Reductive and Nonreductive Aromatization of Quinol Ketal Glycals. Models for the Preparation of *C*-Aryl Glycoside Natural Products

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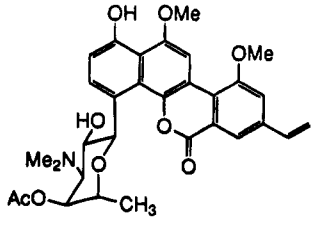
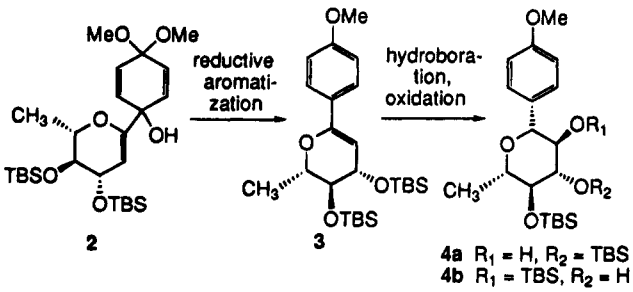
The gilvocarcin class of antitumor antibiotics[3] (e.g. ravidomycin, **1**)[4] has provided inspiration for the development of novel methods for establishing the *C*-aryl glycoside connection.[5] Key steps in our own approach to the synthesis of ravidomycin are the reductive aromatization of a glycal-substituted quinol ketal (e.g. **2** → **3**) and the concurrent or subsequent hydroboration of the enol ether double bond (i.e. **3** → **4**).[6,7]



1 ravidomycin
(or enantio ravidomycin)



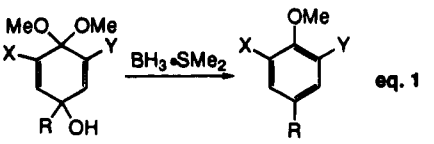
2 **3**

4a R_1 = H, R_2 = TBS
4b R_1 = TBS, R_2 = H

We have examined the potential of several hydride reducing agents for effecting the reductive aromatization of quinol ketals, particularly glycal-substituted quinol ketals. In this paper, we report the details of those studies which have resulted in optimization of the conversion of quinol ketal **2** to *C*-aryl glycal **3**.[6] Furthermore, we describe a new and potentially useful transformation, the nonreductive aromatization of the quinol ketal substrates, a process which takes place with concomitant 1,2-migration of the glycal substituent (see below).

In our early studies with Lewis acidic hydride reagents, we found that borane–dimethyl sulfide (BMS) effects the reductive aromatization of quinol ketals (**5** → **6**, Table 1). Excellent yields were obtained when the reaction was allowed to proceed at room temperature.

Table 1. Reductive Aromatization of Quinol Ketals[a]



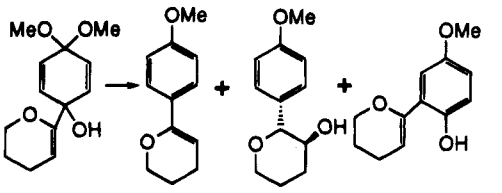
5 **6** eq. 1

entry	substrate 5	X	Y	R	yield (%) of **6**
1	**5a**	H	H	CH_3	96
2	**5b**	H	H	n-Bu	88
3	**5c**	H	H	Ph	83
4	**5d**	H	Br	CH_3	85
5	**5e**	OCH_3	OCH_3	CH_3	82

[a] 1.22 moles BMS/mol of substrate.

However, treatment of the model substrate **7** under similar conditions (1.3 mol of BMS, room temperature), but for 14 h and with an oxidative workup, afforded not only the *C*-aryl glycal **8** and its hydroboration product **9** but a phenolic byproduct **10** (ratio approx. 3:2:1, Table 2, entry 3).

Table 2. Product Distribution as a Function of Amount of Borane



7 **8** **9** **10** eq. 2

entry	molar ratio BMS/**7**	**8**	**9**	**10**	low R_f
1	2/3	52	0	39	0
2	3/3	52	24	24	0
3	4/3	47	36	17	0
4	5/3	26	47	11	0
5	6/3	0	45	0	28
6	7/3	0	50	0	32

Our immediate concern was to improve the yield of glycal **8** and/or hydroxypyran **9** so that we could proceed with confidence to the hydroboration of the more elaborate substrate, quinol ketal **2**. The studies of Fleming and Bolker[8] had indicated that the reductive cleavage of ketals by diborane is third order in borane and that each of the three hydrogens of borane is available for participation in the reduction. Therefore we chose to test the influence of borane concentration on the distribution of products derived from model compound **7**.

