated 2,2′-bipyridine **21** as the only isolable product. (*ca.* 80% yield), although considerable losses occurred during purification. The ketone derived substrate **8c** was less satisfactory in the double IMDA reaction, and gave a poor yield of the unsymmetrical 2,2′-bipyridine **22** in which one of the benzopyran rings has undergone oxidation at the activated CH_2 position to give the observed lactone (Scheme 8). As with



Scheme 8

the mono-alkynes **7b** and **7d**, the diynes **8b** and **8d** failed to undergo IMDA reaction. The *N*-benzoyl compound **11**, a nitrogen containing analogue of **8a**, underwent smooth double IMDA reaction on heating in xylene to give, after loss of dimethylamine, the *N*-benzoylated dihydro 4,4′-bi(benzo[*c*]-[2,7]naphthyridine) **23** in 68% yield. Compound **23** could be deprotected by reaction with DIBAL-H, and the resulting dihydro compound dehydrogenated with palladium-on-carbon to give the aromatic bi(benzonaphthyridine) **25** (Scheme 9).



Scheme 9

Finally, in the series of substrates **15**, in which the azadiene fragment is connected to the alkyne dienophile by a simple alkyl chain, compound **15a** readily underwent the desired double IMDA reaction in boiling xylene to give the 1,1′-bi(cyclo-penta[*c*]pyridine) **24** in good yield. Unfortunately no bipyridine products were isolated from the hydrazones **15b**, **15c**, or **15d**.

Although the IMDA reactions of 1,3-diyne bis(hydrazones) successfully demonstrated our aim of achieving a 2,2′-bipyridine synthesis in which both heterocyclic rings are formed in a single step from an acyclic precursor, the results are somewhat mixed. For a successful double IMDA reaction to occur the substrates need to be carefully designed, and this is clearly a major consideration if chiral 2,2′-bipyridines are to be made by this route.

Experimental

General

Commercially available reagents and solvents were used throughout without further purification unless otherwise stated. Light petroleum refers to the fraction that boils between 40 and 60 °C and was distilled from calcium chloride through a 36 cm Vigreux column before use. Ether, which refers to diethyl ether, and THF were distilled from sodium–benzophenone ketyl under nitrogen prior to use. Dichloromethane was purified and dried by distillation from phosphorus pentaoxide under nitrogen.

Analytical thin layer chromatography was carried out using aluminium or glass backed plates coated with Merck Kieselgel 60 GF_{254}. Developed plates were visualised under ultraviolet light (254 nm) and/or potassium permanganate or ninhydrin dip. Flash chromatography was carried out using Merck Kieselgel 60 H silica. Fully characterised compounds were chromatographically homogeneous.

IR Spectra were recorded on Nicolet FT-205, Nicolet Magna 550 or Perkin Elmer Paragon 1000 FT-IR spectrometers with internal calibration. Spectra were recorded as thin films on sodium chloride plates, in solution or potassium bromide discs. NMR spectra were recorded on Bruker AC-250, AM-300 or Advance DRX-400 spectrometers at the frequencies stated. Chemical shifts are recorded in ppm and J values in Hz. Multiplets less than 0.2 ppm in width were recorded from the centre, those greater were reported as a range. Chemical shift values are referenced against residual chloroform at 7.27 ppm for $CDCl_3$, and are accurate to ±0.01 ppm (δ_H) and ±0.10 ppm (δ_C). High resolution mass spectra (CI and EI) were obtained either on Kratos MS80 or Profile HV3 spectrometers or at the EPSRC National Mass Spectrometry Service at the University of Wales, Swansea.

Reagents and starting materials

N-tert-Butylacetaldehyde imine was prepared by the condensation of acetaldehyde with *tert*-butylamine in 54% yield.[23] Diethyl formylmethylphosphonate was prepared by hydrolysis of the commercially available diethyl acetal (diethyl 2,2-diethoxyethylphosphonate) in 62% yield.[24] Hept-6-ynol **12b** was prepared by the base catalyzed isomerization of hept-3-ynol (52% yield).[19] IBX (1-hydroxy-3-oxo-1,3-dihydro-1,2-benziodoxole 1-oxide) (**CAUTION!** IBX has been reported to explode when heated above 200 °C and when subjected to shock) was prepared from 2-iodobenzoic acid, according to the method of Dess and Martin[25] in 71% yield.

α,α-Bis(trimethylsilyl)-*tert*-butylacetaldehyde imine

Diisopropylamine (14 ml, 100 mmol) was stirred in THF (50 ml) at −20 °C, *n*-butyllithium (1.6 M in hexane; 63 ml, 100 mmol) was added slowly and the temperature reduced to −60 °C. *tert*-Butylacetaldehyde imine[23] (5.0 g, 50 mmol) was added dropwise, the solution was stored at −78 to −60 °C for 18 h and then chlorotrimethylsilane (6.5 ml, 50 mmol) was added dropwise. After 5 h another portion of chlorotrimethylsilane (6.5 ml, 50 mmol) was added, the solution was stirred for 45 min and then allowed to warm to room temperature. The suspension was filtered through Celite and the solvent removed *in vacuo*. The residue was purified by distillation under reduced pressure and the *title compound* was obtained as a yellow oil (5.0 g, 41%); bp 104–107 °C at 20 mmHg (lit.,[16] 93–94 °C at 12 mmHg); ν_{max} (film)/cm^{-1} 2964, 2900, 2868, 1637, 1252, 840; δ_H (300 MHz; $CDCl_3$) 7.49 (1 H, d, J 10.1, CH=N), 1.58 (1 H, d, J 10.1, $(TMS)_2CH$), 1.14 (9 H, s, CMe_3), 0.04 (18 H, s, $SiMe_3$); δ_C (75 MHz; $CDCl_3$) 157.9 (CH), 56.4 (C), 31.6 (CH), 30.0 (Me), −0.2 (Me).

Diethyl formylmethylphosphonate *N*,*N*-dimethylhydrazone

Diethyl formylmethylphosphonate[24] (2.1 g, 12 mmol) was stirred in dichloromethane (26 ml) at 0 °C, and *N*,*N*-dimethylhydrazine (3.54 ml, 46.6 mmol) was added dropwise. After 3 h, the mixture was filtered and the solvent removed *in vacuo* to give the *title compound* as a light yellow oil (2.4 g, 92%) (lit.,[15] bp 122–124 °C at 10 mmHg) (Found: M^+, 222.1136. $C_8H_{19}N_2O_3P$ requires 222.1133); ν_{max} (film)/cm^{-1} 2938, 2907, 2805, 2827, 1256, 1026; δ_H (300 MHz; $CDCl_3$) 6.44 (1 H, dt, J 10.3, 5.8, CH=N), 4.07 (4 H, m, OCH_2), 2.78 (2 H, dd, J 21.4, 5.8, PCH_2), 2.74 (6 H, s, NMe_2), 1.28 (6 H, td, J 7.0, 0.3, Me); δ_C (75 MHz; $CDCl_3$) 126.2 (CH), 62.0 (CH_2), 43.0 (Me), 31.4 (CH_2), 16.4 (Me); δ_P (121 MHz; $CDCl_3$) 26.6; *m*/*z* (EI) 222 (M^+, 12%), 180 (4), 152 (51), 125 (68), 108 (22), 97 (37), 85 (100).

(*E*)-3-(2-Prop-2-ynyloxyphenyl)propenal 4a

Method 1. To a stirred suspension of (formylmethylene)-triphenylphosphorane (486 mg, 1.6 mmol) in dry tetrahydrofuran was added a solution of salicylaldehyde (100 mg, 0.8 mmol) in tetrahydrofuran (1 ml). The reaction mixture was stirred at room temperature for 3 h. The solvent was evaporated and the crude residue was filtered through a pad of silica gel (light petroleum–ethyl acetate 2 : 1) to remove base line impurities. Concentration of the filtrate yielded (*E*)-3-(2-hydroxyphenyl)propenal **2** as a yellow solid (100 mg, 83%), mp 131–132 °C (lit.,[16] mp 122 °C); δ_H (250 MHz; $CDCl_3$) 9.60 (1 H, d, J 8.0, CHO), 7.91 (1 H, d, J 16.0, PhC*H*=), 7.57 (1 H, td, J 16.0, 8.0, =C*H*CHO), 6.93–6.86 (4 H, m, ArH); δ_C (62.5 MHz; $CDCl_3$) 199.5 (CHO), 161.2 (C), 154.7 (CH), 136.4 (CH), 133.0 (CH), 131.8 (CH), 124.9 (C), 123.3 (CH), 119.6 (CH). On a larger scale, this reaction was irreproducible, and gave yields of *ca*. 30%.

A mixture of the above hydroxyaldehyde **2** (100 mg, 0.6 mmol), propargyl chloride (50 µl, 1.0 mmol) and potassium carbonate (80 mg) in anhydrous ethanol (10 ml) was heated to reflux for 18 h under an inert atmosphere. The mixture was filtered, evaporated *in vacuo*, diluted with dichloromethane, washed with sodium hydroxide solution (3 × 50 ml, 10% solution), and washed with water (3 × 50 ml). The organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to leave a yellow oil which was chromatographed on silica gel (light petroleum–ethyl acetate 2 : 1) to give the title compound as a yellow semi-solid (113 mg, 90%), data given below.

