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Regiospecific substitution of the carbon–boron bond of *tris*(4-trimethylsilylfuran-3-yl)boroxine and *tris*(4-methylfuran-3-yl)boroxine. Model approaches towards sesquiterpenoid furanoeudesmanes☆

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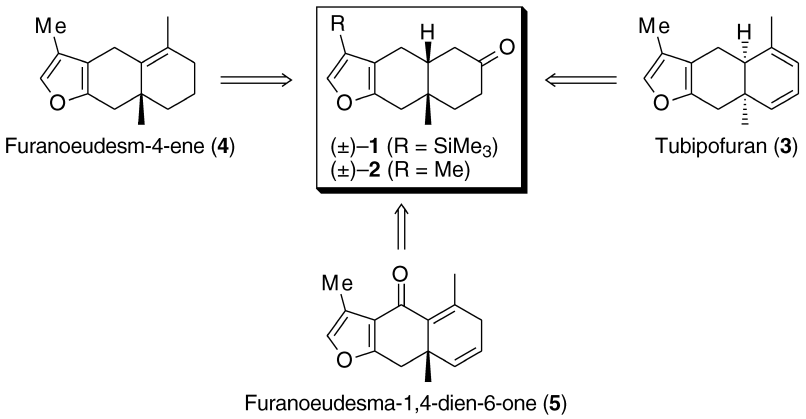
Dedicated to Professor Wei-Shan Zhou on the occasion of his 80th birthday

Abstract—Furan-containing compounds occur abundantly in nature. Among them, the sesquiterpenoid furanoeudesmanes are particularly interesting due to their allergenic, plant-growth inhibiting, antibacterial as well as antitumor properties. Recently an organoboron protocol has been developed in our laboratory for the preparation of regiospecific-substituted furans. By utilizing such methodology, two common intermediates **1** and **2** that may lead to the synthesis of naturally occurring tubipofuran (**3**) furanoeudesm-4-ene (**4**) and furanoeudesma-1,4-dien-6-one (**5**) were obtained.

1. Introduction

During the last few decades, a large number of furanoeudesmanes were isolated from higher plants, and more recently this group of compounds have also been encountered in marine organisms.[2] Because of their potent biological activities,[3] much effort has been devoted to the synthesis and studies of these molecules. However, due to the highly diversified structures of the eudesmane units and the instability of some of the products, synthesis of this family of compounds is still a challenge to organic chemists. It is not surprising that up to now, only very few papers reported the total synthesis of this class of natural products.[4]

Employing our experience in the preparation of regiospecifically substituted furans,[5] we targeted to extend our protocol towards the synthesis of furanoeudesmanes through an intermediate **1** (Scheme 1). In this connection,



Scheme 1.

☆ See Ref. 1.

Keywords: Friedel–Crafts reactions; furans; Suzuki reaction; terpenes and terpenoids.

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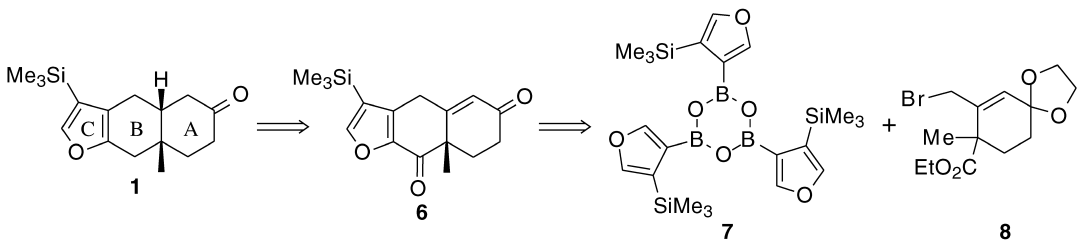
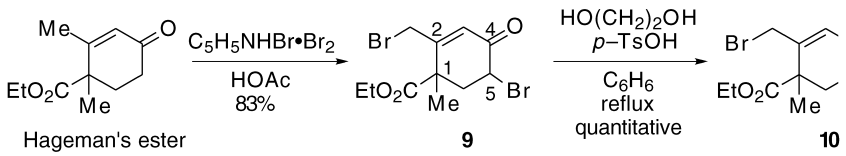


Scheme 2.



Scheme 3.

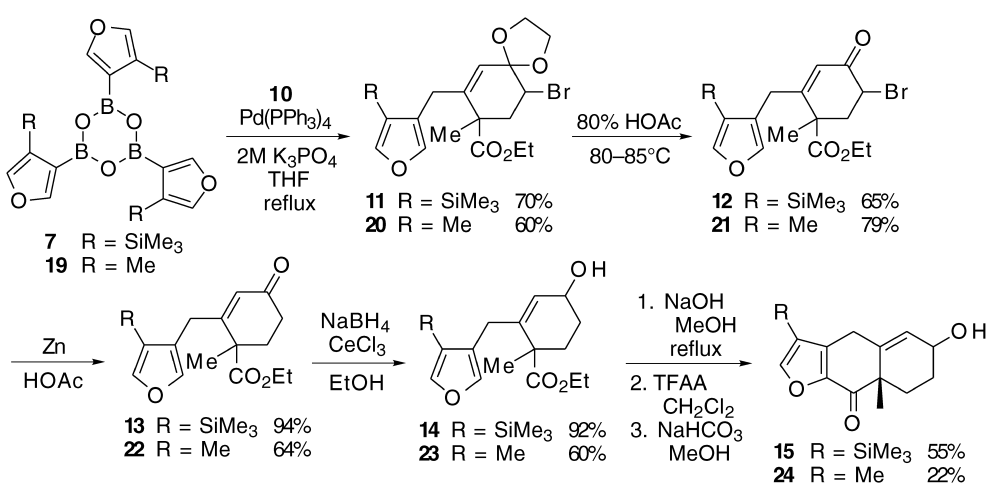
our latest achievement in synthesizing angular analogs of **1** is noteworthy.[6] It was hoped that **1** could be easily converted to **2**,[5] precursor for our eudesmane program of which tubipofuran (**3**), furanoeudesm-4-ene (**4**) and furanoeudesma-1,4-dien-6-one (**5**) are our targets (Scheme 1).

