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Suzuki–Miyaura homocoupling of naphthyl triflates using bis(pinacolato)diboron: approaches to the biaryl skeleton of crisamicin A

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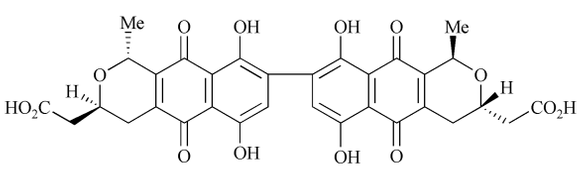
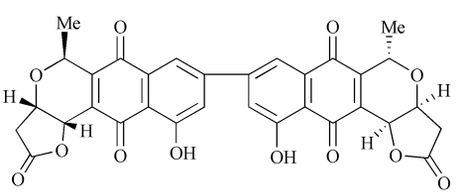
Homocoupling of naphthyl triflates **27**, **16**, **17** to the respective binaphthyls **28**, **31** and **35** has been achieved in a one-pot procedure using bis(pinacolato)diboron and $PdCl_2$(dppf). Use of potassium acetate as the base provides access to the initial naphthylboronate intermediates whereas the stronger base potassium phosphate is required in order to promote subsequent coupling of the naphthylboronate with a second equivalent of the naphthyl triflate. Attempts to convert binaphthyl **35** into bis-acetylnaphthalene **14**, a key intermediate for the synthesis of the dimeric pyranonaphthoquinone antibiotic crisamicin A **2**, *via* double Fries rearrangement of bis-acetate **37** derived from binaphthyl **35**, were unsuccessful. Attempts to introduce the acetyl groups at C-7 and C-7′ on bis-acetylnaphthalene **14** *via* Fries rearrangement of the monomeric precursors **21** and **15**, before effecting homocoupling to a biaryl were unsuccessful. Introduction of an acetyl group *via* initial bromination *ortho* to the hydroxyl group in naphthol **18**, which bears an electron rich benzyl ether at C-7, was plagued by the formation of phenolic coupling product **42** and naphthoquinone **43**. Bromination of naphthol **45**, bearing a less electron rich triflate group at C-7, also afforded binaphthol **47** resulting from phenolic coupling as well as naphthoquinone **48** when using *N*-bromosuccinimide at low temperature.

Introduction

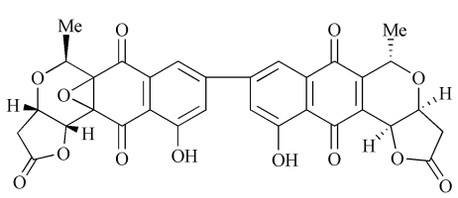
Members of the pyranonaphthoquinone family of antibiotics contain a basic naphtho[2,3-*c*]pyran-5,10-dione skeleton that is built up from acetate/malonate units *via* a polyketide pathway.[1] These antibiotics exhibit activity against a variety of Gram-positive bacteria, pathogenic fungi and yeasts, as well as antiviral activity. In addition, they have been proposed to act as bioreductive alkylating agents.[2] The diversity of chemical structures found within the pyranonaphthoquinone family of antibiotics has prompted a number of syntheses of this class of compound.[3] Our initial synthetic work in this area focused on the synthesis of the monomeric pyranonaphthoquinone antibiotics *via* addition of 2-trimethylsilyloxyfuran to a 2-acetyl-1,4-naphthoquinone followed by rearrangement of the resultant furonaphthofuran ring system to a furonaphthopyran ring system using ceric ammonium nitrate (CAN). This approach has been successfully used to prepare analogues of the carbohydrate containing pyranonaphthoquinone antibiotics griseusin A[4] and medermycin[5] as well as simpler members of the family such as the arizonins[6] and kalafungin.[7] The focus of the work reported herein is directed towards the synthesis of the more complex dimeric pyranonaphthoquinones such as actinorhodin **1** and the crisamicins A **2** and C **3**.



actinorhodin **1**



crisamicin A **2**



crisamicin C **3**

Whilst efficient syntheses of several monomeric pyranonaphthoquinones have been achieved, only one synthesis of a dimeric pyranonaphthoquinone has been reported in which a novel double furofuran annulation—oxidative rearrangement strategy was used to prepare an analogue **4** (Scheme 1) of the aphid pigment actinorhodin **1**.[8] In this case Suzuki–Miyaura coupling of a bromonaphthalene **5** allowed construction of the key biaryl linkage in **6** *ortho* to a methoxy group on the naphthalene ring, before the ensuing double furofuran annulation of the bis-quinone **7** with 2-trimethylsilyloxyfuran **8** and oxidative rearrangement of the resultant adduct **9** to the bis-lactol **10**. In this case the bromine in naphthalene **5** was strategically placed *via ortho*-selective bromination of a naphthol precursor, at the position where biaryl formation later took place.

It was envisaged that previous methodology employed for the synthesis of the actinorhodin analogue **4** could be applied to the synthesis of crisamicins A **2** and C **3**, that were isolated from the microorganism *Micromonospora purpureochromogenes*.[9] Crisamicin A **2** exhibits activity against B16 murine melanoma cells, herpes simplex virus and vesicular stomatitis virus.[10] Our strategy for the synthesis of crisamicin A **2** is outlined in retrosynthetic terms (Scheme 2) and features the double oxidative rearrangement of furonaphthofuran **12** to furonaphthopyran **11** as a key step. In turn bisfuronaphthofuran **12** is formed by double furofuran annulation of bis-naphthoquinone **13** with 2-trimethylsilyloxyfuran **8**. The precursor to bis-naphthoquinone **13** is bis-naphthalene **14** for which it is envisaged that the critical biaryl linkage be constructed *via*

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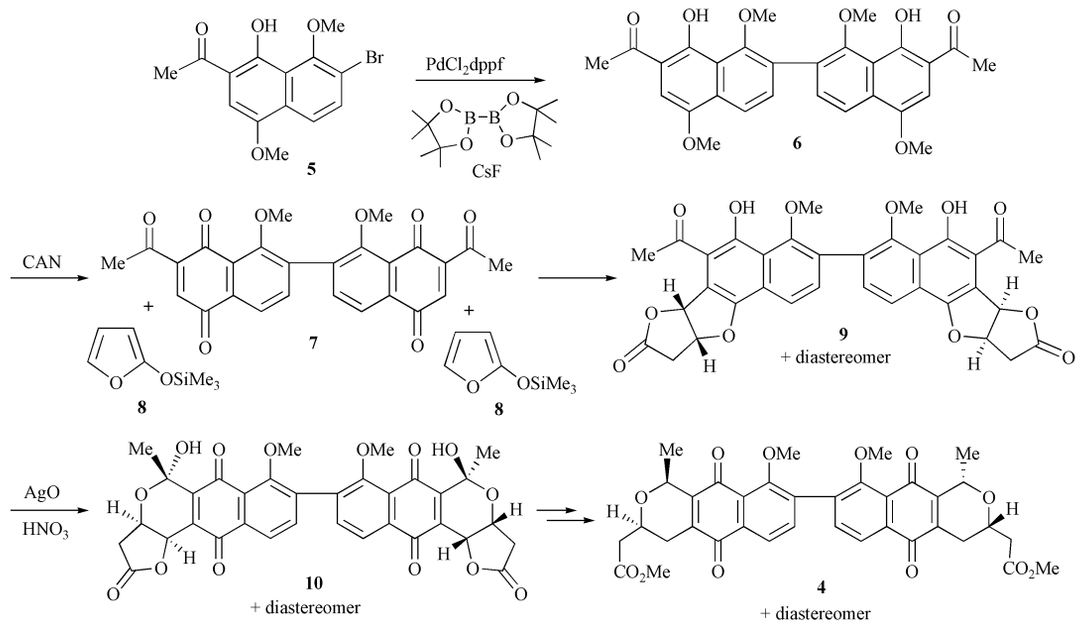
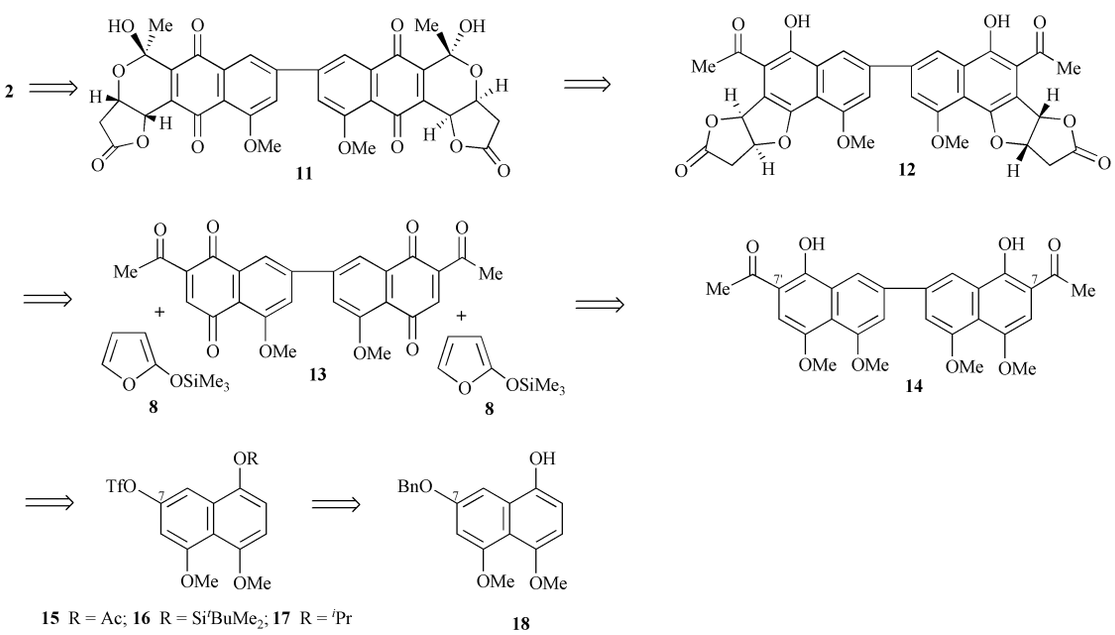


Scheme 1



Scheme 2

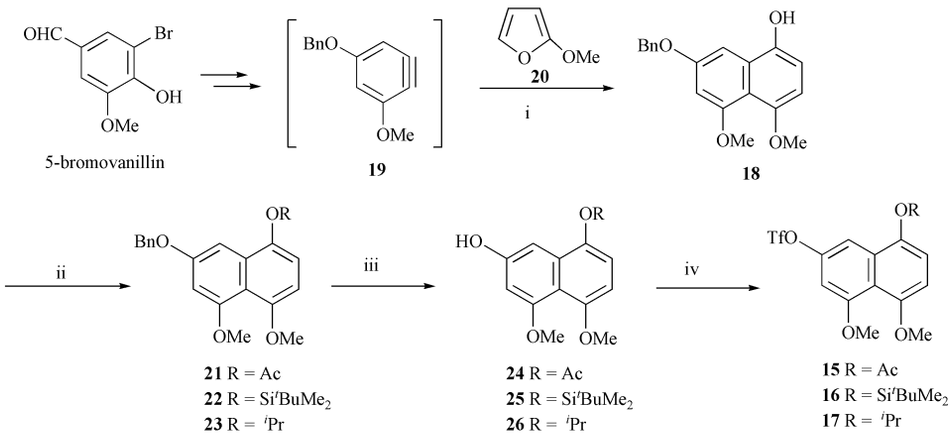
Suzuki–Miyaura homocoupling of one of the protected naphthyl triflates **15**,**16** or **17** that are derived from readily prepared benzyl ether **18**.[11] Thus, in the case of crisamicin A **2** the lack of an oxygen substituent *ortho* to the biaryl linkage precluded the possibility of using a bromine atom to construct a biaryl hence the use of a triflate to achieve this was a critical goal in the present work.

Results and discussion

Miyaura and co-workers[12] have reported the use of bis(pinacolato)diboron and $PdCl_2$(dppf†)–KOAc as a method to prepare aryl boronates from aryl triflates. In the same paper they also report the synthesis of unsymmetrical biaryls by cross-coupling the '*in-situ*' generated boronate esters with another triflate in the presence of potassium phosphate. As an extension to this work we proposed that homocoupling of one of the protected triflates **15**, **16** or **17** with the '*in-situ*' generated boronates derived from the same triflate, would provide an efficient entry to the bis-naphthalene skeleton of crisamicin A **2**. An important consideration was the choice of protecting group for the hydroxyl group at the alpha position that is compatible with the Suzuki–Miyaura coupling hence triflates **15**, **16** and **17** bearing an acetate, *tert*-butyldimethylsilyl or isopropyl ether were selected. It was envisaged that after Suzuki–Miyaura coupling and removal of the protecting group the resultant hydroxyl group would provide functionality for introduction of an acetyl group to the two *ortho* positions. Alternatively, it was hoped that acetate **15** would undergo homocoupling and the acetate groups on the resultant biaryl could then be subjected to double Fries rearrangement in order to introduce the *ortho*-acetyl groups in bis-naphthalene **14**.

