Articles

Benzo[*d*]naphtho[1,2-*b*]pyran-6-one C-Glycosides: Aryltri-*n*-butylstannanes in Palladium-Mediated Coupling with 2,3-Dihydropyran and Furanoid Glycals

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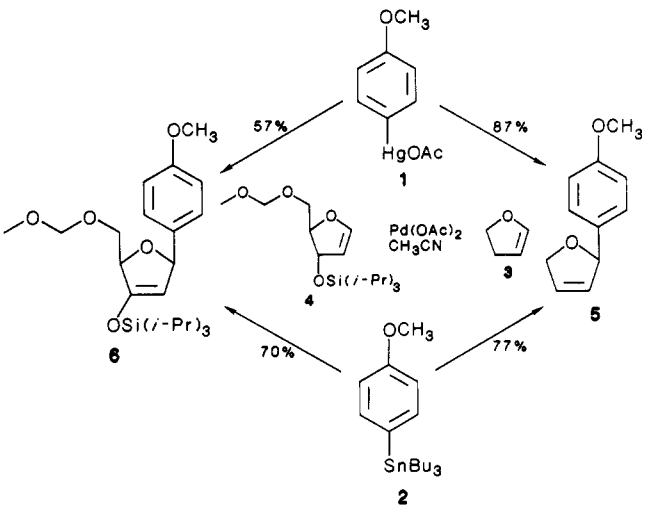
Synthesis of benzo[*d*]naphtho[1,2-*b*]pyran-6-one furanoid C-glycosides, related to the gilvocarcin, ravidomycin, and chrysomycin class of antibiotics, has been accomplished by regio- and stereospecific coupling of a furanoid glycal, 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol with tri-*n*-butylstannyl derivatives of benzo[*d*]naphtho[1,2-*b*]pyran-6-ones in the presence of stoichiometric palladium(II) acetate. Comparison of arylmercurial and aryltri-*n*-butylstannane precursors to the reactive arylpalladium reagent that undergoes glycal (enol ether) coupling indicated both of these organometallic species to be equally effective.

We have in progress a research program directed toward synthesis of benzo[*d*]naphtho[1,2-*b*]pyran-6-one C-glycosides[1,2] that are structural analogues of several important anticancer antibiotics. Antibiotics of this class include ravidomycin,[3] the gilvocarcins[4] (toromycin[5]), and chrysomycins A and B[6] (virenomycin[7]). Initially, we undertook the preparation of appropriate tetracyclic aryl aglycone–mercuric acetate derivatives for use in palladium-mediated coupling with glycals (enol ethers).[8-10] In this reaction, organomercurials serve as precursors to the reactive organopalladium reagents (formed in situ[10,11]), which undergo regio- and stereospecific coupling with glycals.[8-11] In the benzo[*d*]naphtho[1,2-*b*]pyran-6-one series, the organomercurials obtained were too insoluble for effective use; as a result, we[1] have prepared the corresponding tri-*n*-butylstannyl[12] derivatives, which exhibit much more favorable solubility properties. These aryltri-*n*-butylstannanes have been used successfully in palladium-mediated coupling reactions with furanoid glycals to produce the first synthetic benzo[*d*]naphtho[1,2-*b*]-pyran-6-one C-glycosides.[1]

Scheme I



In the present report, we describe (a) a limited investigation carried out to compare the reactivities of aryltri-*n*-butylstannanes[12] and corresponding arylmercuric actates[8-11] in palladium-mediated coupling reactions of enol ethers and (b) the use of tri-*n*-butylstannyl derivatives as intermediates in the synthesis of benzo[*d*]naphtho[1,2-

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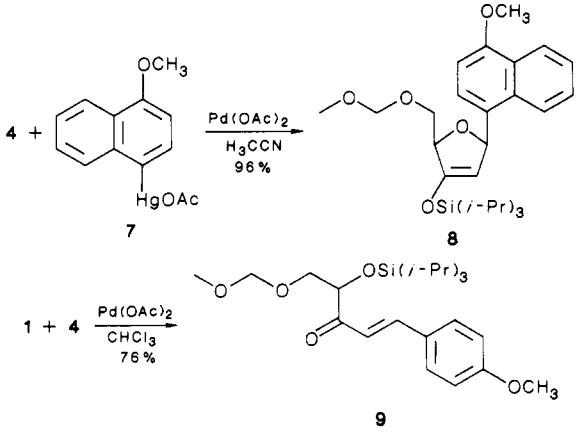
b]pyran-6-one C-glycosides.[1]

Comparison of RHgOAc with $RSnBu_3$ as RPdX Precursors. The palladium-mediated reactions of (4-methoxyphenyl)mercuric acetate[13,14] (**1**) and (4-methoxyphenyl)tri-*n*-butylstannane[15] (**2**) with 2,3-dihydrofuran (**3**) and 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol[16] (**4**) were carried out and the results compared (Scheme I). When a solution of arylmercuric acetate **1**, 2,3-dihydrofuran (**3**), and an equivalent of palladium(II) acetate in acetonitrile were stirred at room temperature for 12 h, the coupled product 2-(4-methoxyphenyl)-2,5-dihydrofuran[14] (**5**) was produced in 87% isolated yield. Repetition of the reaction using the corresponding tri-*n*-butylstannyl derivative **2** as the precursor for formation of the reactive arylpalladium reagent (by transmetalation[11,17,18]) produced a comparable yield (77%) of **5**. From this latter reaction mixture the aryl dimer, 4,4′-dimethoxybiphenyl[19] (22%), was also isolated.[20]

Similar parallel reactions of **1** and **2** with furanoid glycal **4**[16] produced the corresponding C-glycoside **6** in 57% and 70% isolated yields, respectively. The related organomercurial, (4-methoxynaphthyl)mercuric acetate[14] (**7**) underwent palladium-mediated coupling with glycal **4** to produce the corresponding C-glycoside **8** in essentially quantitative yield. When the reaction solvent used for coupling of glycal **4** with the tri-*n*-butylstannyl derivative **2** was chloroform rather than acetonitrile,[14] the yield of **6** was reduced to 43%. However, in chloroform, when the aglycone precursor was organomercurial **1**, C-glycoside **6** was not isolated; rather a 76% yield of the rearranged, acyclic C-glycoside **9** was obtained.



These experiments indicate that both arylmercuric derivative **1** and aryltri-*n*-butylstannyl derivative **2** are effective in enol ether arylation under the conditions of the palladium-mediated coupling reaction. It is particularly noteworthy that stannane **2** exhibits the same reaction regio- and stereochemistry as the more thoroughly studied arylmercurial derivatives.[8-11,14,16,18] Also noted is the fact that reactions involving arylstannane **2** produces the aryl dimer[19] as a side product, whereas this product was not observed when arylmercurial **1** was employed.[20]

Tri-*n*-butylstannyl Derivatives of 1-Methoxy-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]pyran-6-ones. The successful use of (4-methoxyphenyl)tri-*n*-butylstannane (**2**) in palladium-mediated coupling reactions led us to extend this chemistry to the tetracyclic benzo[*d*]naphtho[1,2-*b*]pyran-6-one series. The readily available 1-hydroxy-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]-pyran-6-one[21,22] (**10**) was brominated by using either *N*-bromosuccinimide in dimethylformamide[23] or pyridinium hydrobromide bromide in acetic acid[24]to form the 2-bromo derivative **11**. Methylation of **11** (dimethyl sulfate, potassium carbonate in acetone) yielded **12**, which, upon reaction[25] with hexa-*n*-butylditin in the presence of a catalytic quantity of tetrakis(triphenylphosphine)palladium(0),[26] produced the corresponding tri-*n*-butylstannyl derivative **13**. Alternatively, reversal of the order of the first two reactions, that is initial methylation of the phenolic oxygen of **10** to form **14** followed by bromination, produced the isomeric 4-bromo compound **15**, which, upon catalytic stannylation,[25] yielded the corresponding 4-tri-*n*-butyl analogue **16** (Scheme II).

