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# Addition of silyloxydienes to 2,6-dibromo-1,4-benzoquinone: an approach to highly oxygenated bromonaphthoquinones for the synthesis of thysanone

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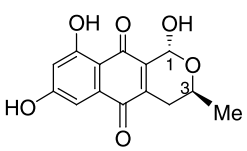
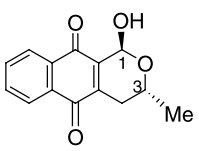
**Abstract**—The synthesis of tetraoxygenated bromonaphthoquinones **6a**, **6b**, **6c**, **6d**, key intermediates for a synthesis of the 3C protease inhibitor, thysanone, were investigated. Addition of 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene **8** to 2,6-dibromo-1,4-benzoquinone **10** in benzene afforded a mixture of naphthoquinone **6a**, arising from Diels–Alder addition followed by aromatisation, and Michael adduct **12**. The Michael adduct **12** predominated when THF was used as solvent whereas **6a** predominated when benzene was used. Naphthoquinone **6a** underwent benzylation to naphthoquinone **6c**. Addition of 1,1-dimethoxy-3-trimethylsilyloxy-1,3-butadiene **9** to 2,6-dibromo-1,4-benzoquinone **10** followed by benzylation failed to afford the desired bromonaphthoquinone **6d** yet methylation did afford naphthoquinone **6b**. Bromonaphthoquinone **6d** was finally prepared from naphthol **18**, obtained from addition of diene **9** to 1,4-benzoquinone **17**, followed by *ortho*-bromination and oxidation. Attempted Sakurai allylation of bromonaphthoquinone **6d** afforded naphthodihydrofuran **21**. A similar observation was observed for 2-carbomethoxy-1,4-naphthoquinone **22** that also underwent Sakurai allylation to afford naphthodihydrofuran **23**. The structure of Michael adduct **12** was confirmed by X-ray crystallography. 

The replication of many animal and plant viruses relies on proteolytic processing and is dependent upon two virally encoded proteases 3C-protease and 2A-protease. Human rhinoviruses belong to a family of picornaviruses that are responsible for causing common colds[1] as well as polio, hepatitis A and foot and mouth disease.[2] Human rhinovirus 3C-protease is therefore an attractive target for the screening of lead compounds for eventual control or cure of the common cold. Thysanone **1**, isolated from *Thysanophora penicilloides*[3] was found to exhibit potent activity ($IC_{50}$ 13 ug/ml) against human rhinovirus 3C-protease by scientists at Merck, Sharp and Dohme who were screening microbial extracts against this enzyme. Thysanone **1** is closely related to the pyranonaphthoquinone family of antibiotics[4] and the absolute stereochemistry of thysanone **1** was established to be (1*R*,3*S*) by an elegant total synthesis recently reported by Donner and Gill.[5]



(1*R*,3*S*)-thysanone **1**



(1*S*,3*R*)-dideoxythysanone **2**

In the synthesis of thysanone **1** by Donner and Gill[5] the (*S*)-stereochemistry at C-3 was derived in nine steps from (*S*)-mellein which in turn was prepared in several steps from (*S*)-propylene oxide. The oxygenated naphthalene ring was assembled at a late stage via Diels–Alder addition of a silyloxydiene to a bromobenzoquinone that already contained a dihydrobenzopyran ring appended to it. Our synthetic approach to thysanone **1** was based on a strategy wherein the stereochemistry at C-3 is controlled using an asymmetric reduction and an efficient synthesis of (1*S*,3*R*)-dideoxythysanone **2** was recently reported[6] using this strategy. This approach to thysanone **1** differed from that used by Donner and Gill[5] in that construction of the dihydrobenzopyran was envisaged to take place from bromoalcohol **3** that is derived from reduction of ketone **4**. Ketone **4** is formed from allylbromonaphthalene **5** via Wacker oxidation. Allylbromonaphthalene **5** in turn is available from Sakurai allylation of a suitably oxygenated bromonaphthoquinone **6** that is obtained by oxidative demethylation of tetraoxygenated bromonaphthalene **7** (Scheme 1). We therefore herein report our efforts to prepare suitable oxygenated bromonaphthoquinones **6** that will enable us to complete our synthesis of thysanone **1** based on our initial synthesis of dideoxythysanone **2**.

Thysanone **1** has the same oxygenation pattern as quinone A, quinone A′ and deoxyquinone A which are derivatives of the aphid pigments protoaphin-*fb*,17 protoaphid-*sl*,[7] and deoxyprotoaphin.[8] Giles et al.[9,10] have developed a

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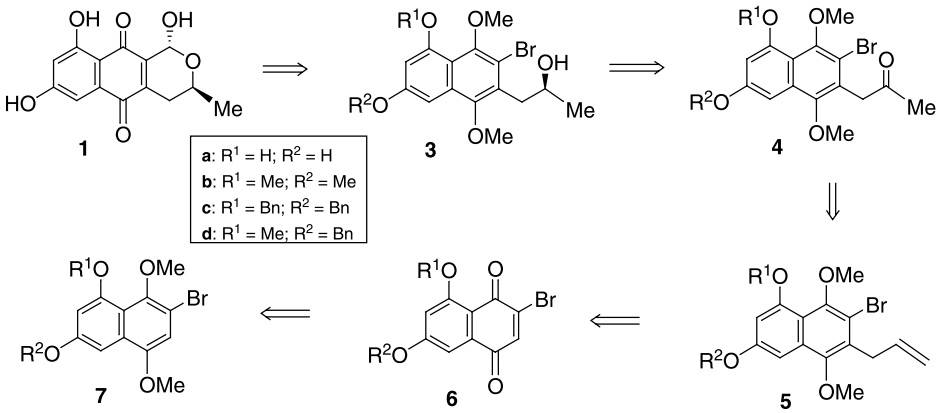
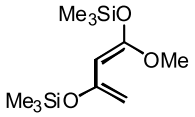
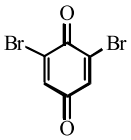
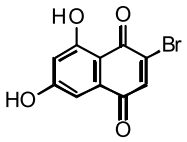
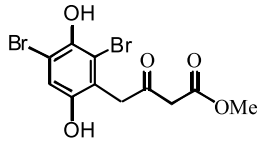
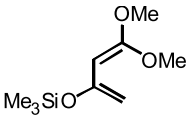
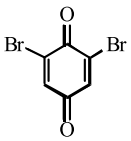
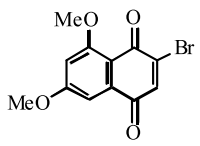
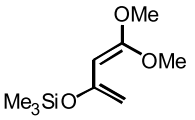
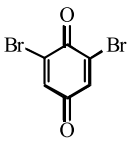
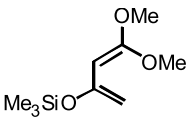
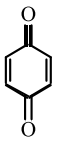
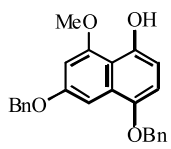
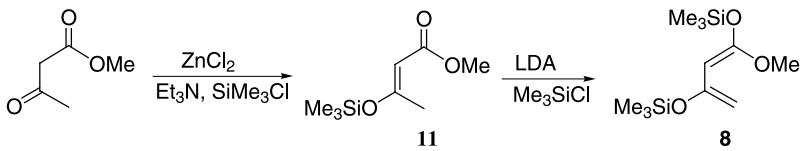



