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Synthesis of regioisomeric analogues of crisamicin A

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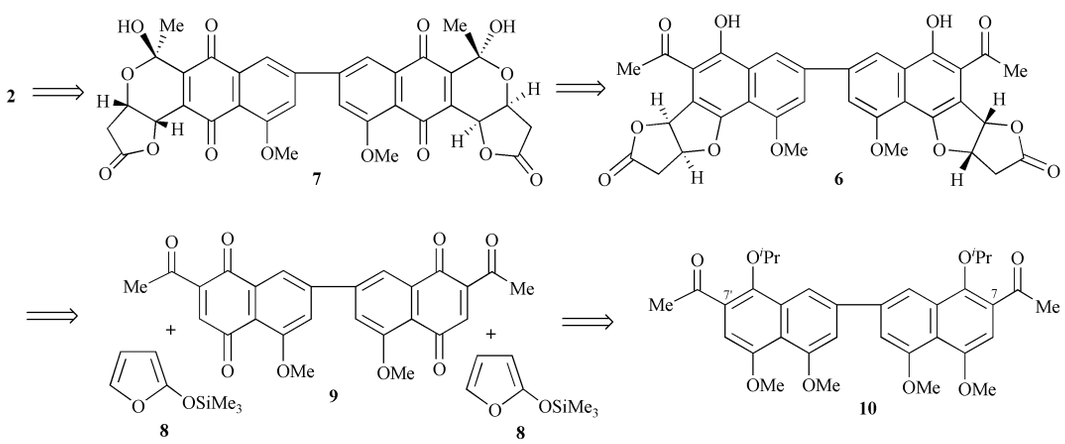
The synthesis of bis-furonaphthopyrans **12a** and **12b**, regioisomeric analogues of the dimeric pyranonaphthoquinone antibiotic crisamicin A **1** is described. The key intermediate **16** was prepared *via* a one-pot *in situ* Suzuki–Miyaura homocoupling of naphthyl triflate **23** using bis(pinacolato)diboron. Oxidation of binaphthyl **16** to bis-naphthoquinone **14** was then effected with silver(II) oxide and nitric acid. Efficient double furofuran annulation of bis-naphthoquinone **14** with 2-trimethylsilyloxyfuran **8** afforded bis-furonaphthofuran adducts **13a** and **13b** as an inseparable 1 : 1 mixture of diastereomers. Oxidative rearrangement of this mixture of bis-furonaphthofuran adducts **13a** and **13b** using silver(II) oxide and nitric acid afforded unstable bis-furonaphthopyrans **12a** and **12b** also as a 1 : 1 mixture of diastereomers. Addition of 2-trimethylsilyloxyfuran **8** to naphthoquinone **25** afforded adduct **26** that underwent oxidative rearrangement to furonaphthopyran **27**, however attempts to effect Suzuki–Miyaura homocoupling of triflates **26** and **27** to their respective dimers **13** and **12**, was unsuccessful.

Introduction

The pyranonaphthoquinone (or isochromanquinone) family of antibiotics exhibit activity against a variety of Gram-positive bacteria, pathogenic fungi and yeasts[1] and have been proposed to act as bioreductive alkylating agents.[2] Whilst the synthesis of monomeric members of this important family of antibiotics is well documented,[3] the total synthesis of a naturally occurring dimeric pyranonaphthoquinone antibiotic has yet to be achieved. Our synthetic work in this area has 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] Herein we report a synthesis of analogues of the dimeric pyranonaphthoquinone antibiotics, the crisamicins.

Crisamicins A **1** and C **2** were isolated from the microorganism *Micromonospora purpureochromogenes*.[8] Crisamicin A **1** exhibits activity against B16 murine melanoma cells, and the herpes simplex and vesicular stomatitis viruses.[9] More recently a new cytotoxic isochromanquinone antibiotic GTRI-BB **3** was isolated from cultures of *Micromonospora sp.* SA246.[10] We have previously reported the use of a double furofuran annulation–oxidative rearrangement strategy to prepare a dimeric pyranonaphthoquinone **5** that is structurally related to the aphid pigment actinorhodin **4**.[11] It was envisaged that previous methodology employed for the synthesis of the actinorhodin analogue **5** could be applied to the synthesis of crisamicin A **1**. Our strategy for the synthesis of crisamicin A **1** (Scheme 1) hinged on the double oxidative rearrangement of furonaphthofuran **6** to furonaphthopyran **7** as the key step with bisfuronaphthofuran **6** being formed by double furofuran annulation of bis-naphthoquinone **9** with 2-trimethylsilyloxyfuran **8**. In turn bis-naphthoquinone **9** is available from bis-naphthalene **10** in which the acetyl groups at C-7 and C-7′ control the regioselectivity of the subsequent annulation step.

We have previously reported[12] the construction of the biaryl framework of crisamicin A **1** *via* Suzuki–Miyaura[13] homocoupling of a naphthyl triflate, however it transpired that attempts to introduce the required acetyl groups at C-7 and C-7′ in bis-acetylnaphthalene **10** proved problematic, thereby prompting a rethink of our synthetic approach to crisamicin A **1**. It was therefore decided to focus on the synthesis of the regioisomer **11** of crisamicin A *via* the intermediacy of bis-furonaphthopyran **12** and bis-furonaphthofuran **13**. This approach requires the initial synthesis of bis-acetylnaphthoquinone **14** from bis-acetylnaphthalenes **15** or **16** (Scheme 2) in which the acetyl groups are positioned at the more electron rich C-6 and C-6′ sites and are therefore more easily introduced by



Scheme 1

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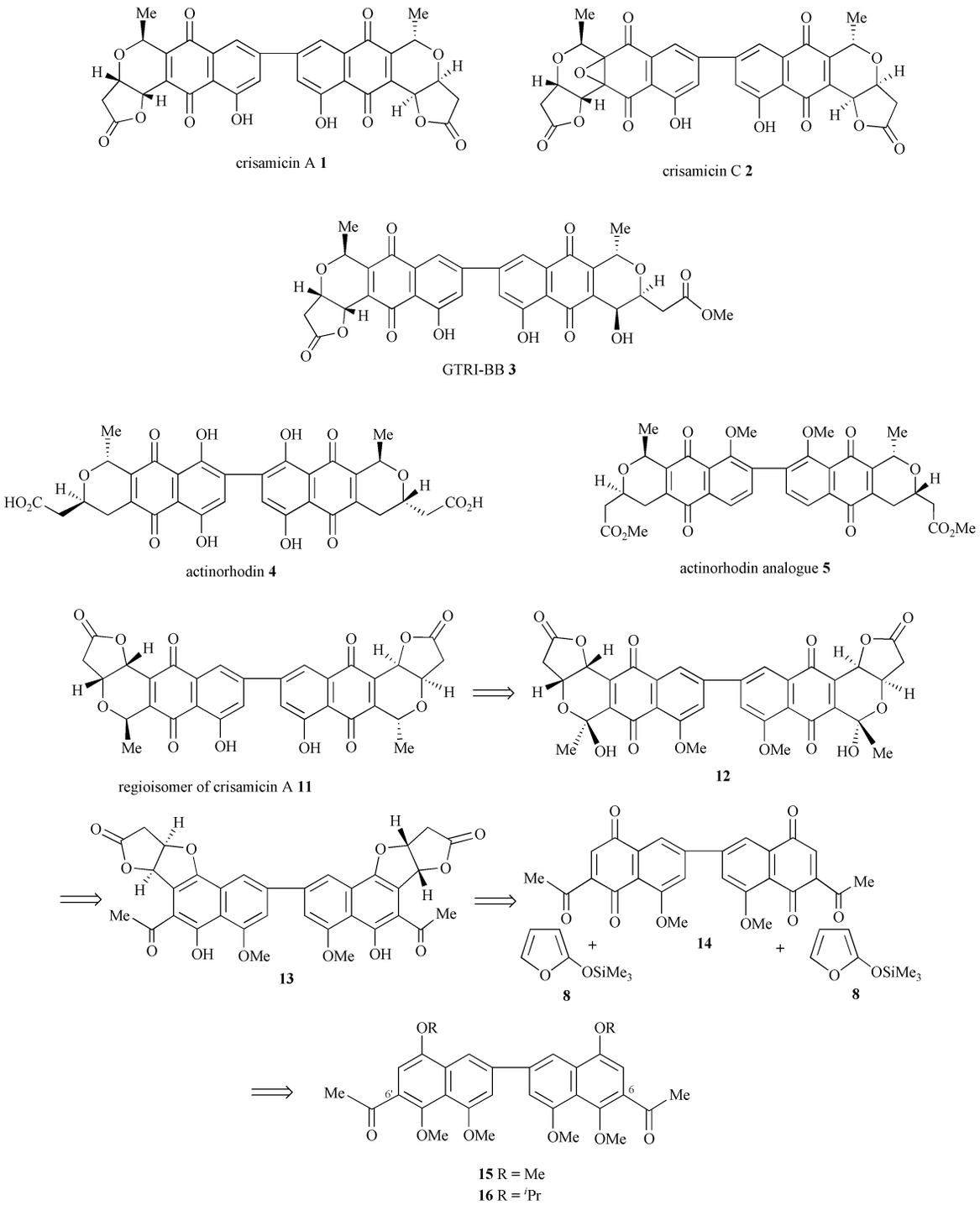