Aromatization of the tetrahydro rings of **12**, **14**, and **15** was accomplished by a two-step sequence involving benzoyl peroxide catalyzed allylic bromination, forming the intermediates **19**, **21**, and **22**, respectively, which upon dehydrohalogenation yield **20**, **23**, and **24**. Catalytic stannylation of **24** yielded aryltri-*n*-butylstannane **25**. Alternately, aromatization of **10** was accomplished by using a mixture of palladium on carbon and sulfur[22] to yield **17**, which was subsequently brominated (**18**) and O-methylated (**20**).

Palladium-Mediated Coupling Reactions of Tetracyclic Arylstannanes. Coupling of 2- and 4-tri-*n*-butylstannyl derivatives (**13** and **16**) with 2,3-dihydrofuran (**3**) in the presence of palladium acetate was accomplished, producing **26** and **27**, respectively, in modest yield. Similar coupling of **13** and **16** with furanoid glycal **4** was accomplished, furnishing the corresponding C-glycosides **28** (53%) and **29** (92%); no other coupled products were isolated. Analogously, by palladium-mediated coupling of tri-*n*-butylstannane **25** with glycal **4**, C-glycoside **30** was obtained; again only a single coupled product was isolated from the reaction mixture (Scheme III).

C-Glycosides **29** and **30** were assigned to the β-C-glycoside series by nuclear magnetic resonance (NMR) spectrometry. 2,3-Unsaturated furans exhibit $^4J_{1,4} > 5$ Hz for trans 1,4 hydrogens and <4 Hz for 1,4 cis hydrogens.[16,27] The coupling constants $^4J_{1',4'} = 3.42$ Hz for C-glycoside **29**

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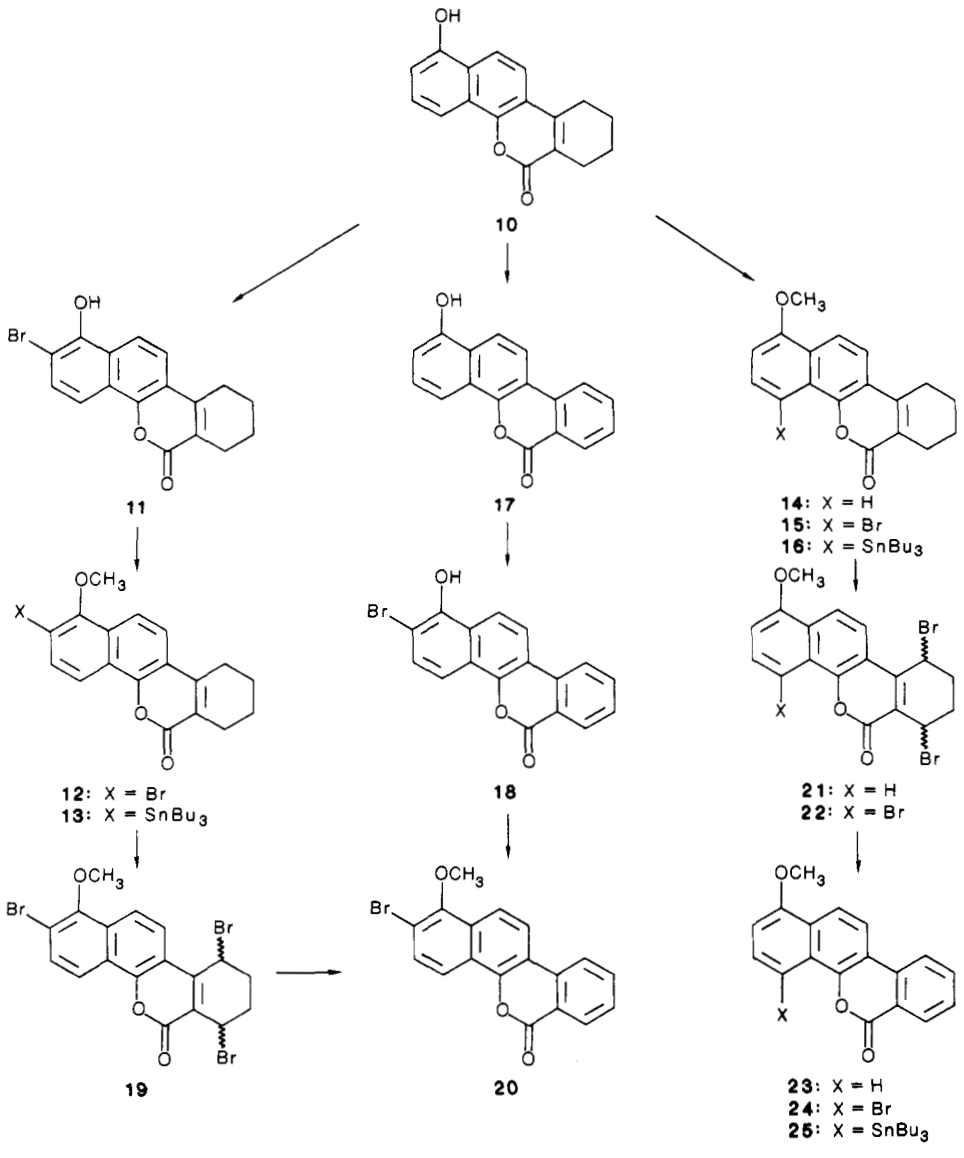
Scheme II



and 3.75 Hz for **30**, establish the 1′ and 4′ hydrogens as cis in each compound and establish the anomeric configuration as β. We were unable to determine the value of $^4J_{1',4'}$ from the ^{1}H NMR spectrum of **28**; the assignment of this C-glycoside to the β series is made by analogy with **29** and **30** and in accord with the stereochemical outcome of other palladium-mediated coupling reactions using glycal **4**.[9,10,16]

Discussion

The present study has demonstrated the efficacy of the palladium-mediated coupling reaction developed in our laboratory[8-10] for synthesis of C-glycosides of the tetracyclic benzo[d]naphtho[1,2-b]pyran-6-one aglycone series[1] and presages the employment of this route for synthesis of C-glycosides closely related to the antibiotics of this series.[1-7] It is noteworthy that syntheses of the aglycone, defucogilvocarcin V,[28-31] and of the carbohydrate portion of ravidomycin, (−)-methyl ravidosaminide,[32] have been reported.

Experimental Section

General Comments. Thin-layer chromatography (TLC) was carried out on prescored silica gel GF plates (Analtech). Preparative TLC was carried out on 1 mm thick, 20 × 20 cm^2, silica gel GF plates (Analtech). For flash chromatography, silica gel 60 (230–400 mesh ASTM, E. Merck) was used. Columns were eluted with a positive nitrogen pressure. Nuclear magnetic resonance spectra were obtained on a JEOL FX 90Q spectrometer or on a GE GN-300 spectrometer and are referenced to tetramethylsilane. Mass spectra (EI) were obtained with a Finnegan 4023 GC/MS/DS system operating at 70 eV, using a direct insertion probe. High resolution mass measurements were performed by Dr. I. Wachs, Department of Chemistry, Cornell University. Melting points were measured with a Thomas-Hoover capillary apparatus and are uncorrected. Elemental analyses were carried out by Dr. G. Robertson, Florham Park, NJ.

4-(2′,5′-Dihydrofuran-2′-yl)anisole (5). (a) To a solution of 4-(tri-*n*-butylstannyl)anisole[15] (**2**) (0.397 g, 1.00 mmol) in 10 mL of dry acetonitrile was added 2,3-dihydrofuran (**3**) (0.10 mL, 1.3 mmol). To the resulting solution was added a solution of pal-