Triflates **15**, **16** and **17** were prepared from benzyl ether **18** which in turn is available in seven steps from 5-bromovanillin *via* acid catalysed fragmentation of the Diels–Alder adduct formed from addition of benzyne **19** to 2-methoxyfuran **20** (Scheme 3).[11] Protection of the hydroxyl group as either an

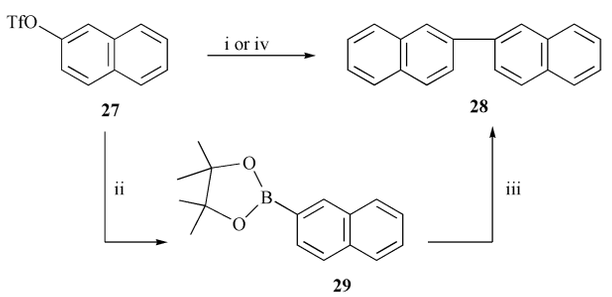
† dppf = 1,1′-Bis(diphenylphosphino)ferrocene.



Scheme 3 *Reagents, conditions and yields*: (i) see ref. 11; (ii) **21**, Ac_2O, py, 18 h, 73%; **22**, $ClSi^tBuMe_2$, imid., DMAP, CH_2Cl_2, room temp., 20 h, 67%; **23**, NaH, DMF, 1 h, then 2-bromopropane, room temp., 3.5 h, 89%; (iii) 10% Pd/C, H_2, EtOAc, **24**, 5 h, 81%; **25**, 1 h, 89%; **26**, 1.5 h, 78%; (iv) **15**, Tf_2O, Et_3N, CH_2Cl_2, −20 °C, 18.5 h, 82%; **16**, 23.5 h, 96%; **17**, $PhNTf_2$, Et_3N, CH_2Cl_2, −25 °C, 15 h, 81%.

acetate **21**, a *tert*-butyldimethylsilyl ether **22** or an isopropyl ether **23** was then effected under standard conditions. Removal of the benzyl ether by hydrogenolysis over palladium on charcoal afforded naphthols **24**, **25** or **26** respectively, that were then treated with trifluoromethanesulfonic anhydride or *N*-phenyltrifluoromethanesulfonimide to afford triflates **15**, **16** and **17** in good yield.

In preparation for the key Suzuki–Miyaura coupling of triflates **15**, **16** and **17** to binaphthyls it was initially decided to investigate the homocoupling of 2-naphthyl triflate **27**[13] into binaphthyl **28**. One method for direct reduction of 2-naphthyl triflate **27** using zinc metal catalysed by palladium(II) acetate and (±)-1,1′-BINAP, as reported by Jutand and Mosleh,[14] afforded binaphthyl **28** in 67% yield (Scheme 4).



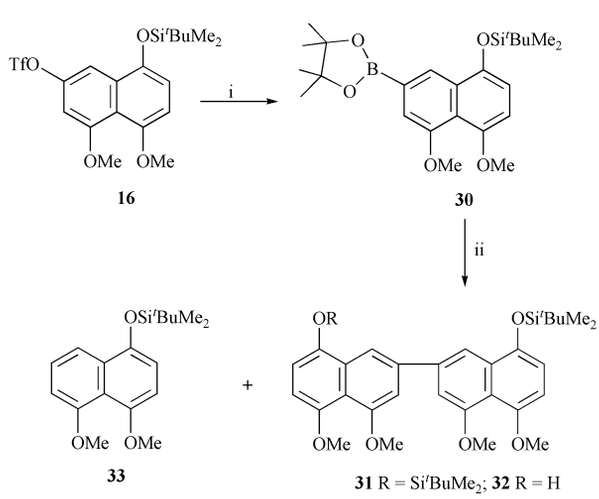
Scheme 4 *Reagents, conditions and yields*: (i) Zn, $Pd(OAc)_2$, (±)-1,1′-BINAP, DMF, 120 °C, 1.5 h, 67%; (ii) pinacolborane (3.0 equiv., 1.0 M in THF), $PdCl_2$(dppf), Et_3N, 1,2-dichloroethane, 110 °C, 53%; pinacolborane (1.5 equiv., 97%), $PdCl_2$(dppf), Et_3N, 1,2-dichloroethane, 110 °C, 50%; bis(pinacolato)diboron (1.1 equiv.), $PdCl_2$(dppf), dppf, KOAc, dioxane, reflux, 2.5 h, 54%; (iii) triflate **27**, $PdCl_2$(dppf), K_3PO_4, dioxane, reflux, 5 h, 58%; (iv) bis(pinacolato)diboron (1.1 equiv.), $PdCl_2$(dppf), dppf, KOAc, dioxane, reflux, 2.5 h, then K_3PO_4, heat, 18 h, 84%.

In an attempt to improve the yield of binaphthyl **28** we next turned to Suzuki–Miyaura coupling using pinacolboronate **29** (Scheme 4). Pinacolboronate **29** was generated from 2-naphthyl triflate **27** using pinacolborane in 50–53% yield using pinacolborane (1.0 M in THF, 3.0 equiv.), triethylamine and $PdCl_2$(dppf) in 1,2-dichloroethane at 110 °C following the method of Murata *et al*.[15] Use of neat pinacolborane (1.5 equiv., 97%) did not improve the yield of naphthylboronate **29** with substantial formation of naphthalene as a by-product also being formed in this case. This observation may be attributed to the pinacolborone acting as a hydride source and effecting cross-coupling with the pinacolboronate.[15,16]

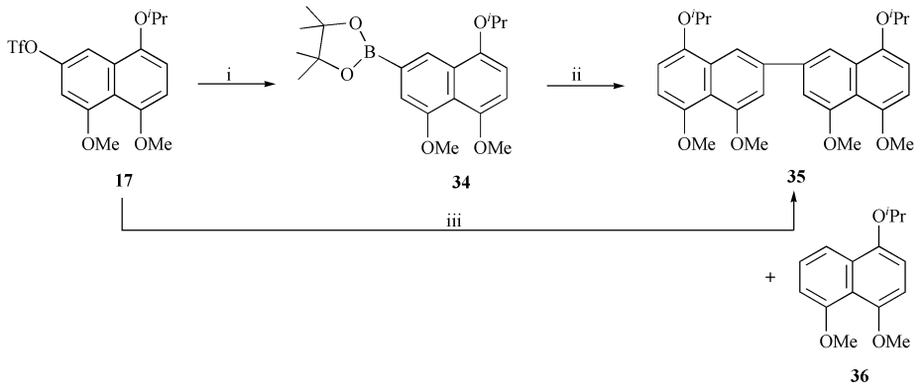
We next focussed on the use of bis(pinacolato)diboron as the boronating agent following the method reported by Miyaura *et al*.[12] In this case one can either form the arylboronate first and then effect homocoupling to the biaryl or one can employ a one-pot '*in situ*' coupling directly to the biaryl. Potassium acetate is used as the base to form the naphthylboronate whereas the stronger base potassium phosphate is required to effect formation of the biaryl. Comparison of these two procedures described by Miyaura *et al*.[12] using 2-naphthyl triflate **27** led to the conclusion that the best yielding method was the one-pot '*in situ*' coupling of boronate **29** with 2-naphthyl triflate **27** affording binaphthyl **28** in 84% yield compared to 31% yield when using the stepwise coupling. The use of potassium acetate for the initial formation of the naphthylboronate **29** was important in order to minimize the formation of the by-product, naphthalene.

Having established the optimum method for effecting homocoupling of 2-naphthyl triflate **27** attention turned to the homocoupling of triflates **15**, **16** and **17** using similar conditions. Treatment of triflate **15** bearing an acetate group at C-1, with zinc and palladium(II) acetate afforded mainly recovered starting material as did attempts to effect Suzuki–Miyaura homocoupling using bis(pinacolato)diboron. On the other hand, silyl ether **16** underwent smooth conversion into naphthylboronate **30** (Scheme 5) with bis(pinacolato)diboron and subsequent coupling of **30** with triflate **16** afforded biaryl **31** in low yield together with deprotected material **32** and reduced product **33**. In this case use of the one pot method did not improve the yield of biaryl **31**.

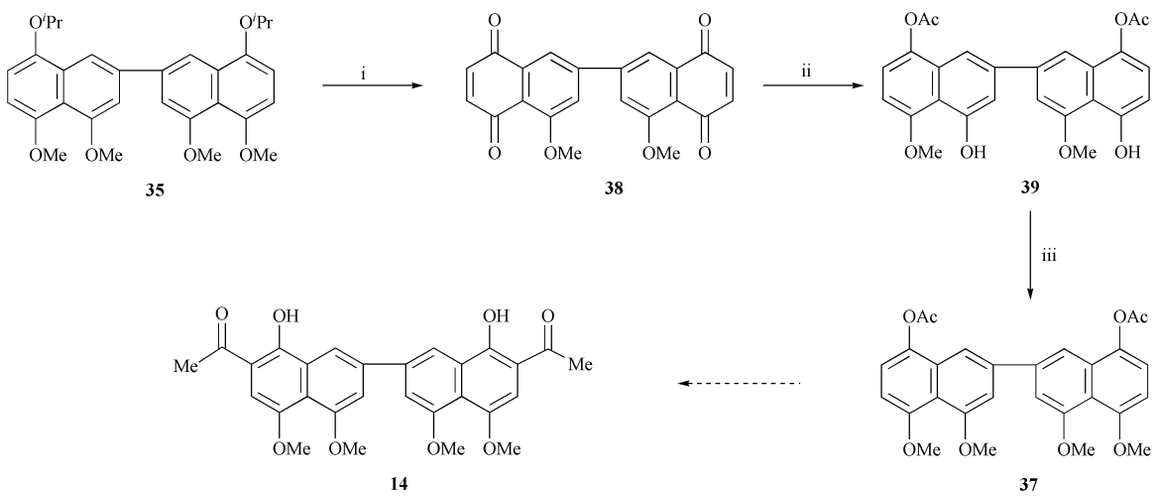
In the case of the isopropyl protected triflate **17**, naphthylboronate **34** was prepared in 50% yield by treatment with bis(pinacolato)diboron in 1,2-dichloroethane using $PdCl_2$(dppf)



Scheme 5 *Reagents, conditions and yields*: (i) bis(pinacolato)diboron (1.1 equiv.), $PdCl_2$(dppf), dppf, KOAc, dioxane, reflux, 1.5 h, 80%; (ii) triflate **16**, $PdCl_2$(dppf), K_3PO_4, dioxane, reflux, 1.5 h, **31**, 22%; **32**, 16%; **33**, 4%.



Scheme 6 *Reagents, conditions and yields*: (i) bis(pinacolato)diboron (1.1 equiv.), $PdCl_2$(dppf), Et_3N, 1,2-dichloroethane, reflux, 1.5 h, 50%; (ii) triflate **17**, $PdCl_2$(dppf), K_3PO_4, dioxane, reflux, 21.5 h, 59%; (iii) bis(pinacolato)diboron (1.1 equiv.), $PdCl_2$(dppf), dppf, KOAc, dioxane, reflux, 1.5 h, then triflate **17**, $PdCl_2$(dppf), K_3PO_4, reflux, 18 h, 77%.



Scheme 7 *Reagents, conditions and yields*: (i) AgO (16 equiv.), 6 M HNO_3, dioxane, 10 min, then AgO (16 equiv.), 100%; (ii) Ac_2O, py, Zn, $CHCl_3$, heat, 10 min, 71%; (iii) dimethyl sulfate, acetone, reflux, 7 h, 67%.

with triethylamine as the base (Scheme 6). Subsequent conversion to binaphthyl **35** took place in 59% yield by further reaction with triflate **17** and $PdCl_2$(dppf) using potassium phosphate as base in dioxane. The homocoupling was then achieved in better yield (77%) using a one-pot procedure wherein naphthylboronate **34** was generated in dioxane with $PdCl_2$(dppf) using potassium acetate as base, triflate **17** was added with a second portion of $PdCl_2$(dppf) together with the stronger base potassium phosphate. Attempts to optimize this homocoupling further using $Pd_2(dba)_3$ rather than $PdCl_2$-(dppf) using the phosphine ligands (dicyclohexylphosphino)-biphenyl and 2-(dimethylamino)-2′-(dicyclohexylphosphino)-biphenyl did not offer any improvement in the yield of binaphthyl **35** obtained, rather substantial quantities of the reduced product **36** were afforded.