**Scheme 1.**

synthesis of these aphid derivatives and have established that a benzyl ether was a suitable protecting group for 7-OH. However, the use of methyl or isopropyl ethers at this position led to destruction of the sensitive pyran ring during deprotection in related synthetic studies towards quinone A.[11] A benzyl ether at the C-7 position is thought be to more suitable as it can be removed by hydrogenolysis over palladium on charcoal. This milder deprotection would be less damaging to the pyran ring in thysanone **1**. The 9-OH group can be protected as either a methyl or benzyl ether, as

**Table 1**. Addition of silyloxydienes **8** and **9** to 2,6-dibromo-1,4-benzoquinone **10**

| Diene | Quinone | Conditions | Products, yield (%) | |
|---|---|---|---|---|
|  **8** |  **10** | |  **6a** |  **12** |
| Entry 1 | | Benzene, room temperature, 18 h. | 32 | 12 |
| Entry 2 | | Benzene, reflux, 4 h. | 19 | 8 |
| Entry 3 | | $CH_2Cl_2$ reflux, 12 h. | 26 | 12 |
| Entry 4 | | THF, room temperature, 4 h | 6 | 15 |
| Entry 5 | | THF, −78°C, 2 h. then HCl | 14 | 40 |
|  **9** |  **10** | |  **6b** | |
| Entry 6 | | (i) Benzene, reflux, 1 h, (ii) MeOH, 5% HCl, (iii) MeI, $Ag_2O$ | 25 | |
|  **9** |  **10** | | | |
| Entry 7 | | (i) Benzene, reflux, 1 h, (ii) MeOH, 5% HCl, (iii) BnBr, $Ag_2O$ | Complex mixture no **6d** isolated | |
|  **9** |  **17** | |  **18** | |
| Entry 8 | | (i) Benzene, room temperature, 1 h, (ii) BnBr, $K_2CO_3$ DMF, 60°C | 31 | |




**Scheme 2.**

it is *peri* to the quinone carbonyl group at C-10 and can therefore be more easily removed than a 7-OMe group using boron tribromide.

Bromonaphthoquinones **6c** and **6d** in which the hydroxyl group at C-7 is protected as a benzyl ether were considered suitable intermediates for our synthesis of thysanone **1**. These compounds were envisaged to be assembled by Diels–Alder addition of 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene **8** or 1,1-dimethoxy-3-trimethylsilyloxy-1,3-butadiene **9** to 2,6-dibromo-1,4-benzoquinone **10** (Table 1). The presence of strategically placed halogen substituents in benzoquinone and naphthoquinone dienophiles controls the regiochemistry of the cycloaddition such that the nucleophilic end of an electron rich diene adds to the unsubstituted carbon of the quinone.[12–18]

Our initial attention focused on the synthesis of bromonaphthoquinone **6c** available from benzylation of bromonaphthoquinone **6a**, the anticipated Diels–Alder adduct formed from 1-methoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene **8** and 2,6-dibromo-1,4-benzoquinone **10** (entries 1–5, Table 1). 2,6-Dibromo-1,4-benzoquinone **10** was prepared uneventfully from 2,4-dibromo-4-nitrophenol using the procedure reported by van Erp.[19] Diene **8** was prepared[20–22] from silyl enol ether **11** (Scheme 2) that in turn was available from methyl acetoacetate.[23,24] In the reported procedure[24] for the preparation of silyl enol ether **11**, a mixture of methyl acetoacetate, zinc chloride and triethylamine in benzene was treated with trimethylsilyl chloride and the reaction left to stir overnight. In our hands we found that the reaction required stirring for 2–3 days in order to obtain an acceptable 70% yield of the silyl ether **11**. Reaction of silyl ether **11** with lithium diisopropylamide in THF at −78°C for 2 min followed by the addition of trimethylsilyl chloride afforded diene **8** in over 90% yield. Diene **8** could only be stored in the freezer at −5°C for 1 week due to the facile migration[25] of the trimethylsilyl group attached to the oxygen at C-1 to C-4.

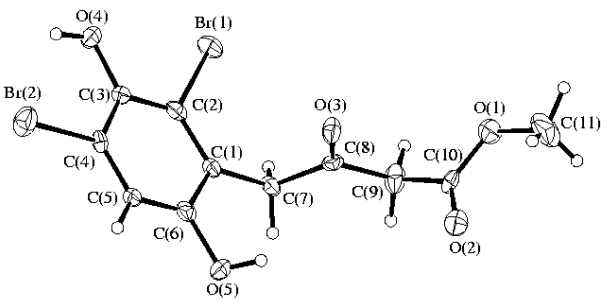


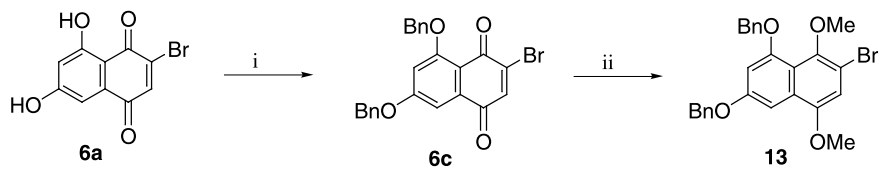

**Figure 1.**

Addition of diene **8** to 2,6-dibromo-1,4-benzoquinone **10** in dry benzene under nitrogen for 18 h. afforded the Diels–Alder adduct **6a** as an orange solid in 32% yield together with the conjugate addition product **12** in 12% yield. Bromonaphthoquinone **6a** exhibited a broad absorbance at 3400–3500 $cm^{-1}$ consistent with the presence of the two hydroxyl groups and an absorbance at 1653 $cm^{-1}$ due to the quinonoid carbonyls. The $^1H$ NMR spectrum of **6a** exhibited *meta*-coupled aromatic doublets at $\delta_H$ 6.63 and $\delta_H$ 7.04 ($J$ 2.5 Hz), assigned to 8-H and 6-H, respectively, and a singlet at $\delta_H$ 7.49 was assigned to the quinonoid proton, 2-H. The two hydroxyl protons, 7-OH and 5-OH resonated at $\delta_H$ 10.32 and $\delta_H$ 11.87, respectively, with 5-OH resonating further downfield due to hydrogen bonding to the C-4 quinone carbonyl group.