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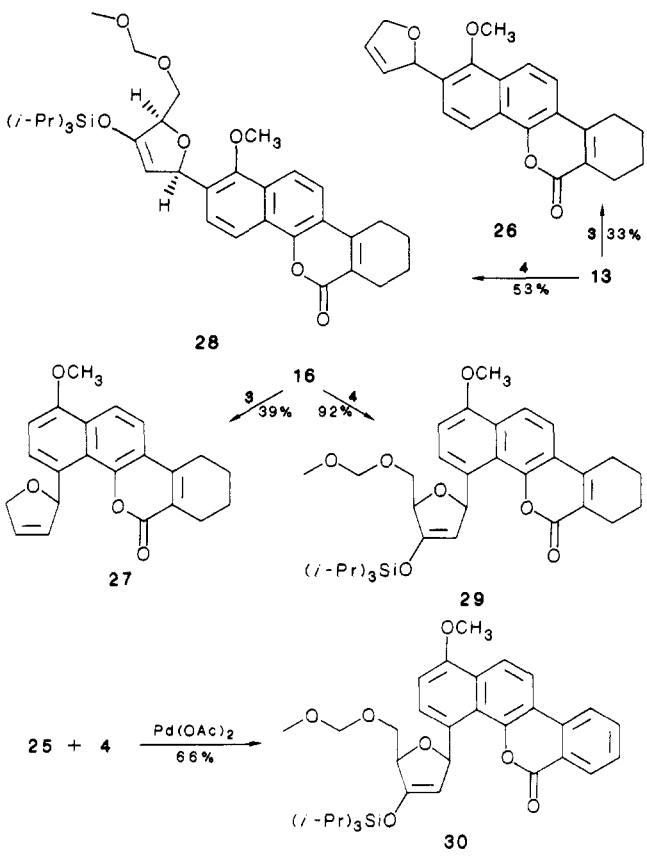
Scheme III



ladium acetate (0.224 g, 1.00 mmol) in 10 mL of dry acetonitrile. The mixture was stirred at room temperature for 8 h. Then the reaction mixture was diluted with 50 mL of chloroform, filtered through Celite, washed with water (2 × 15 mL), and dried over sodium sulfate. The sodium sulfate was removed and then the solvent was removed in vacuo followed by purification by preparative TLC ($CHCl_3$) to afford two products **5** (0.136 g, 77%), R_f = 0.75 as a yellow oil,[14] and 4,4′-dimethoxybiphenyl (0.023 g, 22%), R_f = 0.78 as white platelets, mp 171–172 °C (ref.[19] mp 172–173 °C). **Compound 5**:[14] ^{13}C NMR ($CDCl_3$): 159.29 (C1), 134.05 (C4), 129.93 (C2′), 127.76 (C3, C5), 126.57 (C3′), 113.78 (C2, C6), 99.86 (C1′), 75.37 (C4′), 55.17 (OCH_3). **4,4′-Dimethoxybiphenyl**:[19] ^1H NMR ($CDCl_3$) 7.49 (4 H, ddd, H3, H3′, H5, H5′), 6.96 (4 H, ddd, H2, H2′, H6, H6′), 3.85 (6 H, s, OCH_3's); mass spectrum, *m/z* (relative intensity) 214 (100, $M^{\bullet+}$), 199 (79, $M^{\bullet+} - CH_3$), 171 (26, $M^{\bullet+} - C_2H_3O$), 107 (21, $M^{\bullet+}$).

(b) To a suspension of (4-methoxyphenyl)mercuric acetate[13,14] (**1**) (0.367 g, 1.00 mmol) and palladium acetate (0.224 g, 0.998 mmol) in 20 mL of acetonitrile was added 2,3-dihydrofuran (**3**) (0.1 mL, 1.32 mmol). The resulting black solution was stirred for 12 h at room temperature. The mixture was then diluted with 25 mL of acetonitrile and filtered through Celite. The solvent and other volatiles were removed in vacuo and the residual oil was purified by preparative TLC (chloroform) to afford **5**[14] (0.176 g, 87%) R_f = 0.8 as a yellow oil indistinguishable from a sample prepared by method a.

(2′*R*)-*cis*-4-[2′,5′-Dihydro-5′-[(methoxymethoxy)-methyl]-4′-[[tris(1-methylethyl)silyl]oxy]-2′-furanyl]anisole (6). (a) To a solution of 4-(tri-*n*-butylstannyl)anisole[15] (**2**) (0.075 g, 0.19 mmol) and 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol[16] (**4**) (0.075 g, 0.24 mmol) in 3 mL of acetonitrile was added a solution of palladium acetate (0.042 g, 0.19 mmol) in 2.0 mL of acetonitrile. After 1 min, sodium bicarbonate (0.064 g, 0.76 mmol) was added and then the resulting mixture was stirred at room temperature for 18 h. The reaction mixture was then diluted with 25 mL of acetonitrile, filtered through Celite, and dried (sodium sulfate). The solvent was removed and the resulting crude oil was separated by preparative TLC (ether/petroleum ether, 1:2) to yield **6** (0.056 g, 70%) as a yellow oil: IR (neat) ν 3005, 2980, 2970, 2960, 2880, 1680, 1665, 1580, 1520, 1470, 1260, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (2 H, ddd, H2, H6), 6.86 (2 H, ddd, H3, H5), 5.67 (1 H, dd, $J_{1',4'}$ = 3.57 Hz, $J_{1',2'}$ = 0.16 Hz, H1′), 4.60–4.83 (4 H, m, H2′, H4′, OCH_2O), 3.68–3.91 (5 H, m, H5′, H5″, $ArOCH_3$), 3.33 (3 H, s, OCH_3), 1.09 (21 H, narrow m, $Si(CH(CH_3)_2)_3$); ^{13}C NMR ($CDCl_3$) δ 159.35 (C1), 150.95 (C3′), 135.02 (C4), 128.63 (C3, C5), 113.52 (C2, C6), 101.76 (C2′), 96.56 (OCH_2O), 84.64 (C1′), 82.15 (C4′), 68.98 (C5′), 55.17, 55.01 (OCH_3's), 17.79 (CH_3's), 12.21 (CH); mass spectrum, *m/z* (relative intensity) 422 (17, $M^{\bullet+}$), 347 (78, $M^{\bullet+} - C_3H_7O_2$), 135 (100, $M^{\bullet+} - C_{15}H_{31}O_3Si$).

Anal. Calcd for $C_{23}H_{38}O_5Si$: C, 65.36; H, 9.06. Found: C, 65.36; H, 9.14.

(b) To a solution of (4-methoxyphenyl)mercuric acetate[13,14] (**1**) (0.069 g, 0.188 mmol) and 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol[16] (**4**) (0.075 g, 0.237 mmol) in 3 mL of dry acetonitrile was added a solution of palladium acetate (0.042 g, 0.187 mmol) in 2 mL of acetonitrile. After 1 min, sodium bicarbonate (0.064 g, 0.762 mmol) was added and the resulting black solution was stirred for 18 h at room temperature. The reaction mixture was then diluted with 25 mL of acetonitrile and filtered through Celite. The solvent was removed under vacuum and the residual oil was separated by preparative TLC (petroleum ether/ether, 2:1) to afford **6** (0.045 g, 57% as a pale yellow oil indistinguishable from that obtained by method a).

(2′*R*)-*cis*-4-[2′,5′-Dihydro-5′-[(methoxymethoxy)-methyl]-4′-[[tris(1-methylethyl)silyl]oxy]-2′-furanyl]-1-methoxynaphthalene (8). To a solution of (4-methoxynaphthyl)mercuric acetate[14] (**7**) (0.078 g, 0.19 mmol) and 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol[16] (**4**) (0.075 g, 0.28 mmol) in 3.0 mL of acetonitrile was added a solution of palladium acetate (0.042 g, 0.19 mmol) in 2.0 mL of acetonitrile. The resulting solution was stirred for 1 min and then sodium bicarbonate (0.064 g, 0.76 mmol) was added. The reaction mixture was then stirred at room temperature for 12 h. After this time period, the reaction mixture was diluted with 25 mL of acetonitrile and filtered through Celite. The solvent was removed under vacuum and the crude product was purified by preparative TLC (ether/petroleum ether, 1:1) to afford **8** (0.085 g, 96%) as a yellow oil: IR (neat) ν 3080, 3005, 2975, 2945, 2900, 2878, 1690, 1605, 1580, 1518, 1468, 1225, 1042, 1027 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.31 (1 H, ddd, H8), 8.22 (1 H, ddd, H5), 7.58 (1 H, ddd, H6), 7.56 (1 H, d, H3), 7.46 (1 H, ddd, H7), 6.80 (1 H, d, H2), 6.48 (1 H, dd, $J_{1',4'}$ = 3.83 Hz, $J_{1',2'}$ = 1.49 Hz, H1′), 5.05 (1 H, dd, $J_{2',4'}$ = 1.61 Hz, H2′), 4.74–4.96 (1 H, m, H4′), 4.59 (2 H, s, OCH_2O), 4.00 (3 H, s, $ArOCH_3$), 3.81 (1 H, dd, $J_{4',5'}$ = 2.64 Hz, $J_{5',5''}$ = 11.13 Hz, H5′), 3.68 (1 H, dd, $J_{4',5''}$ = 5.86 Hz, H5″), 3.25 (3 H, s, OCH_3), 1.25–1.00 (21 H, m, $Si(CH(CH_3)_2)_3$); ^{13}C NMR ($CDCl_3$) δ 155.23 (C1), 151.11 (C3′), 132.26 (C3), 130.42 (C10), 126.41 (C4), 125.65 (C9), 124.73, 124.46 (C5, C6), 123.37 (C7), 122.34 (C8), 103.11 (C2), 101.00 (C2′), 96.50 (OCH_2O), 82.36 (C1′), 81.17 (C4′), 69.09 (C5′), 55.39, 54.90 ($ArOCH_3$, OCH_3), 17.84 (CH_3), 12.27 (CH); mass spectrum, *m/z* (relative intensity) 472 (6.0, $M^{\bullet+}$), 441 (2.0, $M^{\bullet+} - OCH_3$), 397 (4.0, $M^{\bullet+} - C_3H_7O_2$).