Method 2. Propargyl chloride (3.6 ml, 50 mmol) was added dropwise to a stirred solution of salicylaldehyde (1.1 ml, 10 mmol) and potassium carbonate (2.1 g, 15 mmol) in ethanol (50 ml). The solution was heated at reflux for 20 h and then allowed to cool to room temperature and the solvent removed *in vacuo*. The residue was partitioned between sodium hydroxide solution (2 M; 70 ml) and ether (70 ml), the organic phase was washed with further sodium hydroxide solution (2 M; 2 × 70 ml) and water (2 × 70 ml) and dried ($MgSO_4$). The mixture was filtered and concentrated *in vacuo* and purified by flash chromatography (elution with 2 : 1 light petroleum–ether) to give 2-prop-2-ynyloxybenzaldehyde **3a** as a colourless solid (1.2 g, 76%); mp 69 °C (from light petroleum) (lit.,[26] 68 °C); δ_H (300 MHz; $CDCl_3$) 10.5 (1 H, s, CHO), 7.86 (1 H, dd, J 7.7, 1.7, ArH), 7.57 (1 H, ddd, J 8.6, 7.3, 1.7, ArH), 7.13–7.06 (2 H, m, ArH), 4.83 (2 H, d, J 2.4, OCH_2), 2.57 (1 H, t, J 2.4, ≡CH).

Prop-2-ynyloxybenzaldehyde **3a** (640 mg, 4.0 mmol) and zinc bromide (900 mg, 4.0 mmol) were stirred in THF (4 ml) at room temperature. α,α-Bis(trimethylsilyl)-*tert*-butylacetaldehyde imine (1.1 g, 4.4 mmol) in THF (2 ml) was added dropwise. After 3 h the reaction was quenched by addition of aqueous zinc chloride (800 mg in 8 ml of water) and ether (10 ml) with stirring for 1 h. After filtration through Celite the solution was extracted with ether (2 × 40 ml) and the combined organic extracts were washed with water (3 × 40 ml) and dried ($MgSO_4$). The solution was concentrated *in vacuo* and the residue purified by flash chromatography (elution with 3 : 2 light petroleum–ether and then 1 : 1 light petroleum–ether) to give the *title compound* as a yellow solid (530 mg, 71%); mp 77–79 °C (from ether–light petroleum) (Found: M^+, 186.0681. $C_{12}H_{10}O_2$ requires 186.0681); ν_{max} (KBr)/cm^{-1} 3209, 2833, 2121, 1675, 1622, 1616, 1600; δ_H (300 MHz; $CDCl_3$) 9.70 (1 H, d, *J* 7.8, CHO), 7.86 (1 H, d, *J* 16.1, PhC*H*=), 7.58 (1 H, dd, *J* 7.6, 1.6, ArH), 7.42 (1 H, ddd, *J* 8.6, 7.4, 1.6, ArH), 7.06–7.03 (2 H, m, ArH), 6.77 (1 H, dd, *J* 16.1, 7.8, =C*H*CHO), 4.81 (2 H, d, *J* 2.4, OCH_2), 2.56 (1 H, t, *J* 2.4, ≡CH); δ_C (75 MHz; $CDCl_3$) 194.5 (CHO), 156.1 (C), 147.7 (CH), 132.5 (CH), 129.3 (CH), 128.8 (CH), 123.6 (C), 121.8 (CH), 112.8 (CH), 77.9 (C), 76.3 (CH), 56.2 (CH_2); *m*/*z* (EI) 186 (M^+, 25%), 157 (23), 147 (47), 131 (93), 118 (28), 91 (100).

2-But-3-ynyloxybenzaldehyde 3b

Salicylaldehyde (2.3 g, 19 mmol) was stirred in toluene (100 ml), sodium ethoxide (21% w/w in ethanol, 1.1 g, 15 mmol) in ethanol was added dropwise and the suspension stirred for 1.5 h. But-3-yn-1-yl methanesulfonate[27] (4.6 g, 31 mmol) was added slowly and the mixture heated to reflux for 7 days. The solution was cooled and partitioned between ether (300 ml) and sodium hydroxide solution (2 M; 300 ml). The organic layer was washed with more sodium hydroxide solution (2 M; 2 × 300 ml), water (3 × 300 ml) and dried ($MgSO_4$). The mixture was filtered and evaporated *in vacuo* and the residue purified by flash chromatography (elution with 2 : 1 light petroleum–ether) to give the *title compound* as a red oil (580 mg, 21%) (Found: M^+, 174.0685. $C_{11}H_{10}O_2$ requires 174.0681); ν_{max} ($CHCl_3$)/cm^{-1} 3309, 2956, 2889, 2764, 2125, 2125, 1732, 1689, 1601; δ_H (300 MHz; $CDCl_3$) 10.5 (1 H, s, CHO), 7.82 (1 H, dd, *J* 7.7, 1.9, ArH), 7.53 (1 H, ddd, *J* 8.5, 7.4, 1.9, ArH), 6.95–7.05 (2 H, m, ArH), 4.20 (2 H, t, *J* 6.8, OCH_2), 2.73 (2 H, td, *J* 6.8, 2.7, C*H*$_2$C≡), 2.05 (1 H, t, *J* 2.7, ≡CH); δ_C (75 MHz; $CDCl_3$) 189.6 (CHO), 160.8 (C), 135.8 (CH), 128.3 (CH), 125.2 (C), 121.2 (CH), 112.3 (CH), 79.9 (C), 70.3 (CH), 66.6 (CH_2), 19.5 (CH_2); *m*/*z* (EI) 174 (M^+, 12%), 144 (44), 135 (42), 121 (100), 110 (16).

(*E*)-3-(2-But-3-ynyloxyphenyl)propenal 4b

2-But-3-ynyloxybenzaldehyde **3b** (100 mg, 0.57 mmol) and zinc bromide (130 mg, 0.57 mmol) were stirred in THF (1 ml), α,α-bis(trimethylsilyl)-*tert*-butylacetaldehyde imine (150 mg, 0.63 mmol) in THF (0.5 ml) was added dropwise and the solution stirred at room temperature for 3 h. The reaction was quenched by addition of aqueous zinc chloride solution (0.73 M; 3 ml) and ether (4 ml), after stirring for 15 min the aqueous phase was extracted with more ether (2 × 20 ml) and the combined organic extracts were washed with water (3 × 20 ml) and dried ($MgSO_4$). The mixture was filtered and the solvent removed *in vacuo*, the residue was purified by flash chromatography (elution with 1 : 1 light petroleum–ether) to give the *title compound* as a light yellow oil (82 mg, 72%) (Found: M^+, 200.0831. $C_{13}H_{12}O_2$ requires 200.0837); ν_{max} (film)/cm^{-1} 3293, 2949, 2817, 2741, 2122, 1675, 1621, 1599; δ_H (300 MHz; $CDCl_3$) 9.70 (1 H, d, *J* 7.8, CHO), 7.86 (1 H, d, *J* 16.1, PhC*H*=), 7.56 (1 H, dd, *J* 7.8, 1.7, ArH), 7.40 (1 H, ddd, *J* 8.4, 7.4, 1.7, ArH), 7.02 (1 H, m, ArH), 6.94 (1 H, d, *J* 8.4, ArH), 6.81 (1 H, dd, *J* 16.1, 7.8, =C*H*CHO), 4.19 (2 H, t, *J* 6.8, OCH_2), 2.76 (2 H, td, *J* 6.8, 2.7, C*H*$_2$C≡), 2.08 (1 H, t, *J* 2.7, ≡CH); δ_C (75 MHz; $CDCl_3$) 194.6 (CHO), 157.1 (C), 148.0 (CH), 132.6 (CH), 129.2 (CH), 129.0 (CH), 123.3 (C), 121.4 (CH), 112.4 (CH), 80.1 (C), 70.3 (CH), 66.5 (CH_2), 19.6 (CH_2); *m*/*z* (EI) 200 (M^+, 28%), 171 (14), 147 (38), 131 (100), 118 (25), 103 (18), 91 (53).

(*E*)-4-(2-Hydroxyphenyl)but-3-en-2-one 5

Salicylaldehyde (2.0 g, 16 mmol) in THF (2 ml) was added to a stirred suspension of (acetylmethylene)triphenylphosphorane (7.8 g, 25 mmol) in THF (50 ml) at room temperature. After 16 h, the mixture was filtered and solvent removed *in vacuo*, the *title compound* was isolated by flash chromatography (elution with 2 : 1 ether–light petroleum) and obtained as a colourless solid (2.40 g, 91%); mp 139–140 °C (from light petroleum–ether) (lit.,[28] mp 140.5–141.5 °C) (Found: C, 73.9; H, 6.2. $C_{10}H_{10}O_2$ requires C, 74.1; H, 6.2%); δ_H (300 MHz; d_6-acetone) 7.93 (1 H, d, *J* 16.5, ArC*H*=CH), 7.63 (1 H, dd, *J* 7.8, 1.7, ArH), 7.27 (1 H, ddd, *J* 8.2, 7.3, 1.7, ArH), 7.00 (1 H, dd, *J* 8.2, 1.1, ArH), 6.92 (1 H, m, ArH), 6.88 (1 H, d, *J* 16.5, ArCH=C*H*), 2.34 (3 H, s, Me); δ_C (75 MHz; d_6-acetone) 198.4 (C=O), 157.5 (C), 139.1 (CH), 132.4 (CH), 129.4 (CH), 127.9 (CH), 126.0 (C), 120.9 (CH), 117.1 (CH), 27.4 (Me).