2. Results and discussion

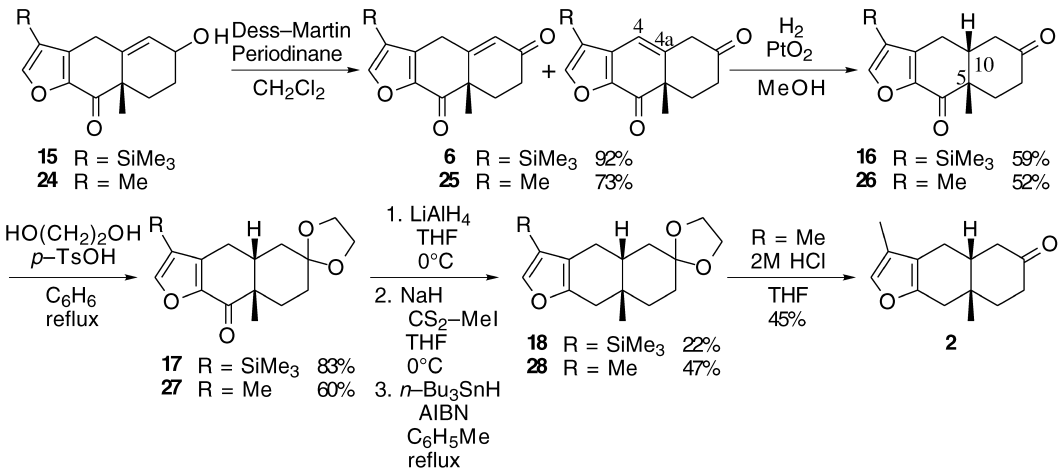
The retrosynthetic pathway for the preparation of **1** is shown in Scheme 2. The ring C building block, *tris*(4-trimethylsilylfuran-3-yl)boroxine (**7**), was easily accessible through our silicon–boron protocol,[5] whose preparation can be easily carried out in a large scale manner. Disconnection of **6** in ring B leads to compound **8** that is a Hageman's ester derivative.[7] Hence, the allyl bromide group of **8** would serve as a handle for the palladium(0)-catalyzed coupling reaction with boroxine **7**, while the ester group of **8** would be important for ring B closure through a Friedel–Crafts acylation.[8] Lastly, catalytic hydrogenation of the double bond in **6** followed by the removal of the carbonyl group next to the furan would furnish **1**, whose trimethylsilyl group would then be transformed to a methyl group, leading to **2**.

The preparation of ring A precursor is shown in Scheme 3. Starting from the Hageman's ester,[7] bromination was expected to take place in an endocyclic mode.[9] Thus, the enone was first protected as an acetal, which was allowed to react with bromine. Disappointingly, the reaction resulted in a messy mixture. On the other hand, a direct bromination of the Hageman's ester with pyridinium bromide perbromide in acetic acid gave cleanly a 2:1 diastereomeric mixture of dibromide **9** whose structure is supported by its ^{1}H NMR spectrum. A direct coupling of **9** with boroxine **7** was not successful due to the instability of **9** under the basic condition normally employed for the Suzuki coupling.[10] Therefore, ketone **9** was protected with ethylene glycol, resulting in an cyclic acetal **10** in a quantitative yield (Scheme 3).

As illustrated in Scheme 4, reaction of **10** with boroxine **7** proceeded smoothly in 10 M equivalents of aqueous K_3PO_4 and 5 mol% $Pd(PPh_3)_4$ in refluxing THF, affording **11** in 70% yield. The remaining bromine substituent was effectively removed in two steps. Thus, hydrolysis of acetal **11** in refluxing 80% acetic acid gave ketone **12** in 65% yield. It is noteworthy that **12** is very unstable and decomposes readily. Despite this, a debromination reaction was



Scheme 4.



Scheme 5.

performed by stirring **12** with activated zinc in glacial acetic acid to complete the reaction in 94% yield. Attempted reprotection of the carbonyl group with ethylene glycol only resulted in an unstable acetal which hydrolyzed readily once in contact with silica gel or alumina during the chromatographic purification. The generation of thioketal that requires the addition of boron trifluoride as catalyst is not recommended due to the likely protodesilylation problem. The resulting ketone **13** was then reduced with $NaBH_4$ in the presence of $CeCl_3$ in ethanol to afford a diastereomeric mixture of compound **14** in a diastereomeric ratio of 2:1. The final hurdle of ring B construction was smoothly completed through a Friedel–Crafts acylation.[8] Thus, saponification of **14** with NaOH was followed immediately by the addition of trifluoroacetic anhydride. After usual work-up, the triflate intermediate was hydrolyzed with methanolic sodium hydrogen carbonate to provide alcohol **15** in an overall yield of 55%. The diastereomeric mixture of **15** was separable by chromatography on silica gel.

As can be seen in Scheme 5, when compound **15** was treated with the Dess–Martin periodinane,[11] the reaction proceeded instantly and completed within 15 min. After usual work-up, ^1H NMR spectroscopic study of the crude product showed a strong signal at δ 5.95, indicating the formation of the desired enone **6**. However, due to the highly acidic methylene protons on ring B, the C–C double bond shifted easily during chromatographic purification on silica gel. For this reason, the $\Delta^{4,4a}$ isomer was isolated along with compound **6** in the ratio of 3:1 after purification. This isomeric mixture was hydrogenated with Adams' catalyst to afford a *cis*-decalin skeleton **16**. The carbonyl group of ring A was selectively protected with ethylene glycol in refluxing benzene, providing the corresponding acetal **17** in 83% yield. The remaining carbonyl group was removed successfully by the Barton–McCombie radical deoxygenation method.[12] Thus, treatment of **17** with $LiAlH_4$ offered a diastereomeric mixture of the corresponding alcohol. A diastereomeric mixture of xanthate was obtained employing a standard procedure.[12] Finally, treatment with *n*-Bu_3SnH and AIBN in refluxing toluene completed the synthesis of **18** (a protected form of **1**) in a total yield of 22%.

The *cis*-stereochemistry at the AB ring junction of **17** was further confirmed by an X-ray crystallographic study (CCDC 196030).[13] The ORTEP plot of **17** is showed in Figure 1.

After obtaining a sufficient amount of **18**, efforts had been made to convert the trimethylsilyl group to a methyl group.[14] Unfortunately, several experiments had been attempted but no positive result was secured in the conversion of **18** to **2** (Scheme 6). In order to obtain a proper precursor for our synthetic program, we therefore started another program whose aim was to realize **2**.

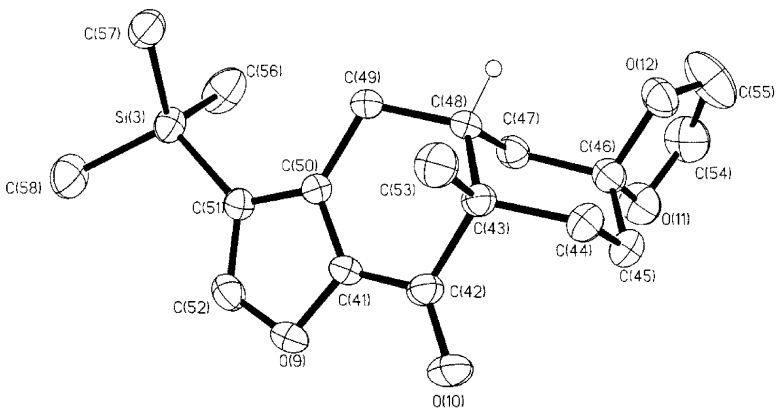
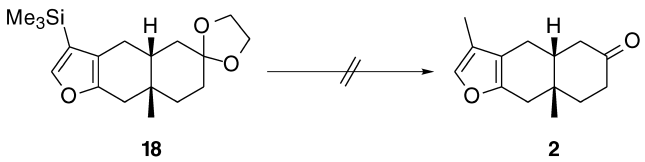


Figure 1. X-Ray crystal structure of **17**.



Scheme 6.

As can also be seen in Scheme 4, a palladium-catalyzed reaction between **10** and **19**[6] gave **20** that is a methyl version of **11**. Standard transformations of **20** via steps (**20→21→22→23→24**) identical to those for **11** led eventually to compound **24** (Scheme 4). In Scheme 5, compound **24** was oxidized to afford diketone **25**, whose C–C double bond was hydrogenated to form **26**. The *cis*-stereochemistry **26** was established by a 2D $^{1}H-^{1}H$ NOESY study whose results are illustrated in Figure 2. As can be seen, the *cis*-configuration of **26** is suggested by the correlation of the methyl group at C-5 (δ 1.32) and the proton at C-10 (δ 1.51), and is in line with our own observation of the configuration shown in **17**. With **26** in hand, protection and removal of the conjugated keto group led to **28**. Deprotection by treatment with 2N HCl in THF finally converted **28** to one of our targets **2**. The realization of **3**, **4** and **5** employing **2** as a pivotal precursor is in progress.