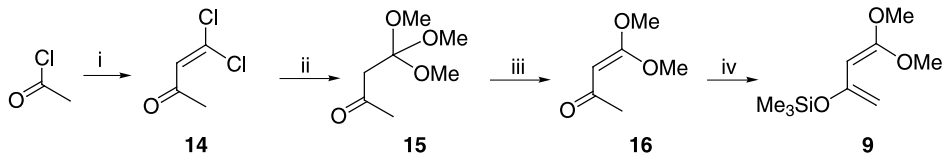
Considerable effort was made to improve the yield of the desired naphthoquinone **6a** by conducting the reaction in a variety of solvents and at different temperatures, however these efforts were fruitless. Representative examples of these attempts are summarized (entries 1–5, Table 1). Adding base to the initial reaction mixture (pyridine or $NaHCO_3$) in order to mop up any hydrogen bromide formed did not improve the yield. Alternatively, use of an acidic workup or the addition of silica gel to the reaction in an effort to facilitate the aromatization step, did not help.

It was found that use of THF as the solvent increased the yield of the conjugate addition product **12** (entries 4 and 5, Table 1) that was only observed as a minor product when benzene was used as the solvent. The formation of Michael adducts such as **12** is not without precedence in related systems using highly electrophilic dienophiles.[6,12] The $^1H$ NMR spectrum of Michael adduct **12** was difficult to assign due to the presence of tautomers, however the structure of **12** was confirmed by X-ray crystallography (Fig. 1).

Benzylation of dihydroxynaphthoquinone **6a** was carried out using freshly prepared silver(I) oxide and benzyl bromide in chloroform in the dark for 3 days (Scheme 3). Although this procedure only afforded bis(benzyloxy)-naphthoquinone **6c** in 30% yield, alternative conditions such as the use of sodium hydride in DMF or potassium




**Scheme 3.** *Reagents and conditions*: (i) $Ag_2O$, $CHCl_3$, BnBr, room temperature, 3 days, 30%; (ii) $Na_2S_2O_4$, $Bu_4NI$, $Me_2So_4$, 50% KOH, THF, 75%.




**Scheme 4.** *Reagents and conditions*: (i) vinylidence chloride, $AlCl_3$, 82%; (ii) NaOMe, MeOH, 0°C, 63%; (iii) 150°C, 5 h, 44%; (iv) LDA, $Me_3SiCl$, −78°C, 97%.

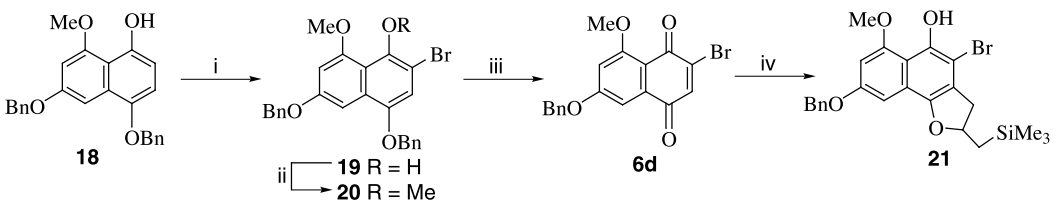
carbonate in acetone, only resulted in decomposition of the starting material. Bis(benzyloxy)naphthoquine **6c** was unstable, thus in order to facilitate characterisation, reductive methylation to dimethoxynaphthalene **13** was carried out in 75% yield using sodium dithionite in aqueous THF with tetrabutylammonium iodide followed by the addition of potassium hydroxide and dimethyl sulfate.

Given the disappointing yield of naphthoquinone **6a** from the addition of diene **8** to 2,6-dibromo-1,4-benzoquinone **10**, we next focused our attention on the synthesis of naphthoquinone **6d** from reaction of diene **9** with 2,6-dibromo-1,4-benzoquinone **10** followed by benzylation of the C-7 hydroxyl group (entry 7, Table 1). 1,1-Dimethoxy-3-trimethylsilyloxy-1,3-butadiene **9** was prepared in four steps from acetyl chloride (Scheme 4) using procedures that were slightly modified from that given in the literature.[26]

The first step in the synthesis of diene **9** involved preparation of 4,4-dichlorobut-3-en-2-one **14** in 82% yield via Friedel–Craft acylation of vinylidene chloride by acetyl chloride using aluminium trichloride as reported by Heilbron et al.[27] In our hands, a slightly modified procedure was used. Finely powdered aluminium chloride was added to acetyl chloride at −9°C. Conversion of enone **14** into the trimethyl orthoester **15** was then effected using the method of Banville and Brassard[26] upon treatment with sodium methoxide in methanol at 0°C. Pyrolysis of orthoester **15** to enone **16** proved to be the most difficult step. Banville and Brassard[26] reported that this pyrolysis proceeded in 35% yield, however, it was hoped that modification of the procedure might increase the yield of the desired product. The literature procedure involved heating orthoester **15** in a pear-shaped flask at 160°C for 5 h. After cooling, the mixture was distilled at reduced pressure to afford the product **16** in 44% yield together with recovered **15** in 25% yield. It was found that leaving the pyrolysis for longer periods of time led to decreased yields of enone **16** whilst the yield of recovered starting material **15** did not change. The reaction was also carried out at a higher temperature, namely 190°C for 5 h, however this also led to decomposition of the desired product. Thus it was found that the optimum yield of enone **16** was obtained by adhering to the literature procedure which involved heating the orthoester **15** at 150°C for exactly 5 h. Finally, enone **16** was treated with lithium diisopropylamide and trimethylsilyl chloride to afforded diene **9** in 97% yield. This procedure proved better than using the literature method[26] that used triethylamine and trimethylsilyl chloride in benzene to effect the final silylation step. Diene **9** needed to be redistilled immediately before use in order to remove trace quantities of enone **15** that formed upon storage.

Grandmaison and Brassard[28] reported a procedure wherein diene **9** and 2,6-dibromo-1,4-benzoquinone **10** were reacted to form a Diels–Alder adduct that was hydrolysed using methanol and 5% HCl. The crude adduct was not isolated but immediately treated with methyl iodide and silver(I) oxide to produce dimethoxynaphthoquinone **6b** in 25% yield. In order to generate naphthoquinone **6d** in which 7-OH is protected as a benzyl ether rather than a methyl ether, it was thought that the above procedure could be used replacing methyl iodide with benzyl bromide. Disappointingly, substituting benzyl bromide for methyl iodide in this procedure, afforded a complex mixture of products with none of the desired product **6d** being isolated (entry 7, Table 1). On the other hand, when the literature procedure with methyl iodide was used the desired product **6b** was afforded in the anticipated 25% yield (entry 6, Table 1). Considerable experimentation did not avail us of the desired naphthoquinone **6d** when using benzyl bromide in the alkylation step thereby leading us to conclude that addition of diene **9** to 2,6-dibromo-1,4-benzoquinone **10** is an unfavourable process and other side products are generated in preference to the required product **6d**.