Scheme 2

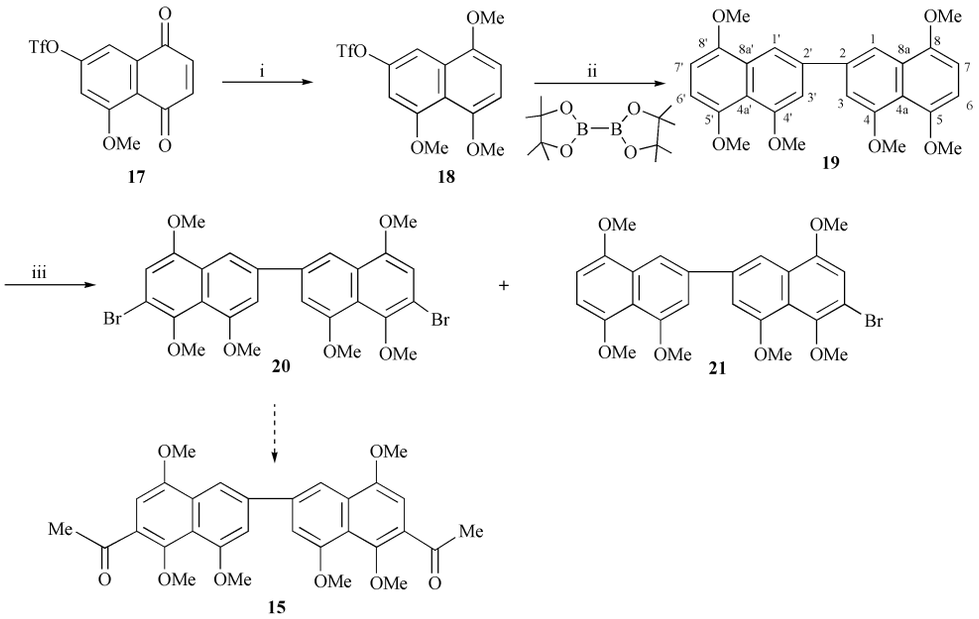
electrophilic aromatic substitution. The synthesis of the regioisomer **11** of crisamicin A provides a useful compound for evaluation of its biological activity compared to the natural product.

Results and discussion

Initial attention focused on the synthesis of binaphthyl **15** from known naphthoquinone **17**[12] (Scheme 3) *via* homocoupling of triflate **18** followed by introduction of acetyl groups at C-6 and C-6′ of binaphthyl **19**. Reduction of naphthoquinone **17** with sodium dithionite followed by methylation with dimethyl sulfate afforded naphthalene **18** in 64% yield. Triflate **18** was then heated with bis(pinacolato)diboron in dry dioxane in the presence of $PdCl_2$(dppf), dppf ligand and the weak base KOAc at reflux for 0.5 h to afford the boronate ester that was directly coupled with a further equivalent of triflate **18**. This latter step was assisted with a second addition of the palladium catalyst and a stronger base, K_3PO_4 to drive the homocoupling reaction to completion furnishing binaphthyl **19** in 84% yield after purification by flash chromatography.

The mass spectrum of **19** confirmed the molecular formula $C_{26}H_{26}O_6$ by the observation of a molecular ion at *m*/*z* 434.1730. The ^{1}H NMR spectrum exhibited two downfield doublets, each with a coupling constant of *J* 1.6 Hz, at δ 7.31 and δ 8.22, assigned to H-3 and H-1 respectively. H-6 and H-7 were shifted upfield resonating as doublets, each with a large *ortho* coupling constant, *J* 8.5 Hz, at δ 6.78 and δ 6.81 respectively.

With binaphthyl **19** in hand, attention turned to the direct introduction of the acetyl groups at C-6 and C-6′. Attempts to effect a double Vilsmeier reaction of binaphthyl **19** using either



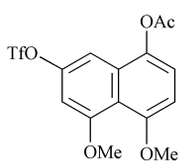
Scheme 3 *Reagents, conditions and yields*: (i) CH_2Cl_2–Et_2O (1 : 3), $Na_2S_2O_4$, H_2O, 20 min, then dry acetone, K_2CO_3, Me_2SO_4, 60 °C, 23 h, 64%; (ii) bis(pinacolato)diboron (1.1 equiv.), $PdCl_2$(dppf), dppf, KOAc, dioxane, reflux, 0.5 h, then triflate **18**, $PdCl_2$(dppf), K_3PO_4, dioxane, reflux, 2 h, 84%; (iii) NBS (2.0 equiv.), CH_2Cl_2, 2.5 h, **20**, 13%, **21**, 3%.

N,*N*-dimethylacetamide or *N*,*N*-dimethylformamide and phosphorus oxychloride were unsuccessful. Our efforts thus turned to the synthesis of bis-acetylnaphthalene **15** from dibromonaphthalene **20** *via* Stille coupling with α-(ethoxyvinyl)tributylstannane followed by hydrolysis of the resultant enol ether.

Initially, a standard bromination procedure using *N*-bromosuccinimide in dry dichloromethane was employed in an attempt to convert binaphthyl **19** to dibromonaphthalene **20**. After chromatography on alumina, the desired dibromide **20** was obtained in a low 13% yield together with bromide **21** in 3% yield. The high resolution mass spectrum of dibromide **20** featured molecular ions with intensities of 1 : 2 : 1 at *m*/*z* 589.9933, 591.9924 and 593.9881 consistent with the molecular formula $C_{26}H_{24}Br_2O_6$, whilst molecular ions of equal intensities at *m*/*z* 512.0840 and 514.0823 supported the molecular formula $C_{26}H_{25}BrO_6$ for bromide **21**. In the ^{1}H NMR spectrum of dibromide **20**, there were only three distinct aromatic protons at δ 6.99, δ 7.29 and δ 8.12. On the other hand, seven distinct aromatic protons were observed for bromide **21** at δ 6.80, δ 6.81, δ 6.99, δ 7.14, δ 7.33, δ 8.14 and δ 8.18 consistent with an unsymmetrical binaphthyl structure.