1′-(4-Anisyl)-4′(*R*)-[[tris(1-methylethyl)silyl]oxy]-5′-(methoxymethoxy)-1′-penten-3′-one (9). To a solution of (4-methoxyphenyl)mercuric acetate[13,14] (**1**) (0.0690 g, 0.188 mmol) and 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol[16] (**4**) (0.0750 g, 0.237 mmol) in 3.0 mL of chloroform was added a solution of palladium acetate (0.0420 g, 0.187 mmol) in 2.0 mL of chloroform. After 1 min of stirring, sodium bicarbonate (0.0640 g, 0.762 mmol) was added and the resulting black solution was stirred for 2 days. After this time, the reaction mixture was diluted with 25 mL of chloroform and filtered through Celite. The solvent was removed in vacuo and the residual oil was purified by preparative TLC (petroleum ether/ether 2:1) to yield **9** (0.061 g, 76%) R_f = 0.52, as a deep yellow oil: IR (neat) ν 3020, 3000, 2950, 2900, 2878, 1680, 1597, 1511, 1260, 1110, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.72 (1 H, d, $J_{1',2'}$ = 15.82 Hz, H1′), 7.55 (2 H, dd, H3, H5), 7.21 (1 H, d, H2′), 6.91 (2 H, dd, H2, H6), 4.61 (2 H, s, OCH_2O), 4.46 (1 H, t, $J_{4',5'}$ = 4.90 Hz, H4′), 3.85 (3 H, s, $ArOCH_3$), 3.78 (2 H, dd, H5′, H5″), 3.32 (3 H, s, OCH_3), 1.096 (21 H, s, $Si(CH(CH_3)_2)_3$); ^{13}C NMR ($CDCl_3$) δ 200.14 (C3′), 161.67 (C1), 143.35 (C1′), 130.25 (C3, C5), 127.60 (C4), 118.88 (C2′), 114.38 (C2, C6), 96.61 (OCH_2O), 78.25

(C4'), 70.39 (C5'), 55.39, 55.22 (OCH_3's), 17.90 (CH_3), 12.21 (CH); mass spectrum, m/z (relative intensity) 422 (0.11, $M^{\bullet+}$), 379 (23, $M^{\bullet+} - C_3H_7$), 161 (30, $M^{\bullet+} - C_{13}H_{29}O_3Si$), 147 (22, $M^{\bullet+} - C_{14}H_{31}O_3Si$).

2-Bromo-1-hydroxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (11). To a solution of 1-hydroxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (**10**)[21] (1.00 g, 3.76 mmol) in 40 mL of acetic acid was added a solution of pyridinium hydrobromide bromide (1.20 g, 3.76 mmol) in 40 mL of acetic acid. The mixture was stirred at room temperature for 14 h. Then the reaction mixture was poured onto ice and the precipitate that formed was collected. Recrystallization of the crude product from ethanol afforded **11** (1.16 g, 89%) as a light tan solid, mp 228–230 °C: IR (KBr) ν 3380, 2930, 2860, 1680, 1608, 1565, 1415, 1248, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.07 (1 H, dd, H12), 7.98 (1 H, dd, H4), 7.61 (1 H, d, H3), 7.61 (1 H, d, H11), 6.05 (0.5 H, br s, ArOH), 2.55–3.00 (4 H, m, H7, H10), 1.80–2.00 (4 H, m, H8, H9); ^{13}C NMR ($CDCl_3$) δ 165.47 (C=O), 153.75 (C1), 147.75 (C5a, C10a), 133.41 (C11a), 129.52 (C3, C12a), 124.62 (C7a), 123.92 (C4a), 119.96 (C11), 118.23 (C4), 115.73 (C12), 106.74 (C2), 25.70 (C7), 24.13 (C10), 21.47 (C8, C9); mass spectrum, m/z (relative intensity) 344, 346 (49, 45, $M^{\bullet+}$), 228, 290 (54, 52, $M^{\bullet+} - C_4H_8$).

2-Bromo-1-methoxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (12). A mixture of **11** (2.59 g, 7.51 mmol), potassium carbonate (4.04 g, 29.2 mmol), and dimethyl sulfate (2.0 mL, 21 mmol) in 80 mL of acetone was heated at reflux for 12 h. The reaction mixture was cooled, the solvent was removed under vacuum, and the resulting residue was dissolved in chloroform, washed with a dilute alkali solution, and dried (sodium sulfate). Removal of chloroform in vacuo followed by recrystallization of the crude product from ethanol gave **12** (2.45 g, 91%) as yellow needles, mp 174–176 °C: IR (KBr) ν 2940, 2860, 1708, 1602, 1458, 1405, 1260, 1080, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.06 (1 H, dd, H12), 7.84 (1 H, dd, H4), 7.62 (1 H, d, H3), 7.50 (1 H, d, H11), 3.99 (3 H, s, OCH_3), 2.50–2.90 (4 H, m, H7, H10), 1.75–1.98 (4 H, m, H8, H9); ^{13}C NMR ($CDCl_3$) δ 161.08 (C=O), 152.90 (C1), 148.35 (C5a), 147.48 (C10a), 131.07 (C3), 129.52 (C12a), 123.75, 123.43 (C7a, C11a), 120.56 (C11), 119.36 (C4), 117.74 (C12), 115.63, 115.25 (C4a, C2), 61.51 (OCH_3), 25.53 (C7), 24.02 (C10), 21.36 (C8, C9); mass spectrum, m/z (relative intensity) 358, 360 (72, 67, $M^{\bullet+}$), 302, 304 (37, 35, $M^{\bullet+} - C_4H_8$).

Anal. Calcd for $C_{18}H_{15}BrO_3$: C, 60.18; H, 4.21; Br, 22.24. Found: C, 59.92; H, 4.20; Br, 22.13.

2-(Tri-n-butylstannyl)-1-methoxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (13). A mixture of **12** (0.889 g, 2.48 mmol), hexa-*n*-butylditin (2.50 mL, 4.95 mmol), and tetrakis(triphenylphosphine)palladium(0)[26] (0.044 g, 0.039 mmol) in 20 mL of dry toluene at reflux was stirred for 12 h under an atmosphere of nitrogen. The reaction mixture was cooled and the solution diluted with 50 mL of toluene. The resulting solution was treated with decolorizing carbon and filtered through Celite. The toluene and low boiling products were removed under vacuum to give a crude brownish yellow oil. The crude oil was purified by flash column chromatography (ether/petroleum ether, 1:1) to yield **13** (1.15 g, 82%), R_f = 0.71, as a viscous yellow oil: IR (neat) ν 2985, 2950, 2890, 1724, 1635, 1605, 1570, 1465, 1376, 1263, 1032 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.30 (1 H, d, H4), 7.91 (1 H, d, H12), 7.60 (1 H, d, H3), 7.58 (1 H, d, H11), 3.93 (3 H, s, OCH_3), 2.55–3.00 (4 H, br m, H7, H10), 1.70–2.10 (4 H, br m, H8, H9), 1.00–1.75 (18 H, br m, CH_2's), 0.75–1.10 (9 H, br t, CH_3's).

