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Preparation of Functionalised Aryl Alkynes as Precursors to Extended Cyclophanes

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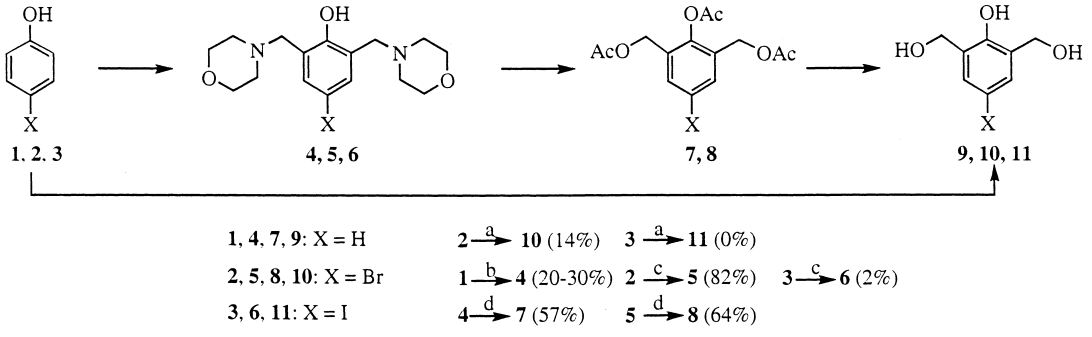
Abstract—The preparation of 2,6-substituted arylhalides and triflates is described. These compounds are suitable precursors for cyclophane formation.

Introduction

Structures based on cyclophanes continue to arouse interest because of their unique physical properties, and their ability to act as model compounds for the study of intramolecular processes[1,2] and host–guest chemistry.[3] Cyclophanes containing extended π-conjugation have been investigated as mimics for solid-state interactions involving photoexcitation[4] and for electron transfer processes involving extended orthogonal π-systems.[5] The classical, and still often used, methodology for the preparation of cyclophanes relies on the formation of a benzyl halide precursor.[2] Two basic methodologies exist for the preparation of functionalised or π-extended cyclophanes. The first involves functionalisation of the benzyl halide precursor with cyclophane formation as the final step.[6] The second involves the functionalisation of the cyclophane itself, and often suffers from the disadvantage of the close proximity of the two aryl rings which alters the outcome of functional group manipulation.[7] We required a series of π-conjugated cyclophanes in order to investigate the relationship between aromatic rings in close proximity and their optoelectronic properties. The report herein presents methodologies for the preparation of 2,6-bis(hydroxymethyl)aryl and 2,6-bis(halomethyl)aryl compounds as precursors for cyclophane formation. The palladium-catalysed coupling of 2,6-bis(substituted)aryl compounds with arylalkynes is described, along with subsequent functional group transformations of the aryl side chains.

Results and Discussion

The direct route to aryl alkynes containing side-arms suitable for cyclophane formation would be the bis-hydroxymethylation of *p*-bromo- **2**[8] and *p*-iodophenol **3**. Whilst *p*-bromophenol could be readily bis-hydroxymethylated to give the desired compound **10** in a low yield of 14%, the reaction involving *p*-iodophenol produced no isolable material (Scheme 1). Both halophenols appeared to undergo extensive polymerisation and, for *p*-iodophenol, the aryl iodide bond appeared to be reduced.



Scheme 1. Conditions: (a) CH_2O, NaOH; (b) CH_2O, morpholine; (c) CH_2O, morpholine, AcOH; (d) Ac_2O, AcOH; (e) base hydrolysis.

Keywords: arylhalides; cyclophanes; triflates.

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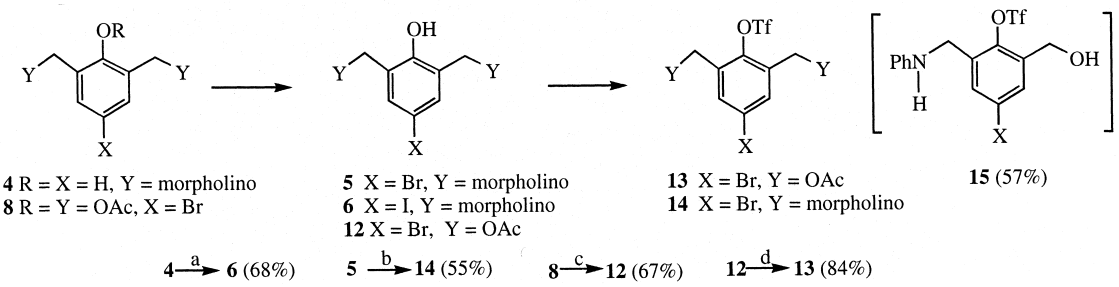


Scheme 2. Conditions: (a) NaI, Chloramine-T, DMSO; (b) NaH, $PhNTf_2$, THF; (c) guanidine, CH_3OH; (d) K_2CO_3, $PhNTf_2$, THF.

An indirect route was therefore sought for the introduction of the 2,6-functionality and the formation of bis(morpholinomethyl) compounds via a Mannich reaction[9] was investigated. The literature conditions for the Mannich reaction of *p*-bromophenol[10] with morpholine and formaldehyde met with little success in our hands. When acetic acid was used as both solvent and activator the desired material **5** was isolated in 82% yield (Scheme 1). Unfortunately, application of this procedure to *p*-iodophenol gave compound **6** in only 2% yield. Extensive decomposition of the starting materials and formation of molecular iodine took place during the reaction. Formation of the parent compound, 2,6-bis(morpholinomethyl)phenol **4**, could also be achieved using this procedure without acetic acid, yielding the 2,6-bis(morpholinomethyl)phenol **4** in 20–30% yield. Although the yield was low, it was reproducible on a large scale (~60 g).

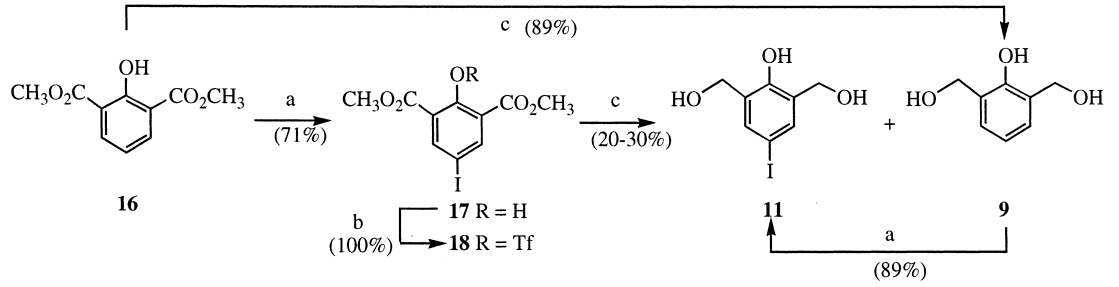
Morpholinomethylphenol **4** was converted to the triacetate **7** in 57% yield by heating **4** in acetic anhydride.[11] The analogous bromophenol **5** was also readily converted to the corresponding triacetate 8 in 64% yield using a modification to this procedure in which both acetic anhydride and acetic acid were necessary.

The iodination of triacetate **7** under a variety of conditions met with little success with starting material being recovered in each case.[12] Attempts to selectively deacetylate only the phenolic acetate of **7** to the corresponding phenol with either guanidine in methanol,[13] sodium hydroxide in ethanol, potassium carbonate in methanol or zinc in methanol[14] gave either decomposition or complete hydrolysis of all the acetate protecting groups. However, triacetate **8** could be selectively deacetylated using a methanolic solution of guanidine at −10 to −20°C, whereas at higher temperatures there was no selectivity for the deacetylation (Scheme 2). To gain access to the iodinated analogue of **12**, direct iodination of **4** with NaI/Chloramine-T in dimethylsulphoxide[15] was investigated and gave 2,6-bis(morpholinomethyl)-4-iodophenol **6** in 68% yield (Scheme 2).