Use of pyridinium hydrobromide perbromide afforded complex mixtures using a range of solvents and reaction conditions. In a further attempt to brominate **19**, a mild, highly chemo- and regioselective method for bromination of electron rich aromatic molecules was used wherein electrophilic Br^+ was generated *in situ* from lithium bromide in acetonitrile using ceric ammonium nitrate as an oxidant.[14] Disappointingly, only a mixture of products was obtained in this case.

Our inability to access bis-acetylnaphthalene **15** *via* homocoupling of triflate **18** followed by bis-acetylation focused our attention on the introduction of an acetyl group at C-6 of triflate **22**[12] to form acetylnaphthalene **23** that would then undergo homocoupling to the desired binaphthyl **16** (Scheme 4). Acetylation of triflate **22** using trifluoroacetic anhydride (TFAA) in glacial acetic acid at room temperature as used by Giles *et al*.[15] furnished acetylnaphthalene **23** in 32% yield together with acetate **24** (14% yield) and recovered starting material. Increasing the temperature of the reaction to 60 °C afforded more of the undesired acetate **24** with no improvement in the yield of the desired acetylnaphthalene **23**. The ^{1}H NMR spectrum of triflate **23** featured a three-proton singlet at δ 2.76 characteristic of a methyl ketone. A singlet at δ 7.12 was assigned to H-7, whilst H-1 and H-3 resonated as doublets, each with a coupling constant of *J* 2.4 Hz, at δ 6.80 and δ 7.78 respectively. The ^{13}C NMR spectrum confirmed the presence of the newly introduced acetyl group with a carbonyl carbon resonating at δ 200.8.



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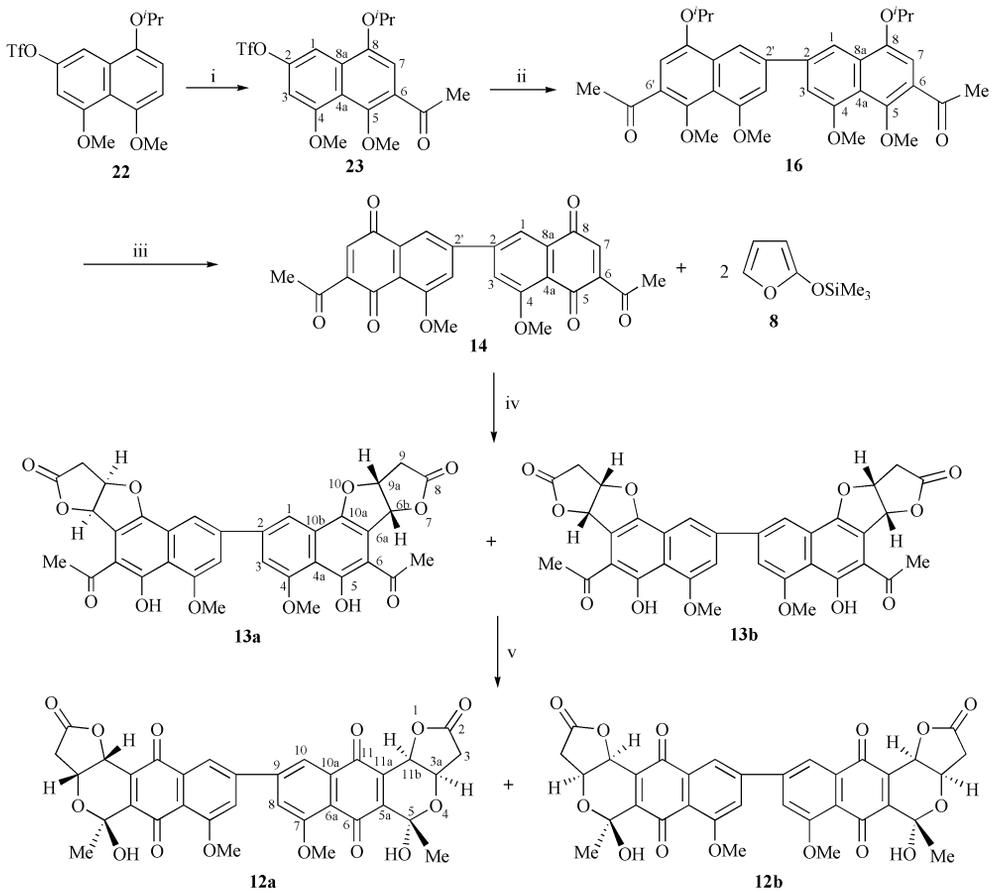
An alternative acetylation procedure[16] was tried using acetic anhydride, catalysed by a combination of ruthenium(III) chloride trihydrate and silver hexafluoroantimonate in dry dichloromethane at 40 °C. In this case, acetate **24** was the only product and none of the desired triflate **23** was afforded. This latter observation suggested that this combination of transition metals efficiently acts as a Lewis acid to facilitate deisopropylation of **22**, subsequently leading to acetate **24** in the presence of acetic anhydride.

With triflate **23** in hand, our focus next turned to the construction of biaryl **16**, a critical step required for the formation of bis-naphthoquinone **14**, a key intermediate in the preparation of a regioisomer of crisamicin A, using a double furofuran annulation–double oxidative rearrangement strategy (Scheme 4). Following now well-established procedures in our laboratory for the construction of binaphthyls *via* homocoupling of naphthyl triflates, triflate **23** was subjected to Suzuki–Miyaura coupling using bis(pinacolato)diboron, $PdCl_2$(dppf), dppf and KOAc in dry dioxane followed by addition of K_3PO_4 to drive the homocoupling to completion, affording binaphthyl **16** in 58% yield. High resolution mass spectrometry established the molecular formula $C_{34}H_{38}O_8$ for binaphthyl **16** by the observation of a molecular ion at *m*/*z* 574.2561. The ^{1}H NMR spectrum featured two mutually coupled downfield doublets at δ 7.31 and δ 8.26 (J_{meta} 1.4 Hz) that were assigned to H-3 and H-1 respectively.

With binaphthyl **16** in hand, it next remained to effect the conversion of **16** to bis-naphthoquinone **14**. Treatment of **16** with freshly prepared silver(II) oxide and 6 M nitric acid afforded bis-naphthoquinone **14** in 91% crude yield and the



Scheme 4 *Reagents, conditions and yields*: (i) HOAc, TFAA, room temp., 5 h, **23** 32%, **24**, 14%; (ii) bis(pinacolato)diboron (1.1 equiv.), $PdCl_2$(dppf), dppf, KOAc, dioxane, reflux, 1.75 h, then triflate **23**, $PdCl_2$(dppf), K_3PO_4, dioxane, reflux, 2.5 h, 58%; (iii) AgO, 6 M HNO_3, dioxane, 10 min, 91%; (iv) **8** (3.0 equiv.), CH_3CN, 0 °C, 1 h, **13a** : **13b** (1 : 1), 41%; (v) CAN, acetonitrile, 15 min, 28%

material obtained was not purified further due to its inherent instability. The infrared spectrum of **14** displayed strong absorptions at 1715 and 1665 cm^{-1} that were assigned to the acetyl and quinone C=O bond stretches respectively. The ^1H NMR spectrum featured a single methoxy group at δ 4.13 and a methyl group at δ 2.64 was assigned to the acetyl group. A singlet at δ 7.08 was assigned to H-7, whilst H-3 and H-1 resonated as doublets at δ 7.51 and δ 7.97 with a small *meta* coupling constant, J 1.6 Hz.