(*E*)-4-(2-Prop-2-ynyloxyphenyl)but-3-en-2-one 6a

A suspension of 4-(2-hydroxyphenyl)but-3-en-2-one **5** (800 mg, 4.9 mmol) and potassium carbonate (2.0 g) in ethanol (30 ml) was stirred at 45 °C. Propargyl chloride (1.8 ml, 25 mmol) was added. After 3 days, the mixture was filtered and solvent was removed, the residue was dissolved in dichloromethane (100 ml) and washed with aqueous sodium hydroxide (2 M; 3 × 50 ml) and water (3 × 50 ml), the organic layer was dried ($MgSO_4$). The mixture was filtered and the solvent removed *in vacuo*, the residue was purified by flash chromatography (elution with 3 : 1 light petroleum–ethyl acetate) to give the *title compound* as a yellow oil (750 mg, 76%) (Found: M^+, 200.0841. $C_{13}H_{12}O_2$ requires 200.0837); ν_{max} ($CHCl_3$)/cm^{-1} 3307, 2125, 1667, 1600, 1485; δ_H (300 MHz; $CDCl_3$) 7.87 (1 H, d, *J* 16.5, ArC*H*=), 7.55 (1 H, dd, *J* 7.7, 1.7, ArH), 7.35 (1 H, ddd, *J* 8.5, 7.7, 1.7, ArH), 7.05 (1 H, dd, *J* 8.5, 0.8, ArH), 7.01 (1 H, br t, *J* 7.7, ArH), 6.72 (1 H, d, *J* 16.5, PhCH=C*H*), 4.78 (2 H, d, *J* 2.4, C*H*$_2$C≡), 2.54 (1 H, t, *J* 2.4, ≡CH), 2.37 (3 H, s, Me); δ_C (75 MHz; $CDCl_3$) 198.9 (C=O), 156.2 (C), 138.3 (CH), 131.5 (CH), 128.3 (CH), 128.1 (CH), 124.1 (C), 121.8 (CH), 112.9 (CH), 78.1 (C), 76.1 (CH), 56.2 (CH_2), 27.1 (Me); *m*/*z* (EI) 200 (M^+, 12%), 185 (16), 157 (16), 145 (100), 128 (17), 118 (26), 89 (15).

(*E*)-4-(2-But-3-ynyloxyphenyl)but-3-en-2-one 6b

To a stirred suspension of (acetylmethylene)triphenylphosphorane (1.2 g, 3.6 mmol) in THF (10 ml) was added 2-but-3-ynyloxybenzaldehyde **3b** (420 mg, 2.4 mmol). After 16 h, the mixture was filtered and concentrated *in vacuo* and the residue purified by flash chromatography (elution with 3 : 1 light petroleum–ether) to give the *title compound* as a colourless solid (260 mg, 51%); mp 61–62 °C (from ether) (Found: C, 78.3; H, 6.6. $C_{14}H_{14}O_2$ requires C, 78.5; H, 6.5%) (Found: M^+, 214.0990. $C_{14}H_{14}O_2$ requires 214.0994); ν_{max} (KBr)/cm^{-1} 3268, 3061, 2964, 2916, 1668, 1646, 1618, 1599; δ_H (400 MHz; $CDCl_3$) 7.91 (1 H, d, *J* 16.7, PhC*H*=), 7.55 (1 H, dd, *J* 7.8, 1.6, ArH), 7.53 (1 H, ddd, *J* 8.3, 7.3, 1.6, ArH), 6.99 (1 H, m, ArH), 6.92 (1 H, dd, *J* 8.3, 0.9, ArH), 6.79 (1 H, d, *J* 16.5, =C*H*C(Me)O), 4.18 (2 H, t, *J* 6.7, OCH_2), 2.75 (2 H, td, *J* 6.7, 2.6, C*H*$_2$C≡), 2.38 (3 H, s, Me), 2.07 (1 H, t, *J* 2.6, ≡CH); δ_C (100 MHz; $CDCl_3$) 199.0 (C=O), 157.1 (C), 138.5 (CH), 131.7 (CH), 128.6 (CH), 128.0 (CH), 123.9 (C), 121.4 (CH), 112.5 (CH), 80.2 (C), 70.1 (CH), 66.5 (CH_2), 27.2 (Me), 19.6 (CH_2); *m*/*z* (EI) 215 (48), 214 (M^+, 20%), 172 (17), 146 (100), 119 (49), 104 (41).

(*E*)-3-(2-Prop-2-ynyloxyphenyl)propenal *N*,*N*-dimethylhydrazone 7a

(*E*)-3-(2-Prop-2-ynyloxyphenyl)propenal **4a** (88 mg, 0.47 mmol) and magnesium sulfate (200 mg) were stirred in dichloromethane (10 ml) at 0 °C. *N*,*N*-Dimethylhydrazine (110 µl, 1.4 mmol) was added dropwise and then the mixture allowed to warm to room temperature. The solution was filtered and the solvent was removed *in vacuo*. The crude residue was purified by flash chromatography (elution with 1 : 1 light petroleum–ether) to give the *title compound* as a yellow oil (93 mg, 87%) (lit.,[15] no data given) (Found: M^+, 228.1264. $C_{14}H_{16}N_2O$ requires 228.1263); ν_{max} (film)/cm^{-1} 3290, 2955, 2859, 2787, 2121, 1522, 1485, 1457, 750; δ_H (400 MHz; $CDCl_3$) 7.53 (1 H, dd, *J* 7.8, 1.4, ArH), 7.21 (1 H, m, ArH), 7.20 (1 H, d, *J* 7.0, CH=N), 7.00–6.95 (4 H, m, C*H*=C*H*-, 2 × ArH), 4.74 (2 H, d, *J* 2.4, OCH_2), 2.92 (6 H, s, NMe_2), 2.52 (1 H, t, *J* 2.4, ≡CH); δ_C (100 MHz; $CDCl_3$) 154.5 (C), 136.3 (CH), 128.24 (CH), 128.21 (CH), 127.1 (C), 126.23 (CH), 126.18 (CH), 121.8 (CH), 78.7 (C), 75.5 (CH), 56.3 (CH_2), 42.8 (Me); *m*/*z* (EI) 228 (M^+, 100%), 184 (43), 169 (23), 156 (15), 146 (52), 131 (76), 118 (34), 91 (29).

(*E*)-3-(2-But-3-ynyloxyphenyl)propenal *N*,*N*-dimethylhydrazone 7b

(*E*)-3-(2-But-3-ynyloxyphenyl)propenal **4b** (67 mg, 0.34 mmol) and magnesium sulfate (200 mg) were stirred in dichloromethane (10 ml) at 0 °C. *N*,*N*-Dimethylhydrazine (76 µl, 1.0 mmol) was added dropwise, and after 15 min the reaction mixture was allowed to warm to room temperature and stirred for a further 3 h. The mixture was then filtered and the solvent removed *in vacuo*. The crude residue was filtered through a short plug of silica (elution with 1 : 1 light petroleum–ether) to give the *title compound* as a viscous yellow oil (69 mg, 84%) (Found: M^+, 242.1414. $C_{15}H_{18}N_2O$ requires 242.1419); ν_{max} (film)/cm^{-1} 3295, 2953, 2882, 2858, 2827, 2786, 2122, 1616, 1597, 750; δ_H (400 MHz; $CDCl_3$) 7.53 (1 H, dd, *J* 7.7, 1.6, ArH), 7.20–7.16 (1 H, m, ArH), 7.19 (1 H, d, *J* 8.1, CH=N), 7.01 (1 H, d, *J* 16.1, PhC*H*=), 6.95 (1 H, dd, *J* 16.1, 8.1, =C*H*CHN), 6.94 (1 H, m, ArH), 6.86 (1 H, dd, *J* 8.3, 1.0, ArH), 4.14 (2 H, t, *J* 7.0, OCH_2), 2.92 (6 H, s, NMe_2), 2.73 (2 H, td, *J* 7.0, 2.6, CH_2C≡), 2.05 (1 H, t, *J* 2.6, ≡CH); δ_C (100 MHz; $CDCl_3$) 155.3 (C), 136.4 (CH), 128.4 (CH), 127.9 (CH), 126.8 (C), 126.2 (CH), 126.0 (CH), 121.4 (CH), 112.5 (CH), 80.5 (C), 70.0 (CH), 66.6 (CH_2), 42.8 (Me), 19.6 (CH_2); *m*/*z* (EI) 242 (M^+, 100%), 173 (55), 158 (7), 146 (16), 131 (74), 118 (23), 103 (9), 91 (18), 71 (16).

(*E*)-4-(2-Prop-2-ynyloxyphenyl)but-3-en-2-one *N*,*N*-dimethylhydrazone 7c

N,*N*-Dimethylhydrazine (0.21 ml, 2.7 mmol) was added to a mixture of 4-(2-prop-2-ynyloxyphenyl)but-3-en-2-one **6a** (705 mg, 0.27 mmol) and magnesium sulfate (240 mg) in THF (4 ml) at room temperature. After 3 days, the mixture was filtered and the solvent removed *in vacuo*, the residue was purified by flash chromatography (elution with: 2 : 1 light petroleum–ethyl acetate) to give the *title compound* as a yellow oil (590 mg, 69%) (inseparable mixture of 2 isomers: TLC, 2 : 1 light petroleum–ethyl acetate, isomer 1: R_f = 0.29, isomer 2: R_f = 0.25) (Found: M^+, 242.1413. $C_{15}H_{18}N_2O$ requires 242.1419); ν_{max} ($CHCl_3$)/cm^{-1} 3307, 2959, 2864, 2823, 2779, 2475 (br), 2125, 1734, 1599; δ_H (400 MHz; $CDCl_3$) 7.65–6.83 (6 H, m, 4 × ArH, PhC*H*=C*H*), 4.74 (2 H, d, *J* 2.4, OCH_2), 2.56 (1.8 H, s, NMe_2), 2.53 (4.2 H, s, NMe_2), 2.51 (1 H, t, *J* 2.3, ≡CH), 2.20 + 2.14 (3 H, s, Me); δ_C (75 MHz; $CDCl_3$) isomer 1: 163.1 (C), 155.0 (C), 130.4 (CH), 129.9 (CH), 129.3 (CH), 126.7 (CH), 126.2 (C), 121.8 (CH), 112.8 (CH), 78.5 (C), 75.7 (CH), 56.3 (CH_2), 47.3 (Me), 13.5 (Me); isomer 2: 161.7 (C), 155.4 (C), 130.4 (CH), 129.9 (CH), 129.3 (CH), 127.1 (CH), 126.2 (C), 121.8 (CH), 112.8 (CH), 78.5 (C), 75.8 (CH), 56.3 (CH_2), 48.1 (Me), 21.0 (Me); *m*/*z* (EI) 242 (M^+, 71%), 187 (75), 158 (57), 145 (100), 118 (54), 91 (50), 85 (69).