3. Experimental

3.1. General

All reagents and solvents were reagent grade. Further purification and drying by standard methods were employed when necessary. All organic solvents were evaporated under reduced pressure with a rotary evaporator. The plates used for thin-layer chromatography (TLC) were E. Merck silica gel $60F_{254}$ (0.25 mm thickness) precoated on aluminum plates, and they were visualized under short (254Nm) UV light. Compounds on TLC plates were visualized with a spray of 5% dodecamolybdophosphoric acid in ethanol and with subsequent heating. Column chromatography was performed using E. Merck silica gel (230–400 mesh).

Melting points were measured on a Reichert Microscope apparatus and were uncorrected. NMR spectra were recorded on a Bruker DPX-300 spectrometer (300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C). All NMR measurements were carried out at 300 K in deuterated chloroform solution unless otherwise stated. Chemical shifts are reported as parts per million (ppm) in δ unit in the scale relative to the resonance of $CDCl_3$ (7.26 ppm in the ^{1}H, 77.00 ppm for the central line of the triplet in the ^{13}C modes, respectively). Coupling constants (J) are reported in Hz. Splitting patterns are described by using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. ^{1}H NMR data are reported in this order: chemical shift; multiplicity, coupling constant(s), number of proton. Mass spectra (MS and HRMS) were obtained with a Thermo-finnigan MAT 95XL spectrometer and determined at an ionized voltage of 70 eV unless otherwise stated. Relevant data were tabulated as *m/z*. Elemental analyses were performed at Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, China.

3.1.1. Ethyl 5-bromo-2-bromomethyl-1-methyl-4-oxo-cyclohex-2-ene-1-carboxylate (9). To a solution of the Hageman's ester[7] (5.4 g, 27.5 mmol) in acetic acid (20 mL) was added pyridinium bromide perbromide (26.4 g, 82.5 mmol). The mixture was stirred at rt for 3 h. After pouring into saturated aqueous $NaHCO_3$ solution (80 mL), it was extracted with diethyl ether (3×100 mL). The combined organic extract was washed with water (50 mL) and brine (50 mL). Upon drying ($MgSO_4$) and evaporation

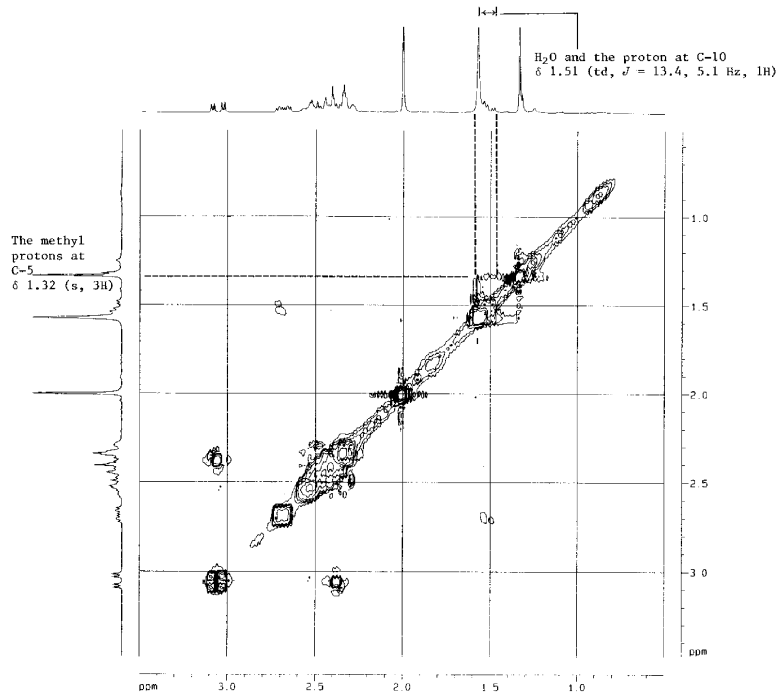


Figure 2. 2D NOESY of 26.

of solvent under reduced pressure, the residue was chromatographed on silica gel (200 g, hexanes–ethyl acetate, 15:1) to afford **9** (7.8 g, 80%) as a yellow oil, which consisted of a pair of *anti* and *syn* diastereomers in a ratio of 2:1. NMR data of the *anti*-isomer: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J=7.2 Hz, 3H, ethyl ester's methyl protons), 1.57 (s, 3H, C-1 methyl protons), 2.44 (t, J=13.8 Hz, 1H, one of C-6 protons), 2.92 (dd, J=13.8, 5.1 Hz, 1H, one of the C-6 protons), 4.07 (d, J=19.8 Hz, 1H, one of the bromomethyl protons), δ 4.17–4.25 (m, 3H, one of the bromomethyl protons and ethyl ester's methylene protons), 4.92 (dd, J=13.8, 5.1 Hz, 1H, C-5 proton), 6.35 (s, 1H, C-3 olefinic proton); ^{13}C NMR ($CDCl_3$) δ 14.0, 23.2, 29.9, 45.7, 48.2, 48.8, 62.4, 129.4, 157.5, 172.0, 190.7. NMR data of the *syn* isomer: ^{1}H NMR ($CDCl_3$) δ 1.30 (t, J=7.2 Hz, 3H, ethyl ester's methyl protons), 1.64 (s, 3H, C-1 methyl protons), 2.52 (dd, J=14.4, 4.5 Hz, 1H, one of the C-6 protons), 2.98 (dd, J=14.4, 8.4 Hz, 1H, one of the C-6 protons), 4.03 (d, J=19.8 Hz, 1H, one of the bromomethyl protons), δ 4.17–4.25 (m, 3H, one of the bromomethyl protons and ethyl ester's methylene protons), 4.59 (dd, J=8.4, 4.5 Hz, 1H, C-5 proton), 6.38 (s, 1H, C-3 olefinic proton); ^{13}C NMR ($CDCl_3$) δ 13.9, 23.2, 29.5, 43.4, 45.8, 47.6, 62.3, 128.9, 159.0, 172.7, 189.9; MS (FAB) m/z 354 (M^+). Anal. calcd for $C_{11}H_{14}Br_2O_3$: C, 37.32; H, 3.99. Found: C, 37.43; H, 4.02.