Having successfully prepared bis-naphthoquinone **14** from triflate **22** it next remained to effect a double furofuran annulation to bis-furonaphthofurans **13a** and **13b** followed by double oxidative rearrangement to bis-furonaphthopyrans **12a** and **12b**. Treatment of bis-naphthoquinone **14** in dry acetonitrile at 0 °C with 2-trimethylsilyloxyfuran **8** for 1 h afforded a mixture of bis-furonaphthofurans **13a** and **13b** in 41% yield after purification by flash chromatography. Adducts **13a** and **13b** were not separable by flash chromatography and the ratio of diastereomers **13a**:**13b** was determined to be 1 : 1 using analytical HPLC.

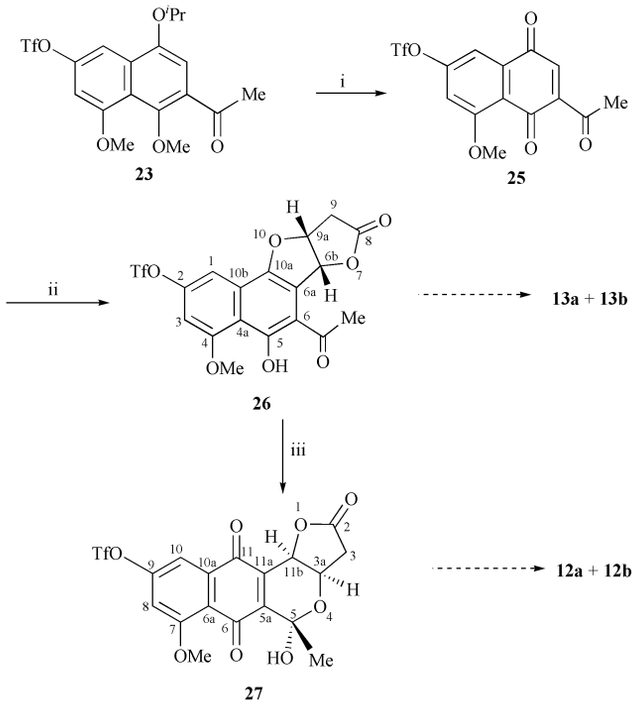
The ^1H NMR spectrum of adducts **13a** and **13b** only showed one set of resonances for the individual protons of both diastereomers **13a** and **13b**. However, analytical HPLC clearly indicated that a 1 : 1 mixture of the two diastereomers was present. A doublet resonating at δ 6.65 with coupling constant J 6.0 Hz was assigned to the bridgehead proton H-6b, whilst the other bridgehead proton H-9a was observed as an unresolved multiplet at δ 5.42–5.55. Another unresolved multiplet at δ 3.10–3.12 was assigned to H-9 and H-9′. A singlet at δ 2.80 was assigned to the protons of the methyl ketone, whilst H-3 and H-1 were observed as doublets at δ 7.19 and δ 7.82 respectively, both with a coupling constant of J 1.4 Hz. A singlet at δ 11.8 was assigned to the hydroxy group.

The bridgehead protons in furonaphthofuran adducts **13a** and **13b** resonated at similar chemical shifts to those reported for the analogous monomeric furonaphthopyrans[6,7] and the coupling constant of $J_{3a,11b}$ 3.2 Hz supported the presence of a *cis*-fused furonaphthopyran ring system.[6,7] The stereochemistry of hemiacetals **13a** and **13b** was assigned by analogy to the monomeric system[6,7] and a dimeric analogue of actinorhodin.[11]

The ^{13}C NMR spectrum was also consistent with the proposed structure and exhibited one set of signals for the individual carbons of the two diastereomers **13a** and **13b** with the methylene carbon at δ 35.7 being assigned to C-9 and the two methine carbons at δ 81.3 and δ 85.3 being assigned to the bridgehead carbons C-9a and C-6b respectively. The two carbonyl carbons at δ 174.4 and δ 200.3 were assigned to the lactone and ketone respectively.

With furonaphthofuran adducts **13a** and **13b** in hand, attention next turned to the oxidative rearrangement step. This step was rather capricious and was best effected using ceric ammonium nitrate in aqueous acetonitrile at 0 °C as previously used by this research group for the synthesis of an analogue of actinorhodin.[11] In contrast to our experience with the actinorhodin work, the product of the present double oxidative rearrangement, namely bis-furonaphthopyran **12**, was highly unstable and rapidly decomposed upon attempts to purify it by flash chromatography or reverse-phase HPLC. The inherent instability of this product, coupled with the disappointing low yield for this step (28%), precluded further synthetic work on this material and prompted investigation of an alternative synthetic strategy.

As an alternative strategy to prepare regioisomer of crisamicin A (Scheme 5), it was proposed that triflate **23** would undergo oxidation to naphthoquinone **25**, which would under-



Scheme 5 *Reagents, conditions and yields*: (i) AgO, 6 M HNO_3, dioxane, 10 min, 96%; (ii) **8** (3.0 equiv.), CH_3CN, 0 °C, 1 h, 74%; (iii) CAN, CH_3CN, H_2O, 0 °C, 15 min, 62%.

go addition with 2-trimethylsilyloxyfuran **8** to afford furonaphthofuran **26**. Subsequent oxidative rearrangement of this adduct **26** then affords furonaphthopyran **27**, which could then be subjected to a one-pot *in situ* Suzuki–Miyaura homocoupling to furnish the desired bis-furonaphthopyrans **12a** and **12b**.

Treatment of naphthalene **23** with silver(II) oxide and 6 M nitric acid in dioxane for 10 min, followed by standard workup afforded naphthoquinone **25** in 96% yield which was used in the next step without further purification. Treatment of naphthoquinone **25** with 2-trimethylsilyloxyfuran **8** (3.0 equiv.) in acetonitrile at 0 °C for 1 h followed by purification by flash chromatography then afforded the desired adduct **26** in 74% yield. Its ^{1}H NMR spectrum featured a doublet resonating at δ 6.55 with a coupling constant of J 6.0 Hz, assigned to the bridgehead proton H-6b, and the other bridgehead proton, H-9a, resonated as an unresolved multiplet at δ 5.48–5.52. A multiplet at δ 3.12–3.13 was assigned to H-9 and H-9′, a three proton singlet at δ 2.78 was assigned to the methyl protons of the acetyl group and H-3 and H-1 resonated as doublets at δ 6.83 and δ 7.44, with a coupling constant of J 2.4 Hz. A singlet at δ 12.2 was assigned to the hydroxy group.

It was next envisaged that Suzuki–Miyaura homocoupling of triflate **26** would afford bis-furonaphthofurans **13a** and **13b** which could then be converted to bis-furonaphthopyrans **12a** and **12b** using a double oxidative rearrangement as described above. Unfortunately, use of the conditions that had been successfully used to convert triflate **23** to binaphthyl **16**, afforded none of the desired bis-furonaphthofuran **13**.