(*E*)-4-(2-But-3-ynyloxyphenyl)but-3-en-2-one *N*,*N*-dimethylhydrazone 7d

4-(2-But-3-ynyloxyphenyl)but-3-en-2-one **6b** (210 mg, 1.0 mmol) was stirred in THF (15 ml) with magnesium sulfate (700 mg), and *N*,*N*-dimethylhydrazine (0.76 ml, 10 mmol) was added dropwise. After 7 days, the mixture was filtered, the solution was concentrated *in vacuo* and the residue was purified by flash chromatography (elution with 1 : 1 ether–light petroleum containing 3% triethylamine) to give the *title compound* as an orange oil (130 mg, 50%) (inseparable mixture of 2 isomers) (Found: M^+, 256.1575. $C_{16}H_{20}N_2O$ requires 256.1576); ν_{max} ($CHCl_3$)/cm^{-1} 3309, 2960, 2929, 2858, 1599, 1489, 1454, 1261; δ_H (300 MHz; $CDCl_3$) 7.64–6.77 (6 H, m, 4 × ArH, PhC*H*=C*H*), 4.13 (2 H, m, OCH_2), 2.73 (2 H, m, CH_2C≡), 2.56 (4.2 H, s, NMe_2), 2.54 (1.8 H, s, NMe_2), 2.20 (3 H, s, Me), 2.05 (1 H, t, *J* 2.7, ≡CH); δ_C (75 MHz; $CDCl_3$) major isomer: 163.2 (C), 155.7 (C), 130.0 (CH), 129.5 (CH), 128.3 (CH), 126.3 (CH), 126.0 (C), 121.5 (CH), 112.6 (CH), 80.4 (C), 69.9 (CH), 66.6 (CH_2), 47.4 (Me), 19.6 (CH_2), 13.5 (Me); minor isomer: 161.9 (C), 156.3 (C), 130.7 (CH), 130.1 (CH), 127.2 (CH), 125.9 (C), 121.3 (CH), 120.6 (CH), 112.5 (CH), 80.3 (C), 70.0 (CH), 66.5 (CH_2), 48.1 (Me), 20.5 (Me), 19.6 (CH_2); *m*/*z* (EI) 256 (M^+, 25%), 240 (41), 201 (24), 188 (71), 171 (25), 160 (24), 145 (100), 131 (33).

1,6-Bis[2-(2-formylethenyl)phenoxy]hexa-2,4-diyne bis(*N*,*N*-dimethylhydrazone) 8a

A solution of 3-(2-prop-2-ynyloxyphenyl)propenal *N*,*N*-dimethylhydrazone **7a** (200 mg, 0.88 mmol) in ether (5 ml) was added to a stirred solution of ether (80 ml), methanol (20 ml) and pyridine (20 ml) containing copper(II) acetate monohydrate (530 mg, 2.6 mmol) for 16 h at 55 °C. The cooled solution was then filtered and the solvents removed *in vacuo*, the residue was partitioned between HCl (2 M; 100 ml) and dichloromethane (100 ml), the organic phase was washed with water (2 × 100 ml) and brine (100 ml) and dried (Na_2SO_4). After filtration and evaporation of the solvent *in vacuo*, the crude residue was purified by flash chromatography (elution with 3 : 1 ether–light petroleum) to give the *title compound* as a light yellow solid (97 mg, 48%); mp 130–132 °C (from ether) (Found: M^+, 454.2375. $C_{28}H_{30}N_4O_2$ requires 454.2369); ν_{max} (KBr)/cm^{-1} 2997, 2958, 2784, 2146, 1670, 1616, 1597, 1578, 1485, 746; δ_H (300 MHz; $CDCl_3$) 7.52 (2 H, dd, *J* 7.7, 1.6, ArH), 7.22–7.17 (4 H, m, 2 × CH=N, 2 × ArH), 7.01–6.91 (8 H, m, 2 × PhC*H*=C*H*, 4 × ArH), 4.79 (4 H, s, OCH_2), 2.92 (12 H, s, NMe_2); δ_C (75 MHz; $CDCl_3$) 154.3 (C), 136.2 (CH), 128.34 (CH), 128.30 (CH), 127.0 (C), 126.2 (CH), 125.9 (CH), 122.0 (CH), 112.6 (CH), 74.7 (C), 71.1 (C), 56.7 (CH_2), 42.8 (Me); *m*/*z* (EI) 454 (M^+, 0.06%), 409 (1), 365 (4), 277 (39), 144 (45), 106 (80), 88 (66), 57 (100).

1,8-Bis[2-(2-formylethenyl)phenoxy]octa-3,5-diyne bis(*N*,*N*-dimethylhydrazone) 8b

A solution of 3-(2-but-3-ynyloxyphenyl)propenal *N*,*N*-dimethylhydrazone **7b** (100 mg, 0.42 mmol) was stirred in ether (40 ml), methanol (10 ml) and pyridine (10 ml) with copper(II) acetate monohydrate (250 mg, 1.3 mmol) at reflux. After 16 h, the reaction mixture was filtered and the solvent removed *in vacuo*, the residue was partitioned between HCl (2 M; 80 ml) and dichloromethane (80 ml), and the organic extracts were washed with water (2 × 80 ml) and brine (80 ml) and dried ($MgSO_4$). After filtration the solvent was removed *in vacuo* and the crude residue purified by flash chromatography (elution with 2 : 1 ether–light petroleum containing 3% triethylamine) to give the *title compound* as a viscous orange oil (31 mg,

31%) (Found: M^+, 482.2683. $C_{30}H_{34}N_4O_2$ requires 482.2682); ν_{max} (film)/cm^{-1} 3034, 2953, 2787, 1676, 1597, 1487, 750; δ_H (300 MHz; $CDCl_3$) 7.53 (2 H, dd, *J* 7.9, 1.8, ArH), 7.20 (2 H, d, *J* 8.1, CH=N), 7.18 (2 H, ddd, *J* 9.0, 7.5, 1.8, ArH), 7.01 (2 H, d, *J* 16.0, PhC*H*=), 6.96 (2 H, dd, *J* 16.0, 8.1, PhCH=C*H*), 6.94 (2 H, m, ArH), 6.83 (2 H, dd, *J* 7.5, 0.9, ArH), 4.12 (4 H, t, *J* 7.0, OCH_2), 2.92 (12 H, s, NMe_2), 2.79 (4 H, t, *J* 7.0, $CH_2C{\equiv}$); δ_C (75 MHz; $CDCl_3$) 155.1 (C), 136.4 (CH), 128.4 (CH), 127.9 (CH), 126.8 (C), 126.1 (CH), 125.9 (CH), 121.5 (CH), 112.5 (CH), 73.9 (C), 66.7 (C), 66.3 (CH_2), 42.9 (Me), 20.4 (CH_2); *m*/*z* (EI) 482 (M^+, 4%), 438 (4), 395 (13), 248 (10), 218 (10), 173 (13), 146 (19), 131 (100), 91 (19), 77 (42).

1,6-Bis[2-(3-oxobut-1-enyl)phenoxy]hexa-2,4-diyne bis(*N*,*N*-dimethylhydrazone) 8c

(*E*)-4-(2-Prop-2-ynyloxyphenyl)but-3-en-2-one *N*,*N*-dimethylhydrazone **7c** (300 mg, 1.2 mmol) was added to a stirred mixture of copper(II) acetate monohydrate (740 mg, 3.7 mmol) in ether (100 ml), methanol (30 ml) and pyridine (30 ml). The reaction mixture was heated to 55 °C for 16 h, the cooled solution was filtered and the solvents were removed *in vacuo*. The residue was then partitioned between HCl (2 M; 150 ml) and dichloromethane (150 ml). The organic phase was washed with brine (2 × 150 ml) and water (150 ml) and dried (Na_2SO_4). After filtration the solvent was evaporated *in vacuo* and the crude residue purified by flash chromatography (elution with ether containing 3% triethylamine) to give the *title compound* as a viscous yellow oil (148 mg, 50%) (unseparated mixture of 2 isomers) (Found: M^+, 482.2694. $C_{30}H_{34}N_4O_2$ requires 482.2682); ν_{max} ($CHCl_3$)/cm^{-1} 2961, 2862, 2779, 1668, 1599, 1485, 1456; δ_H (300 MHz; $CDCl_3$) 7.88–7.22 (6 H, m, 2 × PhC*H*=, 4 × ArH), 7.06–6.70 (6 H, m, 2 × PhCH=C*H*, 4 × ArH), 4.81 (4 H, s, OCH_2), 2.58 (9 H, m, NMe_2), 2.54 (3 H, m, NMe_2), 2.20 (6 H, m, Me); δ_C (100 MHz; $CDCl_3$) major isomer: 163.0 (C), 154.8 (C), 130.6 (CH), 129.4 (CH), 128.0 (CH), 126.8 (CH), 126.3 (C), 122.1 (CH), 112.7 (CH), 74.7 (C), 71.2 (C), 56.7 (CH_2), 47.3 (Me), 13.6 (Me); minor isomer: 161.6 (C), 155.2 (C), 131.6 (CH), 130.2 (CH), 130.0 (CH), 127.3 (CH), 126.3 (C), 122.1 (CH), 112.7 (CH), 74.5 (C), 71.3 (C), 56.2 (CH_2), 48.1 (Me), 20.5 (Me); *m*/*z* (EI) 482 (M^+, 0.8%), 468 (1), 437 (9), 393 (44), 379 (40), 352 (19), 234 (76), 145 (100), 91 (26).