We next considered that the desired bromonaphthoquinone **6d** could be formed by bromination and oxidation of naphthol **18** (Scheme 5). Naphthol **18** in turn, has been prepared albeit in low yield, from cycloaddition of diene **9** to 1,4-benzoquinone **17** followed by benzylation.[10] Following the procedure described by Giles et al.[10] a solution of diene **9** and 1,4-benzoquinone **17** in benzene was stirred at room temperature for 12 h. The solvent was removed and the crude adduct redissolved in DMF then treated with benzyl bromide and anhydrous potassium carbonate. After




**Scheme 5.** *Reagents and conditions*: (i) $Br_2$, $CCl_4$, 0°C, 83%; (ii) NAH, MeI, DMF, 83%; (iii) $Ce(NH_4)_2(NO_3)_6$, $CH_3CN$, 1 h, 0°C, 79%; (iv) $MeAlCl_2$, $CH_2Cl_2$, −78°C, allyltrimethylsilane, 48%.

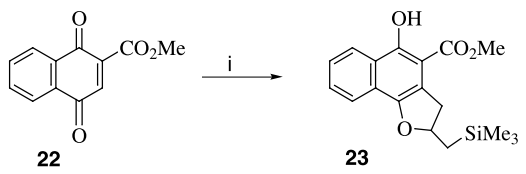
further stirring at 40°C for 18 h. naphthol **18** was isolated in 31% yield after purification by flash chromatography and was found to be unstable when stored at room temperature.

With naphthol **18** in hand, a bromine can now be introduced at the *ortho* position as required for a synthesis of thysanone **1**, that then serves as a vital tool for introduction of an aldehyde group. *ortho*-Bromination of naphthol **18** was therefore effected smoothly using bromine in carbon tetrachloride at 0°C affording unstable bromonaphthol **19** in 83% yield that then underwent methylation under standard conditions to tetraoxygenated bromonaphthalene **20**. The $^1$H NMR spectrum for bromonaphthol **19** exhibited two *meta*-coupled doublets with $J$=2 Hz at $\delta_H$ 6.64 ppm and $\delta_H$ 7.25 ppm assigned to 6-H and 8-H respectively, together with a singlet at $\delta_H$ 7.02 ppm assigned to H-2, thereby providing strong evidence for introduction of a bromine at C-3. Bromonaphthol **19** also underwent smooth oxidation with ceric ammonium nitrate (2.5 equiv.) in acetonitrile to bromonaphthoquinone **6d** thereby providing a suitable intermediate for our projected synthesis of thysanone **1**. Successful introduction of a bromine substituent onto the quinonoid nucleus was important in order to control the regiochemistry of the subsequent allylation step by bidentate coordination with the quinone carbonyl group at C-4 to a Lewis acid.

With bromonaphthoquinone **6d** finally in hand, our attention turned to the introduction of an allyl group at C-2. Attempts to effect oxidative allylation of bromonaphthoquinone **6d** with vinylacetic acid, potassium persulfate and silver nitrate as successfully used by Kometani et al.[29] on a simpler system, was unsuccessful and only starting material was recovered from the reaction. We therefore turned to the use of allyltrimethylsilane with methylaluminium dichloride as the Lewis acid at −78°C as these conditions had been successfully used by us in our earlier synthesis of dideoxythysanone **2**.[6]

More recently, attempted allylation of bromonaphthoquinone **6d** using these same conditions afforded the highly unstable naphthodihydrofuran **21**. Naphthodihydrofuran **21** arises from trapping of the initial β-silyl carbocation formed upon Michael addition of the allylsilane to the naphthoquinone, by the incumbent naphthol OH group at C-1 that is generated upon aromatization of the aromatic ring. Further support for the formation of naphthodihydrofuran **21** was also observed by us when attempted Sakurai allylation of naphthoquinone **22** afforded naphthodihydrofuran **23** (Scheme 6).

The difficulties described herein with our attempts to obtain bromonaphthoquinones **6a**, **6b**, **6c** or **6d** in a respectable yield, as required for the synthesis of a key intermediate at




22 23

**Scheme 6.** *Reagents and conditions*: (i) $MeAlCl_2$, $CH_2Cl_2$, −78°C, allyltrimethylsilane, 51%.

the early stages of a longer synthesis, have now prompted us to rethink our synthetic strategy to thysanone **1** in a direction far removed from our original synthesis of dideoxythysanone **2**.[6] The formation of the unusual naphthodihydrofurans **21** and **23** upon attempts to effect Sakurai reaction of the highly electrophilic benzoquinones **6d** and **22** with allyltrimethylsilane, have also provided impetus for development of an alternative strategy.

## 1. Experimental

### 1.1. General details

All reactions were conducted in flame-dried or oven-dried glassware under a dry nitrogen atmosphere unless otherwise noted. Tetrahydrofuran was dried over sodium/benzophenone and distilled prior to use. Flash chromatography was performed using Merck Kieselgel 60 (230–400 mesh) with the indicated solvents. Thin layer chromatography (TLC) was carried out on precoated silica plates (Merck Kieselgel $60F_{254}$) and compounds were visualized by UV fluorescence or by staining with vanillin in methanolic sulfuric acid and heating. Infrared spectra were recorded with a Perkin–Elmer 1600 series Fourier-transform infrared spectrometer as thin films between sodium chloride plates. Absorption maxima are expressed in wavenumbers ($cm^{-1}$) with the following abbreviations: s=strong, m=medium, w=weak and br=broad. $^1$H and $^{13}$C NMR spectra were obtained using a Bruker AC 200B or a Bruker AM 400 spectrometer. All chemical shifts are given in parts per million (ppm) downfield from tetramethylsilane as internal standard ($^1$H) or relative to $CDCl_3$ ($^{13}$C) and $J$ values are given in Hz. $^1$H NMR data are tabulated as s, singlet; d, doublet; t, triplet; q, quartet, m, multiplet, br, broad. High-resolution mass spectra were recorded using a VG70-SE spectrometer operating at nominal accelerating voltage of 70 eV. Chemical ionisation (CI) mass spectra were obtained with ammonia as the reagent gas.

**1.1.1. Methyl 3-trimethylsilyloxybut-2-enoate 11.** Anhydrous powered zinc chloride (0.2 g, 1.47 mmol) was added to triethylamine (15.8 $cm^3$, 0.11 mol) and the mixture stirred at room temperature for 1 h. or until the salt had become suspended in the amine. To this suspension was added a solution of methyl acetoacetate (10.8 $cm^3$, 0.05 mol) in dry benzene (15 $cm^3$) followed by trimethylsilyl chloride (10.85 g, 0.1 mol). The reaction mixture was heated to 40°C and stirred for 30 min, after which time the reaction mixture was cooled to room temperature and stirred for 2 days. Ether (100 $cm^3$) was added and the reaction mixture filtered. The filtrate and ether washes were combined and concentrated in vacuo to give a yellowish oil. Distillation of the crude oil at reduced pressure using a Vigreux column gave the title compound **11** (13.9 g, 70%) as a clear oil, bp 82–84°C/30 mm Hg (lit.[20] bp 71–72°C/9 mm Hg).