1-Methoxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (14). A mixture of 1-hydroxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (**10**) (1.00 g, 3.75 mmol),[21] potassium carbonate (2.02 g, 14.6 mmol), and dimethyl sulfate (1.00 mL, 10.6 mmol) in 40 mL of acetone was heated under reflux for 12 h. The reaction mixture was cooled, the solvent was removed under vacuum, and the residue was dissolved in chloroform. The resulting solution was washed with dilute aqueous sodium hydroxide and dried (magnesium sulfate). Removal of solvent in vacuo followed by recrystallization of the residual crude product from acetone afforded **14** (0.98 g, 93%) as beige crystals, mp 161–162 °C (lit.[21] mp 164 °C): IR (KBr) ν 3000, 2930, 2870, 1710, 1610, 1570, 1450, 1257, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.12 (1 H, ddd, H4), 8.07 (1 H, dd, H12), 7.52 (1 H, d, H11), 7.49 (1 H, dd, H3), 6.93 (1 H, dd, H2), 4.02 (3 H, s, OCH_3), 2.55–2.95 (4 H, m, H7, H10), 1.75–1.95 (4 H, m, H8, H9); ^{13}C NMR ($CDCl_3$) δ 161.84 (C=O), 155.77 (C1), 147.96 (C5a), 147.31 (C10a), 127.11 (C3), 125.97 (C12a), 124.25 (C7a), 122.60 (C4a), 118.61 (C11), 117.40 (C12), 115.84 (C11a), 114.38 (C4), 106.04 (C2), 55.66 (OCH_3), 25.70 (C7), 24.07 (C10), 21.53 (C8, C9).

Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 76.99; H, 5.82.

4-Bromo-1-methoxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (15). A solution of *N*-bromosuccinimide (0.668 g, 3.73 mmol) in 20 mL of dry dimethylformamide (DMF) was added to a solution of **14** (1.05 g, 3.76 mmol) in 20 mL of dry DMF and stirred for 15 min at room temperature. The precipitate that formed was collected and recrystallized from ethanol to give **15** (1.10 g, 82%) as light yellow needles, mp 216–217 °C: IR (KBr) ν 3065, 2990, 2922, 2830, 1700, 1603, 1550, 1455, 1415, 1251, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.09 (1 H, d, H12), 7.79 (1 H, d, H3), 7.54 (1 H, d, H11), 6.73 (1 H, d, H2), 3.99 (3 H, s, OCH_3), 2.50–2.95 (4 H, m, H7, H10), 1.70–2.00 (4 H, m, H8, H9); ^{13}C NMR ($CDCl_3$) δ 160.60 (C=O), 154.52 (C1), 147.26 (C5a), 141.90 (C10a), 134.10 (C3), 127.92 (C12a), 124.02 (C7a), 121.64 (C4a), 119.69 (C11), 118.28 (C12), 117.20 (C11a), 107.18 (C4), 106.53 (C2), 55.87 (OCH_3), 25.86 (C7), 24.02 (C10), 21.58, 21.42 (C8, C9).

Anal. Calcd for $C_{18}H_{15}BrO_3$: C, 60.87; H, 4.21; Br, 22.24. Found: C, 60.80; H, 4.26; Br, 22.50.

4-(Tri-n-butylstannyl)-1-methoxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (16). A mixture of **15** (0.889 g, 2.48 mmol), hexa-*n*-butylditin (1.5 mL, 2.97 mmol), and tetrakis(triphenylphosphine)palladium(0)[26] (0.0220 g, 0.196 mmol) in 20 mL of dry toluene at reflux was stirred for 12 h under an atmosphere of nitrogen. The reaction mixture was cooled, and the resulting solution was diluted with 50 mL of toluene, treated with decolorizing carbon, and filtered through Celite. The toluene and low boiling products were removed in vacuo to afford a crude yellow brown oil. Purification of the crude oil by flash column chromatography (ether/petroleum ether, 2:1) yielded **16** (1.17 g, 83%), R_f = 0.64 as a yellow oil: IR (neat) ν 3015, 2990, 2960, 2905, 2880, 1720, 1600, 1557, 1465, 1382, 1365, 1320, 1258, 1043 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.17 (1 H, dd, H12), 7.72 (1 H, d, H3), 7.55 (1 H, d, H11), 6.96 (1 H, dd, H2), 4.02 (3 H, s, OCH_3), 2.50–3.00 (4 H, m, H7, H10), 1.70–2.10 (4 H, m, H8, H9), 1.10–2.70 (18 H, br m, CH_2's), 0.65–1.05 (9 H, br t, CH_3's); ^{13}C NMR ($CDCl_3$) δ 160.75 (C=O), 155.44 (C1), 149.59 (C10a), 147.91 (C5a), 136.86 (C3), 129.60 (C12a), 127.71 (C4), 127.11 (C7a), 122.83 (C4a), 118.50, 118.28 (C11, C12), 115.79 (C11a), 105.79 (C2), 55.49 (OCH_3), 29.22 (3-CH_2), 27.38 (2-CH_2), 25.86 (C7), 24.02 (C10), 21.58 (C8, C9), 13.73 (4-CH_3), 11.62 (1-CH_2Sn); mass spectrum, m/z (relative intensity) 567, 569, 571 (1.0, 1.5, 2.6, $MH^{\bullet+}$), 509, 511, 513 (3.1, 5.2, 11, MH - $Bu^{\bullet+}$), 395, 397, 399 (0.23, 0.42, 0.52, $MH^{\bullet+}$ - 3Bu), 280 (65, $MH^{\bullet+} - SnBu_3$).

1-Hydroxybenzo[d]naphtho[1,2-b]pyran-6-one (17). Following the procedure of Chebaane et al.,[22] an intimate mixture of 1-hydroxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one[21] (**10**) (0.500 g, 0.188 mmol), 10% palladium on carbon (0.300 g), and sublimed sulfur (0.250 g, 0.780 mmol) was heated on a sand bath at 260 °C for 30 h. The residue was extracted with benzene and filtered, and the volume of the solvent was reduced under vacuum to promote crystallization to give **17** (0.322 g, 65%) as off-white needles, mp 295–297 °C: IR (KBr) ν 3384, 3036, 1695, 1605, 1557, 1509, 1438, 1253, 1089, 1027 cm^{-1}; ^1H NMR (DMSO-d_6) δ 10.47 (0.5 H, br s, ArOH), 8.53 (1 H, dd, H4), 8.33 (1 H, dd, H12), 8.21 (1 H, d, H11), 7.65–8.15 (4 H, m, H3, H7, H9, H10), 7.51 (1 H, dd, H8), 7.05 (1 H, dd, H2); ^{13}C NMR (DMSO-d_6) δ 160.38 (C=O), 153.37 (C1), 146.31 (C5a), 135.44 (C9), 134.85 (C10a), 129.75 (C7), 129.10 (C7a), 127.97 (C10), 125.04 (C8), 124.34 (C4a), 122.93 (C3), 120.49 (C12a), 118.59, 118.38 (C11, C11a), 113.00 (C4), 111.71 (C12), 110.41 (C2).

Anal. Calcd for $C_{17}H_{10}O_3$: C, 77.86; H, 3.84. Found: C, 77.60; H, 4.10.

2-Bromo-1-hydroxybenzo[d]naphtho[1,2-b]pyran-6-one (18). To a solution of **17** (0.320 g, 1.20 mmol) in 15 mL of acetic acid (warmed to dissolve **17**) was added a solution of pyridinium hydrobromide bromide (0.385 g, 1.20 mmol) in 5 mL of acetic acid. The resulting mixture was stirred for 24 hours at room temperature; the precipitate which formed was collected and recrystallized from ethanol to yield **18** (0.327 g, 80%) as a beige solid, mp 256–257 °C: IR (KBr) ν 3430, 1732, 1630, 1605, 1590, 1430, 1245, 1225, 1080, 1060 cm^{-1}; ^1H NMR (DMSO-d_6) δ 10.27 (0.7 H,

br s, ArOH), 8.52 (1 H, dd, H4), 8.41 (1 H, d, H12), 8.32 (1 H, dd, H3), 8.17 (1 H, d, H11), 8.02 (1 H, ddd, H9), 7.60–7.85 (3 H, m, H7, H8, H10).

Anal. Calcd for $C_{17}H_9BrO_3$: C, 59.85; H, 2.66. Found: C, 60.06; H, 2.81.