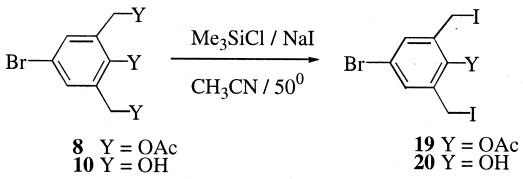
Phenol **12** could be readily converted to triflate **13** using *N*-phenyltriflimide and potassium carbonate, whereas phenol **6** required NaH and *N*-phenyltriflimide for conversion to triflate **14**.[16] When the unprotected phenol **10** was treated with NaH and *N*-phenyltriflimide the anilinomethyl triflate **15** was formed in 57% yield (Scheme 2). The formation of **15** could have resulted from either direct triflation of the hydroxymethyl group or by an intramolecular transfer of a triflate group from the phenoxy position. The use of milder bases such as potassium carbonate or triethylamine gave no triflation and starting material was recovered.

The isophthalate compound **16**[17] proved to be an efficient entry into a variety of functionalised aryl alkynes. The direct iodination of diester **16** could not be achieved with either chloramine-T/NaI[15] in DMF, or *t*BuOCl/NaI in acetonitrile.[18] However, BTMA·ICl_2[19] iodinated **16** readily and **17** was isolated in 71%. Triflation of **17** was performed using *N*-phenyltriflimide and triethylamine in acetonitrile and gave **18** in a quantitative yield (Scheme 3).

On a small scale (0.020 g) the reduction of **17** with lithium aluminium hydride in THF at 0°C gave reasonable yields (20–30%) of the desired alcohol **11**, provided the suspension was allowed to warm gradually to room temperature over 3 h after the addition of hydride. By NMR, integration of the benzyl peaks gave the ratio of **11**:**9** as 11:1. However, on a larger scale (0.30 g), under the same conditions, the ratio was reversed and increased to a disappointing 1:29 for **11**:**9**. A more successful approach to the formation of **11**



Scheme 3. Conditions: (a) BTMA·ICl_2, $NaHCO_3$, MeOH; (b) $PhNTf_2$, Et_3N, CH_3CN; (c) $LiAlH_4$, THF, 0°C to rt.



Scheme 4.

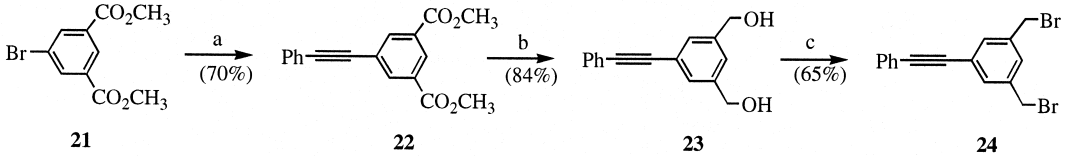
was to perform an initial hydride reduction on the parent diester **16** to form **9** in 94%, followed by iodination to give the aryl–iodide **11** in 89% yield. Of interest with the phenol **9** was a reversible enantiotropic polymorphism which was observed as two distinct melting points.[20]

The conversion of the acetoxy or hydroxy groups into good leaving groups for cyclophane formation was then investigated. Trimethylsilyl iodide, generated in situ, from trimethylsilyl chloride and sodium iodide,[21] could convert triacetoxy **8** to **19** in 62% yield (Scheme 4). The phenolic acetoxy group remains unchanged during this reaction. The same reagent at room temperature converted trihydroxy compound **10** into **20** in 64% yield.

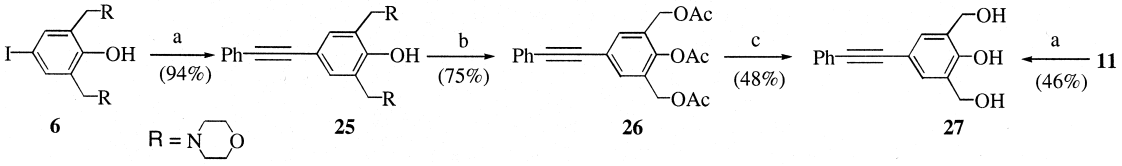
The preparation of π-conjugated aryl alkynes was then investigated with the coupling of diester **21**[22] to phenylacetylene using $Pd(PPh_3)_4$, NaI, $ZnCl_2$ and piperidine in DMF[23] at 60°C to give **22** in 70% yield. The reduction of the ester groups of **22** proceeded selectively at room temperature giving the desired bis-hydroxymethyl compound **23** in 84% yield (Scheme 5).

Conversion of the hydroxyl groups of **23** to the corresponding iodides could not be achieved with trimethylsilyl iodide as decomposition of the starting materials occurred. The conversion of the hydroxyl groups to bromides was then investigated and PPh_3/CBr_4 in ether[24] proved efficacious with the desired material **24** being isolated in 65% yield (Scheme 5).

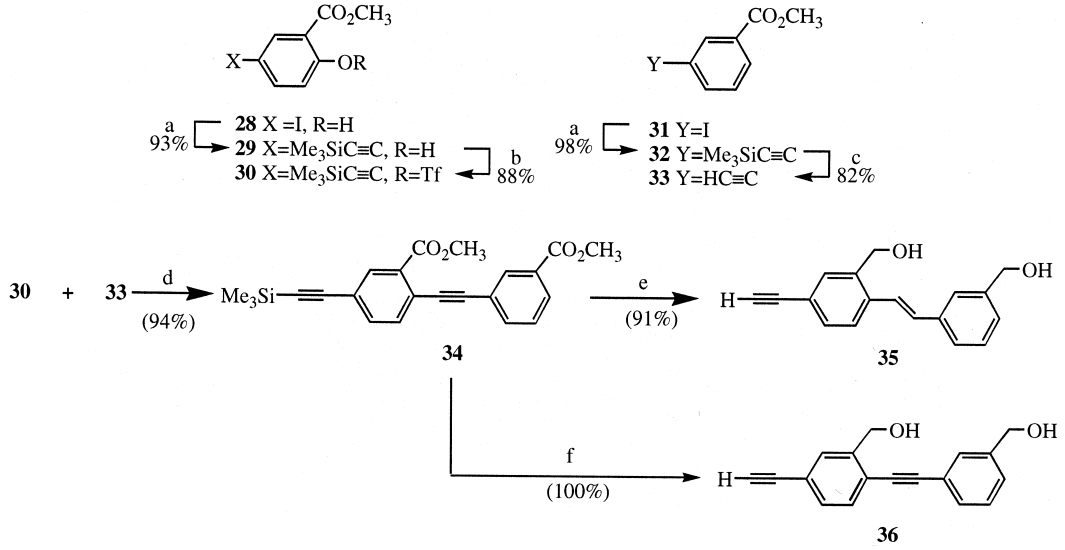
Palladium-catalysed coupling of phenylacetylene with **6** gave **25** in 94% yield. Treatment of **25** with acetic anhydride and acetic acid at reflux successfully produced the



Scheme 5. Conditions: (a) $Pd(PPh_3)_4$, NaI, $ZnCl_2$, piperidine, DMF; (b) $LiAlH_4$, THF; (c) PPh_3, CBr_4, ether.



Scheme 6. Conditions: (a) PhC≡CH, $Pd(PPh_3)_4$, CuI, piperidine; (b) Ac_2O, AcOH; (c) 5M H_2SO_4, THF.