3.1.2. Ethyl 5-bromo-2-bromomethyl-4-(1,3-dioxolan-2-yl)-1-methyl-cyclohex-2-ene-1-carboxylate (10). A mixture of **9** (3.5 g, 10 mmol), ethylene glycol (1.7 mL, 30 mmol) and a trace amount of *p*-toluenesulfonic acid in benzene (30 mL) was refluxed with a Dean-Stark trap for 48 h. After cooled to rt, the mixture was washed with saturated $NaHCO_3$ (5 mL), water (5 mL) and brine (5 mL). Drying ($MgSO_4$) and evaporation of solvent under reduced pressure provided **10** (3.9 g, quantitative) as a viscous colorless oil, which consisted of a pair of diastereomers deriving from **9**. NMR data of the major component: ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J=7.2 Hz, 3H, ethyl ester's methyl protons), 1.44 (s, 3H, C-1 methyl protons), 2.32 (t, J=13.8 Hz, 1H, one of the C-6 protons), 2.59 (dd, J=13.5, 3.6 Hz, 1H, one of the C-6 protons), 4.56 (dd, J=13.8 Hz, 3.6 Hz, 1H, C-5 proton), 5.90 (s, 1H, C-3 olefinic proton), the dioxolanyl protons, ethyl ester's methylene protons and bromomethyl protons appeared as a multiplet in the region at δ 3.78–4.29; ^{13}C NMR ($CDCl_3$) δ 14.0, 23.8, 31.0, 43.6, 48.4, 51.8, 61.7, 66.1, 104.2, 131.1, 138.9, 173.6. NMR data of the minor component: ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J=7.2 Hz, 3H, ethyl ester's methyl protons), 1.49 (s, 3H, C-1 methyl protons), 2.25 (dd, J=13.2, 3.3 Hz, 1H, one of C-6 protons), 2.82 (t, J=13.2 Hz, 1H, one of the C-6 protons), 4.36 (dd, J=12.9, 3.6 Hz, 1H, C-5 proton), 5.90 (s, 1H, C-3 olefinic proton); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.2, 30.3, 42.7, 48.9, 51.0, 61.7, 65.9, 66.5, 104.1, 130.4, 140.1, 173.6; MS (EI) m/z 398 (M^+). Anal. calcd for $C_{11}H_{18}Br_2O_4$: C, 39.40; H, 4.58. Found: C, 39.54; H, 4.53.

3.1.3. Ethyl 5-bromo-4-(1′,3′-dioxolan-2′-yl)-1-methyl-2-(4-trimethylsilylfuran-3-yl)methylcyclohex-2-ene-1-carboxylate (11). A mixture of **10** (1.5 g, 3.8 mmol), *tris*(4-trimethylsilylfuran-3-yl)boroxine (**7**) (650 mg, 1.3 mmol), $Pd(PPh_3)_4$ (220 mg, 0.2 mmol) in THF (50 mL) and aqueous K_3PO_4 (2 M, 20 mL) was refluxed for 3 h under a nitrogen atmosphere. After being cooled to rt, THF was removed under reduced pressure. The aqueous residue was extracted with ethyl acetate (3×20 mL). The combined organic extract was washed with brine (10 mL). After drying ($MgSO_4$) and evaporation of solvent under reduced pressure, the residue was chromatographed on silica gel (100 g, hexanes–ethyl acetate, 20:1) to afford **11** (1.2 g, 70%) as a colorless oil, which consisted of a pair of diastereomers in a ratio of 2:1. NMR data of the major component: ^{1}H NMR ($CDCl_3$) δ 0.20 (s, 9H, trimethylsilyl protons), 1.27 (t, J=7.2 Hz, 3H, ethyl ester's methyl protons), 1.37 (s, 3H, methyl protons), 2.34 (t, J=13.5 Hz, 1H, one of the C-6 protons), 2.60 (dd, J=13.5, 3.6 Hz, 1H, one of the C-6 protons), 3.14 (d, J=17.4 Hz, 1H, one of the furanylmethylene protons), 3.24 (d, J=17.4 Hz, 1H, one of the furanylmethylene protons), 3.94–3.97 (m, 2H, ethyl ester's methylene protons), 4.10–4.21 (m, 4H, dioxolanyl protons), 4.66 (dd, J=13.8, 3.6 Hz, 1H, C-5 proton), 5.23 (t, J=1.5 Hz, 2H, C-3 olefinic protons), 7.25 (s, 1H, one of the furan α protons), 7.27 (s, 1H, one of the furan α protons); ^{13}C NMR ($CDCl_3$) δ −0.5, 14.1, 24.4, 27.8, 43.7, 48.9, 52.9, 61.4, 65.9, 66.3, 104.6, 119.5, 124.7, 126.5, 141.8, 142.1, 148.5, 174.0; NMR data of the minor component: ^{1}H NMR ($CDCl_3$) δ 0.20 (s, 9H, trimethylsilyl protons), 1.26 (t, J=7.2 Hz, 3H, ethyl ester's methyl protons), 1.44 (s, 3H, C-1 methyl protons), 2.23 (dd, J=13.2, 3.6 Hz, 1H, one of the C-6 protons), 2.92 (t, J=13.5 Hz, 1H, one of the C-6 protons), 3.07 (s, 2H, furanylmethylene protons), 3.94–3.97 (m, 2H, ethyl ester's methylene protons), 4.10–4.21 (m, 4H, dioxolanyl protons), 4.41 (dd, J=13.8, 3.6 Hz, 1H, C-5 proton), 5.17 (t, J=1.5 Hz, 1H, C-3 olefinic proton), 7.25 (s, 1H, one of the furan α protons), 7.27 (s, 1H, one of the furan α protons); ^{13}C NMR ($CDCl_3$) δ −0.5, 14.1, 21.6, 27.6, 43.0, 49.7, 52.2, 61.4, 65.7, 66.4, 104.5, 119.5, 124.4, 125.3, 141.8, 143.0, 148.5, 174.0; MS (EI) m/z 456 (M^+). HRMS (EI) calcd for $C_{20}H_{29}BrO_5Si$: 456.0968. Found: 456.0968.

3.1.4. Ethyl 5-bromo-4-(1′,3′-dioxolan-2′-yl)-1-methyl-2-(4-methylfuran-3-yl)methylcyclohex-2-ene-1-carboxylate (20). Similar to the preparation of **11**, compound **20** was prepared from **19** (13.3 g, 41.2 mmol) in THF (20 mL) and a mixture of **10** (48.6 g, 123.7 mmol), $Pd(PPh_3)_4$ (2.4 g, 2.0 mmol), 2 M aqueous K_3PO_4 (500 mL) in THF (260 mL). The mixture was refluxed for 21 h. Usual work-up and column chromatography on silica gel (420 g, hexanes–ethyl acetate, 9:1) afforded **20** (29.4 g, 60%) as a pale yellow oil, which consisted of a pair of diastereomers in a ratio of 7:3. Data of the major component: ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J=7.1 Hz, 3H), 1.38 (s, 3H), 1.86 (s, 3H), 2.33 (t, J=13.7 Hz, 1H), 2.40 (s, 1H), 2.55 (dd, J=13.6, 3.7 Hz, 1H), 3.00 (d, J=17.1 Hz, 1H), 3.88–4.02 (m, 2H), 4.04–4.23 (m, 4H), 4.63 (dd, J=13.7, 3.7 Hz, 1H), 5.22 (t, J=1.5 Hz, 1H), 7.16 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 7.8, 14.1, 23.9, 25.9, 43.6, 48.7, 52.6, 61.4, 65.9, 66.4, 104.5, 116.4, 120.9, 125.5, 139.7, 140.9, 141.3, 173.8; Data of the minor component: ^{1}H NMR ($CDCl_3$) δ 1.34 (t, J=7.1 Hz, 3H), 1.44 (s, 3H), 1.86 (s, 3H), 2.13 (s, 1H), 2.22 (dd, J=13.0, 3.5 Hz, 1H), 2.89 (t, J=13.3 Hz, 1H), 3.15 (dd, J=17.3, 1.7 Hz, 1H), 4.04–4.23 (m, 4H), 4.23–4.33 (m, 2H), 4.40 (dd, J=13.6, 3.5 Hz, 1H), 5.16 (t, J=1.5 Hz, 1H), 7.16 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 7.8, 13.9, 21.3, 25.6, 42.9, 49.4, 52.0, 61.4, 65.8, 66.5, 104.5, 116.4, 120.2, 124.4, 139.6, 140.8, 142.1, 173.8; MS (EI) m/z 398 (M^+). HRMS (FAB)

(MH^+) calcd for $C_{18}H_{24}O_5Br$: 399.0807, 401.0782. Found: 399.0800, 401.0787. Anal. calcd for $C_{18}H_{23}O_5Br$: C, 54.15; H, 5.81. Found: C, 54.17; H, 5.98.