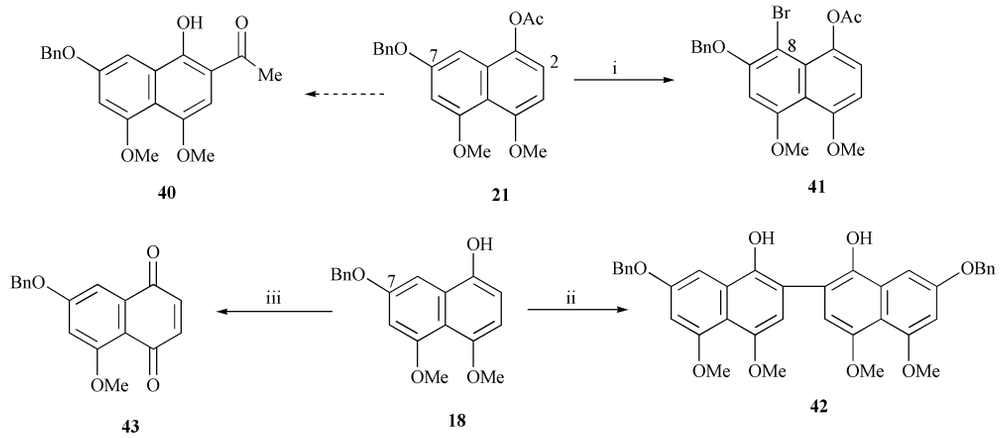
With binaphthyl **35** in hand, attention turned to introduction of acetyl groups at C-7 and C-7′ in order to provide binaphthyl **14** as required for the proposed synthesis of crisamicin A **2** (Scheme 2). It was initially envisaged that selective removal of the isopropyl ethers and acetylation of the resultant bis-naphthol would provide bis-acetate **37** that would undergo double Fries rearrangement to the bis-acetylnaphthalene **14** (Scheme 7). This approach was put on hold when attempts to selectively deprotect the isopropyl groups in binaphthyl **35** using aluminium trichloride,[17] boron trichloride,[18] trifluoroacetic acid,[19] iron trichloride[20] and ruthenium trichloride[21] were not selective for removal of the isopropyl groups and afforded complex mixtures of products.

In light of the inability to effect deprotection of the isopropyl ethers in binaphthyl **35**, as required for preparation of bis-acetate **37**, we next decided to effect oxidation of binaphthyl **35** to bis-naphthoquinone **38** that would then undergo reductive acetylation and methylation to bis-acetate **37** (Scheme 7). Bis-acetate **37** would then provide bis-acetylnaphthalene **14** upon double Fries rearrangement. Towards this end binaphthyl **35** was oxidized quantitatively with silver(II) oxide and nitric acid to bis-naphthoquinone **38** that then underwent double selective reductive acetylation to **39** in 71% yield using zinc and acetic anhydride. Finally methylation of **39** by heating with dimethyl sulfate and potassium carbonate in acetone[22] afforded bis-acetate **37** in 67% yield.

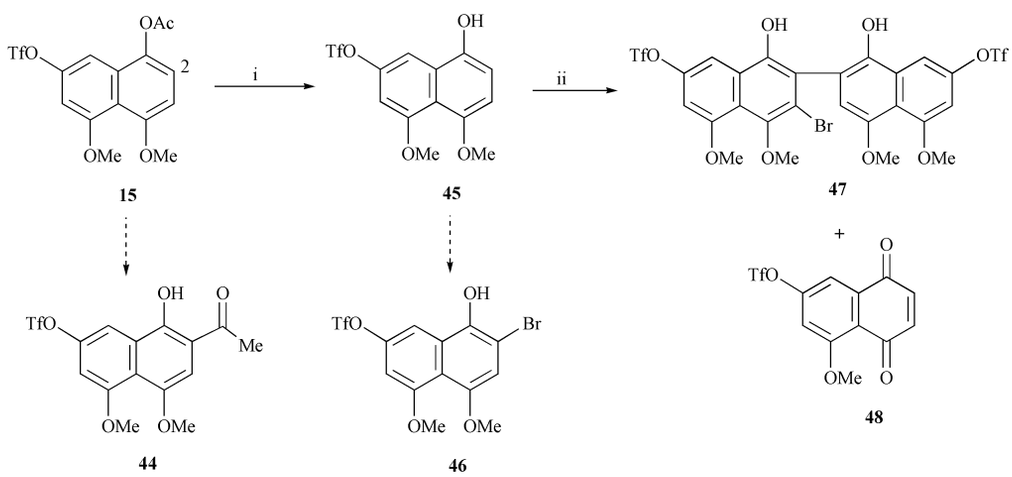
Considerable effort was made to effect a double Fries rearrangement of bis-acetate **37** to the desired bis-acetylnaphthalene **14** using boron trifluoride, aluminium trichloride and scandium triflate using a variety of solvents and conditions, however these attempts were fruitless. Similarly, attempts to effect introduction of acetyl groups at C-7 and C-7′ on binaphthyl **35** using trifluoroacetic anhydride in acetic acid[22] and acetic anhydride with ruthenium trichloride[21] afforded complex mixtures.

Given that the acetyl groups at C-7 and C-7′ in binaphthyl **14** that are required for our proposed synthesis of crisamicin A **2**, could not be effectively introduced onto binaphthyl **35**, an alternative pathway was adopted wherein the required acetyl groups were introduced onto a monomeric naphthalene before effecting construction of the biaryl linkage.

With acetate **21** already in hand, its conversion to 2-acetylnaphthalene **40** was investigated (Scheme 8). Disappointingly, attempts to effect Fries rearrangement of **21** to **40** were frustrated by the formation of complex mixtures in which loss of the benzyl and methyl ethers were observed. Alternatively, 2-acetylnaphthalene **40** could be prepared from acetate



Scheme 8 *Reagents, conditions and yields*: (i) NBS (1.0 equiv.), DMF, 1.5 h, 75%; (ii) NBS (1.0 equiv.). $^{i}Pr_2EtN$, CH_2Cl_2, 2 h, 79%; (iii) NBS (1.0 equiv.), DMF, 22 h, 37%.



Scheme 9 *Reagents, conditions and yields*: (i) K_2CO_3, MeOH–THF (95 : 5), 15 min, 91%; (ii) NBS, toluene, −78 °C, 1 h, **47**, 22%; **48**, 14%.

21 *via* selective bromination at C-2 followed by Stille coupling with α-(ethoxyvinyl)tributylstannane as used by this research group in the synthesis of *C*-glycosylpyranonaphthoquinones.[5] Unfortunately bromination of acetate **21** took place in the more electron rich ring affording the undesired C-8 bromide **41**. In an attempt to direct bromination to the C-2 position naphthol **18** was treated with *N*-bromosuccinimide and diisopropylamine in dichloromethane, however this resulted in a 79% yield of dimer **42**, a product of phenolic coupling formed due to the presence of electron donating groups on naphthol **18**. Use of *N*-bromosuccinimide in DMF afforded naphthoquinone **43** in 37% yield whereas use of molecular bromine and iodine afforded complex mixtures of products.

The electron donating effects of the two methoxy groups at C-4 and C-5 in benzyl ether **21** resulted in increased electron density at C-8 that was reinforced by the benzyloxy group at C-7. It was therefore decided to focus on electrophilic aromatic substitution of triflate **15** as a method for introduction of an acetyl group at C-2, hoping that the presence of the more electron withdrawing triflate group at C-7 would direct reaction to the hydroquinonoid ring (Scheme 9). Numerous attempts to effect Fries rearrangement of triflate **15** to acetylnaphthalene **44** only afforded naphthol **45**. Naphthol **45**, however, could potentially undergo *ortho*-selective bromination to bromide **46** that could then serve as precursor for introduction of an acetyl group at this position.

In order to investigate this approach larger quantities of naphthol **45** were prepared by hydrolysis of acetate **15** using potassium carbonate in methanol–THF (Scheme 9). Unfortunately attempts to effect *ortho*-bromination of naphthol **45** gave complex mixtures of phenolic coupling products and naphthoquinones as exemplified by the formation of dimer **47** and naphthoquinone **48** upon treatment of naphthol **45** with *N*-bromosuccinimide in toluene at low temperature. It was therefore concluded that introduction of an acetyl group at C-2 on naphthol **45** *via ortho*-bromination followed by Stille coupling using α-(ethoxyvinyl)tributylstannane was not viable due to the initial inability to successfully brominate naphthol **45** at C-2.

In summary, the homocoupling of naphthyl triflates **27**, **16**, **17** to the binaphthyls **28**, **31** and **35** respectively, has been achieved providing the first examples of the use of a Suzuki–Miyaura coupling using bis(pinacolato)diboron and $PdCl_2$-(dppf) to effect homocoupling of aryl triflates to biaryls. Although the main focus of the present work was to prepare bis-acetylnaphthalene **14** as a key intermediate for our proposed synthesis of crisamicin A **2** using a double furofuran annulation–double oxidative rearrangement strategy, it transpired that attempts to introduce the required acetyl groups at C-7 and C-7′ in bis-acetylnaphthalene **14** *via* double Fries rearrangement of acetate **37**, Fries rearrangement of monomeric acetates **21** and **15**, or regioselective bromination of monomeric benzyl ether **8** and triflate **45**, proved problematic thereby prompting a rethink of our synthetic approach to crisamicin A **2**.

Experimental

General

Mps were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded using a Perkin-Elmer 1600 Fourier Transform IR spectrophotometer as thin films between sodium chloride plates. Absorption spectra are expressed in wavenumbers (cm^{-1}) with the following abbrevi-

ations: s = strong, m = medium, w = weak and br = broad. ^{1}H NMR spectra were recorded on a Bruker AC 200 (200 MHz) or a Bruker DRX 400 (400 MHz) spectrometer at ambient temperature. All *J*-values are given in Hz. Chemical shifts are expressed in parts per million downfield shift from tetramethylsilane as an internal standard, and reported as position (δ_H), relative integral, multiplicity (s = singlet, br s = broad singlet, d = doublet, dd = double doublet, ddd = double double doublet, t = triplet, q = quartet, m = multiplet) and assignment. ^{13}C NMR spectra were recorded on a Bruker AC 200 (50.3 MHz) or a Bruker DRX 400 (100.5 MHz) spectrometer at ambient temperature with complete proton decoupling. Low resolution mass spectra were recorded on a VG70-250S, a VG70-SD or a AEI model MS902 double focusing magnetic sector mass spectrometer operating with an ionisation potential of 70 eV (EI, DEI, CI and DCI). High resolution mass spectra were recorded at nominal resolution of 5000 or 10 000 as appropriate. Major fragments are given as percentages relative to the base peak and assigned where possible. Ionisation methods employed were either electron impact or chemical ionisation with ammonia or methane as reagent gas (CI). Low resolution chemical ionisation mass spectra were also recorded on a Hewlett Packard 5989A mass spectrometer using ammonia as reagent gas with the sample dissolved in methanol. Flash chromatography was performed using Merck Kieselgel 60 (230–400 mesh) with the indicated solvents. Thin layer chromatography (TLC) was performed using 0.2 mm thick pre-coated silica gel plates (Merck Kieselgel 60 F_{254} or Riedel-de Haen Kieselgel S F_{254}). Compounds were visualised by ultraviolet fluorescence or by staining with iodine or vanillin in methanolic sulfuric acid.

7-Benzyloxy-4,5-dimethoxynaphthalen-1-ol (18)

The following procedure is adapted from the method of Giles, Hughes and Sargent.[23]

A solution of *n*-butyllithium (0.54 mL of a 1.6 M solution in hexane, 0.857 mmol) was added to a stirred solution of 4-benzyloxy-2-bromo-6-methoxyphenyl toluene-*p*-sulfonate[11] (0.209 g, 0.451 mmol) and 2-methoxyfuran **20** (0.084 mL, 0.90 mmol) in dry tetrahydrofuran (10 mL), under an atmosphere of nitrogen at −100 °C. The solution was stirred at −100 °C for 13 min then allowed to warm to room temperature for 2 h. The mixture was acidified by the addition of conc. HCl (~6 drops), stirred at room temperature for 15 min. then poured into water (2 mL), extracted with ethyl acetate (2 × 50 mL), washed with water (20 mL) and brine (20 mL) then dried over magnesium sulfate. Concentration under reduced pressure afforded a red–orange oil which was purified by flash column chromatography using 2:8 ethyl acetate–hexane as eluent to yield naphthol **18** (84 mg, 60%) as a dark green solid, mp 155.2–156.8 °C. The ^{1}H NMR data were in agreement with those reported in the literature.[11] δ_H (200 MHz, $CDCl_3$) 3.90 (3 H, s, 4-OCH_3), 3.95 (3 H, s, 5-OCH_3), 5.18 (2 H, s, OCH_2), 6.57 (1 H, d, $J_{3,2}$ 8.3 Hz, H-3), 6.63 (1 H, d, $J_{6,8}$ 2.4 Hz, H-6), 6.73 (1 H, d, $J_{2,3}$ 8.3 Hz, H-2), 7.18 (1 H, d, $J_{8,6}$ 2.3 Hz, H-8), 7.34–7.52 (5 H, m, PhH); δ_C (50 MHz, $CDCl_3$) 56.2 (CH_3, OCH_3), 57.3 (CH_3, OCH_3), 69.7 (CH_2, OCH_2), 94.0 (CH, C-6), 99.8 (CH, C-8), 104.9 (CH, C-3), 109.5 (CH, C-2), 114.3 (quat., C-4a), 127.8 (CH, C-2′ and C-6′), 128.0 (CH, C-4′), 128.3 (quat., C-8a), 128.5 (CH, C-3′ and C-5′), 136.8 (quat., C-1′), 144.7 (quat., C-1), 151.3 (quat., C-4), 157.1 (quat., C-7), 158.1 (quat., C-5).