1-Methoxy-2,7,10-tribromo-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]pyran-6-one (19). A suspension of **12** (1.35 g, 3.76 mmol), benzoyl peroxide (0.0090 g, 0.037 mmol), and *N*-bromosuccinimide (1.67 g, 9.39 mmol) in 50 mL of carbon tetrachloride was heated at reflux for 12 h. The reaction mixture was cooled, and the resulting precipitate was collected and triturated with carbon tetrachloride. Removal of solvent from the resulting solution, followed by recrystallization of the residue from acetone/water, yielded **19** (1.50 g, 78%) as pale yellow crystals, mp 88–91 °C dec: IR (KBr) ν 2960, 2930, 2865, 1723, 1605, 1590, 1478, 1255, 1080, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.19 (1 H, dd, H12), 8.06 (1 H, dd, H4), 7.81 (1 H, d, H3), 7.75 (1 H, d, H11), 5.55–5.75 (2 H, m, H7, H10), 4.03 (3 H, s, OCH_3), 2.35–2.90 (4 H, m, H8, H9); mass spectrum, m/z (relative intensity) 435, 437, 439 (0.12, 0.21, 0.07, $M^{\bullet+}$ – Br), 358 (5.7, $M^{\bullet+}$ – 2Br), 356 (33, $M^{\bullet+}$ – 2Br and $M^{\bullet+}$ – 2HBr), 354 (25, $M^{\bullet+}$ – 2HBr).

2-Bromo-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (20). (a) A mixture of **18** (0.305 g, 0.894 mmol), potassium carbonate (0.462 g, 3.34 mmol) and dimethyl sulfate (0.25 mL, 2.6 mmol) in 10 mL of acetone was heated at reflux for 48 h. The reaction mixture was cooled, the solvent was removed under vacuum, and the resulting residue was dissolved in chloroform. The solution was washed with saturated aqueous $NaHCO_3$ (2 × 25 mL) and saturated aqueous NaCl (1 × 25 mL) and dried (sodium sulfate). Evaporation of the chloroform solution and crystallization gave **20** (0.306 g, 96%) as yellow-brown crystals, mp 232–234 °C.

(b) To a solution of **19** (3.41 g, 6.59 mmol) in 66 mL of dry toluene at 25 °C under nitrogen was added triethylamine (11.6 mL, 83.2 mmol), dropwise over 30 min. After the addition of the triethylamine was complete, the reaction mixture was heated at reflux for 8 h. The precipitate that formed was collected and triturated with chloroform. The chloroform solution was extracted with water and dried over sodium sulfate. The sodium sulfate was removed and evaporation of the chloroform to induce recrystallization afforded **20** (1.63 g, 70%) as yellow brown crystals, mp 232–234 °C: IR (KBr) ν 3010, 3000, 2990, 2980, 1740, 1620, 1395, 1280, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.45 (1 H, dd, H7), 8.21 (1 H, dd, H12), 8.18 (1 H, dd, H10), 8.12 (1 H, dd, H4), 8.02 (1 H, d, H11), 7.87 (1 H, ddd, H8), 7.71 (1 H, d, H3), 7.60 (1 H, ddd, H9), 4.04 (3 H, s, OCH_3); ^{13}C NMR ($CDCl_3$) δ 160.2 (C=O), 156.1 (C1), 153.0 (C5a), 147.2 (C10a), 138.0 (C12a), 135.02 (C9), 131.55 (C7), 130.74 (C7a, C3), 130.0 (C10), 128.90 (C8), 122.07 (C11), 120.23 (C11a), 119.58 (C4), 118.55 (C12), 61.62 (OCH_3); mass spectrum, m/z (relative intensity) 354, 356 (30, 33, $M^{\bullet+}$), 311, 313 (12, 13, $M^{\bullet+}$ – C_2H_3O).

7,10-Dibromo-1-methoxy-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]pyran-6-one (21). A suspension of **14** (1.05 g, 3.76 mmol), benzoyl peroxide (0.0090 g, 0.037 mmol), and *N*-bromosuccinimide (1.34 g, 7.51 mmol) in 50 mL of carbon tetrachloride was heated at reflux for 24 h. The reaction mixture was cooled and the resulting precipitate was collected and washed with 50 mL of carbon tetrachloride. Evaporation of the carbon tetrachloride in vacuo afforded **21** (1.24 g, 75%) as yellow crystals, mp 98–100 °C: IR (KBr) ν 3070, 2940, 2835, 1710, 1605, 1568, 1422, 1390, 1260, 1073, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (1 H, dd, H12), 8.10 (1 H, dd, H4), 7.71 (1 H, d, H11), 7.52 (1 H, dd, H3), 6.78 (1 H, dd, H2), 5.45–5.65 (1 H, m, H10), 4.35–4.70 (1 H, m, H7), 4.02 (3 H, s, OCH_3), 2.10–2.75 (4 H, m, H8, H9); mass spectrum, m/z (relative intensity) 436, 438, 440 (3.4, 6.0, 4.9, $M^{\bullet+}$), 357, 359 (57, 58, $M^{\bullet+}$ – Br), 278 (100, $M^{\bullet+}$ – 2Br).

1-Methoxy-4,7,10-tribromo-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]pyran-6-one (22). A suspension of **15** (3.16 g, 8.79 mmol), benzoyl peroxide (0.0270 g, 0.112 mmol) and *N*-bromosuccinimide (4.01 g, 22.5 mmol) in 150 mL of carbon tetrachloride was heated at reflux for 10 h. The reaction mixture was then cooled, and the precipitate that formed was collected and triturated with 50 mL of carbon tetrachloride. The carbon tetrachloride was removed in vacuo to yield **22** (4.38 g, 96%) as yellow crystals, mp 164–166 °C: IR (KBr) ν 2960, 2920, 2830, 1718, 1597, 1418, 1251, 1072, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.20 (1 H, d, H12), 7.81 (1 H, d, H3), 7.74 (1 H, d, H11), 6.79 (1 H, d, H2), 5.52–5.72 (2 H, br app s, H7, H10), 4.00 (3 H, s, OCH_3), 2.35–2.95 (4 H, m, H8, H9); ^{13}C NMR ($CDCl_3$) δ 158.0 (C=O), 154.52 (C1), 145.75 (C5a), 134.75 (C3), 130.5, 129.0 (C12a, C10a), 123.05 (C7a), 120.01 (C11, C4a), 118.99 (C11a), 114.22 (C12), 107.72 (C2), 107.28 (C4), 56.04 (OCH_3), 43.20 (C10), 42.01 (C7), 27.70, 27.43 (C8, C9); mass spectrum, m/z (relative intensity) 435, 437, 439 (0.15, 0.30, 0.20, $M^{\bullet+}$ – Br), 358 (0.07, $M^{\bullet+}$ – 2Br), 356 (0.41, $M^{\bullet+}$ – 2Br and $M^{\bullet+}$ – 2HBr), 254 (0.24, $M^{\bullet+}$ – 2HBr).

1-Methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (23). (a) By use of the procedure of Chebaane, Guyot, and Molho,[22] a mixture of **14** (1.05 g, 3.76 mmol), sublimed sulfur (0.0510 g, 1.56 mmol), and 0.601 g of 10% palladium on charcoal was heated in a sand bath at 270 °C for 30 h. After this time, the reaction mixture was cooled, and the black tar was extracted with hot benzene and filtered. The solvent was removed in vacuo and the crude beige solid was recrystallized from ethanol to give **23** (0.875 g, 84%), mp 205–206 °C (lit.[21] mp 205 °C).