Scheme 7. Conditions: (a) i. $Me_3SiC{\equiv}CH$, $Pd(PPh_3)_4$, Et_3N, CuI, DMF; (b) $PhNTf_2$, Et_3N, CH_3CN; (c) K_2CO_3, MeOH; (d) $Pd(PPh_3)_4$, CuI, Et_3N; (e) i. $LiAlH_4$, THF; ii. Bu_4NF, CH_2Cl_2; (f) i. DIBAL-H, THF; ii. Bu_4NF, CH_2Cl_2.

tri-acetate **26** in 75% yield (Scheme 6). Treatment of **25** under a range of basic conditions, including guanidine in methanol, sodium methoxide in methanol and potassium hydroxide in methanol gave only partial hydrolysis. Even with extensive heating of the reaction mixture only one, or at most two, of the acetates could be cleaved and no trihydroxy **27** could be isolated. Hydrolysis of **27** under acidic conditions, THF with 5M H_2SO_4 at reflux for 17 h, gave the desired bis-hydroxymethyl compound **27** in 48% yield. These last two steps confirmed the fact that the acetylenic functionality would remain intact under strongly acidic conditions whilst the linker-arm precursor was manipulated. A more convenient methodology for the preparation of **27** was the palladium catalysed coupling of **11** with phenylacetylene and this gave **27** in 46% yield.

Attention was then directed to the synthesis of extended aryl alkynes containing side arms suitable for cyclophane formation. Triflate **30** was prepared from methyl 4-iodosalicylate **28**[15] via the phenol **29**,[26] using a palladium catalysed coupling reaction followed by mild triflation with *N*-phenyltriflimide. Arylalkyne **33** was a known compound,[25] however, it was prepared from methyl 3-iodobenzoate **31**[27] via the protected alkyne **32**[25] using an alternative method to that described in the literature. Coupling of triflate **30** to arylalkyne **33** using $Pd(PPh_3)_4$ and CuI resulted in a 94% isolated yield of **34** (Scheme 7). Conversion of the diester **34** to the bis-hydroxymethyl compound **34** was attempted using lithium aluminium hydride at 0°C, followed by deprotection with Bu_4NF. The isolated product was the *trans* vinyl derivative **35** resulting from the reduction of the triple bond in addition to the ester groups. This reaction was reminiscent of the reduction of propargyl alcohols to allylic alcohols via the anti-addition of hydride. Evidence to support the assignment of the double bond as *trans* has been obtained by a homonuclear decoupling experiment.

The problem of over-reduction was solved by the use DIBAL-H at −20°C in THF. Reduction under these conditions, followed by deprotection with Bu_4NF gave the desired bis-hydroxymethyl compound **36** in a quantitative yield from the ester **34**.

In summary, we have prepared a series of aryl alkynes containing hydroxymethyl and bromomethyl side chains. We will report in the near future how these precursors have been converted into orthogonal π-conjugated aryl alkynes and subsequently into cyclophanes.

Experimental

^1H NMR spectra were recorded at 300 MHz on a Varian Gemini NMR (75.47 MHz for ^{13}C) or at 200 MHz on a Varian Gemini spectrometer (50.28 MHz for ^{13}C) using a dual 5 mm $^{13}C/^1H$ probe. All spectra were recorded as dilute solutions in deuteriochloroform using tetramethylsilane as an internal standard. Melting points were determined on a Kofler hot-stage micro-melting point apparatus equipped with a Reichart microscope and are uncorrected. Electron impact (EI) and fast atom bombardment (FAB) mass spectra were recorded at 70 eV on a Vacuum Generators ZAB 2HF mass spectrometer. Liquid secondary ionisation mass spectrometry (LSIMS) and accurate mass spectra were performed by the University of Tasmania mass spectrometric service. Infrared spectra were recorded on an ATI Mattison Genesis FTIR as nujol mulls between sodium chloride plates. Elemental analyses were performed at the University of Otago, New Zealand. Solvents were purified and dried using standard laboratory procedures and all organic extracts were dried over anhydrous magnesium sulphate. All solvents for palladium catalysed coupling reactions were degassed by the freeze–pump–thaw method and kept under an atmosphere of nitrogen.

A typical extractive workup for the palladium catalysed coupling reactions involved addition of the reaction mixture to saturated NH_4Cl and extraction with two portions of organic solvent. The organic layers were then combined, washed with water, dried and the solvent removed under vacuum.

The following compounds were prepared according to published procedures: 1-acetoxy-2,6-bis(acetoxymethyl)-benzene **7**,[11] 2,6-bis(hydroxymethyl) phenol **9**,[20] 2,6-bis-(hydroxymethyl)-4-bromophenol **10**,[8] dimethyl 2-hydroxyisophthalate **16**,[17] dimethyl 5-bromoisophthalate **21**,[22] and methyl 4-iodosalicylate **28**[15].

2,6-Bis(morpholinomethyl)phenol 4. To a 38% formaldehyde solution (35.2 mL, 450 mmol) was added phenol (20.0 g, 210 mmol) followed by morpholine (38.6 mL, 440 mmol). The resulting suspension was stirred vigorously and heated at 50°C for 15 h. Water (100 mL) and ethyl acetate (20 mL) were then added with cooling to 0°C. Over 0.5 h a white precipitate formed which was collected by vacuum filtration and washed with a solution of water/ethyl acetate (10:1) (100 mL). The solid was recrystallised from hexane to give the title compound as colourless plates (12.0 g, 20%); mp 123.5–124.5°C; Anal. Calcd for $C_{16}H_{24}N_2O_3$: C, 65.73; H, 8.27, Found: C, 66.02; H, 8.07; δ_H (300 MHz) 2.51 (8H, t, J=4.6 Hz), 3.61 (4H, s, ArCH_2R), 3.71 (8H, t, J=4.6 Hz), 6.74 (1H, t, J=7.5 Hz, Ar*H*), 7.04 (2H, d, J=7.5 Hz, Ar*H*); δ_C (75.47 MHz) 53.1, 59.2, 66.7 (ArCH_2R), 118.5, 122.0 (*Ar*CH_2R), 129.0, 155.9 (*Ar*OH); *m*/*z* (EI) 292 (M^+, 75%), 205 (100);); ν_{max} 3430 cm^{-1}.

2,6-Bis(morpholinomethyl)-4-bromophenol 5. To a solution of *p*-bromophenol (8.65 g, 50 mmol) in acetic acid (10 mL) was added morpholine (9.60 mL, 110 mmol) and 38% formaldehyde solution (11 mL, 110 mmol). The resulting solution was then heated at 80°C for 6 h. The reaction mixture was then taken up into dichloromethane (200 mL) and washed with water (100 mL), saturated $NaHCO_3$ (100 mL) and finally water (100 mL). The solution was dried and passed through a short squat column of Silica gel 60. The solvent was removed in vacuo, to yield a yellow solid (16.45 g, 82%); mp 115.0–115.5°C; Anal. Calcd for $C_{16}H_{23}N_2O_3Br$: C, 51.76; H, 6.24; N, 7.54, Found: C, 52.03; H, 6.23; N, 7.42; δ_H (300 MHz) 2.53 (8H, t, J=4.6 Hz), 3.59 (4H, s, ArCH_2R), 3.74 (8H, t, J=4.6 Hz), 7.20 (2H, s, Ar*H*); δ_C (75.47 MHz) 52.7, 58.2, 66.3, 110.1 (*Ar*Br), 124.0, 130.8, 154.7 (*Ar*OH); *m*/*z* (EI) 372 (M^+, ^{81}Br, 40%), 370 (M^+, ^{79}Br, 41%), 285 (100), 283 (84); ν_{max} 3400 cm^{-1}.

2,6-Bis(morpholinomethyl)-4-iodophenol 6. To a solution of phenol **4** (2.00 g, 6.85 mmol) in dimethylsulphoxide (10 mL) was added NaI (1.23 g, 8.22 mmol) and chloramine-T trihydrate (2.32 g, 8.22 mmol) with stirring. The resulting suspension was heated at 50°C for 45 min after which time the reaction mixture was taken up into dichloromethane (50 mL) and washed with water (50 mL). The aqueous layer was re-extracted with dichloromethane (50 mL), the organic layers combined and washed with saturated $Na_2S_2O_3$ (2×50 mL) and water (50 mL). The solvent was dried and removed in vacuo to give a yellow oil. The product was purified by flash chromatography on silica gel [ethyl acetate, R_f 0.36] to give a colourless oil which was taken up into hot hexane and upon cooling gave off-white prisms (1.95 g, 68%); mp 108.0–109.0°C; Exact Mass Calcd for $C_{16}H_{23}IN_2O_3$: 418.0755. Found: 418.0763; δ_H (300 MHz) 2.52 (8H, t, J=4.6 Hz), 3.59 (4H, s, ArCH_2R), 3.74 (8H, t, J=4.6 Hz), 7.34 (2H, s, ArH); δ_C (75.47 MHz) 53.1, 58.5, 66.7, 113.1 (*Ar*I), 125.0, 137.3, 156.1 (*Ar*OH); *m/z* (EI) 418 (M^+, 44%), 331 (98); ν_{max} 3410 cm^{-1}.