It was next decided to prepare triflate **27** *via* oxidative rearrangement of adduct **26** with the idea that homocoupling of triflate **27** would provide a more expeditious route to bis-furonaphthopyran **12**. With this idea in mind, furonaphthofuran **26** was treated with ceric ammonium nitrate (2 equiv.) in aqueous acetonitrile for 15 min affording furonaphthopyran **27** in 62% yield after workup and purification by chromatography on florisil. In a one-pot *in situ* homocoupling reaction, triflate **27** was then reacted with bis(pinacolato)diboron in the presence of $PdCl_2$(dppf), dppf ligand and KOAc in dry dioxane. Following the reaction by TLC showed complete consumption of the starting triflate **27** and a new fluorescent spot, consistent with the formation of a boronate ester, was observed. The resulting boronate was therefore coupled *in situ* with another molecule of triflate **27** upon addition of more palladium catalyst and the stronger base, K_3PO_4. Unfortunately, this procedure afforded a complex mixture of products and the ^{1}H NMR spectrum of the crude product mixture did not exhibit characteristic resonances for the desired bisfuronaphthopyran **12**.

In conclusion, the work described herein constitutes a synthesis of a dimeric pyranonaphthoquinone employing a double furofuran annulation–oxidative rearrangement strategy previously developed by this research group for the synthesis of analogues of actinorhodin wherein the biaryl linkage is *ortho* to an oxygen substituent. The present work further extends the use of this methodology to access dimeric pyranonaphthoquinones which lack an oxygen substituent *ortho* to the biaryl linkage.

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 spectrometer; samples were measured as thin films between sodium chloride plates. Absorption spectra are expressed in wavenumbers (cm^{-1}) with the following abbreviations: 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 from tetramethylsilane as an internal standard, and are 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 a 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.

4,5,8-Trimethoxynaphthalen-2-yl trifluoromethanesulfonate (18)

Naphthoquinone **17**[12] (94 mg, 0.280 mmol) was dissolved in dichloromethane–diethyl ether (1 : 3) (7.5 mL) and shaken with a freshly prepared solution of sodium dithionite (0.49 g, 2.80 mmol) in water (4.5 mL) for 20 min under an atmosphere of nitrogen. The organic layer was separated, washed with brine (9 mL) and dried over magnesium sulfate. The solvent was removed under reduced pressure to give the crude hydroquinone as a pale brown solid. This solid was dissolved in dry acetone (5 mL) in a flat-bottomed flask and added to a stirred suspension of finely ground potassium carbonate (0.502 g, 3.63 mmol) in dry acetone (1.6 mL). Dimethyl sulfate (0.32 mL, 3.35

mmol) was added and the solution stirred and heated under reflux for 24 h. The mixture was then cooled, filtered through Celite and the solvent removed under reduced pressure. The resultant red–brown oil was redissolved in diethyl ether (6.5 mL) and stirred with triethylamine (0.31 mL, 2.24 mmol). After 20 min, the solution was washed with HCl (1 M, 2 × 10 mL), water (10 mL) and brine (10 mL). The organic extract was then dried over magnesium sulfate and concentrated *in vacuo* to give a dark brown oil which was purified by flash column chromatography using ethyl acetate–hexane (1.5 : 8.5) as eluent to afford the *title compound* **18** (66 mg, 64%) as a yellow solid, mp 79–82 °C [Found (EI): M^+, 366.0377; $C_{14}H_{13}F_3O_6S$ requires M^+, 366.0385]; ν_{max} (CH_2Cl_2 solution) 1412 (SO_2–O), 1206 (C–F), 1072 (C–O) cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.91, 3.95 and 3.99 (each 3 H, s, OCH_3), 6.73 (1 H, d, $J_{3,1}$ 2.5 Hz, H-3), 6.81 (1 H, d, $J_{6,7}$ 8.6 Hz, H-6), 6.85 (1 H, d, $J_{7,6}$ 8.6 Hz, H-7), 7.75 (1 H, d, $J_{1,3}$ 2.5 Hz, H-1); δ_C (75 MHz, $CDCl_3$) 55.9 (CH_3, OCH_3), 56.7 (CH_3, OCH_3), 57.4 (CH_3, OCH_3), 100.5 (CH, C-1), 106.0 (CH, C-3), 106.2 (CH, C-6), 108.1 (CH, C-7), 116.7 (quat., C-4a), 128.1 (quat., C-8a), 147.3 (quat., C-5), 149.4 (quat., C-8), 151.0 (quat., C-4), 158.9 (quat., C-2); *m/z* 366 (M^+, 62%), 351 (M − CH_3, 10), 205 (100).

4,4′,5,5′,8,8′-Hexamethoxy-2,2′-binaphthalenyl (19)

A mixture of potassium acetate (20 mg, 0.205 mmol), dry dioxane (2.5 mL), $PdCl_2$(dppf) (1.7 mg, 0.0021 mmol), dppf (1.2 mg, 0.0021 mmol), bis(pinacolato)diboron (19 mg, 0.0751 mmol) and 4,5,8-trimethoxynaphthalen-2-yl trifluoromethanesulfonate **18** (25 mg, 0.0682 mmol) was heated under argon, with stirring at 110 °C for 0.5 h. Potassium phosphate (43 mg, 0.205 mmol), $PdCl_2$(dppf) (1.7 mg, 0.0021 mmol) and 4,5,8-trimethoxynaphthalen-2-yl trifluoromethanesulfonate **18** (25 mg, 0.0682 mmol) were then added and the resultant mixture heated with stirring at 110 °C 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 dirty green solid. Further purification by flash column chromatography using gradient elution (from 2.5 : 7.5 to 5 : 5 ethyl acetate–hexane to dichloromethane) to afford the *title compound* **19** (25 mg, 84%) as a yellow solid, mp 186–189 °C [Found (EI): M^+, 434.1730; $C_{26}H_{26}O_6$ requires M^+, 434.1729]; ν_{max} (CH_2Cl_2 solution) 1594 (C=C), 1057 (C–O) cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.96 (3 H, s, 5-OCH_3), 4.00 and 4.09 (each 3 H, s, OCH_3), 6.78 (1 H, d, $J_{6,7}$ 8.5 Hz, H-6), 6.81 (1 H, d, $J_{7,6}$ 8.5 Hz, H-7), 7.31 (1 H, d, $J_{3,1}$ 1.6 Hz, H-3), 8.22 (1 H, d, $J_{1,3}$ 1.6 Hz, H-1); δ_C (75 MHz, $CDCl_3$) 55.8 (CH_3, OCH_3), 56.8 (CH_3, OCH_3), 57.5 (CH_3, OCH_3), 104.7 (CH, C-3), 107.1 (CH, C-6), 107.3 (CH, C-7), 113.2 (CH, C-1), 117.7 (quat., C-4a), 128.9 (quat., C-8a), 138.9 (quat., C-2), 149.9 (quat., C-5), 150.8 (quat., C-8), 157.2 (quat., C-4); *m/z* 434 (M^+, 100%), 419 (M − CH_3, 34), 404 (M − C_2H_6, 30), 389 (M − C_3H_9, 24), 373 (2), 359 (3), 345 (2).

6,6′-Dibromo-4,4′,5,5′,8,8′-hexamethoxy-2,2′-binaphthalenyl (20) and 6-bromo-4,4′,5,5′,8,8′-hexamethoxy-2,2′-binaphthalenyl (21)

To a solution of dimer **19** (10 mg, 0.023 mmol) in dry dichloromethane (1.5 mL) was added *N*-bromosuccinimide (8.2 mg, 0.046 mmol) in a single portion. The mixture was stirred for 2.5 h, then quenched with sodium sulfite (1.0 mL) and stirred for an additional 5 min. The phases were separated, and the aqueous phase was extracted with dichloromethane (10 mL). The combined organic phases were washed with water (10 mL), dried over magnesium sulfate and concentrated *in vacuo* to give a yellow oil. Purification by flash column chromatography on alumina using ethyl acetate–hexane (1 : 9) as eluent afforded *title compounds* **20** and **21**.