(b) To a solution of **21** (0.876 g, 2.00 mmol) in 40 mL of acetone at −10 °C under a nitrogen atmosphere was added triethylamine (6.90 mL, 49.5 mmol), dropwise over 30 min. After the addition of the triethylamine, the reaction mixture was allowed to warm to room temperature and was then heated at reflux for 8 h. The precipitate that formed was collected and washed with chloroform. The chloroform solution was washed with water and dried (sodium sulfate). The solvent was then removed in vacuo to afford a crude solid; recrystallization from ethanol/water afforded **23** (0.406 g, 75%) as off-white crystals, mp 204–205 °C (lit.[21] mp 205 °C): IR (KBr) ν 3050, 3010, 2960, 2940, 1738, 1610, 1430, 1260, 1090, 1045 cm^{-1}; ^1H NMR (DMSO-d_6) δ 8.25–8.60 (3 H, m, H4, H12, H10), 7.85–8.20 (3 H, m, H7, H9, H11), 7.50–7.84 (2 H, m, H8, H3), 7.16 (1 H, dd, H2), 4.02 (3 H, s, OCH_3); ^{13}C NMR (DMSO-d_6) δ 172.0 (C=O), 154.5 (C1), 146.0 (C5a), 135.4 (C9), 134.5 (C10a), 130.0 (C7), 129.1 (C7a), 127.9 (C10), 125.2 (C4a), 124.0 (C8), 123.0 (C3), 119.2 (C12a), 118.0 (C11, C11a), 113.0 (C4, C12), 116.9 (C2), 55.5 (OCH_3); mass spectrum, m/z (relative intensity) 276 (100, $M^{\bullet+}$), 233 (74, $M^{\bullet+}$ – C_2H_3O).

Anal. Calcd for $C_{18}H_{12}O_3$: C, 78.25; H, 4.38. Found: C, 77.99; H, 4.46.

4-Bromo-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (24). (a) A solution of **23** (0.065 g, 0.24 mmol) in 1.0 mL of dry dimethylformamide (DMF) was treated with a solution of *N*-bromosuccinimide (0.052 g, 0.29 mmol) in 1.0 mL of dry DMF, and the resulting mixture was stirred for 24 h. The solution was then poured into 20 mL of water and the precipitate that formed was collected and recrystallized from acetone to yield **24** (0.068 g, 81%) as a beige solid, mp 243–245 °C.

(b) To a solution of **22** (1.03 g, 2.00 mmol) in 40 mL of toluene at room temperature under nitrogen was added triethylamine (7.0 mL, 50 mmol), dropwise over 10 min. After the addition of triethylamine was complete, the reaction mixture was stirred for 15 min at room temperature and then heated at reflux for 15 h. The reaction mixture was cooled, and the toluene was removed in vacuo to yield a crude product that was dissolved in chloroform. This solution was washed with dilute HCl (3 × 75 mL) and water (2 × 75 mL) and then dried over sodium sulfate. Evaporation of the dried chloroform solution and recrystallization afforded **24** (0.565 g, 80%) as a beige solid, mp 245–246 °C: IR (KBr) ν 2940, 2925, 2830, 1745, 1600, 1515, 1425, 1260, 1250, 1085, 1055, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.48 (1 H, ddd, H7), 8.27 (1 H, d, H12), 8.22 (1 H, dd, H10), 8.05 (1 H, d, H11), 7.88 (1 H, ddd, H8), 7.84 (1 H, d, H3), 7.63 (1 H, ddd, H9), 6.76 (1 H, d, H2), 4.02 (3 H, s, OCH_3); mass spectrum, m/z (relative intensity) 354, 356 (100, 77, $M^{\bullet+}$).

Anal. Calcd for $C_{18}H_{11}BrO_3$: C, 60.87; H, 3.12. Found: C, 60.80; H, 3.20.

4-(Tri-*n*-butylstannyl)-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (25). A mixture of **24** (0.440 g, 1.24 mmol), hexa-*n*-butylditin (1.50 mL, 2.97 mmol) and tetrakis(triphenylphosphine)palladium(0)[26] (0.0220 g, 0.0196 mmol) in 20 mL of dry toluene at reflux was stirred for 12 h under an atmosphere of nitrogen. The reaction mixture was cooled, and the resulting solution was diluted with 50 mL of toluene and filtered through Celite. The toluene and low boiling products were removed under vacuum to give a crude brown oil, which was purified by flash chromatography (ether/petroleum ether, 2:1) to afford **25** (0.455

g, 65%), R_f = 0.67, as a bright yellow solid: IR (KBr) ν 3015, 3005, 2985, 2960, 2885, 1725, 1620, 1600, 1578, 1385, 1263, 1047 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.40 (1 H, dd, H7), 8.22 (1 H, d, H12), 8.16 (1 H, dd, H10), 7.99 (1 H, d, H11), 7.81 (1 H, ddd, H8), 7.71 (1 H, d, H3), 7.53 (1 H, ddd, H9), 6.92 (1 H, d, H2), 4.02 (3 H, s, OCH_3), 1.00–1.80 (18 H, br m, CH_2's), 0.70–1.05 (9 H, br t, CH_3's); mass spectrum, m/z (relative intensity) 505, 507, 509 (2.9, 5.2, 7.3, $MH^{\bullet+}$ – Bu), 391, 393, 395 (2.9, 4.9, 5.4, $MH^{\bullet+}$ – 3Bu), 276 (6.4, $MH^{\bullet+}$ – $SnBu_3$).

1-Methoxy-2-(2′,5′-dihydrofuran-2′-yl)-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (26). To a solution of **13** (0.143 g, 0.251 mmol) and 2,3-dihydrofuran (**3**) (0.025 mL, 0.33 mmol) in 3 mL of a 1:1 solution of chloroform/acetonitrile was added a solution of palladium acetate (0.0560 g, 0.249 mmol) in 2 mL of a 1:1 solution of chloroform/acetonitrile. The resulting solution was stirred at room temperature for 12 h. Then the reaction mixture was diluted with 25 mL of chloroform and filtered through Celite. The resulting solution was washed with H_2O and dried over sodium sulfate. The solvent and other volatiles were removed under vacuum to produce a crude oil, which was purified by preparative TLC, affording **26** as a beige solid (0.029 g, 33%), mp 171–173 °C: IR (KBr) ν 2938, 2860, 1710, 1610, 1570, 1412, 1262, 1225, 1080, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.32 (1 H, d, H4), 7.95 (1 H, dd, H12), 7.13 (1 H, d, H11), 7.52 (1 H, d, H3), 6.25–6.50 (1 H, m, H2′), 6.05–6.20 (1 H, m, H4′), 5.85–6.05 (1 H, m, H3′), 4.70–5.10 (2 H, m, H5′), 4.01 (3 H, s, OCH_3), 2.50–3.00 (4 H, m, H7, H10), 1.65–2.05 (4 H, m, H8, H9); mass spectrum, m/z (relative intensity) 348 (100, $M^{\bullet+}$), 307 (22, $M^{\bullet+}$ – C_3H_5).

1-Methoxy-4-(2′,5′-dihydrofuran-2′-yl)-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (27). A solution of **16** (0.143 g, 0.251 mmol) and 2,3-dihydrofuran (**3**) (0.025 mL, 0.33 mmol) in dry acetonitrile was stirred at room temperature for 10 min. A solution of palladium acetate (0.0560 g, 0.0250 mmol) in 5 mL of dry acetonitrile was added and the reaction mixture was stirred for 24 h at room temperature. After this period, TLC indicated the presence of unreacted **16**, so 5.0 mL of 2,3-dihydrofuran (**3**) was added and the resulting reaction mixture was stirred at room temperature for 48 h. Then stirring was discontinued, and the reaction mixture was diluted with 50 mL of acetonitrile and filtered through Celite. The solvent and excess 2,3-dihydrofuran (**3**) was removed under vacuum and the residual solid was purified by preparative TLC (ether/petroleum ether, 2:1) to afford **27** (0.034 g, 39%) as yellow crystals, mp 177–179 °C, R_f = 0.58: IR (KBr) ν 3105, 2935, 2925, 1717, 1600, 1570, 1445, 1257, 1080, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (1 H, d, H12), 7.84 (1 H, dd, H3), 7.54 (1 H, d, H11), 7.05–7.35 (1 H, m, H2′), 6.94 (1 H, d, H2), 6.70–6.90 (1 H, m, H4′), 5.85–6.02 (1 H, m, H3′), 4.90–5.10 (2 H, m, H5′), 4.00 (3 H, s, OCH_3), 2.50–3.00 (4 H, m, H7, H10), 1.75–2.05 (4 H, m, H8, H9); ^{13}C NMR ($CDCl_3$) δ 161.02 (C=O), 154.14 (C1), 149.0 (C5a), 147.91 (C10a), 132.15 (C12a), 131.93 (C2′, C3), 126.89 (C4a), 125.05, 124.78 (C3′, C7a), 122.78 (C4), 118.66 (C11, C12), 116.76 (C11a), 106.09 (C2), 86.64 (C1′), 75.59 (C4′), 55.71 (OCH_3), 25.91 (C7), 23.96 (C10), 21.63, 21.47 (C8, C9); mass spectrum, m/z (relative intensity) 348 (61, $M^{\bullet+}$), 320 (72, $M^{\bullet+}$ – C_2H_4), 307 (38, $M^{\bullet+}$ – C_3H_5).