**1.1.2. 1-Methoxy-1,3-bis(trimethylsilyloxy)-buta-1,3-diene 8.** Butyllithium in hexanes (9 $cm^3$, 22.5 mmol, 2.5 mol $l^{-1}$) was added dropwise to a stirred solution of diisopropylamine (2.16 g, 3 $cm^3$, 21.3 mmol) in THF (75 $cm^3$) under nitrogen at 0°C. The solution was then

cooled to −78°C and methyl 3-trimethylsilyloxybut-2-enoate **11** (3.3 g, 17.7 mmol) added dropwise, over 5 min. After stirring for 3 min, trimethylsilyl chloride (3.07 g, 3.6 $cm^3$, 28.5 mmol) was added. The reaction mixture was allowed to warm to room temperature and the solvent removed in vacuo. The residue was washed with dry hexane, filtered and concentrated in vacuo to yield the title compound **8** (4.57 g, 99%) as a clear oil for which the $^1H$ NMR spectrum was in agreement with the literature.[20]

**1.1.3. 4,4-Dichlorobut-3-en-2-one 14.** Finely powered aluminium chloride (100.3 g, 0.75 mol) was added in portions, over 10 min, to acetyl chloride (100.8 g, 91 $cm^3$, 1.27 mol) at −9°C (ice/salt bath). Upon completion of the addition, the reaction was allowed to warm to room temperature. Vinylidene chloride (60.1 g, 50 $cm^3$, 0.62 mol) was then added dropwise over 1.5 h, with continuous stirring, forming a fine yellow precipitate. The reaction mixture was stirred for 1 h before quenching by slow addition of ice, then water (100 $cm^3$). After extraction into dichloromethane (4×100 $cm^3$), the combined organic layers were washed with water (3×100 $cm^3$), dried ($MgSO_4$) and concentrated in vacuo to yield the crude product. Further purification by distillation under vacuum using a Vigreux column yielded the title compound **14** (70.6 g, 82%), as a pale yellow oil, bp 53–55°C/26 mm Hg (lit.[27] bp 58°C/32 mm Hg).

**1.1.4. 4,4,4-Trimethoxybutan-2-one 15.** Freshly cut sodium metal (6.98 g, 0.302 mol) was added to dry methanol (120 $cm^3$) with vigorous stirring. Upon complete dissolution 4,4-dichlorobut-3-ene-2-one **14** (20 g, 0.144 mol) was added dropwise over 1 h. The reaction mixture was then stirred for 2 h., then quenched by pouring into water (100 $cm^3$) and extracting with dichloromethane (6×50 $cm^3$). The combined organic extracts were washed with water (2×50 $cm^3$), dried ($MgSO_4$) and evaporated in vacuo to yield an oil. The crude oil was purified by distillation under vacuum to yield the title compound **15** (14.9 g, 63%) as a clear oil, bp 48–50°C/2 mm Hg (lit.[26] 82–84°C/12 mm Hg).

**1.1.5. 4,4-Dimethoxybut-3-en-2-one 16.** 4,4,4-Trimethoxybutan-2-one **15** (12 g, 0.07 mol) was pyrolyzed, by heating in a pear-shaped flask, at 160°C for 5 h. After cooling to room temperature, distillation under reduced pressure afforded the title compound **16** (4.2 g, 44%) as a yellow oil, bp 80–82°C/0.8 mm Hg (lit.[26] bp 104–105°C/10 mm Hg) and starting material **15** (3.03 g, 25%). The $^1H$ NMR spectrum of enone **16** was in agreement with the literature.[26]

**1.1.6. 1,1-Dimethoxy-3-trimethylsilyloxy-1,3-butadiene 9.** Butyllithium in hexanes (12.8 $cm^3$, 32 mmol, 2.5 mol $l^{-1}$) was added dropwise to a stirred solution of diisopropylamine (8.64 g, 12 $cm^3$, 21.3 mmol) in THF (75 $cm^3$) under nitrogen at 0°C. The reaction mixture was then cooled to −78°C and a solution of 4,4-dimethoxybutan-2-one **16** (3.45 g, 26.5 mmol) in dry THF (10 $cm^3$) added dropwise, over 10 min. After stirring for 30 min, trimethylsilyl chloride (4.43 g, 5.2 $cm^3$, 39.8 mmol) was added and the reaction mixture allowed to warm to room temperature before the solvent was removed in vacuo. The residue was washed with dry hexane, filtered and concentrated in vacuo to yield the title compound **9** (5.21 g, 97%) as a clear oil for which the $^1H$ NMR spectrum was in agreement with the literature.[26]

**1.1.7. 2,6-Dibromo-1,4-benzoquinone 10.** Tin granules (8 g) were slowly added to a solution of 2,4-dibromo-4-nitrophenol (10 g, 0.33 mol) in acetic acid (40 $cm^3$) over 10 min. and the reaction mixture stirred until most of the tin was consumed (approx. 2 h). The reaction mixture was then filtered and the solid residue washed with boiling acetic acid (5 $cm^3$). The combined filtrate and washes were then quickly added to a solution of chromium trioxide (11 g) in conc. $H_2SO_4$ (50 $cm^3$) and water (500 $cm^3$). The solution instantly darkened and a yellow precipitate was formed. After stirring for 15 min, the solution was filtered, the solid washed with water (2×50 $cm^3$) then left to dry in air overnight. The crude solid was recrystallized from ethanol to give the title compound **10** (5.52 g, 61%) as golden flakes, mp 126–127°C (lit.[19] 129–130°C).

**1.1.8. 3-Bromo-5,7-dihydroxy-1,4-naphthoquinone 6a and methyl 3-oxo-4-(2,4 dibromo-3,6-dihydroxyphenyl)-butanoate 12.** To a solution of 2,6-dibromo-1,4-benzoquinone **10** (0.47 g, 1.75 mmol) in dry benzene (5 $cm^3$) under nitrogen, at room temperature, was added, dropwise over 10 min, a solution of diene **8** (0.5 g, 2 mmol) in dry benzene (5 $cm^3$). The reaction mixture was stirred for 18 h, after which time the solvent was removed in vacuo to yield a crude residue. The residue was purified by flash chromatography (20–30% ethyl acetate–hexane) to afford the title compound **6a** (0.15 g, 32%) as a bright orange solid, mp 192–194°C. (Found: $M^+$, 269.9383; 267.9388. $C_{10}H_5O_4{}^{81}Br$ and $C_{10}H_5O_4{}^{79}Br$ require 269.9350; 267.9371); $\nu_{max}$ (NaCl plates)/$cm^{-1}$ 3425 (OH), 1699 and 1653 (C═O) and 1599 (C═C); $\delta_H$ (200 MHz, $d^6$-acetone) 6.63 and 7.04 (each 1H, d, $J$=2.5 Hz, 6-H and 8-H), 7.49 (1H, s, 2-H), 10.32 (1H, bs, 7-OH) and 11.87 (1H, s, 5-OH); *m/z* (%) 270 ($^{81}Br$ $M^+$, 81), 268 ($^{79}Br$ $M^+$, 83), 189 (M−Br, 26) and 161 (100) and methyl 3-oxo-4-(2,4-dibromo-3,6-dihydroxyphenyl)-butanoate **12** (0.08 g, 12%) as pale crystals, mp 137–138°C. (Found: $M^+$, 383.8878; 381.8880; 379.8899. $C_{11}H_{10}O_5{}^{81}Br_2$, $C_{11}H_{10}O_5{}^{81}Br^{79}Br$ and $C_{11}H_{10}O_5{}^{79}Br_2$ require 383.8854; 381.8875; 379.8895); $\nu_{max}$ (NaCl plates)/$cm^{-1}$ 3300–3500 (OH), 1740 (C═O) and 1696 (C═C); *m/z* (%) 382 ($^{79}Br^{81}Br$ $M^+$, 10), 350 (M−MeOH, 23), 308 (73), 281 (56) and 101 (100). The structure of **12** was confirmed by X-ray crystallography (vide infra).