(i) The *title compound* **20** (1.75 mg, 13%) was a yellow oil [Found (EI): M^+, 589.9933, 591.9924 and 593.9881; $C_{26}H_{24}{}^{79}Br_2O_6$, $C_{26}H_{24}{}^{79}Br^{81}BrO_6$ and $C_{26}H_{24}{}^{81}Br_2O_6$ require M^+, 589.9940, 591.9919 and 593.9899]; ν_{max} (CH_2Cl_2 solution) 1580 (C=C), 1080 (C–O), 1046 (C–Br) cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.89, 4.01 and 4.11 (each 3 H, s, OCH_3), 6.99 (1 H, s, H-7), 7.29 (1 H, d, $J_{3,1}$ 1.6 Hz, H-3), 8.12 (1 H, d, $J_{1,3}$ 1.6 Hz, H-1); *m/z* 594/592/590 (M^+, 100%), 579/577/575 (M − CH_3, 8), 564/562/560 (M − C_2H_6, 13), 549/547/545 (M − C_3H_9, 5), 498/496 (M − CH_3Br, 11), 483/481 (M − C_2H_6Br, 5), 468/466 (M − C_3H_9Br, 6).

(ii) The *title compound* **21** (0.5 mg, 3%) was a pale yellow oil [Found (EI): M^+, 512.0840 and 514.0823; $C_{26}H_{25}{}^{79}BrO_6$ and $C_{26}H_{24}{}^{81}BrO_6$ require M^+, 512.0835 and 514.0814]; ν_{max} (CH_2Cl_2 solution) 1584 (C=C), 1078 (C–O), 1045 (C–Br) cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.88, 3.98, 3.99, 4.00, 4.09 and 4.11 (each 3 H, s, OCH_3), 6.80 (1 H, d, $J_{6',7'}$ 8.6 Hz, H-6′), 6.81 (1 H, d, $J_{7',6'}$ 8.6 Hz, H-7′), 6.99 (1 H, s, H-7), 7.14 (1 H, s, H-3′), 7.33 (1 H, s, H-3), 8.14 (1 H, s, H-1), 8.18 (1 H, s, H-1′); *m/z* 514/512 (M^+, 100%), 499/497 (M − CH_3, 23), 484/482 (M − C_2H_6, 18), 469/467 (M − C_3H_9, 13), 418 (M − CH_3Br, 8), 403 (6), 388 (5).

6-Acetyl-8-isopropoxy-4,5-dimethoxynaphthalen-2-yl trifluoromethanesulfonate (23)

8-Isopropoxy-4,5-dimethoxynaphthalen-2-yl trifluoromethanesulfonate **22**[12] (98 mg, 0.249 mmol) was treated with a premixed solution of glacial acetic acid (0.0142 mL, 0.249 mL) and trifluoroacetic anhydride (0.14 mL, 0.994 mmol) and the mixture was left to stir at room temperature for 5 h. The reaction mixture was diluted with dichloromethane (5 mL) and concentrated at reduced pressure. The resultant residue was redissolved in dichloromethane (10 mL), washed with brine (5 mL), dried over magnesium sulfate then concentrated *in vacuo* to afford a red–brown oil. Flash column chromatography using gradient elution (from 3 : 7 to 10 : 0 dichloromethane–hexane) yielded *title compound* **23** and also **24**.

(i) The *title compound* **23** (34.3 mg, 32%) was a light yellow oil [Found (EI): M^+, 436.0806; $C_{18}H_{19}F_3O_7S$ requires M^+, 436.0804]; ν_{max} (CH_2Cl_2) 1671 (C=O), 1061 (C–O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.43 (6 H, d, *J* 6.0 Hz, CH_3 of isopropyl), 2.76 (3 H, s, $COCH_3$), 3.81 and 4.06 (each 3 H, s, OCH_3), 4.75 (1 H, septet, *J* 6.0 Hz, CH of isopropyl), 6.80 (1 H, d, $J_{3,1}$ 2.4 Hz, H-3), 7.12 (1 H, s, H-7), 7.78 (1 H, d, $J_{1,3}$ 2.4 Hz, H-1); δ_C (100 MHz, $CDCl_3$) 21.9 (CH_3, 2 × CH_3 of isopropyl), 31.3 (CH_3, $COCH_3$), 56.7 (CH_3, 4-OCH_3), 64.1 (CH_3, 5-OCH_3), 71.3 (CH, OCH), 101.2 (CH, C-1), 106.9 (CH, C-3), 107.3 (CH, C-7), 119.9 (quat., C-6), 130.7 (quat., C-4a), 131.5 (quat., C-8a), 148.4 (quat., C-5), 149.6 (quat., C-8), 151.0 (quat., C-4), 158.8 (quat., C-2), 200.8 (quat., C=O); *m/z* 436 (M^+, 42%), 394 (M − C_2H_2O, 73), 379 (11), 233 (100).

(ii) *4,5-Dimethoxy-7-trifluoromethanesulfonyloxynaphthalen-1-yl acetate* **24** (14 mg, 14%) was an off-white solid, mp 132–134 °C, for which the ^1H NMR data were in agreement with that reported in the literature.[12]

6,6′-Diacetyl-8,8′-diisopropoxy-4,4′,5,5′-tetramethoxy-2,2′-binaphthalenyl (16)

A mixture of potassium acetate (34 mg, 0.344 mmol), dry dioxane (1.0 mL), $PdCl_2$(dppf) (2.8 mg, 0.0034 mmol), dppf (1.9 mg, 0.0034 mmol), bis(pinacolato)diboron (32 mg, 0.126 mmol) and 6-acetyl-8-isopropoxy-4,5-dimethoxynapthalen-2-yl trifluoromethanesulfonate **23** (50 mg, 0.115 mmol) was heated under argon, with stirring at 110 °C for 1.75 h. Potassium phosphate (73 mg, 0.344 mmol), $PdCl_2$(dppf) (2.8 mg, 0.0034 mmol) and 6-acetyl-8-isopropoxy-4,5-dimethoxynapthalen-2-yl trifluoromethanesulfonate **23** (50 mg, 0.115 mmol) were then added and the resultant mixture heated with stirring at 110 °C for 2.5 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 brown oil. Further purification by flash column chromatography using 3 : 7 ethyl

acetate–hexane as eluent yielded the *title compound* **16** (38 mg, 58%) as a bright yellow solid, mp 157–160 °C [Found (EI): M^+, 574.2561; $C_{34}H_{38}O_8$ requires M^+, 574.2567]; ν_{max} (CH_2Cl_2 solution) 1666 (C=O), 1591 (C=C), 1373 [$C(CH_3)_2$], 1067 (C–O) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.47 (6 H, d, J 6.0 Hz, CH_3 of isopropyl), 2.81 (3 H, s, $COCH_3$), 3.88 and 4.16 (each 3 H, s, OCH_3), 4.80 (1 H, septet, J 6.0 Hz, CH of isopropyl), 7.16 (1 H, s, H-7), 7.31 (1 H, d, $J_{3,1}$ 1.4 Hz, H-3), 8.26 (1 H, d, $J_{1,3}$ 1.4 Hz, H-1); δ_C (100 MHz, $CDCl_3$) 22.1 (CH_3, CH_3 of isopropyl), 31.5 (CH_3, $COCH_3$), 56.5 (CH_3, 4-OCH_3), 63.9 (CH_3, 5-OCH_3), 71.1 (CH, OCH), 106.6 (CH, C-1), 106.8 (CH, C-3), 114.0 (CH, C-7), 119.8 (quat., C-6), 129.4 (quat., C-4a), 132.4 (quat., C-8a), 140.4 (quat., C-2), 149.9 (quat., C-8), 151.7 (quat., C-4), 157.4 (quat., C-5), 201.0 (quat., C=O); *m/z* 574 (M^+, 100%), 531 [$M - CH(CH_3)_2$, 33], 490 (68), 474 (18).