3.1.5. Ethyl 5-bromo-1-methyl-4-oxo-2-(4-trimethylsilylfuran-3-yl)methylcyclohex-2-ene-1-carboxylate (12). A solution of **11** (500 mg, 1.1 mmol) in 80% acetic acid (10 mL) was heated to 80°C (oil bath) for 2 h. After cooling to rt, the solvent was removed under vacuum. The residue was then chromatographed on silica gel (40 g, hexanes–ethyl acetate, 20:1) to afford **12** (295 mg, 65%) as a colorless oil, which consisted of a pair of diastereomers in a ratio of 9:1. Data of the major component: ^{1}H NMR ($CDCl_3$) δ 0.16 (s, 9H), 1.29 (t, J=7.2 Hz, 3H), 1.52 (s, 3H), 2.41 (t, J=13.5 Hz, 1H), 2.95 (dd, J=13.5, 5.1 Hz, 1H), 3.26 (s, 2H), 4.22 (q, J=7.2 Hz, 2H), 4.98 (dd, J=14.5, 5.4 Hz, 1H), 5.78 (s, 1H), 7.24 (s, 1H), 7.28 (d, J=0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −0.6, 14.0, 24.1, 29.2, 45.7, 48.8, 49.4, 62.1, 119.4, 122.8, 126.7, 141.9, 148.8, 163.4, 172.4, 190.0; MS (EI) m/z 412 (M^+). HRMS (EI) calcd for $C_{18}H_{25}BrO_4Si$: 412.0705. Found: 412.0700.

3.1.6. Ethyl 5-bromo-1-methyl-4-oxo-2-(4-methylfuran-3-yl)methylcyclohex-2-ene-1-carboxylate (21). Similar to the preparation of **12**, compound **21** was prepared from **20** (20.4 g, 51.2 mmol) in 80% acetic acid (255 mL) heated to 85°C for 6 h. Usual work-up and column chromatography on silica gel (600 g, hexanes–ethyl acetate, 9:1) gave **21** (14.3 g, 79%) as a pale yellow oil, which consisted of a pair of diastereomers in a ratio of 4:1. Data of the major component: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J=7.1 Hz, 3H), 1.54 (s, 3H), 1.83 (s, 3H), 2.42 (t, J=13.6 Hz, 1H), 2.91 (dd, J=13.6, 5.3 Hz, 1H), 3.35 (s, 2H), 4.12–4.33 (m, 2H), 4.93 (dd, J=13.6, 5.3 Hz, 1H), 5.79 (s, 1H), 7.18 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 7.9, 14.1, 23.8, 27.6, 44.2, 45.7, 48.8, 62.1, 119.5, 124.8, 125.8, 140.3, 141.1, 162.9, 172.4, 190.8. Data of the minor component: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J=7.1 Hz, 3H), 1.57 (s, 3H), 1.85 (s, 3H), 2.51 (dd, J=13.8, 4.9 Hz, 1H), 3.00 (dd, J=13.7, 10.9 Hz, 1H), 3.00 (dd, J=13.6, 1.5 Hz, 2H), 4.12–4.33 (m, 2H), 4.66 (dd, J=10.9, 4.9 Hz, 1H), 5.75 (s, 1H), 7.18 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 7.8, 14.0, 22.2, 27.2, 45.7, 47.1, 49.4, 62.0, 119.8, 124.8, 125.8, 140.3, 141.1, 164.3, 173.0, 190.0. Anal. calcd for $C_{16}H_{19}$O4Br: C, 54.10; H, 5.39. Found: C, 54.10; H, 5.46.

3.1.7. Ethyl 1-methyl-4-oxo-2-(trimethylsilylfuran-3-yl)methylcyclohex-2-ene-1-carboxylate (13). To a solution of **12** (300 mg, 0.7 mmol) in glacial acetic acid (4 mL) was added zinc dust (150 mg, 2.1 mmol). The mixture was stirred for 0.5 h. The zinc dust was filtered off and the filtrate was concentrated under vacuum. Chromatography on silica gel (10 g, hexanes–ethyl acetate 8:1) afforded **13** (220 mg, 94%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.16 (s, 9H), 1.27 (t, J=7.2 Hz, 3H), 1.49 (s, 3H), 1.93–2.01 (m, 1H), 2.38–2.56 (m, 3H), 3.40 (s, 2H), 4.15–4.23 (m, 2H), 5.66 (s, 1H), 7.23 (s, 1H), 7.26 (d, J=1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −0.6, 14.1, 22.7, 29.2, 34.2, 34.6, 47.2, 61.5, 119.3, 123.1, 128.0, 141.8, 148.7, 163.8, 173.9, 198.1; MS (EI) m/z 334 (M^+). Anal. calcd for $C_{18}H_{26}O_4Si$: C, 64.64; H, 7.83. Found: C, 64.25; H, 7.82.

3.1.8. Ethyl 1-methyl-4-oxo-2-(4-methylfuran-3-yl)methylcyclohex-2-ene-1-carboxylate (22). Similar to the preparation of **13**, compound **22** was prepared from **21** (10.9 g, 30.8 mmol) in glacial acetic acid (141 mL), zinc dust (4.0 g, 61.7 mmol). The mixture was stirred for 3 h at rt. Usual work-up and column chromatography on silica gel (310 g, hexanes–ethyl acetate, 5:1) afforded **22** (5.4 g, 64%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J=7.2 Hz, 3H), 1.53 (s, 3H), 1.86 (s, 3H), 1.90–2.09 (m, 1H), 2.33–2.64 (m, 3H), 3.32 (d, J=6.9 Hz, 2H), 4.08–4.31 (m, 2H), 5.68 (d, J=1.5 Hz, 1H), 7.19 (d, J=8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 7.8, 14.1, 22.6, 27.5, 34.2, 34.7, 47.2, 61.5, 119.9, 120.0, 127.2, 140.1, 141.1, 163.2, 174.0, 198.4. Anal. calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.31; H, 7.41.

3.1.9. Ethyl 1-methyl-4-hydroxy-2-(4-trimethylsilylfuran-3-yl)methylcyclohex-2-ene-1-carboxylate (14). To a stirred solution of **13** (500 mg, 1.5 mmol) in absolute ethanol (5 mL) was added $CeCl_3$ (740 mg, 3 mmol) followed by $NaBH_4$ (86 mg, 2.3 mmol). After 0.5 h, the solution was poured into saturated aqueous NH_4Cl (5 mL) solution and extracted with diethyl ether (3×10 mL). The combined organic extract was washed with brine (10 mL). After drying ($MgSO_4$) and evaporation of solvent under reduced pressure, the crude product was chromatographed on silica gel to afford **14** (460 mg, 92%) as a colorless oil, which consisted of a pair of diastereomers in a ratio of 2:1. Compound **14** showed very complicated ^{1}H and ^{13}C NMR spectra due to the presence of a pair of diastereomers. Compound **14** was used in the subsequent step without further spectroscopic characterization. MS (EI) m/z 336 (M^+). HRMS (EI) calcd for $C_{18}H_{28}O_4Si$: 336.1757. Found: 336.1755.