1-Acetoxy-2,6-bis(acetoxymethyl)-4-bromobenzene 8. A solution of bromophenol **5** (5.00 g, 13.5 mmol) in acetic anhydride (30 mL) and acetic acid (2 mL) was refluxed for 24 h. The reaction mixture was concentrated by rotary evaporation and the resulting red/brown oil taken up into dichloromethane (150 mL), washed with saturated $NaHCO_3$ (3×75 mL) and water (75 mL). The solvent was dried and removed in vacuo to give a red oil. This oil was then shaken with a solution of 3% methanol in hexane (10 mL) for 5 min before being placed in the fridge to crystallise overnight. The crude product was collected and recrystallised from hexane to give colourless needles (3.08 g, 64%); mp 81.0–82.0°C; Anal. Calcd for $C_{14}H_{15}O_6$: C, 46.82; H, 4.21, Found: C, 46.73; H, 4.02; δ_H (300 MHz) 2.10 (6H, s, ArCH$_2$OCOCH_3), 2.35 (3H, s, ArOCOCH_3), 5.00 (4H, s, ArCH_2R), 7.57 (2H, s, ArH); δ_C (75.47 MHz) 20.4, 20.7, 60.5, 119.4 (*Ar*Br), 131.1 (*Ar*CH$_2$OAc), 132.8, 146.3 (*Ar*OAc), 168.7 (*C*=O), 170.3 (*C*=O); *m/z* (FAB) 361 ($(M+H)^+$, ^{81}Br, 60%), 359 ($(M+H)^+$, ^{79}Br, 61%), 301 (13), 209 (13), 259 (16), 257 (17); ν_{max} 1734, 1768 cm^{-1}.

2,6-Bis(hydroxymethyl)-4-iodophenol 11. To a solution of phenol **9** (1.22 g, 7.92 mmol) in methanol (40 mL) was added $NaHCO_3$ (3.32 g, 39.61 mmol) and benzyltrimethylammonium dichloroiodate (2.90 g, 8.32 mmol). The resulting suspension was stirred at room temperature for 2 h. The reaction mixture was concentrated in vacuo and then purified by squat column chromatography [dichloromethane/ethyl acetate 1:1 (v/v), R_f 0.50] to give the title compound as a fawn solid (1.98 g, 89%). A small sample was recrystallised from a methanol/water mixture as orange needles; mp 155.0–156.5°C; Exact Mass Calcd for $C_8H_9IO_3$: 279.9598, Found 279.9608; δ_H (200 MHz, d_6-acetone) 4.72 (4H, s, ArCH_2OH), 7.46 (2H, s, ArH); δ_C (50.28 MHz) 61.2, 81.5 (*Ar*I), 131.0, 135.4, 154.4 (*Ar*OH); *m/z* (EI) 280 (M^+, 37%), 262 (100);(ν_{max} 3330 cm^{-1}.

2,6-Bis(acetoxymethyl)-4-bromophenol 12. A stock solution of 0.5 M guanidine in methanol was prepared by the addition of guanidine hydrogencarbonate (14.20 g, 79 mmol) to sodium methoxide (1.78 g, 77.4 mmol, in 800 mL of dry methanol). A solution of bromobenzene **8** (600 mg, 1.67 mmol) in methanol (8 mL) and dichloromethane (8 mL) was cooled to −25°C before 0.5 M guanidine in methanol (3.34 mL, 1.67 mmol) was added over 0.5 h. During this time the reaction temperature was kept between −20 and −25°C and stirred for a further 3 h. Acetic acid (0.2 mL) was then added to quench the reaction. The mixture was taken up into dichloromethane (75 mL) and washed with 5% NH_4Cl (40 mL) and water (40 mL). The solvent was dried and removed in vacuo to yield an off-white solid which was recrystallised from hexane to give the title compound as a colourless powder (353 mg, 67%); mp 82.0–83.0°C; Exact Mass Calcd for $C_{12}H_{13}O_5Br$: 315.9947, Found: 315.9948; δ_H (300 MHz) 2.13 (6H, s, ArCH$_2$OCOCH_3), 5.10 (4H, s, ArCH_2OAc), 7.41 (2H, s, ArH); δ_C (75.47 MHz) 20.8 (*C*H$_3$CO$_2$CH$_2$Ar), 61.8 (ArCH_2-OAc), 119.9 (*Ar*Br), 125.4, 134.1, 152.9 (*Ar*OH), 172.5 (*C*=O); *m/z* (EI) 318 (M^+, ^{81}Br, 8%), 316 (M^+, ^{79}Br, 8%), 216 (30), 214 (32); ν_{max} 3380, 1745, 1734, 1712, 1693 cm^{-1}.

Phenyl-2,6-bis(acetoxymethyl)-4-bromotrifluoromethylsulphonate 13. Bromophenol **12** (100 mg, 3.16×10^{-4} mol), potassium carbonate (52 mg, 3.78×10^{-4} mol) and *N*-phenyltriflimide (136 mg, 3.78×10^{-4} mol) in THF (6 mL) were stirred together at room temperature for 16 h. The reaction mixture was taken up into dichloromethane (40 mL) and washed with 5% NH_4Cl (2×25 mL) and water (25 mL). The solvent was dried and removed in vacuo to give a colourless oil. The crude product was purified by flash chromatography [dichloromethane, R_f 0.49] to give the title compound as colourless oil that crystallised upon addition of pentane as colourless prisms (118 mg, 84%); mp 59.5°C; Anal. Calcd for $C_{13}H_{12}BrF_3O_7S$: C, 34.76; H, 2.69, Found: C, 34.67; H, 2.46; δ_H (300 MHz) 2.15 (6H, s, ArCH$_2$OCOCH_3), 5.20 (4H, s, ArCH_2OAc), 7.63 (2H, s, ArH); δ_C (75.47 MHz) 20.6 (*C*H$_3$CO$_2$CH$_2$Ar), 60.0 (ArCH$_2$OAc), 118.4 (q, J=319 Hz, *C*F$_3$SO$_2$Ar), 122.6 (*Ar*Br), 132.6, 133.3, 142.3 (*Ar*OTf), 170.2 (*C*=O); *m/z* (FAB) 451 ($(M+H)^+$, ^{81}Br, 4%), 449 ($(M+H)^+$, ^{79}Br, 4%), 391 (18), 289 (18), 301 (20), 299 (20); ν_{max} 1746, 1210 cm^{-1}.