1,8-Bis[2-(3-oxobut-1-enyl)phenoxy]octa-3,5-diyne bis(*N*,*N*-dimethylhydrazone) 8d

A solution of 4-(2-but-3-ynyloxyphenyl)but-3-en-2-one *N*,*N*-dimethylhydrazone **7d** (130 mg, 0.49 mmol) was stirred in ether (40 ml), methanol (10 ml) and pyridine (10 ml) with copper(II) acetate monohydrate (290 mg, 1.5 mmol) at reflux. After 16 h, the reaction mixture was filtered and the solvent removed *in vacuo*. The residue was partitioned between HCl (2 M; 50 ml) and dichloromethane (50 ml), the organic extracts were washed with water (2 × 50 ml) and brine (50 ml) and dried (Na_2SO_4). After filtration the solvent was removed *in vacuo* and the crude residue purified by flash chromatography (elution with ether containing 3% triethylamine) to give the *title compound* as a viscous yellow oil (63 mg, 50%) (inseparable mixture of 2 isomers) (Found: M^+, 510.3007. $C_{32}H_{38}N_4O_2$ requires 510.2995); ν_{max} (film)/cm^{-1} 3059, 2953, 2856, 2819, 2775, 1599, 1489, 1454, 752; δ_H (400 MHz; $CDCl_3$) 7.59–6.81 (12 H, m, 8 × ArH, 2 × PhC*H*=C*H*), 4.14 (4 H, m, OCH_2), 2.80 (4 H, m, $CH_2C{\equiv}$), 2.56 (8.5 H, s, NMe_2), 2.54 (3.5 H, s, NMe_2), 2.22 (6 H, s, Me); δ_C (100 MHz; $CDCl_3$) major isomer: 163.1 (C), 155.6 (C), 130.1 (CH), 129.4 (CH), 128.1 (CH), 126.4 (CH), 126.2 (C), 121.6 (CH), 112.6 (CH), 73.9 (C), 66.7 (C), 66.2 (CH_2), 47.3 (Me), 20.4 (CH_2), 13.5 (Me); minor isomer: 161.9 (C), 156.1 (C), 130.6 (CH), 130.1 (CH), 127.2 (CH), 126.1 (C), 121.5 (CH), 120.7 (CH), 112.6 (CH), 73.8 (C), 66.7 (C), 66.2 (CH_2), 48.1 (Me), 20.42 (Me), 20.39 (CH_2); *m*/*z* (EI) 510 (M^+, 2%), 495 (3), 466 (37), 452 (35), 409 (61), 187 (35), 145 (100), 91 (37).

(*E*)-3-[2-(*N*-Benzoyl-*N*-prop-2-ynylamino)phenyl]propenal *N*,*N*-dimethylhydrazone 10

A solution of 3-[2-(*N*-benzoylamino)phenyl]propenal *N*,*N*-dimethylhydrazone **9**[18] (1.0 g, 3.4 mmol) in DMF (5 ml) was added dropwise to a stirred suspension of potassium hydride (0.15 g, 3.8 mmol) in DMF (5 ml) and stirred at 25 °C for 1 h. Propargyl chloride (0.25 g, 3.5 mmol) was added and the reaction mixture was heated at 60 °C for 18 h. Upon cooling the mixture was diluted with dichloromethane (50 ml) and washed with brine (4 × 50 ml) and water (3 × 50 ml). The organic extracts were pooled, dried (Na_2SO_4), and concentrated *in vacuo*. The crude residue was chromatographed on silica gel (ether) to yield the desired product as a pale yellow solid (0.94 g, 83%), mp 137–138 °C (Found: C, 75.9; H, 6.3; N, 12.4. $C_{21}H_{21}N_3O$ requires C, 76.1; H, 6.4; N, 12.7%) (Found: M^+, 331.1684. $C_{21}H_{21}N_3O$ requires 331.1685); ν_{max} (KBr)/cm^{-1} 3442, 3308, 1641, 1618, 1482; δ_H (400 MHz; $CDCl_3$) 7.51 (1 H, d, *J* 8.0, CH=N), 7.25 (1 H, dd, *J* 16.0, 8.0, =C*H*CHN), 7.20–6.94 (8 H, m, ArH), 6.86 (1 H, d, *J* 8.0, ArH), 6.73 (1 H, d, *J* 16.0, PhC*H*=), 4.91 (1 H, dd, *J* 17.0, 2.0, NC*H*H), 4.21 (1 H, dd, *J* 17.0, 2.0, NCH*H*), 2.90 (6 H, s, NMe_2), 2.22 (1 H, t, *J* 1.0, ≡CH); δ_C (100 MHz; $CDCl_3$) 171.3 (C), 140.0 (CH), 135.4 (CH), 135.2 (CH), 134.4 (CH), 131.0 (C), 130.6 (C), 128.8 (CH), 128.6 (CH), 128.2 (CH), 128.1 (CH), 126.1 (CH), 125.3 (CH), 78.9 (C), 72.8 (CH), 43.1 (2 × Me), 39.8 (CH_2); *m*/*z* (EI) 331 (M^+, 25%), 134 (80), 44 (100).

1,6-Bis[2-(2-formylethenyl)phenylamino]hexa-2,4-diyne bis(*N*,*N*-dimethylhydrazone) 11

The acetylene **10** (134 mg, 0.4 mmol) and copper(II) acetate monohydrate (200 mg, 1.0 mmol) were heated in a mixture of pyridine (10 ml), methanol (10 ml) and ether (40 ml) for 18 h. The cooled mixture was filtered and concentrated *in vacuo*. The residue was washed with dilute hydrochloric acid (50 ml), extracted with dichloromethane (50 ml) and washed with brine (2 × 50 ml) and water (2 × 50 ml). The combined organic extracts were dried (Na_2SO_4), and concentrated *in vacuo*. The residue was chromatographed on silica gel (ether) to yield the desired product as a pale brown solid (110 mg, 83%), mp 179–180 °C (Found: MH^+, 661.3290. $C_{42}H_{40}N_6O_2$ + H requires 661.3291); ν_{max} (KBr)/cm^{-1} 3430, 2212, 1644, 1619, 1482; δ_H (400 MHz; $CDCl_3$) 7.45 (2 H, d, *J* 8, CH=N), 7.21–6.90 (18 H, m, ArH), 6.80 (2 H, dd, *J* 16.0, 8.0, =C*H*CHN), 6.63 (2 H, d, *J* 16.0, PhC*H*=), 4.92 (2 H, d, *J* 17.0, NC*H*H), 4.13 (2 H, d, *J* 17.0, NCH*H*), 2.89 (12 H, s, NMe_2); δ_C (100 MHz; $CDCl_3$) 171.5 (C), 140.3 (C), 135.6 (C), 135.5 (CH), 134.7 (CH), 131.6 (CH), 131.6 (CH), 131.0 (CH), 130.9 (CH), 129.2 (CH), 129.1 (CH), 128.7 (CH), 128.5 (CH), 126.5 (CH), 125.4 (CH), 74.3 (C), 69.6 (C), 43.3 (2 × Me), 40.8 (CH_2); *m*/*z* (CI) 661 (MH^+, 75%), 44 (100).

Dodeca-5,7-diyne-1,12-diol 13a

A solution of copper(II) acetate monohydrate (8.0 g, 40 mmol) in ether (400 ml), methanol (100 ml) and pyridine (120 ml) was stirred at reflux. Hex-5-ynol **12a** (1.0 g, 10 mmol) was added and the solution stirred for 16 h. The mixture was concentrated *in vacuo* and the product was partitioned between HCl (2 M; 500 ml) and dichloromethane (500 ml). The organic layer was washed with water (2 × 500 ml) and brine (2 × 500 ml) and dried (Na_2SO_4). The mixture was filtered and the solvent removed *in vacuo*. The residue was purified by flash chromatography (elution with ether) to give the *title compound* as a colourless solid (600 mg, 61%); mp 51–52 °C (from light petroleum–ethyl acetate) (lit.,[29] mp 49–50 °C) (Found: C, 74.1; H, 9.45. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%); ν_{max} (KBr)/cm^{-1} 3430, 3623, 2175; δ_H (300 MHz; $CDCl_3$) 3.63 (4 H, t, *J* 6.1, CH_2O), 2.28 (4 H, t, *J* 6.7, ≡CC*H*$_2$), 2.11 (2 H, s, OH), 1.62 (8

H, m, CH_2CH_2); δ_C (75 MHz; $CDCl_3$) 76.6 (C), 65.6 (C), 62.1 (CH_2), 31.7 (CH_2), 24.6 (CH_2), 19.0 (CH_2).

Tetradeca-6,8-diyne-1,14-diol 13b

To a stirred solution of copper(II) acetate monohydrate in methanol (100 ml), ether (400 ml) and pyridine (200 ml) was added hept-6-ynol **12b** (2.6 g, 23 mmol) in ether (5 ml). The temperature was raised to 55 °C. After 4 days, the mixture was filtered and resulting solution partitioned between HCl (2 M; 350 ml) and dichloromethane (350 ml). The aqueous phase was extracted with more dichloromethane (100 ml). The combined organic phases were washed with water (2 × 350 ml) and brine (350 ml) and were dried (Na_2SO_4). The solution was filtered and the solvent was removed *in vacuo*; the residue was purified by flash chromatography (elution with 1 : 1 ether–ethyl acetate) to give the *title compound* as a pink solid (2.2 g, 85%); mp 62–64 °C (from ether) (Found: M^+, 222.1619. $C_{14}H_{22}O_2$ requires 222.1620); ν_{max} (KBr)/cm^{-1} 3405 (br), 3444 (br), 2939, 2893, 2860, 1464, 1057; δ_H (300 MHz; $CDCl_3$) 3.62 (4 H, t, *J* 6.4, CH_2O), 2.25 (4 H, t, *J* 6.6, $CH_2C{\equiv}$), 1.74 (2 H, br, OH), 1.41–1.60 (12 H, m, CH_2CH_2CH_2); δ_C (75 MHz; $CDCl_3$) 77.3 (C), 65.5 (C), 62.6 (CH_2), 32.2 (CH_2), 28.1 (CH_2), 25.0 (CH_2), 19.2 (CH_2); *m*/*z* (EI) 223 (11%), 222 (M^+, 3), 179 (8), 149 (51), 131 (28), 117 (53), 105 (54), 91 (100).