Naphthalen-2-yl trifluoromethanesulfonate (27)

Trifluoromethanesulfonic anhydride (0.35 mL, 2.50 mmol) was added to a mixture of 2-naphthol (0.300 g, 2.08 mmol) and dry triethylamine (0.35 mL, 2.50 mmol) in dry dichloromethane (10 mL). The mixture was stirred at −20 °C for 2 h, poured into water (20 mL) then extracted with chloroform (2 × 40 mL). The combined organic extracts were washed with dilute HCl (20 mL) and water (20 mL) then dried over magnesium sulfate, and evaporated to dryness to give a brown oil which was purified by flash column chromatography using 1 : 9 ethyl acetate–hexane as eluent to give the title compound **27** (0.556 g, 97%) as a colourless solid, mp 32–33 °C, lit.[13] mp 31–32 °C; δ_H (200 MHz, $CDCl_3$) 7.39 (1 H, dd, *J* 2.5, 9.0 Hz, H-3), 7.53–7.63 (2 H, m, ArH), 7.76 (1 H, d, *J* 2.4 Hz, H-1), 7.86–7.95 (3H, m, ArH).

4,4,5,5-Tetramethyl-2-naphthalen-2-yl-1,3,2-dioxaborolane (29)

a) Using pinacolborane (1.0 M solution in tetrahydrofuran).[15] To a stirred solution of $PdCl_2$(dppf) (14 mg, 0.017 mmol) in dry 1,2-dichloroethane (1.2 mL) was added naphthalen-2-yl trifluoromethanesulfonate **27** (76 mg, 0.275 mmol), dry triethylamine (0.23 mL, 1.65 mmol) and pinacolborane (0.83 mL of a 1.0 M solution in tetrahydrofuran, 0.83 mmol) under an atmosphere of argon and the mixture stirred at reflux for 2 h. The reaction mixture was extracted with ethyl acetate (2 × 20 mL). The combined organic extracts were washed with water (10 mL), dried over magnesium sulfate, and concentrated *in vacuo* to give a dark brown oil which was purified by flash column chromatography on florisil using gradient elution (from hexane to 5 : 95 ethyl acetate–hexane) to yield boronate **29** (37 mg, 53%) as colourless needles, mp 44–46 °C; δ_H (200 MHz, $CDCl_3$) 1.41 (12 H, s, 4 × CH_3), 7.50 (2 H, m, ArH), 7.85 (4 H, m, ArH), 8.40 (1 H, s, H-1). The ^{1}H NMR data were in agreement with that reported in the literature.[15]

b) Using 97% pure pinacolborane. To a stirred solution of $PdCl_2$(dppf) (18 mg, 0.022 mmol) in dry dichloroethane (1.4 mL) was added naphthalen-2-yl trifluoromethanesulfonate **27** (94 mg, 0.34 mmol), dry triethylamine (0.142 mL, 1.02 mmol) and pinacolborane (0.076 mL, 0.51 mmol) under an atmosphere of argon and the mixture stirred at reflux for 3 h. The reaction mixture was extracted with ethyl acetate (2 × 20 mL). The combined organic extracts were washed with water (10 mL), dried over magnesium sulfate, and concentrated *in vacuo* to give a dark brown oil which was purified by flash column chromatography on florisil using gradient elution (from hexane to 5 : 95 ethyl acetate–hexane) to yield boronate **29** 43.2 mg, 50%) as colourless needles. The ^{1}H NMR data were in agreement with those reported above.

c) Using bis(pinacolato)diboron. A mixture of potassium acetate (16 mg, 0.163 mmol), dry dioxane (0.33 mL), $PdCl_2$(dppf) (1.3 mg, 0.0016 mmol), dppf (0.9 mg, 0.0016 mmol), bis(pinacolato)diboron (15 mg, 0.06 mmol) and naphthalen-2-yl trifluoromethanesulfonate **27** (15 mg, 0.054 mmol) was heated and stirred under argon, at reflux for 2 h. The reaction mixture was diluted with ethyl acetate (10 mL), washed with water (5 mL), dried over magnesium sulfate and concentrated *in vacuo* to a dark brown oil which was purified by flash column chromatography on florisil using gradient elution (from hexane to 5 : 95 ethyl acetate–hexane) to yield boronate **29** (7.5 mg, 54%) as colourless needles. The ^{1}H NMR data were in agreement with that reported above.

2,2′-Binaphthalenyl (28)

a) Stepwise homocoupling of triflate 27 and boronate 29.[12] To a solution of boronate **29** (44.1 mg, 0.174 mmol) in dry dioxane (0.86 mL) was added potassium phosphate (111 mg, 0.523 mmol), $PdCl_2$(dppf) (4.3 mg, 0.005 mmol) and naphthalen-2-yl trifluoromethanesulfonate **27** (48 mg, 0.174 mmol). The mixture was stirred and heated at reflux under an atmosphere of argon for 5 h. The reaction mixture was concentrated *in vacuo* then diluted with ethyl acetate (50 mL), washed with water (30 mL), brine (30 mL), dried over magnesium sulfate and concentrated *in vacuo* to give a dark brown oil. Further

purification by flash column chromatography using hexane as eluent yielded the title compound **28** (26 mg, 58%) as a white solid, mp 186–188 °C, lit.[24] mp 185–187 °C.

b) Generation of boronate 29 followed by *in situ* coupling with triflate 27.[12] A mixture of potassium acetate (37 mg, 0.38 mmol), dry dioxane (0.8 mL), $PdCl_2$(dppf) (3.1 mg, 0.0038 mmol), dppf (2.1 mg, 0.0038 mmol), bis(pinacolato)-diboron (35 mg, 0.138 mmol) and naphthalen-2-yl trifluoromethanesulfonate **27** (35 mg, 0.127 mmol) under argon was heated with stirring at reflux for 2.5 h. Potassium phosphate (81 mg, 0.382 mmol), $PdCl_2$(dppf) (3.1 mg, 0.0038 mmol) and naphthalen-2-yl trifluoromethanesulfonate **27** (35 mg, 0.127 mmol) were added and the reaction mixture heated at reflux for 18 h. The reaction mixture was diluted with ethyl acetate (12 mL), washed with water (6 mL), dried over magnesium sulfate then concentrated *in vacuo* to a dark brown oil. Further purification by flash column chromatography using hexane as eluent yielded the title compound **28** (27 mg, 84%) as a white solid, mp 186–188 °C, lit.[24] mp 185–187 °C.

7-Benzyloxy-4,5-dimethoxynaphthalen-1-yl acetate (21)

To a stirred solution of 7-benzyloxy-4,5-dimethoxynaphthalen-1-ol **18** (78 mg, 0.251 mmol) in dry pyridine (1.5 mL) under a nitrogen atmosphere was added acetic anhydride (0.036 mL, 0.377 mmol) and the mixture left to stir overnight at room temperature. Diethyl ether (60 mL) and water (15 mL) were then added. The aqueous layer was removed and the organic layer was washed with 1 M HCl (30 mL), water (30 mL), sat. sodium bicarbonate (30 mL), water (30 mL), brine (30 mL) then dried over magnesium sulfate and concentrated at reduced pressure to yield a yellow–brown solid. Further purification by flash column chromatography using 3 : 7 ethyl acetate–hexane as eluent gave the title compound **21** (65 mg, 73%) as a yellow solid, mp 108–109 °C, lit.[11] mp 109–109.5 °C. The ^{1}H and ^{13}C NMR data were in agreement with those reported in the literature.[11]

7-Hydroxy-4,5-dimethoxynaphthalen-1-yl acetate (24)

A solution of 7-benzyloxy-4,5-dimethoxynaphthalen-1-yl acetate **21** (63 mg, 0.179 mmol) in ethyl acetate (8 mL) was stirred under an atmosphere of hydrogen over palladium on charcoal (10%, 80 mg, 0.75 mmol). After 5 h, the mixture was filtered through Celite and the solvent was removed *in vacuo* to give a green-white solid. The solid was purified by flash column chromatography using gradient elution (from 3 : 7 to 6 : 4 to 8 : 2 ethyl acetate-hexane) to afford the *title compound* **24** (38 mg, 81%) as a colourless solid, mp 178–180 °C [Found (EI): M^+, 262.0840; $C_{14}H_{14}O_5$ requires M^+, 262.0841]; ν_{max}(CH_2Cl_2 solution) 3200 (OH), 1765 (C=O) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.35 (3 H, s, $COCH_3$), 3.88 (3 H, s, 4-OCH_3), 3.93 (3 H, s, 5-OCH_3), 5.71 (1 H, s, OH), 6.47 (1 H, d, $J_{6,8}$ 2.3 Hz, H-6), 6.62 (1 H, d, $J_{3,2}$ 8.5 Hz, H-3), 6.64 (1 H, d, $J_{8,6}$2.3 Hz, H-8), 7.06 (1 H, d, $J_{2,3}$ 8.5 Hz, H-2); δ_C (50 MHz, $CDCl_3$) 20.9 (CH_3, $COCH_3$), 56.3 (CH_3, OCH_3), 56.5 (CH_3, OCH_3), 95.9 (CH, C-8), 98.9 (CH, C-6), 102.9 (CH, C-3), 113.6 (quat., C-4a), 119.2 (CH, C-2), 130.9 (quat., C-8a), 139.0 (quat., C-1), 155.0 (quat., C-4), 155.4 (quat., C-7), 159.1 (quat., C-5), 170.2 (quat., C=O); *m*/*z* 262 (M^+, 28%), 220 (M − C_2H_2O, 100), 205 (7), 177 (11), 147 (7).

4,5-Dimethoxy-7-trifluoromethanesulfonyloxynaphthalen-1-yl acetate (15)

Trifluoromethanesulfonic anhydride (0.007 mL, 0.04 mmol) was added to a mixture of 7-hydroxy-4,5-dimethoxynaphthalen-1-yl acetate **24** (8.6 mg, 0.033 mmol) and dry triethylamine (0.006 mL, 0.04 mmol) in dry dichloromethane (0.8 mL). The mixture was stirred at −20 °C for 18.5 h, then the solvent was removed under reduced pressure and chloroform (50 mL) added. The organic layer was washed with water (25 mL) and separated. The aqueous layer was extracted with chloroform (50 mL). The combined organic layers were dried over magnesium sulfate and concentrated at reduced pressure to give a dark brown–orange oil which was purified by flash column chromatography using 3 : 7 ethyl acetate–hexane as eluent to give the *title compound* **15** (10.6 mg, 82%) as a colourless solid, mp 132–134 °C (Found: C, 45.9; H, 3.6. $C_{15}H_{13}F_3O_7S$ requires C, 45.7; H, 3.3%) [Found (EI): M^+, 394.0331; $C_{15}H_{13}F_3O_7S$ requires M^+, 394.0334]; ν_{max}(CH_2Cl_2 solution) 1763 (C=O), 1422 (SO_2–O), 1215 (C–F), 1040 (C–O) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.42 (3 H, s, $COCH_3$), 3.94 (3 H, s, 4-OCH_3), 3.97 (3 H, s, 5-OCH_3), 6.69 (1 H, d, $J_{6,8}$ 2.2 Hz, H-6), 6.85 (1 H, d, $J_{3,2}$ 8.3 Hz, H-3), 7.24 (1 H, d, $J_{2,3}$ 8.3 Hz, H-2), 7.25 (1 H, d, $J_{8,6}$ 2.2 Hz, H-8); δ_C (50 MHz, $CDCl_3$) 20.9 (CH_3, $COCH_3$), 56.7 (CH_3, 2 × OCH_3), 100.2 (CH, C-8), 104.9 (CH, C-6), 106.4 (CH, C-3), 117.3 (quat., C-4a), 120.5 (CH, C-2), 129.7 (quat., C-8a), 139.7 (quat., C-1), 148.1 (quat., C-4), 155.4 (quat., C-7), 159.7 (quat., C-5), 169.5 (quat., C=O); *m*/*z* 394 (M^+, 14%), 352 (M − C_3H_6, 100), 191 (67).