(2′*R*)-*cis*-2-[2′,5′-Dihydro-5′-[(methoxymethoxy)methyl]-4′-[[tris(1-methylethyl)silyl]oxy]-2′-furanyl]-1-methoxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (28). To a solution of **13** (0.214 g, 0.376 mmol) and 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol (**4**)[16] (0.150 g, 0.474 mmol) in 6.0 mL of dry acetonitrile was added a solution of palladium acetate (0.0840 g, 0.374 mmol) in 4.0 mL of dry acetonitrile. The resulting reaction mixture was stirred for 24 h at room temperature. The reaction mixture was then diluted with acetonitrile and filtered through Celite, and then the solvent was removed in vacuo to yield a residual oil. The crude oil was purified by using preparative TLC (ether/petroleum ether, 2:1) to afford **28** (0.118 g, 53%), R_f = 0.66 as a pale yellow oil: IR (neat) ν 3005, 2985, 2900, 2880, 1715, 1665, 1618, 1575, 1470, 1388, 1225, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.31 (1 H, d, $J_{11,12}$ = 8.79 Hz, H12), 7.91 (1 H, d, $J_{3,4}$ = 8.78 Hz, H3), 7.91 (1 H, d, H4), 7.53 (1 H, d, H11), 6.35 (1 H, m, H1′), 4.81 (2 H, m, H2′, H4′), 4.68 (2 H, s, OCH_2O), 3.98 (3 H, s, $ArOCH_3$), 3.73–3.90 (2 H, m, H5′, H5″), 3.35 (3 H, s, OCH_3), 2.45–2.91 (4 H, m, H7, H10), 1.70–1.95 (4 H, m, H8, H9), 0.99–1.27 (21 H, m, $Si(CH(CH_3)_2)_3$); mass spectrum, m/z (relative intensity) 594 (15, $M^{\bullet+}$), 551 (6.5, $M^{\bullet+}$ – C_2H_3O), 549 (10, $M^{\bullet+}$ – C_2H_5O), 489 (41, $M^{\bullet+}$ – $C_3H_7O_2$), 307 (60, $M^{\bullet+}$ – $C_{15}H_{32}O_3Si$), 280 (2.5, $M^{\bullet+}$ – $C_{16}H_{30}O_4Si$).

(2′*R*)-*cis*-4-[2′,5′-Dihydro-5′-[(methoxymethoxy)methyl]-4′-[[tris(1-methylethyl)silyl]oxy]-2′-furanyl]-1-methoxy-7,8,9,10-tetrahydrobenzo[d]naphtho[1,2-b]pyran-6-one (29). To a solution of **16** (0.107 g, 0.188 mmol) and 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol[16] (**4**) (0.0750 g, 0.237 mmol) in 3 mL of dry acetonitrile was added a solution of palladium acetate (0.0426 g, 0.187 mmol) in 2 mL of dry acetonitrile. The resulting mixture was stirred for 12 h at room temperature. The reaction mixture was diluted with acetonitrile and filtered through Celite. The solvent was removed in vacuo and the resulting crude oil was purified by preparative TLC (petroleum ether/ether, 1:1). Purification afforded **29** (0.102 g, 92%), R_f = 0.48, as a colorless oil: IR (neat) ν 2950, 2940, 2877, 1745, 1725, 1660, 1610, 1575, 1378, 1247, 1090, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.17 (1 H, d, $J_{11,12}$ = 9.08 Hz, H12), 8.14 (1 H, dd, $J_{1',3}$ = 0.71 Hz, $J_{2,3}$ = 8.5 Hz, H3), 7.56 (1 H, d, H11), 7.10 (1 H, ddd, $J_{1',2'}$ = 1.85 Hz, $J_{1',4'}$ = 3.42 Hz, H1′), 6.96 (1 H, d, H2), 5.25 (1 H, dd, $J_{2',4'}$ = 1.56 Hz, H2′), 4.80–5.05 (1 H, br m, H4′), 4.76 (2 H, s, OCH_2O), 3.99 (3 H, s, OCH_3), 3.92 (2 H, dd, H5′, H5″), 3.44 (3 H, s, OCH_3), 2.45–2.95 (4 H, br m, H7, H10), 1.60–2.00 (4 H, br m, H8, H9), 0.80–1.20 (21 H, br app s, $Si(CH(CH_3)_2)_3$); ^{13}C NMR ($CDCl_3$) δ 160.70 (C12), 153.92 (C1), 149.3 (C3′), 149.20 (C5a), 147.58 (C10a), 132.43 (C3), 126.65 (C4), 125.86 (C12a), 122.61 (C7a), 121.25 (C4a), 118.43 (C12, C11), 116.61 (C11a), 105.92 (C2), 104.52 (C2′), 96.64 (OCH_2O), 83.06, 82.13 (C1′, C4′), 69.50 (C5′), 55.59, 55.13 (OCH_3's), 25.86 (C7), 23.97 (C10), 21.55, 21.42 (C8, C9), 17.83, 17.81 (CH_3), 12.20 (CH); mass spectrum, m/z (relative intensity) 594 (0.14, $M^{\bullet+}$), 551 (0.31, $M^{\bullet+}$ – C_2H_3O), 489 (2.3, $M^{\bullet+}$ – $C_3H_7O_2$), 438 (1.8, $M^{\bullet+}$ – $Si(C_3H_7)_3$), 307 (4.8, $M^{\bullet+}$ – $C_{15}H_{32}O_3Si$).

(2′*R*)-*cis*-4-[2′,5′-Dihydro-5′-[(methoxymethoxy)methyl]-4′-[[tris(1-methylethyl)silyl]oxy]-2′-furanyl]-1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one (30). A solution of **25** (0.425 g, 0.752 mmol), 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris(1-methylethyl)silyl]-D-*erythro*-pent-1-enitol[16] (**4**) (0.300 g, 0.949 mmol) and palladium acetate (0.168 g, 0.748 mmol) dissolved in 20 mL of dry acetonitrile was stirred at room temperature for 24 h. The reaction mixture was diluted with 50 mL of acetonitrile and filtered through Celite. The solvent was removed in vacuo to afford a residual oil, which was separated by preparative TLC (ether/petroleum ether, 2:1). Purification afforded **30** (0.294 g, 66%) R_f = 0.60 as a pale yellow oil: IR (neat) ν 3005, 2988, 2965, 2895, 1745, 1612, 1595, 1563, 1467, 1267, 1045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.39 (1 H, dd, $J_{7,9}$ = 1.47 Hz, $J_{7,8}$ = 7.62 Hz, H7), 8.20 (1 H, d, $J_{11,12}$ = 9.08 Hz, H12), 8.15 (1 H, dd, $J_{2,3}$ = 8.20 Hz, $J_{1',3}$ = 0.44 Hz, H3), 8.09 (1 H, dd, $J_{8,10}$ = 1.47 Hz, $J_{9,10}$ = 7.62 Hz, H10), 7.95 (1 H, d, H11), 7.81 (1 H, ddd, $J_{8,9}$ = 7.48 Hz, H9), 7.53 (1 H, ddd, H8), 7.15 (1 H, ddd, $J_{1',2'}$ = 1.76 Hz, $J_{1',4'}$ = 3.75 Hz, H1′), 6.92 (1 H, d, H2), 5.31 (1 H, dd, $J_{2',4'}$ = 1.76 Hz, H2′), 4.85–5.07 (1 H, m, H4′), 4.79 (2 H, s, OCH_2O), 3.98 (3 H, s, $ArOCH_3$), 3.90 (2 H, d, $J_{4',5'}$ = 5.27 Hz, H5′, H5″), 3.46 (3 H, s, OCH_3), 0.98–1.27 (21 H, m, $Si(CH(CH_3)_2)_3$).

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