**1.1.9. 5,7-Bis(benzyloxy)-3-bromo-1,4-naphthoquinone 6c.** To a suspension of 3-bromo-5,7-dihydroxy-1,4-naphthoquinone **6a** (140 mg, 0.52 mmol) in chloroform (8 $cm^3$) under nitrogen, was added silver(I) oxide (0.72 g, 3.12 mmol)[33] and benzyl bromide (0.53 g, 0.37 $cm^3$, 3.12 mmol). The reaction mixture was vigorously stirred for 3 days, within which time two subsequent portions of silver(I) oxide (0.36 g, 1.56 mmol) and benzyl bromide (0.26 g, 0.18 $cm^3$, 1.56 mmol) were added. After this time the reaction mixture was diluted with chloroform (15 $cm^3$), filtered through a small Celite pad and the solvent removed in vacuo to yield an oily residue. The residue was purified by flash chromatography (5–20% ethyl acetate–hexane) to afford the title compound **6c** (69 mg, 30%) as an orange

oil. (Found: $M^+$, 450.0154; 448.0288. $C_{24}H_{17}O_4^{81}Br$ and $C_{24}H_{17}O_4^{79}Br$ require 450.0290; 448.0310); $\nu_{max}$ (NaCl plates)/$cm^{-1}$ 1660 (C═O) and 1592 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 5.18 (2H, s, 5-OC$H_2$Ph), 5.22 (2H, s, 7-OC$H_2$Ph), 7.12 (1H, s, 2-H) and 7.12–7.65 (12H, m, Ar-H); *m/z* (%) 450 ($^{81}Br$ $M^+$, 2), 448 ($^{79}Br$ $M^+$, 2), 357 (M−$CH_2$Ph 10) and 91 ($CH_2$Ph 100).

**1.1.10. 5,7-Bis(benzyloxy)-3-bromo-1,4-dimethoxynaphthalene 13.** To a stirred solution of naphthoquinone **6c** (30 mg, 0.07 mmol) and tetrabutylammonium iodide (5 mg, 0.02 mmol) in aqueous THF (30% water–70% THF) was added a solution of sodium dithionite (70 mg, 0.4 mmol) in water (0.2 $cm^3$). After 30 min a solution of potassium hydroxide (50%, 1 $cm^3$) was added followed 10 min later by dimethyl sulfate (1.3 $cm^3$, 13.75 mmol). After 12 h. the reaction mixture was poured into water (15 $cm^3$), extracted with dichloromethane (2×10 $cm^3$), dried ($MgSO_4$) and the solvent removed in vacuo. The crude residue was purified by flash chromatography (10% ethyl acetate–hexane) to yield the title compound **13** (34 mg, 75%) as a yellow–green oil. (Found: $M^+$, 480.0743; 478.0758. $C_{26}H_{23}O_4^{81}Br$ and $C_{26}H_{23}O_4^{79}Br$ require 480.0759; 478.0780); $\nu_{max}$ (NaCl plates)/$cm^{-1}$ 1592 (C═C); $\delta_H$ (200 MHz, $CDCl_3$) 3.95 (3H, s, 4-OMe), 3.97 (3H, s, 1-OMe), 5.18 (2H, s, 5-OC$H_2$Ph), 5.21 (2H, s, 7-OC$H_2$Ph), 6.92–7.63 (13H, m, Ar-H); *m/z* (%) 480 ($^{81}Br$ $M^+$, 2), 478 ($^{79}Br$ $M^+$, 2), 389 ($^{81}Br$ M−$CH_2$Ph, 5), 387 ($^{79}Br$ M−$CH_2$Ph, 5), 91 ($PhCH_2$, 100).

**1.1.11. 1,7-Bis(benzyloxy)-5-methoxy-4-naphthol 18.** A solution of recrystallized 1,4-benzoquinone (**52**) (0.4 g, 3.7 mmol) and freshly distilled diene **9** (0.97 g, 4.8 mmol) in dry benzene (6 $cm^3$) was stirred for 14 h under nitrogen. The initial dark reddish solution turned to dark yellow. The solvent was evaporated under reduced pressure to afford the crude material. The crude material was dissolved in dimethylformamide (20 $cm^3$) under nitrogen, anhydrous potassium carbonate (3.48 g, 25.2 mmol) and benzyl bromide (4.43 g, 3.07 $cm^3$, 25.2 mmol) were added and the mixture stirred vigorously at 40°C. After 24 h. the reaction mixture was cooled, quenched with water (20 $cm^3$) and extracted with 30% ether–ethyl acetate (5×30 $cm^3$). The combined organic layers were washed with water (2×20 $cm^3$), dried ($MgSO_4$) and the solvent removed in vacuo. The resultant residue was purified by flash chromatography (10% ethyl actetate–hexane) to yield the title compound **18** (438 mg, 31%) as silver flakes, mp 160–161°C (lit.[10] 159–160°C). The $^1H$ NMR spectrum of the product was in agreement with the literature.[10]

**1.1.12. 1,7-Bis(benzyloxy)-3-bromo-5-methoxy-4-naphthol 19.** To a stirred solution of naphthol **18** (60 mg, 0.155 mmol) in carbon tetrachloride (2 $cm^3$) at 0°C was added dropwise a solution of bromine (28.8 mg, 0.18 mmol) in carbon tetrachloride (0.87 $cm^3$). After 5 min 10% aqueous sodium thiosulfate (10%, 2 $cm^3$) was added and the reaction mixture allowed to warm to room temperature. The mixture was then extracted with dichloromethane (10 $cm^3$), washed with water (10 $cm^3$), dried ($MgSO_4$) and the solvent removed in vacuo. The resultant residue was purified by flash chromatography (15% ethyl acetate–hexane) to yield the title compound **19** (60 mg, 83%) as a colourless solid, mp 139–139°C. (Found: $M^+$, 466.0664; 464.0662. $C_{25}H_{21}O_4^{81}Br$ and $C_{26}H_{23}O_4^{79}Br$ require 466.0603; 464.0623); $\nu_{max}$ (NaCl plates)/$cm^{-1}$ 3382 (OH), 1619 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 4.03 (3H, s, 5-OMe), 5.13 (4H, s, 2×OC$H_2$Ph), 6.64 (1H, d, *J*=2.3 Hz, 6-H), 7.02 (1H, s, 2-H), 7.25 (1H, d, *J*=2.3 Hz, 8-H), 7.35–7.48 (10H, m, Ar-H) and 9.43 (1-H, s, 4-OH); $\delta_C$ (100 MHz, $CDCl_3$) 57.2, 70.9, 71.9, 96.7, 100.5, 100.9, 112.3, 113.5, 127.7, 128.2, 128.5, 128.7, 128.9, 129.0, 129.3, 129.4, 137.3, 137.7, 145.6, 147.3, 157.2 and 157.6; *m/z* (%) 466 ($^{81}Br$ $M^+$, 14), 464 ($^{79}Br$ $M^+$, 15), 373 (52), 375 (53), 91 ($PhCH_2$, 100).