(7-Benzyloxy-4,5-dimethoxynaphthalen-1-yloxy)-*tert*-butyl-dimethylsilane (22)

tert-Butylchlorodimethylsilane (61.2 mg, 0.406 mmol) was added to a solution of 7-benzyloxy-4,5-dimethoxynaphthalen-1-ol **18** (70 mg, 0.226 mmol), imidazole (38.4 mg, 0.564 mmol) and 4-(dimethylamino)pyridine (5%) (1.38 mg, 0.0113 mmol) in dry dichloromethane (4.5 mL). The mixture was stirred at room temperature under nitrogen for 20 h. The reaction mixture was diluted with dichloromethane (10 mL), washed with brine (10 mL) then dried over magnesium sulfate and concentrated *in vacuo* to give a yellow–green oil. Further purification by flash column chromatography using 1 : 9 ethyl acetate–hexane as eluent gave the *title compound* **22** (64 mg, 67%) as a pale yellow solid, mp 93–94 °C [Found (EI): M^+, 424.2072; $C_{25}H_{32}O_4Si$ requires M^+, 424.2070]; ν_{max}(CH_2Cl_2 solution) 1620 (C=C) 1252 (SiMe), 1061 (Si–O), 838 ($SiMe_2$) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.25 (6 H, s, $SiCH_3$), 1.10 (9 H, s, *t*-Bu), 3.92 (3 H, s, 4-OCH_3), 3.96 (3 H, s, 5-OCH_3), 5.18 (2 H, s, OCH_2), 6.61 (1 H, d, $J_{3,2}$ 8.4 Hz, H-3), 6.66 (1 H, d, $J_{6,8}$ 2.4 Hz, H-6), 6.79 (1 H, d, $J_{2,3}$ 8.4 Hz, H-2), 7.22 (1 H, d, $J_{8,6}$ 2.4 Hz, H-8), 7.34–7.54 (5 H, m, PhH); δ_C (50 MHz, $CDCl_3$) −4.3 (CH_3, $SiCH_3$), 18.3 (quat., *t*-Bu), 25.9 (CH_3, *t*-Bu), 56.3 (CH_3, OCH_3), 57.0 (CH_3, OCH_3), 69.8 (CH_2, OCH_2), 94.8 (CH, C-6), 99.5 (CH, C-8), 104.6 (CH, C-3), 113.4 (CH, C-2), 114.2 (quat., C-4a), 127.6 (CH, C-2′ and C-6′), 128.0 (CH, C-4′), 128.6 (CH, C-3′ and C-5′), 131.6 (quat., C-8a), 136.8 (quat., C-1′), 144.4 (quat., C-1), 151.6 (quat., C-4), 157.0 (quat., C-7), 158.3 (quat., C-5); *m*/*z* 424 (M^+, 100%), 409 (M − CH_3, 2), 305 (84), 91 (39), 73 (26).

8-(*tert*-Butyldimethylsilyloxy)-4,5-dimethoxynaphthalen-2-ol (25)

A solution of benzyl ether **22** (1.36 g, 3.21 mmol) in ethyl acetate (80 mL) was stirred over palladium on charcoal (10%, 1.43 g, 13.5 mmol) under an atmosphere of hydrogen. After 1 h, the mixture was filtered through Celite and the solvent removed *in vacuo* to give a pale green solid. The solid was purified by flash column chromatography using gradient elution (from 2.5 : 7.5 to 3 : 7 ethyl acetate–hexane) to afford the *title compound* **25** (0.96 g, 89%) as a colourless solid, mp 222.2–224 °C [Found (EI): M^+, 334.1599; $C_{18}H_{26}O_4Si$ requires M^+, 334.1600]; ν_{max}-(CH_2Cl_2 solution) 3370 (O–H), 1635 (C=C), 1275 (SiMe), 1054 (SiO), 842 ($SiMe_2$) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.244 (6 H, s, $SiCH_3$), 1.07 (9 H, s, *t*-Bu), 3.89 (3 H, s, 5-OCH_3), 3.94 (3 H, s, 4-OCH_3), 5.10 (1 H, s, OH), 6.51 (1 H, d, $J_{3,1}$ 2.4 Hz, H-3), 6.55 (1 H, d, $J_{6,7}$ 8.4 Hz, H-6), 6.73 (1 H, d, $J_{7,6}$ 8.4 Hz, H-7), 7.06 (1 H, d, $J_{1,3}$ 2.4 Hz, H-1); δ_C (100 MHz, $CDCl_3$) −4.2 (CH_3,

$SiCH_3$), 18.4 (quat., *t*-Bu), 26.0 (CH_3, *t*-Bu), 56.4 (CH_3, OCH_3), 57.0 (CH_3, OCH_3), 97.6 (CH, C-1), 98.5 (CH, C-3), 104.3 (CH, C-6), 113.2 (CH, C-7), 114.1 (quat., C-4a), 131.8 (quat., C-8a), 144.2 (quat., C-8), 151.6 (quat., C-5), 153.7 (quat., C-4), 158.8 (quat., C-2); *m*/*z* 334 (M^+, 100%), 319 ($M - CH_3$, 10), 277 (60), 246 (22), 73 (37).

8-(*tert*-Butyldimethylsilyloxy)-4,5-dimethoxynaphthalen-2-yl trifluoromethanesulfonate (16)

Trifluoromethanesulfonic anhydride (0.45 mL, 2.69 mmol) was added to a mixture of naphthol **25** (0.5 g, 1.49 mmol) and dry triethylamine (0.38 mL, 2.69 mmol) in dry dichloromethane (80 mL). The mixture was stirred at −20 °C for 23.5 h, concentrated *in vacuo* and chloroform (100 mL) added. The organic layer was washed with water (80 mL) and separated. The aqueous layer was extracted with chloroform (100 mL). The combined organic extracts were dried over magnesium sulfate and concentrated at reduced pressure to give a dark pink oil which was purified by flash column chromatography using 2 : 8 ethyl acetate–hexane as eluent to give the *title compound* **16** (0.67 g, 96%), as a pale yellow solid, mp 64–66 °C (Found: C, 48.8; H, 5.5. $C_{19}H_{25}F_3O_6SSi$ requires C, 48.9; H, 5.4%) [Found (EI): M^+, 466.1599; $C_{19}H_{25}F_3O_6SSi$ requires M^+, 466.1600]; ν_{max}(CH_2Cl_2 solution) 1422 (SO_2–O), 1383 [$C(CH_3)_3$], 1266 (SO_2–O), 1215 (C–F), 1051 (C–O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.24 (6 H, s, $SiCH_3$), 1.07 (9 H, s, *t*-Bu), 3.90 (3 H, s, 5-OCH_3), 3.99 (3 H, s, 4-OCH_3), 6.70 (1 H, d, $J_{3,1}$ 2.4 Hz, H-3), 6.78 (1 H, d, $J_{6,7}$ 8.5 Hz, H-6), 6.86 (1 H, d, $J_{7,6}$ 8.5 Hz, H-7), 7.67 (1 H, d, $J_{1,3}$ 2.4 Hz, H-1); δ_C (100 MHz, $CDCl_3$) −4.4 (CH_3, $SiCH_3$), 18.3 (quat., *t*-Bu), 25.8 (CH_3, *t*-Bu), 56.7 (CH_3, OCH_3), 57.3 (CH_3, OCH_3), 100.3 (CH, C-1), 106.5 (CH, C-3), 108.2 (CH, C-6), 114.4 (CH, C-7), 117.7 (quat., C-4a), 120.4 (quat., C-8a), 130.4 (quat., C-8), 145.3 (quat., C-5), 147.3 (quat., C-4), 151.5 (quat., C–F), 159.1 (quat., C-2); *m*/*z* 466 (M^+, 100%), 319 (M, 10), 277 (60), 246 (22), 73 (37).

2-[8-(*tert*-Butyldimethylsilyloxy)-4,5-dimethoxynaphthalen-2-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (30)

A mixture of potassium acetate (63.1 mg, 0.643 mmol), dry dioxane (1.8 mL), $PdCl_2$(dppf) (5.3 mg, 0.0064 mmol), dppf (3.6 mg, 0.0064 mmol), bis(pinacolato)diboron (0.0599 mg, 0.236 mmol) and triflate **16** (100 mg, 0.214 mmol) was heated under argon, with stirring at reflux for 1.5 h. The reaction mixture was diluted with ethyl acetate (30 mL), washed with water (10 mL), dried over magnesium sulfate and concentrated *in vacuo* to a yellow–brown oil. Further purification by flash column chromatography using gradient elution (from 1 : 9 to 1.5 : 8.5 ethyl acetate–hexane) as eluent to give the *title compound* **30** (76 mg, 80%) as a light yellow-green oil [Found (EI): M^+, 444.2501; $C_{24}H_{37}BO_5Si$ requires M^+, 444.2503]; ν_{max}(neat) 1595 (C=C), 1380 [$C(CH_3)_3$], 1339 (B–O), 1264 (B–C and SiMe), 1052 (SiO), 839 ($SiMe_2$) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.23 (6 H, s, $SiCH_3$), 1.12 (9 H, s, *t*-Bu), 1.37 (12 H, s, 4 × CH_3), 3.91 (3 H, s, 5-OCH_3), 4.02 (3 H, s, 4-OCH_3), 6.78 (2 H, s, H-6 and H-7), 7.20 (1 H, s, H-3), 8.38 (1 H, s, H-1); δ_C (100 MHz, $CDCl_3$) −4.4 (CH_3, $SiCH_3$), 18.4 (quat., *t*-Bu), 24.9 (CH_3,*t*-Bu), 25.9 (CH_3, $CH_3$of boronate), 56.5 (CH_3, OCH_3), 57.4 (CH_3, OCH_3), 83.7 (quat., boronate), 108.5 (CH, C-6), 110.4 (CH, C-3), 113.0 (CH, C-7), 120.1 (quat., C-4a), 124.4 (CH, C-1), 126.0 (quat., C-8a), 130.5 (quat., C-2), 146.0 (quat., C-5), 151.2 (quat., C-8), 156.1 (quat., C-4); *m*/*z* 444 (M^+, 100%), 429 [$M - (CH_3)$, 5], 372 (11), 287 (43), 73 (27).

8,8′-Bis(*tert*-butyldimethylsilyloxy)-4,5,4′,5′-tetramethoxy-2,2′-binaphthalenyl (31)

a) Stepwise homocoupling of triflate 16 and boronate 30. To a solution of boronate **30** (93.5 mg, 0.210 mmol) in dry dioxane (3 mL) was added potassium phosphate (0.134 g, 0.631 mmol), $PdCl_2$(dppf) (5.2 mg, 0.0063 mmol) and triflate **16** (98 mg, 0.21 mmol). The mixture was heated under reflux under argon for 15 h. The reaction mixture was concentrated *in vacuo*, diluted with ethyl acetate (100 mL), washed with water (50 mL) and brine (50 mL) then dried over magnesium sulfate and concentrated *in vacuo* to give a dark green oil. Further purification by flash column chromatography using gradient elution (from 1 : 9 to 1.5 : 8.5 to 5 : 5 ethyl acetate–hexane) yielded *1-tert-butyldimethylsilyloxy-4,5-dimethoxynaphthalene* **33** (3 mg, 4%) as a light brown oil [Found (EI): M^+, 318.1652; $C_{18}H_{26}O_3Si$ requires M^+, 318.1651]; *m*/*z* 318 (M^+, 100%), 261 [$M - (C_4H_9)$, 64], 246 (10), 203 (7), 73(50).

8,8′-Bis(tert-butyldimethylsilyloxy)-4,5,4′,5′-tetramethoxy-2,2′-binaphthalenyl **31** (29 mg, 22%) as a colourless solid, mp 205–207 °C [Found (EI): M^+, 634.3144; $C_{36}H_{50}O_6Si_2$ requires M^+, 634.3146]; ν_{max}(CH_2Cl_2 solution) 1592 (C=C), 1381 [$C(CH_3)_3$], 1264 (SiMe), 1046 (SiO), 839 ($SiMe_2$) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.29 (6 H, s, $SiCH_3$), 1.12 (9 H, s, *t*-Bu), 3.96 (3 H, s, 4-OCH_3), 4.08 (3 H, s, 5-OCH_3), 6.75 (1 H, d, $J_{6,7}$ 8.2 Hz, H-6), 6.82 (1 H, d, $J_{7,6}$ 8.2 Hz, H-7), 7.33 (1 H, s, H-3), 8.18 (1 H, s, H-1); δ_C (100 MHz, $CDCl_3$) −4.3 (CH_3, $SiCH_3$), 18.4 (quat., *t*-Bu), 26.0 (CH_3, *t*-Bu), 56.3 (CH_3, OCH_3), 57.3 (CH_3, OCH_3), 105.8 (CH, C-3), 107.1 (CH, C-6), 113.1 (CH, C-7), 113.6 (CH, C-1), 117.8 (quat., C-4a), 131.2 (quat., C-8a), 138.1 (quat., C-2), 145.7 (quat., C-5), 151.3 (quat., C-8), 157.4 (quat., C-4); *m*/*z* 634 (M^+, 100%), 577 [$M - (C_4H_9)$, 8], 497 (9), 440 (11), 371 (8), 73 (31).