6,6′-Diacetyl-4,4′-dimethoxy-2,2′-binaphthalenyl-5,5′,8,8′-tetraone (14)

Binaphthyl **16** (7 mg, 0.0122 mmol) and freshly prepared AgO (24.1 mg, 0.195 mmol) were mixed in dioxane (0.92 mL). To this mixture was added HNO_3 (0.017 mL of a 6 M solution) and the reaction mixture was stirred for 10 min, after which time further AgO (24.1 mg, 0.195 mmol) and HNO_3 (0.017 mL of a 6 M solution) were added. After stirring for an additional 10 min the reaction mixture was quenched with water (5 mL) and extracted into dichloromethane (4 × 10 mL). The organic layer was washed with water (20 mL), dried over magnesium sulfate and the solvent removed under reduced pressure to yield the *title compound* **14** (5 mg, 91%) as an orange oil which was not purified further. ν_{max}(CH_2Cl_2 solution) 1715 (C=O, acetyl) and 1665 (C=O, quinone) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.64 (3 H, s, $COCH_3$), 4.13 (3 H, s, OCH_3), 7.08 (1 H, s, H-7), 7.51 (1 H, d, $J_{3,1}$ 1.6 Hz, H-3), 7.97 (1 H, d, $J_{1,3}$ 1.6 Hz, H-1).

(6b*R**,6b′*R**,9a*R**,9a′*R**)-6-Acetyl-2-(6-acetyl-6b,8,9,9a-tetrahydro-5-hydroxy-4-methoxy-8-oxofuro[2,3-*b*]naphtho[2,1-*d*]-furan-2-yl)-6b,9a-dihydro-5-hydroxy-4-methoxyfuro[2,3-*b*]naphtho[2,1-*d*]furan-8(9*H*)-one and (6b*R**,6b′*S**,9a*R**,9a′*S**)-6-acetyl-2-(6-acetyl-6b,8,9,9a-tetrahydro-5-hydroxy-4-methoxy-8-oxofuro[2,3-*b*]naphtho[2,1-*d*]furan-2-yl)-6b,9a-dihydro-5-hydroxy-4-methoxyfuro[2,3-*b*]naphtho[2,1-*d*]furan-8(9*H*)-one (13a and 13b)

To a solution of bis-naphthoquinone **14** (9 mg, 0.0196 mmol) in dry acetonitrile (1.2 mL) cooled to 0 °C under an atmosphere of nitrogen was added dropwise, over a period of 2 min, a solution of 2-trimethylsilyloxyfuran **8** (0.01 mL, 0.059 mmol) in dry acetonitrile (0.2 mL). After stirring for 1 h at 0 °C the solvent was removed under reduced pressure to afford an orange oil. Purification by flash column chromatography using ethyl acetate–hexane (2 : 1) as eluent afforded a 1 : 1 mixture of the *title adducts* **13a** and **13b** (5 mg, 41%) as a yellow solid, mp 129–131 °C [Found (FAB): M + H, 627.1495; $C_{34}H_{27}O_{12}$ requires M + H, 627.1503]; ν_{max} (CH_2Cl_2 solution) 3332 (OH), 1778 (C=O, γ-lactone) and 1632 (C=O, *o*-hydroxyaryl ketone) cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.80 (6 H, s, $COCH_3$), 3.10–3.12 (4 H, m, H-9 and H-9′), 4.23 (6 H, s, OCH_3), 5.42–5.55 (2 H, m, H-9a), 6.65 (2 H, d, $J_{6b,9a}$ 6.0 Hz, H-6b), 7.19 (2 H, d, $J_{3,1}$ 1.4 Hz, H-3), 7.82 (2 H, d, $J_{1,3}$ 1.4 Hz, H-1), 11.8 (2 H, s, OH); δ_C (75 MHz, $CDCl_3$) 32.2 (CH_3, $COCH_3$), 35.7 (CH_2, C-9), 56.9 (CH_3, OCH_3), 81.3 (CH, C-9a), 85.3 (CH, C-6b), 107.1 (CH, C-1), 114.3 (CH, C-3), 116.0, 125.5, 128.8, 130.9 (quat., C-4a, C-6, C-6a, C-10b), 141.3, 150.4, 155.5, 158.8 (quat., C-2, C-4, C-5, C-10a), 174.4 (quat., C-8), 200.3 [quat., C=O (ketone)]; *m/z* 627 (M + H, 1%). Analytical HPLC [C_{18} 3μ 33 × 7 mm; 1 min water (0.05% trifluoroacetic acid) flush followed by a 9 min steady gradient to acetonitrile; 2 mL min^{-1}] showed two major components with retention times of 8.6 and 9.1 min with equal peak areas indicating a 1 : 1 mixture of diastereomers.

(3a*R**,3a′*S**,5*S**,5′*R**,11b*R**,11b′*S**)-3,3a,5,11b-Tetrahydro-9-(3,3a,5,11b-tetrahydro-5-hydroxy-7-methoxy-5-methyl-2,6,11-trioxo-2*H*-furo[3,2-*b*]naphtho[2,3-*d*]pyran-9-yl)-5-hydroxy-7-methoxy-5-methyl-2*H*-furo[3,2-*b*]naphtho[2,3-*d*]pyran-2,6,11-trione and (3a*R**,3a′*R**,5*S**,5′*S**,11b*R**,11b′*R**)-3,3a,5,11b-tetrahydro-9-[3,3a,5,11b-tetrahydro-5-hydroxy-7-methoxy-5-methyl-2,6,11-trioxo-2*H*-furo[3,2-*b*]naphtho[2,3-*d*]pyran-9-yl]-5-hydroxy-7-methoxy-5-methyl-2*H*-furo[3,2-*b*]naphtho[2,3-*d*]pyran-2,6,11-trione (12a and 12b)

To a vigorously stirred solution of adducts **13a** and **13b** (5 mg, 0.008 mmol) in acetonitrile (1 cm^3) at 0 °C was added a solution of ceric ammonium nitrate (18 mg, 0.032 mmol) in water (2 cm^3). After 15 min the reaction mixture was extracted with dichloromethane (2 × 10 cm^3). The combined extracts were washed with brine (10 cm^3), dried (Na_2SO_4) and the solvent removed under reduced pressure to afford a yellow oil. Purification by flash chromatography using hexane–ethyl acetate (3 : 7) then ethyl acetate as eluent afforded a 1 : 1 mixture of the *title compounds* **12a** and **12b** (1.5 mg, 28%) as a yellow oil [Found (CI): M + H, 659.1346; $C_{34}H_{27}O_{14}$ requires M + H, 659.1400]; ν_{max}(film) cm^{-1} 3440 (OH), 1786 (C=O, lactone) and 1664 cm^{-1} (C=O, quinone); δ_H [400 MHz, $(CD_3)_2SO$] 1.81 (3H, s, CH_3), 1.82* (3H, s, CH_3), 2.54 (2H, d, J_{gem} 17.5 Hz, 3-H), 3.22 (2H, dd, J_{gem} 17.5 Hz and $J_{3',3a}$ 5.1 Hz, 3-H′), 4.27 (6H, s, OCH_3), 4.95 (2H, dd, $J_{3a,3'}$ 5.1 Hz, $J_{3a,11b}$ 2.9 Hz, 3a-H), 5.37 (2H, d, $J_{11b,3a}$ 2.9 Hz, 11b-H), 5.89–5.92 (2H, br s, OH), 7.21 (1H, d, $J_{8,10}$ 1.4 Hz, 8-H), 7.22* (1H, d, $J_{8,10}$ 1.4 Hz, 8-H), 7.99 (1H, d, $J_{10,8}$ 1.4 Hz, 10-H) and 8.00* (1H, d, $J_{10,8}$ 1.4 Hz, 10-H); *m/z* 659 (M + H, 9%), 643 (M − O, 14).