**1.1.13. 1,7-Bis(benzyloxy)-3-bromo-4,5-dimethoxynaphthalene 20.** To a stirred solution of bromonaphthol **19** (35 mg, 0.076 mmol) and methyl iodide (1.14 g, 0.5 $cm^3$) in dry dimethylformamide (2 $cm^3$) under hydrogen, was added a slurry of sodium hydride (4 mg, 0.15 mmol) in dry dimethylformamide (0.5 $cm^3$). After 5 min, ice (2 $cm^3$) was added to quench the reaction. The reaction mixture was extracted with dichloromethane (2×5 $cm^3$), washed with water (10 $cm^3$), dried ($MgSO_4$) and the solvent removed in vacuo. The resultant residue was purified by flash chromatography (10% ethyl acetate–hexane) to yield the title compound **20** (30 mg, 83%) as a yellow oil. (Found: $M^+$, 480.0766; 478.0712. $C_{26}H_{23}O_4^{81}Br$ and $C_{26}H_{23}O_4^{79}Br$ require 480.0759; 478.0779); $\nu_{max}$ (NaCl plates)/$cm^{-1}$ 1581 (C═C); $\delta_H$ (200 MHz, $CDCl_3$) 3.86 (3H, s, 5-OMe), 3.96 (3H, s, 4-OMe), 5.14 (2H, s, 7-OC$H_2$Ph), 5.16 (2H, s, 5-OC$H_2$Ph), 6.68 (1H, d, *J*=2.4 Hz, 6-H), 7.01 (1H, s, 2-H), 7.21 (1H, d, *J*=2.4 Hz, 8-H), 7.35–7.52 (10H, m, Ar-H); *m/z* (%) 480 ($^{81}Br$ $M^+$, 3), 478 ($^{79}Br$ $M^+$, 3), 389 ($^{81}Br$ M−$CH_2$Ph, 7), 387 ($^{79}Br$ M−$CH_2$Ph, 7), 91 ($PhCH_2$, 100).

**1.1.14. 7-Benzyloxy-3-bromo-5-methoxy-1,4-naphthoquinone 6d.** To a solution of naphthol **19** (409 mg, 0.88 mmol) in acetonitrile (40 $cm^3$) at 0°C, was added dropwise a solution of ceric ammonium nitrate (1.21 g, 2.21 mmol) in water (10 $cm^3$) to give a yellow coloured solution. After stirring at room temperature for 1 h, the reaction mixture was poured into water (100 $cm^3$) and extracted with dichloromethane (3×100 $cm^3$). The combined organic extracts were dried over anhydrous magnesium sulfate and filtered through a layer of florisil. The solvent was removed under reduced pressure to afford a residue. Further purification of the residue by flash chromatography (10% ethyl acetate–hexane) yielded the title compound **6d** (260 mg, 79%) as a yellow solid, mp 130–131°C (dec.). (Found: $M^+$, 373.9987; 371.9963. $C_{18}H_{13}O_4^{81}Br$ and $C_{18}H_{13}O_4^{79}Br$ require 373.9977; 371.9997); $\nu_{max}$ (NaCl plates)/$cm^{-1}$ 1668 (C═O) and 1591 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 3.98 (3H, s, OMe), 5.20 (2H, s, OC$H_2$Ph), 6.80 (1H, d, *J*=2.0 Hz, 6-H), 7.30 (1H, d, *J*=2.0 Hz, 8-H) and 7.35–7.46 (6H, m, Ar-H and 2-H); $\delta_H$ (100 MHz, $CDCl_3$) 57.3, 71.7, 105.5, 106.0, 114.2, 129.0, 129.9, 130.1, 136.4, 139.1, 144.9, 163.9, 165.6, 176.6 and 184.2; *m/z* (%) 374 ($^{81}Br$ $M^+$, 44), 376 ($^{79}Br$ $M^+$, 44), 91 ($PhCH_2$, 100).

**1.1.15. Methyl 5-hydroxy-2-(trimethylsilylmethyl)-2,3-dihydronaphtho[1,2-*b*]furan-4-carboxylate 23.** To methyl 1,4-dimethoxynaphthalene-2-carboxylate[30] (0.89 g, 3.62 mmol) in acetonitrile (30 $cm^3$) at 0°C was added 10%

aqueous ceric ammonium nitrate (3.97 g, 7.2 mmol) with stirring. After 20 min, the mixture was diluted with dichloromethane (60 $cm^3$) and poured into water (100 $cm^3$) containing pH 7 phosphate buffer (0.1 M, 5 $cm^3$). The organic layer was washed with brine (3×50 $cm^3$), dried over anhydrous magnesium sulfate, passed through a short florisil pad and the solvent removed at reduced pressure. The residue (presumed to be naphthoquinone **22**) was dried under high vacuum for 30 min then dissolved in dry dichloromethane (50 $cm^3$) and cooled to −78°C. Methylaluminium dichloride (4.1 $cm^3$, 1.0 M, 4.1 mmol) was then added dropwise with stirring under an atmosphere of nitrogen. After 5 min allyltrimethylsilane (0.57 $cm^3$, 3.6 mmol) was added and the mixture stirred for 90 min at −78°C, followed by gradual warming to room temperature. The reaction was quenched by the dropwise addition of water (1 $cm^3$) with vigorous stirring until the green solution turned yellow. Water (100 $cm^3$) was added, the organic layer washed with brine (3×100 $cm^3$) and dried over anhydrous magnesium sulfate. After concentration in vacuo the crude product was purified by flash chromatography (1% ethyl acetate–hexane) to afford the title compound **23** (0.59 g, 51%) as an unstable pale yellow solid, mp 71–73°C. (Found: $M^+$, 330.1296. $C_{18}H_{22}O_4Si$ requires $M^+$, 330.1287); $\nu_{max}$ (film) ($cm^{-1}$) 3360–2900 (OH), 1662 (C=O, *o*-hydroxyl aryl ester) and 1235 (Si–$CH_3$); $\delta_H$ (200 MHz, $CDCl_3$) 0.24 (9H, s, $SiMe_3$), 1.15 (1H, dd, $J_{gem}$=14.4 Hz, $J_{1',2}$=7.4 Hz, 1′-$H_A$ or 1′-$H_B$), 1.33 (1H, dd, $J_{gem}$=14.4 Hz, $J_{1',2}$=7.4 Hz, 1′-$H_B$ or 1′-$H_A$), 3.13 (1H, dd, $J_{gem}$=16.6 Hz, $J_{3,2}$=8.2 Hz, 3-$H_A$ or 3-$H_B$), 3.67 (1H, dd, $J_{gem}$=16.6 Hz, $J_{3,2}$=8.0 Hz, 3-$H_B$ or 3-$H_A$), 3.97 (3H, s, aryl $CO_2Me$), 5.01–5.12 (1H, m, 2-H), 7.44–7.63 (2H, m, 7-H and 8-H), 7.86 (1H, d, $J_{9,8}$=8.2 Hz, 9-H), 8.36 (1H, d, $J_{6,7}$=8.0 Hz, 6-H), 11.78 (1H, s, OH); $\delta_C$ (100 MHz, $CDCl_3$) −0.09, 26.3, 42.7, 52.7, 82.7, 104.1, 117.0, 122.0, 124.6, 125.0, 125.6, 126.1, 129.7, 147.9, 156.4 and 172.5; *m/z* (%) 330 ($M^+$, 32), 299 (24), 298 (59), 283 (52), 73 (100).