Phenyl-2,6-bis(morpholinomethyl)-4-bromotrifluoromethylsulphonate 14. Bromophenol **5** (500 mg, 1.35 mmol) in dry THF (5 mL) was added dropwise via syringe to a suspension of NaH (50 mg, 2.08 mmol) in dry THF (10 mL) at 0°C under a nitrogen atmosphere. *N*-phenyltriflimide (530 mg, 1.48 mmol) in dry THF (5 mL) was added via syringe and the suspension refluxed for 3 h. The reaction mixture was quenched by dropwise addition of water before being taken up into dichloromethane (50 mL) and washed with water (50 mL). The aqueous layer was re-extracted with dichloromethane (50 mL), the organic layers combined and dried. The solvent was removed in vacuo and the resulting golden oil purified by flash chromatography on silica gel [dichloromethane/ethyl acetate 4:1 (v/v), R_f 0.50] to give the title compound as a colourless oil (374 mg, 55%); Exact Mass Calcd for $C_{17}H_{22}BrF_3N_2O_5S$: 505.0444, Found: 505.0464; δ_H (300 MHz) 2.45 (4H, t, J=4.3 Hz), 3.58 (4H, s, ArCH_2R), 3.71 (8H, t, J=4.6 Hz), 7.72 (2H, s, ArH); δ_C (75.47 MHz) 53.2, 56.4, 66.5, 118.3 (q,

J=321 Hz, CF_3SO_2R), 122.1 (*Ar*Br), 132.6, 134.1, 144.4 (*Ar*OTf); *m/z* 505 ($(M+H)^+$, ^{81}Br, 65%), 503 ($(M+H)^+$ [^{79}Br] and $(M-H)^+$ [^{81}Br], 89%), 501 ($(M-H)^+$, ^{79}Br, 25%); ν_{max} 1210 cm^{-1}.

2-(Anilinomethyl)-4-bromo-6-(hydroxymethyl)phenyltrifluoromethanesulphonate 15. Bromophenol **10** (220 mg, 0.77 mmol) in dry THF (10 mL) was added dropwise via syringe to a suspension of NaH (17 mg, 0.77 mmol) in dry THF (5 mL) at 0°C under a nitrogen atmosphere. *N*-phenyltriflimide (285 mg, 0.80 mmol) was then added and the suspension refluxed for 3 h. The reaction mixture was quenched by dropwise addition of 'wet' ether until no further effervescence was observed. The solvent was removed in vacuo and the resulting oil purified by flash chromatography on silica gel [dichloromethane, R_f 0.22] to give the title compound as a colourless oil which slowly solidified on standing (100 mg, 57); mp 85.0–88.0°C; Exact Mass Calcd for $C_{15}H_{13}BrF_3NO_4S$: 438.9718, Found: 438.9718; δ_H (200 MHz): 4.69 (2H, s, ArCH_2R), 4.96 (2H, s, ArCH_2R), 7.01 (1H, d, J=2.4 Hz, Ar*H*), 7.20–7.33 (6H, m, Ar*H*); δ_C (75.47 MHz) 50.8, 63.9, 111.5, 120.5 (q, J=324.4 Hz, $ArOSO_2CF_3$), 123.6, 126.7, 129.1, 129.2, 129.3, 130.6, 132.6, 136.4, 153.6; *m/z* (EI) 441 (M^+, ^{81}Br, 49%), 439 (M^+, ^{79}Br, 60%), 424 (^{81}Br, 31%), 422 (^{79}Br, 25%), 290 (^{81}Br, 40%), 288 (^{79}Br, 41%); ν_{max} 1230, 1200, 1180 cm^{-1}.

Dimethyl 2-hydroxy-5-iodoisophthalate 17. To a solution of dimethyl 2-hydroxyisophthalate (1.00 g, 4.76 mmol) in methanol (50 mL) was added $NaHCO_3$ (2.00 g, 10.48 mmol) and benzyltrimethylammonium dichloroiodate (1.74 g, 5.00 mmol). The resulting suspension was stirred at rt for 3 h, and then filtered and the solvent removed. The crude product was then taken up into chloroform (150 mL), washed with saturated $Na_2S_2O_3$ (100 mL) and brine (100 mL). The solvent was dried and removed to give the title compound as an off-white solid (1.13 g, 71%). A small sample was purified for analysis by sublimation at 85°C/0.03 mmHg; mp 135.0–138.0°C with rapid heating; Anal. Calcd for $C_{10}H_9O_5I$: C, 35.74; H, 2.70, Found: C, 35.98; H, 2.44; δ_H (300 MHz) 3.96 (6H, s, $ArCO_2CH_3$), 8.32 (6H, s, Ar*H*); δ_C (75.47 MHz) 52.7 ($ArCO_2CH_3$), 78.9 (*Ar*I), 118.6, 114.6, 161.2, 166.8 (*C*=O); *m/z* (EI) 336 (M^+, 100%), 304 (62), 273 (41), 246 (66); ν_{max} 3390, 1733, 1681 cm^{-1}.

Dimethyl 5-iodo-2-{[(trifluoromethyl)sulphonyl]oxy}isophthalate 18. Iodoisophthalate **17** (200 mg, 5.95×10^{-4} mol), triethylamine (0.10 mL, 1.39×10^{-3} mol) and *N*-phenyltriflimide (276 mg, 7.74×10^{-4} mol) in dry CH_3CN (5 mL) were stirred together for 16 h at room temperature under nitrogen. The reaction mixture was then concentrated in vacuo and then purified by flash chromatography [hexane/ethyl acetate 6:1 (v/v), R_f 0.36] to give the title compound as a colourless oil which crystallised upon addition of pentane as colourless needles (278 mg, 100%); mp 96.0–98.0°C; Anal. Calcd for $C_{11}H_8F_3ISO_7$: C, 28.22; H, 1.72, Found: C, 28.43; H, 1.72; δ_H (300 MHz) 3.96 (6H, s, $ArCO_2CH_3$), 8.46 (2H, s, Ar*H*); δ_C (75.47 MHz) 53.2 ($ArCO_2CH_3$), 92.1 (*Ar*I), 118.5 (q, J=321 Hz, CF_3SO_2Ar), 127.5, 144.7, 146.2, 162.9 (*C*=O); *m/z* (EI) 468 (M^+, 100%), 437 (36), 404 (14), 373 (49); ν_{max} 1739, 1726, 1220 cm^{-1}.

1-Acetoxy-2,6-bis(iodomethyl)-4-bromobenzene 19. To a solution of triacetoxybromobenzene **8** (1.00 g, 2.78 mmol) in acetonitrile (20 mL) was added trimethylsilylchloride (2.5 mL, 19.63 mmol) and NaI (2.51 g, 16.71 mmol). The resulting suspension was heated at 50°C for 20 h. The reaction mixture was quenched by addition to Na_2CO_3 (50 mL) and extracted with dichloromethane (2×50 mL). The organic layers were combined and washed with 5% $Na_2S_2O_3$ (50 mL) and finally water (50 mL). The solvent was dried and removed to give a tan solid which was recrystallised from methanol/water to give off-white needles (0.85 g, 62%); mp 190.5–192.0°C; Anal. Calcd for $C_{10}H_9BrI_2O_2$: C, 24.27; H, 1.83, Found: C, 24.42; H, 1.90; δ_H (300 MHz) 2.48 (3H, s, $ArOCOCH_3$), 4.21 (4H, s, $ArCH_2OAc$), 7.46 (2H, s, Ar*H*); δ_C (75.47 MHz) −3.9 ($ArCH_2I$), 20.6 ($ArOCOCH_3$), 119.4 (*Ar*Br), 133.4, 134.8, 146.2, 167.7 (*C*=O); *m/z* (EI) 496 (M^+, ^{81}Br, 17%), 494 (M^+, ^{79}Br, 17%), 454 (^{81}Br, 65%), 452 (^{79}Br, 65%), 369 (^{81}Br, 89%), 367 (^{79}Br, 90%), 327 (^{81}Br, 79%), 325 (^{79}Br, 81%), 199 (^{81}Br, 56%), 197 (^{79}Br, 54%); ν_{max} 1749 cm^{-1}.