*Denotes resonance for diastereomer.

6-Acetyl-4-methoxy-5,8-dioxo-5,8-dihydronaphthalen-2-yl trifluoromethanesulfonate (25)

6-Acetyl-8-isopropoxy-4,5-dimethoxynaphthalen-2-yl trifluoromethanesulfonate **23** (36 mg, 0.0825 mmol) and freshly prepared AgO (82 mg, 0.66 mmol) were mixed in dioxane (6.0 mL). To this mixture was added HNO_3 (0.115 mL of a 6 M solution) and the reaction mixture was stirred for 10 min, after which time further AgO (24.1 mg, 0.195 mmol) and HNO_3 (0.017 mL of a 6 M solution) were added. After stirring for an additional 10 min the reaction mixture was quenched with water (10 mL) and extracted into dichloromethane (4 × 20 mL). The organic layer was washed with water (40 mL), dried over magnesium sulfate and the solvent removed under reduced pressure to yield the *title compound* **25** (30 mg, 96%) as a yellow solid which was not purified further; mp 118–120.5 °C [Found (EI): M^+, 378.0014; $C_{14}H_9F_3O_7S$ requires M^+, 378.0021]; ν_{max} (CH_2Cl_2 solution) 1700 (C=O, acetyl) and 1655 (C=O, quinone) cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.58 (3 H, s, $COCH_3$), 4.04 (3 H, s, OCH_3), 7.07 (1 H, s, H-7), 7.19 (1 H, d, $J_{3,1}$ 2.4 Hz, H-3), 7.97 (1 H, d, $J_{1,3}$ 2.4 Hz, H-1); *m/z* 380 (M + 2, 21%), 378 (M^+, 93), 363 (M − CH_3, 25), 245 (M − CF_3SO_2, 55).

6-Acetyl-6b,8,9,9a-tetrahydro-5-hydroxy-4-methoxy-8-oxofuro[2,3-*b*]naphtho[2,1-*d*]furan-2-yl trifluoromethanesulfonate (26)

To a solution of naphthoquinone **25** (30 mg, 0.0783 mmol) in dry acetonitrile (4.3 mL) cooled to 0 °C under an atmosphere of nitrogen was added dropwise, over a period of 2 min, a solution of 2-trimethylsilyloxyfuran **8** (0.119 mL, 0.24 mmol) in dry acetonitrile (0.72 mL). After stirring for 1 h at 0 °C the solvent was removed under reduced pressure to afford an orange solid. Purification by flash column chromatography using gradient elution (from 2.5 : 7.5 to 4 : 6 ethyl acetate–hexane) afforded the *title compound* **26** (27 mg, 74%) as a bright yellow solid, mp 177–180 °C [Found (EI): M^+, 462.0231; $C_{18}H_{13}F_3O_9S$ requires M^+, 462.0232]; ν_{max} (CH_2Cl_2 solution) 3359 (OH), 1784 (C=O, γ-lactone) and 1633 (C=O, *o*-hydroxyaryl ketone) cm^{-1}; δ_H (400

MHz, $CDCl_3$) 2.78 (3 H, s, $COCH_3$), 3.12–3.13 (2 H, m, H-9 and H-9′), 4.13 (3 H, s, OCH_3), 5.48–5.52 (1 H, m, H-9a), 6.55 (1 H, d, $J_{6b,9a}$ 6.0 Hz, H-6b), 6.83 (1 H, d, $J_{3,1}$ 2.4 Hz, H-3), 7.44 (1 H, d, $J_{1,3}$ 2.4 Hz, H-1), 12.2 (1 H, s, OH); δ_C (100 MHz, $CDCl_3$) 31.8 (CH_3, $COCH_3$), 35.4 (CH_2, C-9), 57.1 (CH_3, OCH_3), 81.4 (CH, C-9a), 84.9 (CH, C-6b), 101.9 (CH, C-1), 107.0 (CH, C-3), 114.9, 116.5, 116.6, 125.1 (quat., C-6a, C-4a, C-6, C-10b), 149.4, 149.8, 156.2, 160.3 (quat., C-5, C-10a, C-4, C-2), 174.0 (quat., C-8), 200.8 [quat., C=O (ketone)]; *m/z* 462 (M^+, 100%), 447 (M − CH_3, 15), 329 (M − CF_3SO_2, 4), 301 (84).

3,3a,5,11b-Tetrahydro-5-hydroxy-7-methoxy-5-methyl-2*H*-furo[3,2-*b*]naphtho[2,3-*d*]pyran-9-yl-2,6,11-trione trifluoromethanesulfonate (27)

A solution of ceric ammonium nitrate (33 mg, 0.061 mmol) in water (1 mL) was added dropwise to a solution of furonaphthofuran **26** (14 mg, 0.030 mmol) in acetonitrile (2 mL) and stirred for 15 min. The mixture was then diluted with dichloromethane (5 mL), washed with water (2 × 3 mL), and dried over magnesium sulfate. Evaporation under reduced pressure yielded an orange oil. Purification by flash column chromatography using 8 : 2 ethyl acetate–hexane as eluent gave the *title compound* **27** (9 mg, 62%) as a yellow oil [Found (DEI): M^+, 478.0159; $C_{18}H_{13}F_3O_{10}S$ requires M^+, 478.0182]; ν_{max} (CH_2Cl_2 solution) 3392 (OH), 1788 (C=O, γ-lactone) and 1673 (C=O, quinone) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.79 (3 H, s, CH_3), 2.75 (1 H, d, J_{gem} 17.6 Hz, H-3′), 2.94 (1 H, dd, J_{gem} 17.6 and $J_{3,3a}$ 4.8 Hz, H-3), 4.06 (3 H, s, OCH_3), 4.90 (1 H, dd, $J_{3,3a}$ 4.8 Hz and $J_{3a,11b}$ 2.9, H-3a), 5.25 (1 H, d, $J_{11b,3a}$ 2.9 Hz, H-11b), 7.20 (1 H, d, $J_{8,10}$ 2.2 Hz, H-8), 7.64 (1 H, d, $J_{10,8}$ 2.2 Hz, H-10), 9.28 (1 H, s, OH); δ_C (100 MHz, $CDCl_3$) 27.5 (CH_3, CH_3), 36.5 (CH_2, C-3), 57.3 (CH_3, OCH_3), 67.1 (CH, C-3a), 68.5 (CH, C-11b), 93.2 (quat., C-5), 111.3 (CH, C-10), 111.6 (CH, C-8), 120.2 (quat., C-6a), 137.0 (quat., C-10a), 148.2 (quat., C-5a), 153.3 (quat., C-11a), 161.6 (quat., C-9), 161.8 (quat., C-7), 174.1 (quat., C-2), 181.0 (quat., C-6), 181.2 (quat., C-11); *m/z* 478 (M^+, 2%), 476 (M − 2H, 3), 463 (M − CH_3, 17).

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