8′-(tert-Butyldimethylsilyloxy)-4,5,4′,5′-tetramethoxy-2,2′-binaphthalenyl-8-ol **32** (18 mg, 16%) as a light yellow oil [Found (EI): M^+, 520.2284; $C_{30}H_{36}O_6Si$ requires M^+, 520.2281]; ν_{max}-(CH_2Cl_2 solution) 3412 (O–H), 1594 (C=C), 1382 [$C(CH_3)_3$], 1270 (SiMe), 1058 (SiO), 838 ($SiMe_2$) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.28 (6 H, s, $SiCH_3$), 1.12 (9 H, s, *t*-Bu), 3.94 (3H, s, 5-OCH_3), 3.95 (3 H, s, 5′-OCH_3), 4.076 (3 H, s, 4′-OCH_3), 4.084 (3 H, s, 4-OCH_3), 5.25 (1 H, br s, OH), 6.72 (1 H, d, $J_{6,7}$ 8.8 Hz, H-6), 6.74 (1 H, d, $J_{6',7'}$ 8.8 Hz, H-6′), 6.80 (1 H, d, $J_{7,6}$ 8.8 Hz, H-7), 6.82 (1 H, d, $J_{7',6'}$ 8.8 Hz, H-7′), 7.32 (1 H, d, $J_{3,1}$ 1.5 Hz, H-3), 7.33 (1 H, d, $J_{3',1'}$ 1.5 Hz, H-3′), 8.16 (1 H, d, $J_{1,3}$ 1.5 Hz, H-1), 8.19 (1 H, d, $J_{1',3'}$ 1.5 Hz, H-1′); δ_C (100 MHz, $CDCl_3$) −4.3 (CH_3, $SiCH_3$), 18.4 (quat., *t*-Bu), 26.0 (CH_3,*t*-Bu), 56.4 (CH_3, OCH_3), 56.8 (CH_3, OCH_3), 57.4 (CH_3, OCH_3), 57.5 (CH_3, OCH_3), 106.3 (CH, C-3′), 106.4 (CH, C-3), 107.3 (CH, C-6′), 107.4 (CH, C-6), 109.4 (CH, C-7′), 112.7 (CH, C-7), 113.2 (CH, C-1′), 114.0 (CH, C-1), 117.7 (quat., C-4a′), 118.0 (quat., C-4a), 128.0 (quat., C-8a), 131.2 (quat., C-8a′), 138.1 (quat., C-2′), 138.5 (quat., C-2), 145.7 (quat., C-5′), 145.9 (quat., C-5), 151.0 (quat., C-8), 151.2 (quat., C-8′), 157.3 (quat., C-4), 157.4 (quat., C-4′); *m*/*z* 520 (M^+, 96%), 505 [$M - (CH_3)$, 6], 463 [$M - (C_4H_9)$,15], 371 (12), 330 (20), 127 (34), 99 (31), 59 (73), 57 (100).

b) Generation of boronate 30 followed by *in situ* coupling with triflate 16. A mixture of potassium acetate (63.1 mg, 0.643 mmol), dry dioxane (1.8 mL), $PdCl_2$(dppf) (5.3 mg, 0.0064 mmol), dppf (3.6 mg, 0.0064 mmol), bis(pinacolato)-diboron (59.9 mg, 0.236 mmol) and triflate **16** (100 mg, 0.214 mmol) was heated under argon, with stirring at reflux for 1 h. Potassium phosphate (137 mg, 0.8643 mmol), $PdCl_2$(dppf) (5.3 mg, 0.0064 mmol) and triflate **16** (100 mg, 0.214 mmol) were then added and the resultant mixture heated with stirring at reflux for 20.5 h. The reaction mixture was diluted with ethyl acetate (30 mL), washed with water (10 mL), dried over magnesium sulfate and concentrated *in vacuo* to a dark brown oil. Further purification by flash column chromatography using gradient elution (from 1 : 9 to 2 : 8 to 3 : 7 to 5 : 5 ethyl acetate–hexane) yielded binaphthyl **31** (34 mg, 22%) as an off-white solid, mp 205–207 °C for which the ^1H NMR data were in agreement with that reported above and binaphthyl **32** (27 mg, 24%) as a yellow oil for which the ^1H NMR data were in agreement with that reported above.

3-Benzyloxy-5-isopropoxy-1,8-dimethoxynaphthalene (23)

A mixture of 7-benzyloxy-4,5-dimethoxynaphthalen-1-ol **18** (110 mg, 0.354 mmol) and sodium hydride (25.4 mg, 1.06 mmol) in dry *N*,*N*-dimethylformamide (12 mL) was stirred at room temperature under a nitrogen atmosphere for 1 h. 2-Bromopropane (0.17 mL, 1.77 mmol) was then added and the reaction mixture left to stir at room temperature for 4.5 h. The reaction mixture was poured into water (3 mL) and extracted with ethyl acetate (4 × 30 mL). The combined organic extracts were washed with water (50 mL) and brine (50 mL) then dried over magnesium sulfate and evaporated to dryness to give a brownish-yellow oil, which was purified by flash column chromatography using 2 : 8 ethyl acetate–hexane as eluent to give the *title compound* **23** (0.11 g, 89%) as a light yellow solid, mp 79.5–81.5 °C [Found (EI): M^+, 352.1672; $C_{22}H_{24}O_4$ requires M^+, 352.1675]; ν_{max}(CH_2Cl_2 solution) 1620 (C=C), 1382 [$C(CH_3)_2$], 1059 (C–O) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.38 (6 H, d, *J* 6.5 Hz, CH_3 of isopropyl), 3.91 (3 H, s, 8-OCH_3), 3.94 (3 H, s, 1-OCH_3), 4.53 (1 H, septet, *J* 6.5 Hz, CH of isopropyl), 5.19 (2 H, s, OCH_2), 6.62 (1 H, d, $J_{7,6}$ 8.5 Hz, H-7), 6.63 (1 H, d, $J_{2,4}$ 2.4 Hz, H-2), 6.78 (1 H, d, $J_{6,7}$ 8.5 Hz, H-6), 7.27 (1 H, d, $J_{4,2}$ 2.4 Hz, H-4), 7.36–7.53 (5 H, m, PhH); δ_C(50 MHz, $CDCl_3$) 22.3 (CH_3, 2 × CH_3 of isopropyl), 56.3 (CH_3, OCH_3), 57.2 (CH_3, OCH_3), 70.0 (CH_2, OCH_2), 71.5 (CH, CH of isopropyl), 94.8 (CH, C-2), 99.6 (CH, C-4), 104.6 (CH, C-7), 109.4 (CH, C-6), 114.8 (quat., C-8a), 127.8 (CH, C-2′ and C-6′), 128.0 (CH, C-4′), 128.6 (CH, C-3′ and C-5′), 130.8 (quat., C-4a), 137.0 (CH, C-1′), 146.9 (quat., C-5), 151.3 (quat., C-8), 157.0 (quat., C-3), 158.2 (quat., C-1); *m*/*z* 352 (M^+, 42%), 309 [M − $CH(CH_3)_2$, 37], 281 (M − C_3H_7CO, 1), 219 (13), 191 (19), 149 (5), 91 (100).

8-Isopropoxy-4,5-dimethoxynaphthalen-2-ol (26)

A solution of 3-benzyloxy-5-isopropoxy-1,8-dimethoxynaphthalene **23** (88.3 mg, 0.251 mmol) in ethyl acetate (8 mL) was stirred under an atmosphere of hydrogen over 10% palladium on charcoal (112 mg, 1.05 mmol). After 1.5 h, the mixture was filtered through Celite and the solvent removed *in vacuo* to give a green–white solid. The solid was purified by flash column chromatography using gradient elution (from 3 : 7 to 6 : 4 to 8 : 2 ethyl acetate–hexane) to afford the *title compound* **26** (50 mg, 78%) as a pale yellow green solid, mp 161–163 °C [Found (EI): M^+, 262.12052; $C_{15}H_{18}O_4$ requires M^+, 262.12051]; ν_{max}(CH_2Cl_2 solution) 3370 (OH), 1384 [$C(CH_3)_2$], 1051 (C–O) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.36 (6 H, d, *J* 6.1 Hz, CH_3 of isopropyl), 3.86 (3 H, s, 5-OCH_3), 3.89 (3 H, s, 4-OCH_3), 4.54 (1 H, septet, *J* 6.1 Hz, CH of isopropyl), 5.66 (1 H, s, OH), 6.49 (1H, d, $J_{3,1}$ 2.3 Hz, H-3), 6.59 (1 H, d, $J_{6,7}$ 8.5 Hz, H-6), 6.74 (1 H, d, $J_{7,6}$ 8.5 Hz, H-7), 7.18 (1 H, d, $J_{1,3}$ 2.3 Hz, H-1); δ_C (50 MHz, $CDCl_3$) 22.2 (CH_3, 2 × CH_3 of isopropyl), 56.2 (CH_3, OCH_3), 57.1 (CH_3, OCH_3), 71.2 (CH, CH of isopropyl), 97.4 (CH, C-3), 98.7 (CH, C-1), 104.3 (CH, C-6), 109.0 (CH, C-7), 113.9 (quat., C-4a), 131.0 (quat., C-8a), 146.5 (quat., C-8), 151.2 (quat., C-5), 154.0 (quat., C-2), 158.5 (quat., C-4); *m*/*z* 262 (M^+, 59%), 219 [M − $CH(CH_3)_2$, 100], 205 (12), 191 (M − C_3H_7CO, 8), 177 (25), 147 (8), 45 (9).

8-Isopropoxy-4,5-dimethoxynaphthalen-2-yl trifluoromethanesulfonate 17

To a solution of 8-isopropoxy-4,5-dimethoxynaphthalen-2-ol **26** (10.4 mg, 0.040 mmol) in dry dichloromethane (1 mL) was added dry triethylamine (0.011 mL, 0.079 mmol), *N*-phenyltrifluoromethanesulfonimide (17 mg, 0.048 mmol) and 4-(dimethylamino)pyridine (2 mg) and the mixture stirred at −25 °C under an atmosphere of nitrogen for 15 h. The mixture was poured into water (2 mL), and extracted with chloroform (25 mL). The organic extract was washed with dilute HCl (10 mL) and water (10 mL) then dried over magnesium sulfate and concentrated *in vacuo* to give a green solid. This solid was purified by flash column chromatography using 2 : 8 ethyl acetate–hexane as eluent to give the *title compound* **17** (14 mg, 91%) as a pale yellow solid, mp 58–60 °C (Found: C, 48.6; H, 4.2. $C_{16}H_{17}F_3O_6S$ requires C, 48.7; H, 4.3) [Found (EI): M^+, 394.0696; $C_{16}H_{17}F_3O_6S$ requires M^+, 394.0698]; ν_{max}(CH_2Cl_2 solution) 1421 (SO_2–O), 1383 [$C(CH_3)_2$], 1265 (SO_2–O), 1216 (C–F), 1050 (C–O) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.40 (6 H, d, *J* 6.1 Hz, CH_3 of isopropyl), 3.91 (3 H, s, 5-OCH_3), 3.98 (3 H, s, 4-OCH_3), 4.60 (1 H, septet, *J* 6.1 Hz, CH of isopropyl), 6.70 (1 H, d, $J_{3,1}$ 2.4 Hz, H-3), 6.82 (1 H, d, $J_{6,7}$ 8.3 Hz, H-6), 6.87 (1 H, d, $J_{7,6}$ 8.3 Hz, H-7), 7.74 (1 H, d, $J_{1,3}$ 2.4 Hz, H-1); δ_C (50 MHz, $CDCl_3$) 22.1 (CH_3, 2 × CH_3 of isopropyl), 56.6 (CH_3, OCH_3), 57.4 (CH_3, OCH_3), 71.8 (CH, CH of isopropyl), 100.3 (CH, C-6), 106.5 (CH, C-7), 108.3 (CH, C-3), 109.8 (CH, C-1), 117.7 (quat., C-4a), 129.4 (quat., C-8a), 147.3 (quat., C-2), 147.6 (quat., C-8), 151.0 (quat., C-5), 158.9 (quat., C-4); *m*/*z* 394 (M^+, 29%), 352 (M − C_3H_6,65), 219 (7), 191 (100), 175 (10), 147 (8), 119 (5), 91(7).