2,6-Bis(iodomethyl)-4-bromophenol 20. To a solution of trihydroxybromophenol **10** (100 mg, 4.29×10^{-4} mol) in dry acetonitrile (3 mL) was added NaI (322 mg, 2.14×10^{-3} mol) and trimethylsilylchloride (0.24 mL, 1.88×10^{-3} mol). The resulting suspension was stirred at room temperature for 1.5 h. The reaction mixture was added to ether (20 mL), washed with water (20 mL) and the aqueous layer re-extracted with ether (20 mL). The organic layers were combined and washed with saturated $Na_2S_2O_3$ (20 mL). The organic layer was dried and the solvent removed. Purification by sublimation at 120°C/0.01 mmHg gave the title compound as a fawn solid (124 mg, 64%); mp 155.5–157.0°C; Exact Mass Calcd for $C_8H_7{}^{79}BrI_2O$: 451.7774, Found: 451.7745; δ_H (200 MHz) 4.36 (4H, s, ArCH_2I), 7.35 (2H, s, Ar*H*); δ_C (50.28 MHz) −0.7 ($ArCH_2I$), 111.7, 128.8, 132.4, 151.5; *m/z* (EI) 454 (M+, ^{81}Br, 32%), 452 (M^+, ^{79}Br, 32%), 200 (^{81}Br, 61%), 198 (^{79}Br, 61%)%); ν_{max} 3380 cm^{-1}.

Dimethyl 5-(2-phenyl-1-ethynyl)isophthalate 22. To a solution of dimethyl 5-bromoisophthalate (200 mg, 0.0733 mmol) in degassed DMF (3 mL) was added $Pd(PPh_3)_4$ (42 mg, 0.0366 mmol), phenylacetylene (0.09 mL, 0.0821 mmol), DBU (0.20 mL, 0.134 mmol), undried $ZnCl_2$ (20 mg, 0.0147 mmol) and NaI (22 mg, 0.01.47 mmol). The resulting suspension was then stirred at 60°C for 3 h. An extractive workup with dichloromethane (20 mL) gave a tan solid. Purification by flash chromatography [dichloromethane/hexane 2:1 (v/v), R_f 0.37] and then recrystallisation from hexane gave the title compound as colourless needles (150 mg, 70%); mp 115.0–116.0°C; Anal. Calcd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.80, Found: C, 73.59; H, 4.57; δ_H (300 MHz) 3.93 (6H, s, $ArCO_2CH_3$), 7.32–7.35 (3H, m, Ar*H*), 7.50–7.53 (2H, m, Ar*H*), 8.31 (2H, d, J=1.5 Hz, Ar*H*), 8.58 (1H, t, J=1.5 Hz, Ar*H*); δ_C (75.47 MHz) 52.4, 87.3 (*C*≡C), 91.2 (*C*≡C), 122.5, 124.4, 128.5, 128.9, 130.0, 130.9, 131.8, 136.5, 165.7 (*C*=O); *m/z* (EI) 294 (M^+, 100%), 263 (47), 235 (10), 220 (13); ν_{max} 2214, 1722 cm^{-1}.

1,3-Bis(hydroxymethyl)-5-(2-phenyl-1-ethynyl)benzene 23. To a suspension of $LiAlH_4$ (69 mg, 2.04 mmol) in dry THF

(15 mL) was added the diester **22** (300 mg, 1.02 mmol) in dry THF (15 mL) dropwise with stirring at room temperature. The suspension was stirred for further 1 h. The reaction mixture was quenched with 'wet' ether and then added to 5% HCl (30 mL). The organic layer was separated, and the aqueous layer extracted with ether (2×30 mL). The organic layers were combined, dried and the solvent removed to give a tan solid. Recrystallisation from a chloroform/hexane mixture gave the title compound as colourless needles (204 mg, 84%); mp 100.0–102.0°C; Exact Mass Calcd for $C_{16}H_{14}O_2$: 238.0994, Found: 238.0988; δ_H (300 MHz) 4.70 (4H, s, ArCH_2OH), 7.33–7.36 (4H, m, Ar*H*), 7.45–7.46 (2H, m, Ar*H*), 7.51–7.54 (2H, m, Ar*H*); δ_C (75.47 MHz) 63.9 (Ar*C*H_2OH), 88.9 (*C*≡C), 89.1 (*C*≡C), 122.9, 123.0, 125.0, 128.1, 128.2, 128.5, 131.3, 141.7; *m*/*z* (EI) 238 (M^+,100); ν_{max} 3326, 2200 cm^{-1}.

1,3-Bis(bromomethyl)-5-(2-phenyl-1-ethynyl)benzene 24. To a solution of the diol **23** (20 mg, 0.0040 mmol) in dry ether (4 mL) was added CBr_4 (61 mg, 0.0185 mmol) and PPh_3 (48 mg, 0.0185 mmol). The resulting solution was refluxed for 16 h. The solvent was removed in vacuo and the residue purified by flash chromatography [hexane/dichloromethane 8:1 (v/v), R_f 0.30] to give the title compound as a colourless oil which solidified on standing (20 mg, 65%). A small sample was sublimed at 100°C/0.05 mmHg to give a colourless powder; mp 111.0–114.0°C; Anal. Calcd for $C_{16}H_{12}Br_2$: C, 52.78; H, 3.32, Found: C, 52.75; H, 3.11; δ_H (300 MHz) 4.46 (4H, s, ArCH_2Br), 7.34–7.38 (4H, m, Ar*H*), 7.49–7.54 (4H, m, Ar*H*); δ_C (75.47 MHz) 32.0 (Ar*C*H_2Br), 88.1 (*C*≡C), 90.4 (*C*≡C), 122.7, 124.5, 128.4, 128.6, 129.3, 131.6, 131.9, 138.6; *m*/*z* (EI) 366 (M^+, $^{81}Br^{81}Br$, 27%), 364 (M^+, $^{81}Br^{79}Br$, 54%), 362 (M^+, $^{79}Br^{79}Br$, 27%), 285 (^{81}Br, 98%), 283 (^{79}Br, 97%); ν_{max} 2208 cm^{-1}.

2,6-Bis(morpholinomethyl)-4-(2-phenyl-1-ethynyl)phenol 25. A solution of iodophenol **6** (1.00 g, 2.03 mmol), $Pd(PPh_3)_4$ (0.23 g, 0.20 mmol), phenyl acetylene (0.45 mL, 4.06 mmol) and CuI (38 mg, 0.20 mmol) in degassed piperidine (15 mL) was stirred at room temperature for 1 h. An extractive workup with dichloromethane (60 mL) gave an orange/red oil. Purification by flash chromatography on silica gel [ethyl acetate, R_f 0.40] gave the title compound as a golden oil (0.83 g, 94%); Exact Mass Calcd for $C_{24}H_{28}N_2O_3$: 392.2100, Found: 392.2103; δ_H (300 MHz) 2.72 (8H, t, *J*=4.4 Hz), 3.80 (4H s, ArCH_2R), 3.92 (8H, t, *J*=4.4 Hz), 7.51 (5H, m, Ar*H*), 7.69 (2H, m, Ar*H*); δ_C (50.28 MHz) 53.1, 58.6, 66.6 (ArCH_2R), 113.2, 122.5, 123.6, 127.7, 128.2, 131.3, 132.3, 156.6 (*Ar*OH); *m*/*z* (EI) 392 (M^+, 23%), 305 (100); ν_{max} 3380, 2208 cm^{-1}.

1-Acetoxy-2,6-bis(acetoxymethyl)-4-(2-phenyl-1-ethynyl)-benzene 26. A solution of phenol **25** (883 mg, 2.25 mmol) in acetic anhydride (25 mL) and acetic acid (1 mL) was refluxed for 14 h. The reaction mixture was concentrated by rotary evaporation and the resulting oil taken up into dichloromethane (100 mL), then washed with sat Na_2CO_3 (3×50 mL) and water (50 mL). The solvent was dried and removed in vacuo to give an off-white solid which was recrystallised from hexane to give the title compound as fine colourless needles (644 mg, 75%); mp 80.0°C; Exact Mass Calcd for $C_{22}H_{20}O_6$: 380.1260, Found: 380.1260; δ_H (300 MHz): 2.07 (6H, s, $ArCH_2OCOCH_3$), 2.32 (3H, s, $ArOCOCH_3$), 5.02 (4H, s, ArCH_2OAc), 7.33 (3H, m, Ar*H*), 7.50 (2H, m, Ar*H*), 7.58 (2H, s, Ar*H*); δ_C (75.47 MHz): 20.2 (*C*H_3COR), 20.5 (*C*H_3COR), 60.9 (ArCH_2OAc), 87.9 (*C*≡C), 90.2 (*C*≡C), 121.9, 123.0, 128.4, 128.6, 129.8, 131.7, 133.4, 147.5 (*Ar*OAc), 168.8 (*C*=O), 170.5 (*C*=O); *m*/*z* (EI) 380 (M^+, 16%), 338 (34), 278 (100), 236 (79); ν_{max} 1761, 1741 cm^{-1}.