**1.1.16. 8-Benzyloxy-4-bromo-6-methoxy-5-hydroxy-2-(trimethylsilylmethyl)-2,3-dihydronaphtho[1,2-*b*]furan 21.** To a solution of bromonaphthoquinone **6d** (0.19 g, 0.51 mmol) in dichloromethane (5 $cm^3$), cooled to −78°C under nitrogen was added methylaluminium dichloride (0.77 $cm^3$, 1.0 M, 0.77 mmol) dropwise with stirring. After 5 min allyltrimethylsilane (0.097 $cm^3$, 0.61 mmol) was added and the mixture stirred for 1 h at −78°C. The reaction was quenched by the dropwise addition of saturated sodium bicarbonate solution (1 $cm^3$) and extracted with dichloromethane (2×10 $cm^3$). The organic extract was washed with brine (1 $cm^3$), dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography (15% ethyl acetate–hexane) using flash silica that had been pre-treated with triethylamine, to afford the title compound **21** (0.12 g, 48%) as an unstable yellow oil that rapidly darkened upon standing. (Found: $M^+$, 488.0822; 486.0844. $C_{24}H_{27}O_4Si^{81}Br$ and $C_{24}H_{27}O_4Si^{79}Br$ require 488.0842; 486.0862); $\nu_{max}$ (film) ($cm^{-1}$) 3389 (OH), and 1607 (C=C); $\delta_H$ (200 MHz, $CDCl_3$) 0.12 (9H, s, $SiMe_3$), 1.03 (1H, dd, $J_{gem}$=14.5 Hz, $J_{1',2}$=7.4 Hz, 1′-$H_A$ or 1′-$H_B$), 1.18 (1H, dd, $J_{gem}$=14.5 Hz, $J_{1',2}$=7.4 Hz, 1′-$H_B$ or 1′-$H_A$), 2.40–2.61 (1H, dd, $J_{gem}$=16.4 Hz, $J_{3,2}$=8.1 Hz, 3-$H_A$ or 3-$H_B$), 3.01–3.22 (1H, dd, $J_{gem}$=16.6 Hz, $J_{3,2}$=7.9 Hz, 3-$H_B$ or 3-$H_A$), 3.99 (3H, s, OMe), 5.02–5.10 (1H, m, 2-H), 6.62 (1H, s, 7-H), 7.01 (1H, s, 8-H), 7.30–7.53 (5H, m, Ar-H) and 9.34 (1H, s, OH); *m/z* (%) 488 ($^{81}Br$ $M^+$, 11), 486 ($^{79}Br$ $M^+$, 11), 408 (32), 91 (86), 73 (100).

**1.1.17. Crystallographic details for Michael adduct 12.** A brown blade like crystal having approximate dimensions of 0.30×0.15×0.08 $mm^3$ was attached to a thin glass fibre, and mounted on a Rigaku AFC7R diffractometer employing graphite monochromated Cu Kα radiation from a rotating anode generator. Primitive orthorhombic cell constants were obtained from a least-squares refinement using the setting angles of 25 reflections in the range 93.88< $2\theta$<109.20°. Diffraction data were collected at a temperature of 21±1°C using $\omega$–$2\theta$ scans to a maximum $2\theta$ value of 130.0°. Omega scans of several intense reflections made prior to data collection, had an average width at half-height of 0.21°, and scans of (1.78+0.35 tan $\theta$)° were made at a speed of 32.0°/min (in omega). The weak reflections ($I$<15.0θ($I$)) were rescanned up to 10 times. Stationary background counts were recorded on each side of the reflection, with a 2:1 ratio of peak to background counting time. The intensities of three representative reflections measured every 150 reflections, did not change significantly during the data collection. An empirical absorption correction based on azimuthal scans of three reflections was applied and the data were also corrected for Lorentz and polarisation effects. All calculations were undertaken with the teXsan[31] crystallographic software package. Neutral atom scattering factors were taken from Cromer and Waber.[32] Anomalous dispersion effects were included in $F_{calc}$[33] and the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley.[34] The values for the mass attenuation coefficients were those of Creagh and Hubbell.[35] The structure was solved[36] and elaborated in the acentric space group *Pna*21 (#33) with Fourier techniques.[37] Non-hydrogen atoms were modelled with anisotropic thermal parameters. Hydrogen atoms were included in the model at calculated positions with group thermal parameters. Refinement of the inversion related structures elevated the residuals by approximately 0.003. An ORTEP projection of the molecule is provided in Figure 1.[38]

### 1.2. Crystal data

Empirical formula $C_{11}H_{10}Br_2O_5$, $M$ 382.01, orthorhombic, space group $Pna2_1$ (#33), $a$=12.148(1) Å, $b$=4.962(1) Å, $c$=21.060(1) Å, $V$=1269.5(2) $Å^3$, $D_c$ 1.999 g $cm^{-3}$, $Z$ 4, crystal size 0.30×0.15×0.08 $mm^3$, $\lambda$ (Cu Kα) 1.5418 Å, $\mu$ (Cu Kα) 82.36 $cm^{-1}$, $T$(analytical)$_{min,max}$ 0.68, 0.99, $\theta_{max}$ 65.0, *hkl* range 0 14, 0 5, −24 0, $N$ 1316, $N_{obs}$ 1043, $R(F)$ 0.038, $R_w(F)$ 0.040. $R=\sum||F_o|-|F_c||/\sum|F_o|$; $R_w=(\sum w(F_o-F_c)^2/\sum(wF_c)^2)^{1/2}$; $w=1/[\sigma^2(F_o)]$. Tables of atomic coordinates, bond angles and bond lengths have been deposited at the Cambridge Crystallographic database.

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