Dodeca-5,7-diyne-1,12-dial 14a

A suspension of IBX (6.52 g, 23.3 mmol) in DMSO (25 ml) was stirred vigorously at room temperature for 1.5 h. Dodeca-5,7-diyne-1,12-diol **13a** (910 mg, 4.7 mmol) in DMSO (7 ml) was added and the mixture stirred overnight. After 16 h, the reaction mixture was diluted with water (100 ml) and the white precipitate was filtered off. The solution was extracted with ether (3 × 80 ml) and the combined organic extracts were washed with water (3 × 150 ml) and dried (Na_2SO_4). The mixture was filtered and the solvent removed to give the *title compound* as a viscous yellow oil (850 mg, 96%) used without further purification; ν_{max} ($CHCl_3$)/cm^{-1} 2944, 2904, 2833, 2729, 2214, 1724, 1391, 1410, 1429; δ_H (300 MHz; $CDCl_3$) 9.77 (2 H, t, *J* 1.2, CHO), 2.56 (4 H, td, *J* 7.0, 1.2, CH_2CHO), 2.32 (4 H, t, *J* 7.0, ≡CCH_2), 1.83 (4 H, quin, *J* 7.0, $CH_2CH_2CH_2$); δ_C (75 MHz; $CDCl_3$) 201.5 (CHO), 76.4 (C), 66.2 (C), 42.5 (CH_2), 20.7 (CH_2), 18.5 (CH_2).

Tetradeca-6,8-diyne-1,14-dial 14b

IBX (340 mg, 1.2 mmol) was stirred in DMSO (0.5 ml) until complete dissolution was achieved (*ca*. 10 min). Tetradeca-6,8-diyne-1,14-diol **13b** (44 mg, 0.2 mmol) was added and the solution stirred for 16 h. Water (10 ml) was added and the precipitate filtered off. The solution obtained was extracted with ether (10 ml) and the organic extracts were washed with water (3 × 10 ml) and dried (Na_2SO_4). The drying agent was removed by filtration and the solvent removed *in vacuo* to give the *title compound* as a viscous yellow oil (40 mg, 92%) used without further purification; ν_{max} ($CHCl_3$)/cm^{-1} 2937, 2867, 2832, 1723, 757; δ_H (300 MHz; $CDCl_3$) 9.75 (2 H, t, *J* 1.6, CHO), 2.45 (4 H, td, *J* 7.2, 1.6, CH_2CHO), 2.27 (4 H, t, *J* 6.9, ≡CCH_2), 1.78–1.68 (4 H, m, CH_2CH$_2$CHO), 1.59–1.51 (4 H, m, ≡CCH$_2$CH_2); δ_C (75 MHz; $CDCl_3$) 202.3 (CHO), 76.8 (C), 65.7 (C), 43.2 (CH_2), 27.6 (CH_2), 21.2 (CH_2), 19.0 (CH_2).

(2*E*,14*E*)-Hexadeca-2,14-diene-7,9-diyne-1,16-dial bis(*N*,*N*-dimethylhydrazone) 15a

Diethyl formylmethylphosphonate *N*,*N*-dimethylhydrazone (330 mg, 1.5 mmol) was stirred in THF (2 ml) at −78 °C. *n*-Butyllithium (1.6 M in hexane; 0.94 ml, 1.5 mmol) was added dropwise and the solution stirred for 10 min. A solution of dodeca-5,7-diyne-1,12-dial **14a** (89 mg, 0.46 mmol) in THF (1.5 ml) was added slowly and after 30 min the reaction mixture was allowed to warm to room temperature. The reaction was then quenched by addition of ammonium chloride solution (saturated aqueous, 50 ml), the solution was extracted with ether (3 × 50 ml) and the combined organic extracts were washed with water (3 × 50 ml) and brine (50 ml) and then dried (Na_2SO_4). The mixture was filtered and the solvent removed *in vacuo*; the crude residue was purified by flash chromatography (elution with 9 : 1 ether–light petroleum) to give the *title compound* as a viscous yellow oil (54 mg, 35%) (Found: M^+, 326.2468. $C_{20}H_{30}N_4$ requires 326.2470); ν_{max} (film)/cm^{-1} 2939, 2858, 2785, 2160, 1560, 1468, 1030; δ_H (300 MHz; $CDCl_3$) 6.97 (2 H, d, *J* 8.9, CH=N), 6.18 (2 H, ddt, *J* 15.6, 8.9, 1.3, C*H*CH=N), 5.73 (2 H, dt, *J* 15.6, 7.0, CH_2C*H*=), 2.80 (12 H, s, NMe_2), 2.26–2.18 (8 H, m, CH_2), 1.61 (4 H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 136.4 (CH), 133.8 (CH), 129.9 (CH), 77.0 (C), 65.7 (C), 42.9 (Me), 31.6 (CH_2), 27.7 (CH_2), 18.6 (CH_2); *m*/*z* (EI) 326 (M^+, 1%), 282 (34), 237 (100), 210 (58), 182 (52), 170 (61), 157 (56), 144 (42), 130 (92).

(2*E*,16*E*)-Octadeca-2,16-diene-8,10-diyne-1,18-dial bis(*N*,*N*-dimethylhydrazone) 15b

Diethyl formylmethylphosphonate *N*,*N*-dimethylhydrazone (420 mg, 1.9 mmol) was stirred in THF (2.5 ml) at −78 °C. *n*-Butyllithium (1.6 M in hexane; 1.2 ml, 1.9 mmol) was added dropwise and the solution stirred for 15 min. A solution of tetradeca-6,8-diyne-1,14-dial **14b** (89 mg, 0.40 mmol) in THF (1.5 ml) was added slowly and after 45 min the reaction was allowed to warm to room temperature. After 2 h, the reaction was quenched by addition of aqueous ammonium chloride solution (saturated, 50 ml), the solution was extracted with ether (3 × 50 ml) and the combined organic extracts were washed with water (3 × 50 ml) and brine (50 ml) and were dried (Na_2SO_4). The mixture was filtered and the solvent removed *in vacuo* to give a crude residue that was purified by flash chromatography (elution with 7 : 3 ether–light petroleum containing 3% triethylamine) to give the *title compound* as a viscous yellow oil (33 mg, 23%) (Found: M^+, 354.2787. $C_{22}H_{34}N_4$ requires 354.2783); ν_{max} (film)/cm^{-1} 2937, 2858, 2784, 1566, 1468, 1032, 733; δ_H (300 MHz; $CDCl_3$) 6.99 (2 H, d, *J* 8.9, CH=N), 6.17 (2 H, ddt, *J* 15.5, 8.9, 1.4, C*H*CH=N), 5.77 (2 H, dt, *J* 15.5, 7.0, CH_2C*H*=), 2.80 (12 H, s, NMe_2), 2.26–2.21 (4 H, m, CH_2), 2.17–2.10 (4 H, m, CH_2), 1.54–1.49 (8 H, m, CH_2CH_2); δ_C (75 MHz; $CDCl_3$) 136.7 (CH), 134.9 (CH), 129.3 (CH), 77.3 (C), 65.4 (C), 42.9 (Me), 32.0 (CH_2), 28.2 (CH_2), 27.7 (CH_2), 19.0 (CH_2); *m*/*z* (EI) 354 (M^+, 1%), 310 (27), 283 (21), 265 (30), 250 (23), 223 (19), 59 (100).

(3*E*,15*E*)-Octadeca-3,15-diene-8,10-diyne-2,17-dione 16a

To a suspension of (acetylmethylene)triphenylphosphorane (3.0 g, 9.3 mmol) in THF (20 ml) was added dodeca-5,7-diyne-1,12-dial **14a** (800 mg, 1.2 mmol) in THF (6 ml). After heating at reflux for 16 h, the solvent was removed and the residue was purified by flash chromatography (elution with 2 : 1 ether–light petroleum) to give the *title compound* as a light yellow oil (340 mg, 34%) (Found: M^+, 270.1618. $C_{18}H_{22}O_2$ requires 270.1620); ν_{max} ($CHCl_3$)/cm^{-1} 2936, 2866, 2162, 1617, 1637, 1627; δ_H (300 MHz; $CDCl_3$) 6.74 (2 H, dt, *J* 16.0, 6.9, CH_2C*H*=), 6.07 (2 H, dt, *J* 16.0, 1.5, =C*H*C(Me)O), 2.36–2.25 (8 H, m, ≡CCH_2, CH_2CH=), 2.21 (6 H, s, Me), 1.68 (4 H, quin, *J* 7.1, $CH_2CH_2CH_2$); δ_C (75 MHz; $CDCl_3$) 198.3 (C=O), 146.4 (CH), 131.0 (CH), 76.6 (C), 66.0 (C), 31.3 (CH_2), 26.9 (Me), 26.6 (CH_2), 18.7 (CH_2); *m*/*z* (EI) 270 (M^+, 0.9%), 227 (100), 213 (21), 199 (44), 174 (26), 149 (42), 128 (38), 115 (37).

(3*E*,17*E*)-Icosa-3,17-diene-9,11-diyne-2,19-dione 16b

A solution of tetradeca-6,8-diyne-1,14-dial **14b** (190 mg, 0.86 mmol) was stirred in toluene (10 ml), (acetylmethylene)-triphenylphosphorane (600 mg, 1.9 mmol) was added and the

suspension heated at reflux for 45 min. The mixture was allowed to cool to room temperature and stirred for a further 16 h and then concentrated *in vacuo*. The crude residue was purified by flash chromatography (elution with 2 : 1 ether–light petroleum) to give the *title compound* as a viscous pale yellow oil (100 mg, 41%) (Found: M^+, 298.1931. $C_{20}H_{26}O_2$ requires 298.1933); ν_{max} (film)/cm^{-1} 3004, 2939, 2862, 1696, 1673; δ_H (300 MHz; $CDCl_3$) 6.77 (2 H, dt, *J* 16.0, 6.9, CH_2CH=), 6.07 (2 H, dt, *J* 16.0, 1.5, =CHC(Me)O), 2.30–2.19 (14 H, m, 4 × CH_2, 2 × Me), 1.61–1.53 (8 H, m, 4 × CH_2); δ_C (75 MHz; $CDCl_3$) 198.6 (C=O), 147.7 (CH), 131.6 (CH), 77.0 (C), 65.6 (C), 31.9 (CH_2), 27.7 (CH_2), 27.1 (CH_2), 26.9 (Me), 19.0 (CH_2); *m*/*z* (EI) 298 (M^+, 2%), 297 (5), 281 (10), 255 (27), 187 (36), 173 (55), 129 (62).