3.1.10. Ethyl 1-methyl-4-hydroxy-2-(4-methylfuran-3-yl)methylcyclohex-2-ene-1-carboxylate (23). Similar to the preparation of **14**, compound **23** was prepared from **22** (6.76 g, 24.5 mmol) in absolute ethanol (72 mL), $CeCl_3$ (9.0 g, 36.7 mmol) and $NaBH_4$ (1.85 g, 48.9 mmol) at 0°C for 4 h. Usual work-up and column chromatography on silica gel (180 g, hexanes–ethyl acetate, 3:1) yielded **23** (4.1 g, 60%) as a colorless oil. Compound **23** showed very complex ^{1}H NMR and ^{13}C NMR spectra due to the presence of a pair of diastereomers. Data of the major component: ^{1}H NMR ($CDCl_3$) δ 1.19–1.27 (m, 3H), 1.31 (s, 3H), 1.45–1.78 (m, 3H), 1.79–1.92 (m, 4H), 2.08–2.20 (m, 1H), 2.92–3.10 (m, 2H), 3.98–4.22 (m, 3H), 5.30–5.39 (m, 1H), 7.13 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 8.0, 14.1, 23.1, 26.3, 28.5, 32.7, 46.4, 60.9, 65.7, 120.4, 121.8, 127.5, 139.6, 139.7, 140.8, 176.1. Data of the minor component: ^{1}H NMR ($CDCl_3$) δ 1.19–1.27 (m, 3H), 1.38 (s, 3H), 1.45–1.78 (m, 3H), 1.79–1.92 (m, 4H), 1.95–2.06 (m, 1H), 2.92–3.10 (m, 2H), 3.98–4.22 (m, 3H), 5.30–5.39 (m, 1H), 7.13 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 8.0, 14.1, 22.9, 26.3, 28.3, 32.2, 46.6, 60.8, 65.6, 120.4, 121.8, 127.1, 139.6, 139.7, 140.6, 176.1. Anal. calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.04; H, 7.91.

3.1.11. 6,7,8,8a-Tetrahydro-6-hydroxy-8a-methyl-3-(trimethylsilyl)naphtho[2,3-*b*]furan-9(4*H*)-one (15). To a solution of **14** (300 mg, 0.9 mmol) in methanol (10 mL) was added slowly an aqueous solution of sodium hydroxide (2 M, 2.5 mL). The mixture was then refluxed for 24 h. After diluted with water (10 mL), the resulting mixture was washed with dichloromethane (10 mL). The aqueous layer

was acidified with 3N HCl until the pH reached 4. It was then extracted with dichloromethane (5×10 mL). The combined organic extract was dried ($MgSO_4$). After removal of solvent under reduced pressure, the crude product was dried under vacuum for a further 3 h and was then dissolved in anhydrous dichloromethane (5 mL). Trifluoroacetic anhydride (0.4 mL, 2.8 mmol) was slowly added. After stirring at rt for 8 h, the reaction was quenched with $NaHCO_3$ (5 mL). The organic layer was separated and the aqueous layer was extracted with diethyl ether (3×5 mL). The combined organic extract was concentrated and redissolved in methanol (5 mL). A drop of saturated aqueous $NaHCO_3$ was added. After 10 min at rt, the mixture was diluted with water (5 mL) and extracted with diethyl ether (5×5 mL). The combined organic extracts were dried ($MgSO_4$). After removal of solvent under reduced pressure, the residue was purified by chromatography on silica gel (50 g, hexanes–ethyl acetate, 3:1) to afford a chromatographically separable diastereomeric mixture of **15** (50 mg, 20% and 90 mg, 35%), both as viscous colorless oils. NMR data of the major compound: ^{1}H NMR ($CDCl_3$) δ 0.27 (s, 9H), 1.33 (s, 3H), 1.55–1.60 (m, 1H), 1.94–1.20 (m, 3H), 2.04 (br s, 1H), 3.22 (d, J=18.3 Hz, 1H), 3.63 (dt, J=18.3, 2.1 Hz, 1H), 4.18–4.21 (m, 1H), 5.67 (s, 1H), 7.43 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.9, 24.0, 27.9, 29.1, 30.6, 47.5, 66.4, 119.8, 128.6, 139.6, 140.6, 146.9, 152.4, 189.8. NMR data of minor compound: ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H), 1.27 (s, 3H), 1.49–1.67 (m, 3H), 1.87–1.94 (m, 1H), 2.36–2.44 (ddd, J=13.5, 11.7, 2.4 Hz, 1H), 3.24 (d, J=18.0 Hz, 1H), 3.68 (dt, J=18.0, 2.1 Hz, 1H), 4.20–4.21 (m, 1H), 5.74 (t, J=2.4 Hz, 1H), 7.43 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.9, 24.1, 26.3, 29.3, 30.8, 47.7, 65.4, 119.9, 128.1, 140.4, 140.6, 147.1, 152.3, 189.1. MS (FAB) m/z 291 (MH^+) (for the diastereomeric mixture). Anal. calcd for $C_{16}H_{22}O_3Si$ (for the diastereomeric mixture): C, 64.25; H, 8.39. Found: C, 64.00; H, 8.17.

3.1.12. 6,7,8,8a-Tetrahydro-6-hydroxy-3,8a-dimethylnaphtho[2,3-*b*]furan-9(4*H*)-one (24). Similar to the preparation of **15**, compound **24** was prepared from **23** (4.3 g, 15.5 mmol) in methanol (116 mL) and 2 M sodium hydroxide (39 mL) for 24 h. Usual work-up gave a product which was treated with trifluoroacetic anhydride (13.2 mL, 92.9 mmol) in dichloromethane (77 mL). After stirring for 10 h, the mixture was again worked up as usual to give a product which was treated with saturated $NaHCO_3$ in methanol (400 mL). Work-up and column chromatography on silica gel (130 g, hexanes–ethyl acetate, 3:1) produced a diastereomeric mixture of **24** (500 mg, 14% and 270 mg, 8%) as colorless oils. Data of the major compound: ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 3H), 1.43–1.66 (m, 2H), 1.75–1.96 (m, 2H), 2.00 (s, 3H), 2.38 (ddd, J=13.9, 10.0, 2.2 Hz, 1H), 3.15 (d, J=18.2 Hz, 1H), 3.55 (dt, J=18.2, 2.2 Hz, 1H), 4.10–4.26 (m, 1H), 5.73 (t, J=2.4 Hz, 1H), 7.36 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 7.7, 24.1, 26.3, 28.4, 29.2, 47.6, 65.4, 120.2, 128.1, 137.0, 140.1, 145.0, 146.1, 189.0. Data of the minor compound: ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3H), 1.44–1.71 (m, 1H), 1.86–1.95 (m, 3H), 1.98 (d, J=0.8 Hz, 3H), 2.12–2.40 (m, 1H), 3.13 (d, J=18.5 Hz, 1H), 3.52 (dt, J=18.5, 2.1 Hz, 1H), 4.09–4.27 (m, 1H), 5.66 (s, 1H), 7.35 (d, J=0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.6, 22.6, 24.0, 28.1, 28.9, 47.3, 66.3, 120.1, 128.6, 137.0, 139.1, 145.1, 145.8, 189.6; MS (EI) m/z 232 (M^+); HRMS (FAB) (MH^+) calcd for $C_{14}H_{17}O_3$: 233.1173. Found: 233.1184.