2,6-Bis(hydroxymethyl)-4-(2-phenyl-1-ethynyl)phenol 27. *Method A:* a solution containing iodophenol **11** (140 mg, 4.16×10^{-4} mol), $Pd(PPh_3)_4$ (48 mg, 4.16×10^{-5} mol), phenylacetylene (0.09 mL, 8.33×10^{-4} mol) and CuI (16 mg, 8.33×10^{-4} mol) in degassed piperidine (3 mL) was stirred at room temperature for 1.5 h. An extractive workup with dichloromethane (40 mL) gave an orange oil. Purification by flash chromatography [dichloromethane/ethyl acetate 1:1 (v/v), R_f 0.48] gave the title compound as a colourless solid (59 mg, 46%).

Method B: 5M sulphuric acid (2 mL) was added to a solution of **26** (50 mg, 1.31×10^{-4} mol) in THF (7 mL). The resulting solution was refluxed for 17 h. The reaction mixture was concentrated by rotary evaporation, taken up into dichloromethane (30 mL) and washed with water (30 mL). The solvent was dried and removed to give a colourless oil that crystallised upon addition of chloroform. The solid was recrystallised from chloroform/hexane to give the title compound as colourless needles (13 mg, 48%); mp 125.0–126.0°C; Exact Mass Calcd for $C_{16}H_{14}O_2$: 238.0994. Found: 238.0988; δ_H (300 MHz) 4.75 (4H, s, ArCH_2OH), 7.33 (5H, m, Ar*H*), 7.48 (2H, m, Ar*H*); δ_C (75.47 MHz) 61.7 (Ar*C*H_2OH), 88.3 (*C*≡C), 90.7 (*C*≡C), 115.4, 125.3, 128.9, 129.1, 129.6, 131.4, 132.4, 155.4 (*Ar*OH); *m*/*z* (LSIMS) 238 (M^+, 100%), 207 (14), 191 (28); ν_{max} 3451, 3275 cm^{-1}.

Methyl 2-hydroxy-5-(trimethylsilylethynyl)salicylate 29. A solution of methyl 5-iodosalicylate (4.00 g, 14.39 mmol), $Pd(PPh_3)_4$ (0.16 g, 0.14 mmol), trimethylsilylacetylene (2.54 mL, 17.99 mmol) and CuI (27 mg, 0.14 mmol) in a degassed solvent system of triethylamine (5 mL)/DMF (10 mL) was stirred at 40°C for 2 h. An extractive workup with ether (100 mL) gave a fawn solid. Purification by squat column chromatography [hexane/dichloromethane 2:1 (v/v), R_f 0.56] yielded the title compound as a colourless oil which solidified on standing (3.30 g, 93%). A small sample was recrystallised from a methanol/water mixture as pale yellow needles; mp 70.0–71.5°C (no lit. mp)[26]; δ_H (200 MHz) 0.24 (9H, s, RSi(CH_3)$_3$), 3.94 (3H, s, $ArCO_2CH_3$), 6.88 (1H, d, *J*=8.6 Hz, Ar*H*), 7.50 (1H, dd, *J*=2.2 and 8.6 Hz, Ar*H*), 7.94 (1H, d, *J*=2.2 Hz, Ar*H*); δ_C (50.28 MHz) −0.2 (RSi(CH_3)$_3$), 52.3 ($ArCO_2CH_3$), 92.8 (*C*≡C), 103.9 (*C*≡C), 112.3, 114.2, 117.8, 133.8, 138.9, 161.6 (*Ar*OH), 169.9 (*C*=O); *m*/*z* (EI) 248 (M^+, 84%), 233 (76), 216 (49), 201 (100); ν_{max} (neat) 2158, 1681 cm^{-1}.

Methyl 5-(trimethylsilylethynyl)-2-{[(trifluoromethyl)-sulphonyl]oxy}benzoate 30. The procedure was analogous to that for **21** using the phenol **29** and purification was performed using flash chromatography [hexane/dichloromethane 2:1 (v/v), R_f 0.40] to give the title compound as a

colourless oil (88%); Exact Mass Calcd for $C_{14}H_{16}O_5F_3SSi$: 381.0458, Found: 381.0421; δ_H (200 MHz) 0.26 (9H, s, RSi(C*H*$_3$)$_3$), 3.96 (3H, s, ArCO$_2$C*H*$_3$), 7.23 (1H, d, *J*=8.6 Hz, Ar*H*), 7.66 (1H, dd, *J*=8.6 and 2.2 Hz, Ar*H*), 8.15 (1H, d, *J*=2.2 Hz, Ar*H*); δ_C (50.28 MHz) −0.4 (RSi(*C*H$_3$)$_3$), 52.7 (ArCO$_2$*C*H$_3$), 98.1 (*C*≡C), 101.7 (*C*≡C), 118.7 (q, *J*=321 Hz, *C*F$_3$SO$_2$Ar), 122.9, 124.2, 124.6, 136.2, 137.1, 147.6, 163.6 (*C*=O); *m*/*z* (LSIMS) 381 ((M+H)$^+$, 100%), 248 (46); ν_{max} (neat) 2164, 1738 cm^{-1}.

Methyl 3-(trimethylsilylethynyl)benzoate 32. A solution of methyl 3-iodobenzoate **31**[27] (10.00 g, 38.16 mmol), Pd(PPh$_3$)$_4$ (0.44 g, 0.14 mmol), trimethylsilylacetylene (6.46 mL, 45.81 mmol), triethylamine (10.62 mL, 76.34 mmol) and CuI (73 mg, 0.38 mmol) in degassed DMF (20 mL) was stirred at 40°C for 16 h. An extractive workup with ether (200 mL) gave a fawn solid. Purification by squat column chromatography [hexane/dichloromethane 2:1 (v/v), R_f 0.43] gave the title compound as a colourless solid (8.69 g, 98%). A small sample was recrystallised from a methanol/water mixture as fawn needles; mp 52.0°C (no lit. mp)[25]; δ_H (200 MHz) 0.29 (9H, s, RSi(C*H*$_3$)$_3$), 3.95 (3H, s, ArCO$_2$C*H*$_3$), 7.41 (1H, t, *J*=7.8 Hz, Ar*H*), 7.67 (1H, dt, *J*=7.8 and 1.6 Hz, Ar*H*), 8.00 (1H, dt, *J*=7.8 and 1.6 Hz, Ar*H*), 8.18 (1H, t, *J*=1.6 Hz, Ar*H*); δ_C (50.28 MHz) −0.3 (RSi(*C*H$_3$)$_3$), 52.1 (ArCO$_2$*C*H$_3$), 95.3 (*C*≡C), 103.9 (*C*≡C), 123.6, 128.3, 129.4, 130.3, 133.1, 135.9, 166.3 (*C*=O); *m*/*z* (EI) 232 (M$^+$, 43%), 217 (100), 201 (62); ν_{max} 2157, 1732 cm^{-1}.