2-(8-Isopropoxy-4,5-dimethoxynaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (34)

To a stirred solution of $PdCl_2$(dppf) (43 mg, 0.0053 mmol) in dry 1,2-dichloroethane (0.52 mL), was added triflate **17** (35 mg, 0.089 mmol), dry triethylamine (0.074 mL, 0.533 mmol) and pinacolborane (0.040 mL, 0.266 mmol) under an atmosphere of argon and the mixture heated with stirring at reflux for 1.5 h. The reaction mixture was extracted with ethyl acetate (2 × 20 mL). The combined organic extracts were washed with water (10 mL), dried over magnesium sulfate then concentrated *in vacuo* to give a dark brown oil. Further purification by flash column chromatography on florisil using gradient elution (from hexane to 5 : 95 ethyl acetate–hexane) yielded *1-isopropoxy-4,5-dimethoxynaphthalene* **36** (3 mg) as a light yellow oil [Found (EI): M^+, 246.1258; $C_{15}H_{18}O_3$ requires M^+, 246.1256]; δ_H (400 MHz, $CDCl_3$) 1.41 (6 H, d, *J* 6.1 Hz, CH_3 of isopropyl), 3.92 (3 H, s, 4-OCH_3), 3.97 (3H, s, 5-OCH_3), 4.61 (1 H, septet, *J* 6.1 Hz, CH of isopropyl), 6.79 (2 H, m, H-2, H-3), 6.90 (1 H, d, $J_{6,7}$ 7.6 Hz, H-6), 7.37 (1 H, dd, $J_{7,6}$ and $J_{7,8}$ 8.1 Hz, H-7), 7.88 (1 H, d, $J_{8,7}$ 8.1 Hz, H-8); δ_C (100 MHz, $CDCl_3$) 22.2 (CH_3, 2 × CH_3 of isopropyl), 56.5 (CH_3, OCH_3), 57.5 (CH_3, OCH_3), 71.2 (CH, CH of isopropyl), 107.0 (CH, C-3), 107.1 (CH, C-6), 108.2 (CH, C-2), 115.1 (CH, C-8), 118.7 (quat., C-4a), 125.7 (CH, C-7), 130.1 (quat., C-8a), 147.7 (quat., C-4), 150.9 (quat., C-1), 156.8 (quat., C-5); *m*/*z* 246 (M^+, 63%), 204 (M − C_3H_6, 100), 189 (16), 161 (17), 131 (13), 115 (10).

2-(8-Isopropoxy-4,5-dimethoxynaphthalen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **34** (43 mg, 50%) as a colourless oil [Found (EI): M^+, 372.2107; $C_{21}H_{29}BO_5$ requires M^+, 372.2108]; ν_{max}(neat) 1598 (C=C), 1379 [$C(CH_3)_2$], 1343 (B–O), 1265 (B–C) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.38 (12 H, s, 4 × CH_3), 1.43 (6 H, d, *J* 6.1 Hz, CH_3 of isopropyl), 3.90 (3 H, s, 5-OCH_3), 4.01 (3 H, s, 4-OCH_3), 4.63 (1 H, septet, *J* 6.1 Hz, CH of isopropyl), 6.76 (1 H, d, $J_{6,7}$ 8.5 Hz, H-6), 6.82 (1 H, d, $J_{7,6}$ 8.5 Hz, H-7), 7.23 (1 H, br s, H-3), 8.37 (1 H, br s, H-1); δ_C (100 MHz, $CDCl_3$) 22.1 (CH_3, CH_3 of isopropyl), 24.9 (CH_3, CH_3 of boronate), 56.5 (CH_3, OCH_3), 57.6 (CH_3, OCH_3), 70.8 (CH, CH of isopropyl), 83.8 (quat., boronate), 107.4 (CH, C-6), 108.7 (CH, C-3), 111.0 (CH, C-7), 123.2 (CH, C-1), 127.6 (C-4a), 128.1 (quat., C-2), 129.3 (quat., C-8a), 148.3 (quat., C-5), 150.5 (quat., C-8), 155.9 (quat., C-4); *m*/*z* 262 (M^+, 59%), 219 [M − $CH(CH_3)_2$,100], 205 (12), 191 (M − C_3H_7CO, 8), 177 (25), 147 (8), 45 (9).

8,8′-Diisopropoxy-4,5,4′,5′-tetramethoxy-2,2′-binaphthalenyl (35)

a) Stepwise homocoupling of triflate 17 and boronate 34. To a solution of boronate **34** (40 mg, 0.107 mmol) in dry dioxane (0.7 mL) was added potassium phosphate (68 mg, 0.32 mmol), $PdCl_2$(dppf) (2.6 mg, 0.003 mmol) and triflate **17** (40 mg, 0.101

mmol). The mixture was heated under reflux under argon for 21.5 h. The reaction mixture was concentrated *in vacuo*, diluted with ethyl acetate (50 mL), washed with water (30 mL) and brine (30 mL) then dried over magnesium sulfate and concentrated *in vacuo* to give a dark brown oil. Further purification by flash column chromatography using 2 : 8 ethyl acetate–hexane as eluent yielded binaphthyl **35** (29 mg, 59%) as a yellow solid, mp 133.5–135 °C (Found: C, 73.2; H, 6.9. $C_{30}H_{34}O_6$ requires C, 73.5; H, 7.0) [Found (EI): M^+, 490.2364; $C_{30}H_{34}O_6$ requires M^+, 490.2355]; $\nu_{max}(CH_2Cl_2$ solution) 1596 (C=C), 1382 [$C(CH_3)_2$], 1059 (C–O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.45 (6 H, d, *J* 6.0 Hz, CH_3 of isopropyl), 3.96 (3 H, s, 5-OCH_3), 4.09 (3 H, s, 4-OCH_3), 4.63 (1 H, septet, *J* 6.0 Hz, CH of isopropyl), 6.80 (1 H, d, $J_{6,7}$ 8.4 Hz, H-6), 6.86 (1 H, d, $J_{7,6}$ 8.4 Hz, H-7), 7.29 (1 H, d, $J_{3,1}$ 1.4 Hz, H-3), 8.25 (1 H, d, $J_{1,3}$ 1.4 Hz, H-1); δ_C (100 MHz, $CDCl_3$) 22.3 (CH_3, CH_3 of isopropyl), 56.8 (CH_3, OCH_3), 57.5 (CH_3, OCH_3), 71.7 (CH, CH of isopropyl), 106.8 (CH, C-6), 107.2 (CH, C-7), 109.2 (CH, C-3), 113.7 (CH, C-1), 117.9 (quat., C-4a), 130.4 (quat., C-8a), 138.6 (quat., C-2), 148.1 (quat., C-8), 151.0 (quat., C-5), 157.2 (quat., C-4); *m*/*z* 490 (M^+, 100%), 447 [$M - CH(CH_3)_2$,70], 405 (66), 390 (45), 203 (30), 199 (7), 129 (8), 69 (22).

b) Generation of boronate 34 followed by *in situ* coupling with triflate 17. A mixture of potassium acetate (86 mg, 0.88 mmol), dry dioxane (2 mL), $PdCl_2$(dppf) (7.1 mg, 0.0088 mmol), dppf (4.9 mg, 0.0088 mmol), bis(pinacolato)diboron (81.5 mg, 0.321 mmol) and triflate **17** (115 mg, 0.292 mmol) was heated under argon, with stirring at reflux for 1.5 h. Potassium phosphate (186 mg, 0.875 mmol), $PdCl_2$(dppf) (7.1 mg, 0.009 mmol) and triflate 17 (115 mg, 0.292 mmol) were then added and the resultant mixture heated with stirring at reflux for 18 h. The reaction mixture was diluted with ethyl acetate (30 mL), washed with water (10 mL), dried over magnesium sulfate and concentrated *in vacuo* to afford a dark brown oil. Further purification by flash column chromatography using 2 : 8 ethyl acetate–hexane as eluent yielded binaphthyl **35** (110 mg, 77%) as a yellow solid, mp 133.5–135 °C for which the ^{1}H NMR data were in agreement with that reported above.

4,4′-Dimethoxy-2,2′-binaphthalenyl-5,8,5′,8′-tetraone (38)

Binaphthyl **35** (26 mg, 0.053 mmol) and freshly prepared AgO (105 mg, 0.848 mmol) were mixed in dioxane (4 mL). To this was added HNO_3 (0.074 mL of a 6 M solution) and the reaction mixture stirred for 10 min, after which time further AgO (105 mg, 0.848 mmol) and HNO_3 (0.074 mL of a 6 M solution) were added. After stirring an additional 10 min the reaction mixture was quenched with water (8 mL) and extracted into dichloromethane (4 × 15 mL). The organic layer was washed with water (30 mL), dried over magnesium sulfate and the solvent removed under reduced pressure to yield the *title compound* **38** (21 mg) as an orange oil which was not purified further [Found (EI): M^+, 374.0784; $C_{22}H_{14}O_6$ requires M^+, 374.0790]; ν_{max}(neat) 1656 (C=O, quinone), 1594 (C=C) and 1017 (C–O) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.12 (3 H, s, OCH_3), 6.93 (2 H, s, H-6 and H-7), 7.53 (1 H, d, $J_{3,1}$ 1.4 Hz, H-3), 7.99 (1 H, d, $J_{1,3}$ 1.4 Hz, H-1); *m*/*z* 374 (M^+, 41%), 357 (4).

8′-Acetoxy-5,5′-dihydroxy-4,4′-dimethoxy-2,2′-binaphthalenyl-8-yl acetate (39)

Bis-naphthoquinone **38** (22 mg, 0.059 mmol) in dry chloroform (2 mL) was treated with acetic anhydride (0.03 mL, 0.317 mmol), dry pyridine (0.03 mL, 0.364 mmol) and zinc powder (0.09 g, 1.30 mmol). The mixture was gently heated under nitrogen with vigorous stirring for 15 min. The mixture was cooled and filtered. The filtrate was poured into water (2 mL) and stirred for 10 min. The organic phase was briefly shaken with water (10 mL) containing concentrated hydrochloric acid (0.33 mL), followed by water (2 × 10 mL). After drying over magnesium sulfate and concentration *in vacuo*, the residue obtained was purified by flash chromatography using 6 : 4 ethyl acetate–hexane as eluent to yield the *title compound* **39** (21 mg, 71%) as a pale yellow solid, mp 256.5–258 °C [Found (FAB): M^+, 462.1308; $C_{26}H_{22}O_8$ requires M^+, 462.1315]; $\nu_{max}(CH_2Cl_2$ solution) 3400 (OH), 1760 (C=O), 1633 (C=C) and 1047 (C–O) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.43 (3 H, s, $COCH_3$), 4.15 (3 H, s, OCH_3), 6.88 (1 H, d, $J_{6,7}$ 8.4 Hz, H-6), 7.02 (1 H, d, $J_{1,3}$ 1.3 Hz, H-1), 7.18 (1 H, d, $J_{7,6}$ 8.4 Hz, H-7), 7.53 (1 H, d, $J_{3,1}$ 1.3 Hz, H-3), 9.24 (1 H, s, OH); δ_C (50 MHz, $CDCl_3$) 20.9 (CH_3, $COCH_3$), 56.4 (CH_3, OCH_3), 104.5 (CH, C-6), 109.9 (CH, C-7), 113.7 (CH, C-1), 114.6 (quat., C-4a), 120.8 (CH, C-3), 129.2 (quat., C-8a), 138.9 (quat., C-2), 139.4 (quat., C-8), 152.5 (quat., C-5), 156.8 (quat., C-4), 169.8 (quat., C=O); *m*/*z* 462 (M^+, 36%), 420 (24), 378 (31), 338 (64).

8′-Acetoxy-4,5,4′,5′-tetramethoxy-2,2′-binaphthalenyl-8-yl acetate (37)

A mixture of naphthol **39** (79 mg, 0.171 mmol), potassium carbonate (0.397 g, 2.87 mmol) and dimethyl sulfate (0.35 mL, 3.67 mmol) in dry acetone (8 mL) was heated under reflux with vigorous stirring for 7 h. The mixture was cooled and filtered. The filtrate was concentrated under reduced pressure and the resultant residue was dissolved in ethyl acetate (15 mL) and washed with concentrated ammonia (5 mL) and water (5 mL). The organic layer was dried over magnesium sulfate and concentrated. The residue was purified by flash chromatography using 6 : 4 ethyl acetate–hexane as eluent to yield the *title compound* **37** (55 mg, 67%) as a yellow solid, mp 231–233 °C [Found (EI): M^+, 490.16284; $C_{28}H_{26}O_8$ requires M^+, 490.16277]; $\nu_{max}(CH_2Cl_2$ solution) 1760 (C=O), 1598 (C=C), 1071 (C–O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.44 (3 H, s, $COCH_3$), 4.00 (3 H, s, OCH_3), 4.06 (3 H, s, OCH_3), 6.84 (1 H, d, $J_{6,7}$ 8.4 Hz, H-6), 7.15 (1 H, d, $J_{3,1}$ 1.3 Hz, H-3), 7.20 (1 H, d, $J_{7,6}$ 8.4 Hz, H-7), 7.59 (1 H, d, $J_{1,3}$ 1.3 Hz, H-1); δ_C (100 MHz, $CDCl_3$) 21.0 (CH_3, $COCH_3$), 56.76 (CH_3, OCH_3), 56.82 (CH_3, OCH_3), 105.5 (CH, C-6), 107.0 (CH, C-7), 112.5 (CH, C-1), 117.6 (quat., C-4a), 119.1 (CH, C-3), 130.2 (quat., C-8a), 140.18 (quat., C-2), 140.20 (quat., C-8), 155.2 (quat., C-5), 157.8 (quat., C-4), 169.8 (quat., C=O); *m*/*z* 490 (M^+, 27%), 448 ($M - C_2H_2O$, 43), 406 ($M - C_4H_4O_2$, 100), 390 ($M - C_4H_4O_3$, 16), 203 (12).