3.1.13. 7,8-Dihydro-8a-methyl-3-(trimethylsilyl)-naphtho[2,3-*b*]furan-6(4*H*),9(8a*H*)-dione (6). A stirred solution of **15** (140 mg, 0.5 mmol) and Dess–Martin periodinane (210 mg, 0.5 mmol) in dichloromethane (5 mL) were kept at 27°C under nitrogen for 1 h. The reaction mixture was then quenched with saturated $NaHCO_3$ (5 mL). The aqueous layer was extracted with diethyl ether (3×5 mL). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to yield **6** (140 mg, 100%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.03 (s, 9H), 1.49 (s, 3H), 2.26–2.40 (m, 3H), 2.48–2.53 (m, 1H), 3.48 (d, J=19.5 Hz, 1H), 3.90 (dd, J=19.5, 2.1 Hz, 1H), 5.96 (d, J=1.8 Hz, 1H), 7.52 (s, 1H); MS (FAB) m/z 289 (MH^+); HRMS (EI) (M^+) calcd for $C_{16}H_{20}O_3Si$: 288.1182. Found: 288.1154. After purification of the above crude product by chromatography on silica gel (20 g, hexanes–ethyl acetate, 3:1), the $\Delta^{4,4a}$ isomer was isolated along with compound **6** (total yield: 130 mg, 92%) in the ratio of 3:1 (**6**: $\Delta^{4,4a}$ isomer) as a viscous yellow oil.

3.1.14. 7,8-Dihydro-3,8a-dimethylnaphtho[2,3-*b*]furan-6(4*H*),9(8a*H*)-dione (25). Similar to the preparation of **6**, compound **25** was prepared from **24** (270 mg, 1.1 mmol), Dess–Martin periodinane (730 mg, 1.7 mmol) in dichloromethane (90 mL) for 3 h. Usual work-up and column chromatography on silica gel (7 g, hexanes–ethyl acetate, 2:1) gave **25** (190 mg, 73%) as a colorless oil, which consisted of a $\Delta^{4,4a}$ isomer in the ratio of 4:1. Data of the major component: ^{1}H NMR ($CDCl_3$) δ 1.48 (d, J=1.6 Hz, 3H), 2.05 (d, J=1.1 Hz, 3H), 2.15–2.46 (m, 3H), 2.47–2.54 (m, 2H), 3.43 (d, J=19.6 Hz, 1H), 3.79 (dd, J=19.6, 1.9 Hz, 1H), 5.97 (d, J=1.8 Hz, 1H), 7.47 (d, J=1.1 Hz, 1H). Compound **25** showed a very complex ^{13}C NMR spectrum due to the presence of the $\Delta^{4,4a}$ isomer. MS (EI) m/z 230 (M^+); HRMS (FAB) (MH^+) calcd for $C_{14}H_{15}O_3$: 231.1021. Found: 231.1012.

3.1.15. 4,5,7,8-Tetrahydro-8a-methyl-3-(trimethylsilyl)-naphtho[2,3-*b*]furan-6(4*H*),10(8a*H*)-dione (16). A solution of **6** (1.97 g, 6.82 mmol) in methanol (170 mL) was hydrogenated from a hydrogen balloon over platinum (IV) oxide (0.17 g, 0.68 mmol). After stirring for 4.5 h, the reaction mixture was filtered, washed with ethyl acetate and hexanes. Upon removal of solvent under reduced pressure, the residue was purified by chromatography on silica gel (37 g, hexanes–ethyl acetate, 3:1) to afford **16** (1.16 g, 59%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.22 (s, 9H), 1.31 (s, 3H), 1.50 (dt, J=13.3, 5.2 Hz, 1H), 2.22–2.56 (m, 6H), 2.63 (dt, J=13.5, 4.5 Hz, 1H), 3.13 (dd, J=17.3, 4.5 Hz, 1H), 7.46 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −1.0, 23.4, 27.1, 32.8, 38.6, 43.8, 44.7, 46.7, 121.1, 139.5, 146.2, 152.8, 188.6, 210.3; MS (FAB) m/z 291 (MH^+); HRMS (FAB) (MH^+) calcd for $C_{16}H_{23}O_3Si$: 291.1411. Found: 291.1423. Anal. calcd for $C_{16}H_{22}O_3Si$: C, 66.17; H, 7.63. Found: C, 66.15; H, 7.68.

3.1.16. 4,5,7,8-Tetrahydro-3,8a-dimethylnaphtho[2,3-*b*]furan-6(4*H*),10(8a*H*)-dione (26). Similar to the preparation of **16**, compound **26** was prepared from the hydrogenation of **25** (55 mg, 0.24 mmol) over platinum (IV)

oxide (11 mg, 0.02 mmol) in methanol (8 mL) for 4 h. Usual work-up and column chromatography on silica gel (5 g, hexanes–ethyl acetate, 2:1) gave **26** (29 mg, 52%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.51 (td, J=13.4, 5.1 Hz, 1H), 1.99 (s, 3H), 2.23–2.59 (m, 6H), 2.66 (dt, J=13.6, 5.4 Hz, 1H), 3.04 (dd, J=17.6, 5.0 Hz, 1H), 7.43 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 7.7, 23.6, 24.8, 33.0, 38.7, 44.0, 44.5, 46.8, 121.4, 135.7, 145.3, 145.6, 188.5, 210.5; MS (EI) m/z 232 (M^+); HRMS (FAB) (MH^+) calcd for $C_{14}H_{17}O_3$: 233.1178. Found: 233.1162.

3.1.17. 4,5,7,8-Tetrahydro-8a-methyl-6,6-(1′,3′-dioxolan-2′-yl)-3-(trimethylsilyl)naphtho[2,3-*b*]furan-9-one (17). A solution of **16** (0.81 g, 2.79 mmol), anhydrous benzene (159 mL), ethylene glycol (3.12 mL, 55 mmol), and *p*-toluenesulfonic acid monohydrate (280 mg, 1.39 mmol) was refluxed for 15 h with a Dean–Stark apparatus. After cooling to rt, the reaction mixture was diluted with ethyl acetate (350 mL), then washed consecutively with saturated aqueous $NaHCO_3$ (350 mL), water (350 mL), and brine (350 mL). The organic solution was then dried over $MgSO_4$. After removal of solvent under reduced pressure, the residue was purified by chromatography on silica gel (26 g, hexanes–ethyl acetate, 5:1) to furnish **17** (0.77 g, 83%) as colorless crystals (hexanes–ethyl acetate); mp 162–164°C; ^{1}H NMR ($CDCl_3$) δ 0.18 (d, J=2.3 Hz, 9H), 1.16 (d, J=2.5 Hz, 3H), 1.25–1.72 (m, 6H), 2.23 2.45 (m, 2H), 3.03–3.18 (m, 1H), 3.79–3.91 (m, 4H), 7.37 (d, J=2.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −1.0, 24.5, 26.9, 30.9, 32.0, 37.8, 42.1, 46.8, 64.1, 64.2, 108.8, 120.8, 139.7, 146.5, 152.1, 189.7. Anal. calcd for $C_{18}H_{26}O_4Si$: C, 64.64; H, 7.83. Found: C, 64.74; H, 7.99.