(3*E*,15*E*)-Octadeca-3,15-diene-8,10-diyne-2,17-dione bis(*N*,*N*-dimethylhydrazone) 15c

Magnesium sulfate (1.0 g) and octadeca-3,15-diene-8,10-diyne-2,17-dione **16a** (340 mg, 1.3 mmol) were stirred in THF (20 ml); *N*,*N*-dimethylhydrazine (950 µl, 13 mmol) was added at 0 °C. After 3 days, the mixture was filtered and the *title compound* isolated by flash chromatography (elution with ether containing 3% triethylamine, TLC showed isomer 1 at R_f = 0.22 and isomer 2 at R_f = 0.19) as a yellow oil (160 mg, 35%) (Found: MH^+, 355.2862. $C_{22}H_{34}N_4$ + H requires 355.2862); ν_{max} ($CHCl_3$)/cm^{-1} 2959, 2864, 1645, 1584, 1468; δ_H (300 MHz; $CDCl_3$) 6.82–6.02 (4 H, m, CH_2CH=, CH_2CH=CH), 2.49 + 2.46 (12 H, s, NMe_2), 2.29–2.24 (8 H, m, CH_2CH=, ≡CCH_2), 2.04 + 2.03 (6 H, s, Me), 1.66 (4 H, quin, *J* 7.2, $CH_2CH_2CH_2$); δ_C (100 MHz; $CDCl_3$) major isomer: 162.8 (C), 135.6 (CH), 132.6 (CH), 76.8 (C), 65.8 (C), 47.2 (Me), 31.7 (CH_2), 27.5 (CH_2), 18.7 (CH_2), 13.3 (Me); minor isomer: 138.5 (C), 135.6 (CH), 123.9 (CH), 76.8 (C), 65.8 (C), 47.8 (Me), 32.1 (CH_2), 27.4 (CH_2), 20.3 (Me), 18.8 (CH_2); *m*/*z* (CI) 355 (MH^+, 20%), 63 (100).

(3*E*,17*E*)-Icosa-3,17-diene-9,11-diyne-2,19-dione bis(*N*,*N*-dimethylhydrazone) 15d

N,*N*-Dimethylhydrazine (220 µl, 2.9 mmol) was added to magnesium sulfate (150 mg) and icosa-3,17-diene-9,11-diyne-2,19-dione **16b** (87 mg, 0.29 mmol) in THF (5 ml), at 0 °C. After 3 days, the mixture was filtered and the solvent removed *in vacuo* to give a residue that was purified by flash chromatography (elution with ether containing 3% triethylamine) to give the *title compound* as a yellow oil (18 mg, 16%) (Found: M^+, 382.3096. $C_{24}H_{38}N_4$ requires 382.3096); ν_{max} ($CHCl_3$)/cm^{-1} 2939, 2858, 2773, 1645, 1583; δ_H (300 MHz; $CDCl_3$) 6.79–6.03 (4 H, m, CH_2CH=CH), 2.50 + 2.47 (12 H, s, NMe_2), 2.27–2.14 (8 H, m, CH_2CH=, CH_2C≡), 2.04 + 2.03 (6 H, s, Me), 1.56–1.53 (8 H, m, $CH_2CH_2CH_2CH_2$); δ_C (75 MHz; $CDCl_3$) major isomer: 163.0 (C), 136.6 (CH), 132.0 (CH), 77.1 (C), 65.8 (C), 47.3 (Me), 32.2 (CH_2), 27.7 (CH_2), 27.9 (CH_2), 19.0 (CH_2), 13.3 (Me); minor isomer: 139.6 (C), 136.6 (CH), 123.4 (CH), 77.1 (C), 65.5 (C), 47.8 (Me), 32.5 (CH_2), 27.9 (CH_2), 27.7 (CH_2), 20.4 (Me), 19.0 (CH_2); *m*/*z* (EI) 382 (M^+, 2%), 367 (6), 338 (43), 324 (100), 304 (24), 281 (96).

Diels–Alder reactions

5*H*-Chromeno[3,4-*c*]pyridine 17

A solution of (*E*)-3-(2-prop-2-ynyloxyphenyl)propenal *N*,*N*-dimethylhydrazone **7a** (69 mg, 0.30 mmol) in xylene (5 ml) was degassed by freeze–pump–thaw techniques in a sealable tube, the headspace in the tube was flushed with nitrogen and the tube sealed. The solution was heated to 165 °C for 1 day and then to 200 °C for 6 days. The solvent was removed *in vacuo* and the residue purified by flash chromatography (elution with ether containing 3% triethylamine followed by 1 : 1 ether–ethyl acetate) to give (i) the *title compound* as a brown oil (33 mg, 59%) (lit.,[15] no data given) (Found: M^+, 183.0685. $C_{12}H_9NO$ requires 183.0684); ν_{max} (film)/cm^{-1} 3034, 2974, 2918, 2853, 1608, 1600, 1476, 1416, 1247; δ_H (400 MHz; $CDCl_3$) 8.58 (1 H, d, *J* 5.2, ArH), 8.41 (1 H, s, ArH), 7.73 (1 H, dd, *J* 7.8, 1.6, ArH), 7.51 (1 H, d, *J* 5.2, ArH), 7.33 (1 H, m, ArH), 7.08 (1 H, m, ArH), 7.01 (1 H, m, ArH), 5.15 (2 H, s, OCH_2); δ_C (100 MHz; $CDCl_3$) 155.7 (C), 150.1 (CH), 145.8 (CH), 137.6 (C), 131.8 (CH), 125.9 (C), 124.0 (CH), 122.4 (CH), 120.4 (C), 117.8 (CH), 115.9 (CH), 65.8 (CH_2); *m*/*z* (EI) 183 (M^+, 99%), 182 (100), 154 (9), 127 (10), 99 (1); and (ii) 3-(2*H*-chromen-8-yl)-propenal *N*,*N*-dimethylhydrazone **18** as a brown oil (4.0 mg, 6%) (Found: M^+, 228.1259. $C_{14}H_{16}N_2O$ requires 228.1263); ν_{max} (film)/cm^{-1} 3045, 2954, 2853, 2827, 1551, 1462, 1443, 1037; δ_H (400 MHz; C_6D_6) 7.48 (1 H, dd, *J* 16.7, 8.8, =CHCHN), 7.38 (1 H, dd, *J* 7.6, 1.8, ArH), 7.23 (1 H, d, *J* 16.4, PhCHCHCHN), 7.12 (1 H, d, *J* 8.8, CH=N), 6.74–6.70 (2 H, m, ArH), 6.19 (1 H, dt, *J* 9.8, 1.9, PhCH=$CHCH_2$), 5.29 (1 H, dt, *J* 9.8, 3.5, =$CH$$CH_2$), 4.48 (2 H, dd, *J* 3.5, 1.9, CH_2O), 2.64 (6 H, s, NMe_2); δ_C (100 MHz; $CDCl_3$) 151.1 (C), 136.5 (CH), 128.1 (CH), 126.1 (CH), 126.0 (CH), 125.7 (CH), 125.0 (C), 124.8 (CH), 122.6 (C), 121.8 (CH), 121.1 (CH), 65.6 (CH_2), 42.8 (Me); *m*/*z* (EI) 228 (M^+, 72%), 182 (57), 169 (100), 154 (35), 141 (32), 128 (75), 115 (57), 102 (32).

2-Methyl-5*H*-chromeno[3,4-*c*]pyridine 19

A solution of 4-(2-prop-2-ynyloxyphenyl)but-3-en-2-one *N*,*N*-dimethylhydrazone **7b** (35 mg, 0.14 mmol) in mesitylene (5 ml) was heated at reflux under an atmosphere of nitrogen for 3 days. The mixture was then transferred to high pressure sealed tube apparatus, the solvent was degassed, the space was filled with nitrogen and the tube sealed. The mixture was then heated to 210 °C for 4 days. The mixture was concentrated *in vacuo* and the *title compound* was isolated by flash chromatography (elution with ether) as a brown oil (11 mg, 41%) (Found: M^+, 197.0845. $C_{13}H_{11}NO$ requires 197.0841); ν_{max} ($CHCl_3$)/cm^{-1} 2962, 2929, 2855, 1609, 1458; δ_H (400 MHz; $CDCl_3$) 8.31 (1 H, s, ArH), 7.74 (1 H, dd, *J* 7.8, 1.6, ArH), 7.41 (1 H, s, ArH), 7.33 (1 H, ddd, *J* 8.2, 7.5, 1.6, ArH), 7.08 (1 H, ddd, *J* 7.8, 7.5, 1.2, ArH), 7.01 (1 H, dd, *J* 8.2, 1.2, ArH), 5.15 (2 H, s, OCH_2), 2.61 (3 H, s, Me); δ_C (100 MHz; $CDCl_3$) 158.7 (C), 155.8 (C), 145.0 (CH), 137.9 (C), 131.6 (CH), 123.9 (CH), 123.2 (C), 122.3 (CH), 120.6 (C), 117.8 (CH), 115.3 (CH), 65.8 (CH_2), 24.5 (Me); *m*/*z* (EI) 197 (M^+, 66%), 196 (73), 168 (7), 141 (5), 118 (36), 83 (100).