Methyl 3-ethynylbenzoate 33. A solution of **32** (500 mg, 2.15 mmol) in methanol (20 mL) was stirred with potassium carbonate (30 mg, 0.22 mmol) at room temperature for 2 h. The solvent was removed in vacuo and the resulting tan solid was sublimed at 45°C/0.03 mmHg to give the title compound as a colourless solid (76 mg, 76%); mp 54.0–55.0°C with rapid heating (lit.[25] 48–50°C); δ_H (200 MHz) 3.13 (1H, s, ArC≡C*H*), 3.93 (3H, s, ArCO$_2$C*H*$_3$), 7.41 (1H, t, *J*=7.8 Hz, Ar*H*), 7.66 (1H, dt, *J*=7.8 and 1.4 Hz, Ar*H*), 8.01 (1H, dt, *J*=7.8 and 1.4 Hz, Ar*H*), 8.17 (1H, t, *J*=1.4 Hz, Ar*H*); δ_C (50.28 MHz) 52.2 (ArCO$_2$*C*H$_3$), 78.1 (*C*≡C), 82.5 (*C*≡C), 122.6, 128.5, 129.8, 130.5, 133.3, 136.3, 166.3 (*C*=O); *m*/*z* (EI) 160 (M$^+$, 60%), 159 (21), 129 (100), 101 (63); ν_{max} 3311, 2106, 1732 cm^{-1}.

Methyl 2-{2-[3-(methoxycarbonyl)phenyl]-1-ethynyl}-5-(trimethylsilylethynyl)-benzoate 34. A solution containing triflate **30** (1.22 g, 3.21 mmol), Pd(PPh$_3$)$_4$ (185 mg, 0.16 mmol), methyl 3-ethynylbenzoate **33** (539 mg, 3.37 mmol) and CuI (31 mg, 0.16 mmol) in a degassed solvent system of triethylamine (4 mL)/DMF (8 mL) was stirred at 50°C for 2 h. An extractive workup with ether (100 mL) gave a tan solid. Purification by flash chromatography [hexane/ethylacetate 5:1 (v/v), R_f 0.46] yielded the title compound as a colourless solid (1.18 g, 94%). A small sample was sublimed at 100°C/0.05 mmHg to give a colourless powder; mp 106.0–107.5°C; Anal. Calcd for $C_{23}H_{22}O_4Si$: C, 70.74; H, 5.68, Found: C, 70.64; H, 5.65; δ_H (300 MHz) 0.26 (9H, s, Si(C*H*$_3$)$_3$), 3.94 (3H, s, ArCO$_2$C*H*$_3$), 3.97 (3H, s, ArCO$_2$C*H*$_3$), 7.46 (1H, t, *J*=7.5 Hz, Ar*H*), 7.57 (2H, br s, Ar*H*), 7.45 (1H, dt, *J*=7.5 and 1.5 Hz, Ar*H*), 8.02 (1H, dt, *J*=7.5 and 1.5 Hz, Ar*H*), 8.09 (1H, br s, Ar*H*), 8.24 (1H, t, *J*=1.5 Hz, Ar*H*); δ_C (75.47 MHz) −0.2 (Si(*C*H$_3$)$_3$), 52.2 (ArCO$_2$*C*H$_3$), 52.3 (ArCO$_2$*C*H$_3$), 88.5 (*C*≡C), 95.0 (*C*≡C), 97.6 (*C*≡C), 103.4 (*C*≡C), 123.1, 123.3, 123.6, 128.5, 129.6, 130.6, 131.9, 132.8, 133.9,134.1, 134.6, 135.8, 165.7 (*C*=O), 166.3 (*C*=O); *m*/*z* (EI) 390 (M$^+$, 16%), 375 (18); ν_{max} 2156, 1718, 1704 cm^{-1}.

4-{[*E*)-2-[3-(hydroxymethyl)phenyl]-1-ethenyl}-3-(hydroxymethyl)ethynylbenzene 35. A suspension of LiAlH$_4$ (10 mg, 0.263 mmol) in dry THF (3 mL) was cooled to 0°C under nitrogen, and then diester **34** (50 mg, 0.128 mmol) in dry THF (3 mL) was added with stirring. The resulting suspension was allowed to warm to room temperature over 5 h. The reaction mixture was quenched with 'wet' ether and then added to 1% HCl (10 mL), followed by extraction with ether (2×10 mL). The organic layers were combined, dried and the solvent removed to give a tan solid. The solid was taken up into dichloromethane (5 mL), Bu$_4$NF (60 mg, 0.192 mmol) was added and the resulting solution stirred for 2 h at rt. The reaction mixture was concentrated in vacuo and purification of the residue by flash chromatography [dichloromethane/ethyl acetate 1:1 (v/v), R_f 0.39] yielded an off-white solid. Recrystallisation from a benzene/hexane mixture gave the title compound as fine off-white needles (30 mg, 91%); mp 138.0–139.0°C; Exact Mass Calcd for $C_{18}H_{16}O_2$: 264.1150, Found: 264.1153; δ_H (300 MHz, CD$_3$CN) 3.43 (1H, s, ArC≡C*H*), 4.58 (2H, d, *J*=3.9 Hz, ArC*H*$_2$OH), 4.71 (2H, d, *J*=3.9 Hz, ArC*H*$_2$OH), 7.17 (1H, d, *J*=16.2 Hz, HC=C*H*), 7.13–7.48 (7H, m), 7.43 (1H, d, *J*=16.2 Hz), 7.68 (1H, d, *J*=8.1 Hz, Ar*H*); δ_C (50.28 MHz, CDCl$_3$/CD$_3$CN) 62.4, 64.6, 79.1 (*C*≡C), 84.3 (*C*≡C), 121.6, 125.4, 125.8, 126.3, 126.4, 127.3, 129.5, 131.8, 132.3, 132.4, 137.3, 138.1, 140.0, 143.4; *m*/*z* (LSIMS) 264 (M$^+$, 100%), 247 (78); ν_{max} 3330, 3275 cm^{-1}.

4-{2-[3-(Hydroxymethyl)phenyl]-1-ethynyl}-3-(hydroxymethyl)ethynylbenzene 36. A solution of diester **34** (19 mg, 0.0487 mmol) in dry THF (3 mL) was cooled to −20°C and 1.5M DIBAL-H in toluene (0.20 mL, 0.300 mmol) was added with stirring. The resulting solution was allowed to warm to 0°C over 0.5 h. The reaction mixture was quenched with 'wet' ether and then added to 1% HCl (10 mL), followed by extraction with ether (2×10 mL). The organic layers were combined, dried and the solvent removed to give a fawn solid. The solid was taken up into dichloromethane (3 mL) and Bu$_4$NF (0.0570 mmol) added. The resulting solution was stirred for 15 min at rt, followed by concentration in vacuo and purification by flash column chromatography [ethyl acetate/dichloromethane 1:1 (v/v), R_f 0.50] to give the title compound as a fawn solid (13 mg, 100%). A sample was recrystallised from a benzene/hexane mixture to give fine pale yellow needles; mp 87.0–88.5°C; Exact Mass Calcd for $C_{18}H_{14}O_2$: 262.0994, Found: 262.0998; δ_H (300 MHz) 3.20 (1H, s, ArC≡C*H*), 4.68 (2H, d, *J*=5.1 Hz, ArC*H*$_2$OH), 4.87 (2H, d, *J*=5.7 Hz, ArC*H*$_2$OH), 7.34–7.47 (5H, m, Ar*H*), 7.53 (1H, s, Ar*H*), 7.63 (1H, d, *J*=0.9 Hz, Ar*H*); δ_C (75.47 MHz) 62.0 (ArCH$_2$OH), 63.5 (ArCH$_2$OH), 78.5 (*C*≡C), 82.9 (*C*≡C), 85.7 (*C*≡C), 95.5 (*C*≡C), 120.9, 121.7, 122.3, 126.8, 128.1, 129.4, 129.8, 129.9, 130.1, 131.4, 141.6, 143.0; *m*/*z* (LSIMS) 262 (M$^+$, 100%), 245 (94); ν_{max} 3340, 3321 cm^{-1}; UV–Vis (nm) 230 (8000),

283 (27 000), 291 (30 000), 300 (38 000), 309 (31 000), 320 (35 000); Fluorescence (nm) 332.

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