3.1.18. 4,5,7,8-Tetrahydro-3,8a-dimethyl-6,6-(1′,3′-dioxolan-2′-yl)naphtho[2,3-*b*]furan-9-one (27). Similar to the preparation of **17**, compound **27** was prepared from **26** (29 mg, 0.1 mmol), ethylene glycol (0.14 mL, 2.5 mmol), *p*-toluenesulfonic acid monohydrate (12 mg, 0.06 mmol) in anhydrous benzene (7 mL) for 24 h. Usual work-up and column chromatography on silica gel (5 g, hexanes–ethyl acetate, 2:1) afforded **27** (21 mg, 60%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 3H), 1.32–1.77 (m, 6H), 1.96 (d, J=1.0 Hz, 3H), 2.27–2.48 (m, 2H), 3.03 (dd, J=17.6, 5.4 Hz, 1H), 3.85–3.96 (m, 4H), 7.36 (d, J=1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.7, 24.5, 24.7, 31.0, 32.0, 38.1, 41.9, 46.9, 64.2, 64.3, 108.9, 121.1, 127.9, 136.0, 145.0, 189.6. Anal. calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.34; H, 7.01.

3.1.19. 4,5,7,8-Tetrahydro-8a-methyl-6,6-(1′,3′-dioxolan-2′-yl)-3-(trimethylsilyl)naphtho[2,3-*b*]furan (18). A solution of **17** (770 mg, 2.31 mmol) in anhydrous THF (60 mL) was added dropwise to an ice cooled (0°C) solution of $LiAlH_4$ (96 mg, 2.31 mmol) in anhydrous THF (200 mL) under nitrogen. After stirring for 1 h at 0°C, the reaction mixture was quenched with saturated aqueous NH_4Cl solution (150 mL), filtered through a bed of Fuller's earth, and rinsed with ethyl acetate (50 mL). The aqueous layer was extracted with ethyl acetate (3×200 mL). The combined organic extract was then washed consecutively with water (300 mL), brine (300 mL), and dried over $MgSO_4$. Upon removal of solvent under reduced pressure, the residue was dissolved in anhydrous THF (19 mL) at 0°C. Carbon disulfide (0.74 mL, 12.2 mmol), iodomethane (0.75 mL, 12.0 mmol), and sodium hydride (60% dispersion in mineral oil) (0.14 g, 3.4 mmol) were subsequently added. The mixture was stirred under nitrogen for 4.5 h at 0°C. The reaction mixture was then quenched with water (20 mL). The aqueous layer was extracted with diethyl ether (3×50 mL). The combined organic extract was washed with brine (50 mL) and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was dissolved in anhydrous toluene (3 mL) and the solution was added dropwise under nitrogen over 30 min into a hot (110°C) solution of tri-*n*-butyltin hydride (6.21 mL, 23.1 mmol) and a catalytic amount of AIBN (3.8 mg, 0.02 mmol) in anhydrous toluene (4 mL). After refluxing for 72 h, the reaction mixture was concentrated under vacuum. The residue was purified by chromatography on silica gel (20 g, hexanes–ethyl acetate, 5:1) to provide **18** (0.16 g, 22%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.19 (s, 9H), 0.98 (s, 3H), 1.36–1.92 (m, 7H), 2.09 (t, J=14.4 Hz, 2H), 2.70–2.89 (m, 2H), 3.87–4.01 (m, 4H), 7.14 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.7, 26.8, 27.4, 28.2, 31.3, 33.4, 36.6, 37.7, 38.5, 64.2, 64.2, 109.5, 116.6, 118.7, 145.7, 149.1; MS (EI) m/z 320 (M^+); HRMS (EI) (M^+) calcd for $C_{18}H_{28}O_3Si$: 320.1808. Found: 320.1791.

3.1.20. 4,5,7,8-Tetrahydro-3,8a-dimethyl-6,6-(1′,3′-dioxolan-2′-yl)naphtho[2,3-*b*]furan (28). Similar to the preparation of **18**, compound **28** was prepared from **27** (30 mg, 0.1 mmol) in three consecutive steps with proper work-ups as shown above, employing the following reagents, solvents and conditions: (1) $LiAlH_4$ (5 mg, 0.13 mmol) in anhydrous THF (17 mL), 1 h at 0°C; (2) carbon disulfide (0.05 mL, 0.83 mmol), iodomethane (0.05 mL, 0.8 mmol) and sodium hydride (60% dispersion in mineral oil) (40 mg, 1 mmol), 5 h at 0°C; (3) tri-*n*-butyltin hydride (0.28 mL, 1 mmol), AIBN (1 mg), anhydrous toluene, refluxed for 72 h. Usual work-up and column chromatography on silica gel (5 g, hexanes–ethyl acetate, 10:1) gave **28** (14 mg, 47%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 3H), 1.37–1.92 (m, 10H), 2.01 (dd, J=16.2, 3.4 Hz, 2H), 2.55–2.70 (m, 1H), 2.78 (d, J=16.9 Hz, 1H), 3.84 (m, 4H), 7.04 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 8.1, 24.3, 27.4, 28.3, 31.3, 33.5, 36.6, 37.7, 38.1, 64.2, 109.5, 113.9, 119.7, 137.2, 148.6; MS (EI) m/z 262 (M^+); HRMS (EI) (M^+) calcd for $C_{16}H_{22}O_3$: 262.1569. Found: 262.1552.

3.1.21. 4,5,7,8-Tetrahydro-3,8a-dimethylnaphtho[2,3-*b*]furan-6(5*H*)-one (2). To a solution of **28** (7 mg, 0.03 mmol) in THF (1 mL), an aqueous solution of 2N HCl (0.02 mL, 0.04 mmol) was added. The reaction mixture was stirred under nitrogen at rt for 15 h. It was then diluted with water (5 mL) and neutralized with saturated aqueous $NaHCO_3$ solution (4 mL) to pH 7. After removal of THF under reduced pressure, the aqueous layer was extracted with diethyl ether (3×15 mL). The combined organic extract was washed with brine (30 mL) and dried over $MgSO_4$. After evaporation under reduced pressure, the residue was purified on a silica gel column (5 g, hexanes–ethyl acetate, 10:1) to provide **2** (3 mg, 45%) as a colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.14 (s, 3H), 1.64–1.78 (m, 1H), 1.85–2.04 (m, 5H), 2.14 (dd, J=16.3, 3.5 Hz, 1H), 2.28 (d, J=8.2 Hz, 2H), 2.36 (dd, J=16.3, 6.7 Hz, 2H), 2.43–2.57 (m, 1H),

2.67–2.79 (m, 1H), 2.88 (d, J=16.8 Hz, 1H), 7.17 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 8.9, 26.6, 26.9, 30.2, 33.5, 36.7, 37.8, 41.2, 43.9, 114.7, 120.5, 138.0, 149.4, 211.7; HRMS (EI) (M^+) calcd for $C_{14}H_{18}O_2$: 218.1307. Found: 218.1310.

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