4,4′-Bi(5*H*-chromeno[3,4-*c*]pyridine) 21

A solution of the bis(*N*,*N*-dimethylhydrazone) **8a** (97 mg, 0.21 mmol) in xylene (6 ml) was degassed by freeze–pump–thaw techniques in a sealable tube. The headspace of the tube was flushed with nitrogen and the solution was heated to 150 °C for 3.5 h. The solvent was removed *in vacuo* and the crude residue purified by flash chromatography (elution with 4 : 1 THF–dichloromethane) to give a brown solid (61 mg, 81%) that was further purified by flash chromatography (elution with chloroform) to give the *title compound* as a light brown solid (14 mg, 18%); mp 208–209 °C (from chloroform) (Found: M^+, 364.1210. $C_{24}H_{16}N_2O_2$ requires 364.1212); ν_{max} ($CHCl_3$)/cm^{-1} 2964, 2856, 1608, 1589, 1581, 1554, 1468; δ_H (400 MHz; $CDCl_3$) 8.63 (2 H, d, *J* 5.2, ArH), 7.80 (2 H, dd, *J* 7.9, 1.5, ArH), 7.62 (2 H, d, *J* 5.2, ArH), 7.37 (2 H, m, ArH), 7.12 (2 H, m, ArH), 7.03 (2 H, dd, *J* 8.2, 1.2, ArH), 5.33 (4 H, s, OCH_2); δ_C (100 MHz; $CDCl_3$) 156.0 (C), 153.1 (C), 147.8 (CH), 139.3 (C), 131.7 (CH), 126.5 (C), 124.1 (CH), 122.3 (CH), 120.8 (C), 117.7 (CH), 116.0 (CH), 65.7 (CH_2); *m*/*z* (EI) 364 (M^+, 100%), 363 (25), 345 (10), 335 (16), 308 (11), 279 (10), 149 (27).

2,2′-Dimethyl-4,4′-bi(5*H*-chromeno[3,4-*c*]pyridin)-5-one 22

A solution of the bis(*N*,*N*-dimethylhydrazone) **8c** (120 mg, 0.25 mmol) in mesitylene (10 ml) was heated at reflux for 48 h. The solvent was removed *in vacuo* and the crude residue

purified by flash chromatography (elution with 2 : 1 ether–ethyl acetate containing 3% triethylamine) to give the *title compound* as a brown oil (17 mg, 17%) (Found: M^+, 406.1310. $C_{26}H_{18}N_2O_3$ requires 406.1317); ν_{max} ($CHCl_3$)/cm^{-1} 2962, 2927, 2856, 1741, 1598, 1262; δ_H (400 MHz; $CDCl_3$) 8.11 (1 H, dd, *J* 8.0, 1.3, ArH), 7.89 (1 H, s, ArH), 7.80 (1 H, dd, *J* 7.8, 1.5, ArH), 7.58 (1 H, ddd, *J* 8.0, 7.5, 1.5, ArH), 7.51 (1 H, s, ArH), 7.40–7.36 (1 H, m, ArH), 7.34 (1 H, dd, *J* 8.3, 1.2, ArH), 7.30 (1 H, ddd, *J* 6.4, 5.7, 1.6, ArH), 7.08 (1 H, m, ArH), 6.95 (1 H, dd, *J* 8.2, 1.6, ArH), 4.90 (2 H, br, OCH_2), 2.79 (3 H, s, Me), 2.64 (3 H, s, Me); δ_C (100 MHz; $CDCl_3$) 163.2 (CO), 160.7 (C), 158.1 (C), 157.6 (C), 155.6 (C), 153.8 (C), 152.9 (C), 143.5 (C), 138.4 (C), 132.8 (CH), 131.3 (CH), 124.7 (CH), 124.1 (CH), 123.6 (CH), 122.1 (CH), 120.9 (C), 120.8 (C), 117.9 (CH), 117.6 (CH), 116.0 (C), 115.3 (CH), 114.5 (CH), 113.2 (C), 64.9 (CH_2), 25.3 (Me), 24.6 (Me); *m*/*z* (EI) 406 (M^+, 100%), 391 (11), 378 (38), 363 (6), 350 (21), 335 (7), 196 (21).

6,6′-Dibenzoyl-5,5′,6,6′-tetrahydro-4,4′-bi(benzo[*c*][2,7]-naphthyridine) 23

A solution of the bis(*N*,*N*-dimethylhydrazone) **11** (100 mg, 0.1 mmol) in xylene (2 ml) was heated at reflux for 2 h. After cooling, the solvent was removed *in vacuo* and the crude residue was chromatographed on silica gel (ether) to yield the desired Diels–Alder adduct as a pale brown solid (58 mg, 68%), mp 163–165 °C (Found: MH^+, 571.2133. $C_{38}H_{26}N_4O_2$ + H requires 571.2134); ν_{max} (KBr)/cm^{-1} 3432, 1653; δ_H (400 MHz; $CDCl_3$) 8.66 (1 H, d, *J* 5.0, ArH), 7.85 (1 H, dd, *J* 8.0, 1.0, ArH), 7.76 (1 H, d, *J* 5.0, ArH), 7.40–7.09 (7 H, m, ArH), 6.83 (1 H, d, *J* 5.0, ArH), 5.16 (2 H, s, NCH_2); δ_C (100 MHz; $CDCl_3$) 169.8 (C), 154.2 (C), 148.3 (CH), 139.8 (C), 138.2 (C), 135.3 (CH), 131.0 (CH), 130.3 (CH), 129.8 (CH), 129.5 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 126.6 (CH), 126.4 (CH), 125.9 (CH), 125.3 (C), 117.6 (CH), 44.9 (CH_2); *m*/*z* (CI) 571 (MH^+, 100%).

6,6′,7,7′-Tetrahydro-1,1′-bi(5*H*-cyclopenta[*c*]pyridine) 24

Hexadeca-2,14-diene-7,9-diyne-1,16-dial bis(*N*,*N*-dimethylhydrazone) **15a** (48 mg, 0.15 mmol) was heated to 145 °C in xylene (3 ml) for 9 h. The solvent was removed *in vacuo* and the residue purified by flash chromatography (elution with ether containing 3% triethylamine) to give the *title compound* as light yellow crystals (27 mg, 76%); mp 106–108 °C (from ether) (Found: M^+, 236.1303. $C_{16}H_{16}N_2$ requires 236.1313); ν_{max} ($CHCl_3$)/cm^{-1} 2962, 1570, 1433; δ_H (300 MHz; $CDCl_3$) 8.42 (2 H, d, *J* 4.9, ArH), 7.18 (2 H, d, *J* 4.9, ArH), 3.12 (4 H, t, *J* 7.5, $ArCH_2$), 2.97 (4 H, t, *J* 7.5, $ArCH_2$), 2.07 (4 H, quin, *J* 7.5, $CH_2CH_2CH_2$); δ_C (75 MHz; $CDCl_3$) 155.0 (C), 153.9 (C), 146.3 (CH), 139.3 (C), 119.4 (CH), 32.9 (CH_2), 31.8 (CH_2), 24.8 (CH_2); *m*/*z* (EI) 236 (M^+, 65%), 235 (100), 208 (2), 157 (10), 117 (30), 91 (22).

4,4′-Bi(benzo[*c*][2,7]naphthyridine) 25

A solution of the dimer **23** (44 mg, 0.07 mmol) in toluene (2 ml) at −78 °C was treated with DIBAL-H (0.1 ml, 25% wt solution). The reaction mixture was allowed to warm to room temperature with stirring over 3 h. Upon completion the reaction mixture was diluted with water (5 ml) and aqueous sodium hydroxide (1 ml, 10% solution) and then extracted with toluene (3 × 15 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to yield 5,5′,6,6′-tetrahydro-4,4′-bi(benzo[*c*][2,7]naphthyridine) as an impure brown semi-solid (29 mg, 97%); δ_H (400 MHz; $CDCl_3$) 8.44 (1 H, d, *J* 8.0, ArH), 7.63 (1 H, d, *J* 8.0, ArH), 7.43 (1 H, d, *J* 5.0, ArH), 7.14 (1 H, t, *J* 8.0, ArH), 6.77 (1 H, t, *J* 8.0, ArH), 6.56 (1 H, d, *J* 8.0, ArH), 4.23 (2 H, s, CH_2); δ_C (100 MHz; $CDCl_3$) 147.5 (CH), 145.3 (C), 131.1 (CH), 129.2 (C), 128.1 (C), 126.6 (C), 124.4 (CH), 119.9 (C), 119.1 (CH), 116.1 (CH), 115.2 (CH), 42.7 (CH_2).

A solution of the above compound (29 mg, 0.07 mmol) in ethyl acetate (2 ml) was treated with excess palladium on charcoal, with stirring for 48 h at 25 °C. The reaction mixture was filtered through a pad of Celite, and concentrated *in vacuo* to yield the *title compound* as a brown semi-solid (27 mg, 97%) (Found: MH^+, 359.1296. $C_{24}H_{14}N_4$ + H requires 359.1298); ν_{max} (CCl_4)/cm^{-1} 1642, 762; δ_H (400 MHz; $CDCl_3$) 9.45 (2 H, s, ArH), 9.26 (2 H, d, *J* 8.0, ArH), 8.64 (2 H, dd, *J* 8.0, 1.0, ArH), 8.54 (2 H, dd, *J* 8.0, 1.0, ArH), 8.16 (2 H, dd, *J* 8.0, 1.0, ArH), 7.87–7.71 (4 H, m, ArH); δ_C (100 MHz; $CDCl_3$) 157.4 (C), 150.0 (CH), 148.1 (C), 135.7 (C), 132.8 (CH), 129.2 (CH), 128.2 (CH), 128.0 (C), 127.8 (CH), 126.3 (CH), 123.5 (CH), 120.8 (C); *m*/*z* (CI) 359 (MH^+, 100%).

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