7-Benzyloxy-8-bromo-4,5-dimethoxynaphthalen-1-yl acetate (41)

A solution of *N*-bromosuccinimide (46 mg, 0.258 mmol) in dry *N*,*N*-dimethylformamide (1.8 mL) was added to a solution of acetate **21** (91 mg, 0.258 mmol) in dry *N*,*N*-dimethylformamide (1.8 mL) and stirred at room temperature under a nitrogen atmosphere for 1.5 h. The mixture was poured into water (20 mL) and extracted with dichloromethane (2 × 20 mL). The combined organic extracts were washed with water (20 mL) then dried over magnesium sulfate and concentrated *in vacuo* to give a yellow–brown solid. Further purification by flash column chromatography using 3 : 7 ethyl acetate–hexane as eluent afforded the *title compound* **41** (34 mg, 75%) as a light yellow solid, mp 96–98 °C [Found (EI): M^+, 430.0413 and 432.0387; $C_{21}H_{19}{}^{79}BrO_5$ and $C_{21}H_{19}{}^{81}BrO_5$ require M^+, 430.0416 and 432.0395]; $\nu_{max}(CH_2Cl_2$ solution) 1654 (C=O), 1594 (C=C), 1026 (C–O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 2.42 (3 H, s, $COCH_3$), 3.86 (3 H, s, 4-OCH_3), 3.91 (3 H, s, 5-OCH_3), 5.25 (2 H, s, OCH_2), 6.65 (1 H, s, H-6), 6.74 (1 H, d, $J_{3,2}$ 8.5 Hz, H-3), 7.08 (1 H, d, $J_{2,3}$ 8.5 Hz, H-2), 7.30–7.52 (5 H, m, PhH); δ_C (100 MHz, $CDCl_3$) 22.0 (CH_3, $COCH_3$), 56.7 (CH_3, OCH_3), 57.8 (CH_3, OCH_3), 71.8 (CH_2, OCH_2), 95.1 (quat., C-8), 98.0 (CH, C-6), 104.6 (CH, C-3), 116.1 (quat., C-4a), 122.8 (CH, C-2), 127.2 (CH, C-2′ and C-6′), 128.0 (CH, C-4′), 128.2 (quat., C-8a), 128.6 (CH, C-3′ and C-5′), 136.5 (quat., C-1), 138.8 (quat., C-1′), 154.5 (quat., C-4), 155.8 (quat., C-5), 158.5

(quat., C-7), 170.7 (quat., C=O); *m*/*z* 432/430 (M^+, 9%), 390/388 ($M - C_2H_2O$, 18), 91(100).

7,7′-Bis(benzyloxy)-4,5,4′,5′-tetramethoxy-2,2′-binaphthalenyl-1,1′-diol (42)

To a solution of naphthol **18** (85 mg, 0.274 mmol) in dichloromethane (1.5 mL) was added a solution of *N*,*N*-diisopropylamine (0.0042 mL, 0.030 mmol) in dichloromethane (0.15 mL). To this mixture was added a solution of *N*-bromosuccinimide (49 mg, 0.274 mmol) in dichloromethane (1.5 mL) dropwise with stirring over 20 min. After stirring for a further 2 h at room temperature, dilute sulfuric acid (2 M solution) was added until the solution became acidic. The organic layer was washed with water (2 × 1.5 mL) then dried over magnesium sulfate and concentrated *in vacuo* to give a dirty green solid. Further purification by flash column chromatography using gradient elution (from 3 : 7 to 5 : 5 ethyl acetate–hexane) yielded the *title compound* **42** (67 mg, 79%), mp 164.4–166.0 °C [Found (EI): M^+, 618.2258; $C_{38}H_{34}O_8$ requires M^+, 618.2254]; δ_H (400 MHz, $CDCl_3$) 3.98 (6H, s, 2 × OCH_3), 5.21 (2 H, s, OCH_2), 7.31–7.43 (5 H, m, PhH), 7.48 (1 H, s, H-6), 7.51 (1 H, s, H-3), 7.53 (1 H, s, H-8); *m*/*z* 618 (M^+, 26%), 505 [$M - (C_7H_6)$,3], 497 (7), 460 (4), 391 (4), 120 (13), 91 (41).

7-Benzyloxy-5-methoxy-1,4-naphthoquinone (43)

A solution of *N*-bromosuccinimide (48.8 mg, 0.274 mmol) in dry *N*,*N*-dimethylformamide (1.5 mL) was added to a solution of naphthol **18** (85 mg, 0.274 mmol) in dry *N*,*N*-dimethylformamide (1.5 mL) and stirred at room temperature under a nitrogen atmosphere for 22 h. The mixture was poured into water (15 mL) and extracted with dichloromethane (2 × 15 mL). The combined organic extracts were washed with water (15 mL) then dried over magnesium sulfate and concentrated *in vacuo* to give a yellow oil. Further purification by flash column chromatography using gradient elution (from 1 : 9 to 2.5 : 7.5 to 4 : 6 ethyl acetate–hexane) afforded the title compound **43** (30 mg, 37%) as an orange–yellow oil [Found (EI): M^+, 294.0890; $C_{18}H_{14}O_4$ requires M^+, 294.0892]; ν_{max}(CH_2Cl_2 solution) 1654 (C=O, quinone), 1594 (C=C), 1057 (C–O) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.94 (3 H, s, OCH_3), 5.24 (2 H, s, OCH_2), 6.81 (2 H, s, H-2 and H-3), 7.32–7.45 (7 H, m, H-6, H-8 and ArH); *m*/*z* 294 (M^+, 15%), 91(100).

8-Hydroxy-4,5-dimethoxynaphthalen-2-yl trifluoromethanesulfonate (45)

To a solution of acetate **15** (64 mg, 0.162 mmol) in methanol–THF (10 mL, 9.5 : 0.5) was added potassium carbonate (25 mg, 0.179 mmol) and the mixture stirred for 15 min under an atmosphere of nitrogen at room temperature. The reaction mixture was concentrated *in vacuo*, and water (5 mL) added and the solution acidified with 1 M hydrochloric acid solution (3 mL). The mixture was extracted with ethyl acetate (2 × 20 mL) and the combined organic extracts washed with water (10 mL), brine (10 mL), dried over magnesium sulfate and concentrated to give a dark brown oil. Purification by flash column chromatography using ethyl acetate–hexane (3 : 7) as eluent afforded the *title compound* **45** (52 mg, 91%) as a pale yellow solid, mp 66–68 °C [Found (EI): M^+, 352.0229; $C_{13}H_{11}F_3O_6S$ requires M^+, 352.0228]; ν_{max}(CH_2Cl_2 solution) 3408 (free OH), 1422 (SO_2–O), 1214 (C–F), 1041 (C–O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.90 (3 H, s, 5-OCH_3), 3.98 (3 H, s, 4-OCH_3), 5.41 (1 H, s, OH), 6.72 (1 H, d, $J_{3,1}$ 2.2 Hz, H-3), 6.76 (1 H, d, $J_{6,7}$ 8.4 Hz, H-6), 6.81 (1 H, d, $J_{7,6}$ 8.4 Hz, H-7), 7.70 (1 H, d, $J_{1,3}$ 2.2 Hz, H-1); δ_C (100 MHz, $CDCl_3$) 56.6 (CH_3, OCH_3), 57.5 (CH_3, OCH_3), 100.5 (CH, C-1), 106.2 (CH, C-3), 108.4 (CH, C-6), 110.6 (CH, C-7), 117.6 (quat., C-4a), 127.1 (quat., C-8a), 145.4 (quat., C-8), 147.2 (quat., C-5), 151.3 (quat., C-4), 158.9 (quat., C-2); *m*/*z* 352 (M^+, 58%), 191 (100).

3-Bromo-1,1′-dihydroxy-4,5,4′,5′-tetramethoxy-7′-trifluoromethanesulfonyloxy-2,2′-binaphthalenyl-7-yl trifluoromethanesulfonate (47) and 4-methoxy-5,8-dioxo-5,8-dihydronaphthalen-2-yl trifluoromethanesulfonate (48)

To a suspension of *N*-bromosuccinimide (23.9 mg, 0.134 mmol) in dry toluene (0.5 mL) cooled to −78 °C under an atmosphere of nitrogen, was added a solution of naphthol **45** (53 mg, 0.134 mmol) in dry dichloromethane (0.5 mL) drop-wise over 10 min. with stirring. After stirring at −78 °C for 1 h, the yellow slurry was allowed to warm to room temperature and stirred for 17 h. The reaction mixture was poured into water (10 mL) and extracted with diethyl ether (4 × 20 mL). The combined organic extracts were washed with water (2 × 40 mL), dried over magnesium sulfate and the solvent removed under reduced pressure to give a brown oil. Purification by flash column chromatography using ethyl acetate–hexane (2 : 8) as eluent afforded the *title compound* **47** (25 mg, 22%) as a brown oil [Found (EI): M^+, 779.9399 and 781.9393; $C_{26}H_{19}{}^{79}BrF_6O_{12}S_2$ and $C_{26}H_{19}{}^{81}BrF_6O_{12}S_2$require M^+, 779.9406 and 781.9385]; ν_{max}(CH_2Cl_2 solution) 3415 (OH), 1424 (SO_2–O), 1213 (C–F), 1046 (C–Br), 1028 (C–O) cm^{-1}; δ_H(400 MHz, $CDCl_3$) 3.79 (3 H, s, 5′-OCH_3), 3.86 (3 H, s, 4′-OCH_3), 3.93 (3 H, s, 5-OCH_3), 3.95 (3 H, s, 4-OCH_3), 6.57 (1 H, s, H-3′), 6.69 (1 H, d, $J_{6,8}$ 2.4 Hz, H-6), 7.02 (1 H, d, $J_{6',8'}$ 2.4 Hz, H-6′), 7.45 (1 H, d, $J_{8,6}$ 2.4 Hz, H-8), 7.64 (1 H, d, $J_{8',6'}$ 2.4 Hz, H-8′); δ_C(100 MHz, $CDCl_3$) 56.7, 56.9, 57.1, 57.2 (CH_3, 4 × OCH_3), 99.3 (quat., C-3), 101.2 (CH, C-8), 105.2 (CH, C-8′), 105.4 (CH, C-6′), 110.2 (CH, C-6), 111.3 (quat., C-4a), 112.0 (CH, C-3′), 112.7 (quat., C-4a′), 113.0 (quat., C-2′), 117.5 (quat., C-2), 120.7 (quat., C-8a′), 124.2 (quat., C-8a), 127.7 (quat., C-1′), 132.4 (quat., C-1), 142.1 (quat., C-4′), 142.3 (quat., C-4), 148.0 (quat., C-5), 152.6 (quat., C-5′), 159.4 (quat., C-7′), 160.9 (quat., C-7); *m*/*z* 780/782 (M^+, 19%), 701/703 (M − Br, 100).

The *title compound* **48** (7 mg, 14%) was also isolated as a yellow solid, mp 115–117 °C [Found (EI): M^+ 335.9910; $C_{12}H_7F_3O_6S$ requires M^+ 335.9915]; ν_{max}(CH_2Cl_2 solution) 1658 (C=O, quinone) 1423 (SO_2–O), 1208 (C–F), 1038 (C–O) cm^{-1}; δ_H(300 MHz, $CDCl_3$) 4.03 (3 H, s, OCH_3), 6.90 (1 H, d, $J_{7,6}$ 10.3 Hz, H-7), 6.95 (1 H, d, $J_{6,7}$ 10.3 Hz, H-6), 7.16 (1 H, d, $J_{3,1}$ 2.4 Hz, H-3), 7.60 (1 H, d, $J_{1,3}$ 2.4 Hz, H-1); δ_C(75 MHz, $CDCl_3$) 57.1 (CH_3, OCH_3), 110.7 (CH, C-6), 111.4 (CH, C-7) 116.5 (quat., C-4a), 136.0 (quat., C-8a), 136.1 (CH, C-3), 141.0 (CH, C-1), 153.2 (quat., C-2), 161.5 (quat., C-4), 182.6, 183.1 (quat., C-5 and C-8); *m*/*z* 336 (M^+, 98%), 203 ($M - CF_3SO_2$, 65), 188 (43), 175 (100).

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