(1) Recipient of an NSF Career Advancement Award, 1992–1993.
(2) Recipient of the 1991–1992 Division of Organic Chemistry (American Chemical Society) Graduate Fellowship Award sponsored by The Rohm and Haas Co.
(3) For a comprehensive survey of the literature on the gilvocarcins and reports of the first syntheses of members of this class, see (a) Matsumoto, T.; Hosoya, T.; Suzuki, K. *J. Am. Chem. Soc.* **1992**, *114*, 3568. (b) Hosoya, T.; Takashiro, E.; Matsumoto, T.; Suzuki, K. *J. Am. Chem. Soc.* **1994**, *116*, 1004.
(4) Findlay, J.; Liu, J.-S.; Radics, L.; Rakhit, S. *Can. J. Chem.* **1981**, *59*, 3018. Rakhit, S.; Eng, C.; Baker, H.; Singh, K. *J. Antibiot.* **1983**, *36*, 1490. Narita, T.; Matsumoto, M.; Mogi, K.; Kukita, K.-I.; Kawahara, R.; Nakashima, T. *J. Antibiot.* **1989**, *42*, 347.
(5) For recent reviews on this subject, see (a) Suzuki, K.; Matsumoto, T. in *Recent Progress in the Chemical Synthesis of Antibiotics and Related Microbial Products*; Lukacs, G., Ed.; Springer: Berlin, 1993; Vol 2, pp 353–403. (b) Jaramillo, C.; Knapp, S. *Synthesis* **1994**, 1–20.
(6) A preliminary report of some of the results described herein has appeared: Parker, K. A.; Coburn, C. A. *J. Am Chem. Soc.* **1991**, *113*, 8516.
(7) For related work on reductive aromatization of quinols, see Parker, K. A.; Coburn, C. A. *J. Org. Chem.* **1991**, *56*, 1666.
(8) (a) Bolker, H. I.; Fleming, B. I. *Can J. Chem.* **1975**, *53*, 2818. (b) Fleming, B. I.; Bolker, H. I. *Can. J. Chem.* **1974**, *52*, 888.

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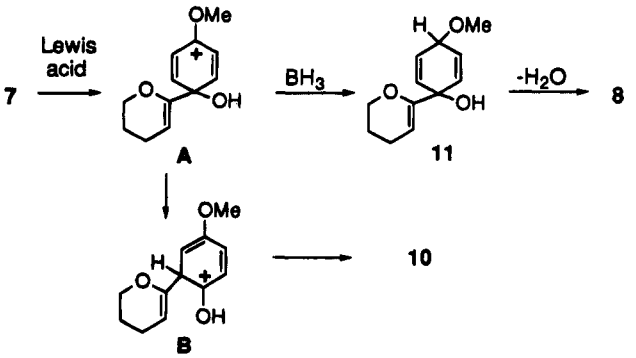
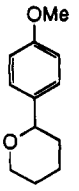
We carried out a series of reactions in which the amount of substrate, the solvent, the time and temperature were constant. Only the amount of borane–dimethyl sulfide was varied. The results are detailed in the Experimental Section and summarized in Table 2.

As expected, with increasing amounts of borane–methyl sulfide, the yield of the hydroboration product **9** increased at the expense of the reductively aromatized product **8**. A decrease in the yield of the rearrangement product **10** with increasing amounts of the borane reagent was also evident. The latter effect is consistent with a mechanism in which reductive aromatization and rearrangement arise from an intermediate such as **A** (Scheme 1). This carbonium ion partitions to **11** (which then dehydrates to **8**) and to **B** which loses a proton to afford **10**. The former transformation (**A** to **8**) involves hydride trapping by the external borane species. However, in the latter transformation (**A** to **10**), no hydride is required.

Scheme 1



In the product mixtures from experiments in which the molar ratio of borane to substrate was at least 2:1 (Table 2), a significant amount of material was found in a low R_f chromatography fraction (last column). One component of this fraction was isolated and identified as tetrahydropyran **12**, presumably the result of over-reduction of enol ether **8**. The reduction of enol ethers to ethers by excess borane[9] is the subject of further study in our labs.

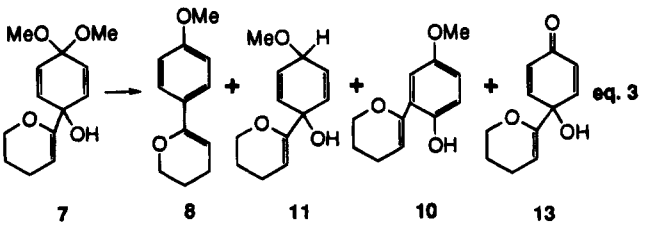


12

Because the product mixture from the borane-induced reductive aromatization could be complex and because the workup was inconvenient on a large scale, we examined alternative reagents for their ability to effect the desired transformation. Product distributions which resulted from the treatment of substrate **7** with a variety of hydride-donating reagents are shown in Table 3. Procedures for those experiments which led to product formation[10] are included in the Experimental Section.

(9) The reduction of indoles by diborane with a sodium methoxide/methanol quench to provide indolines is a relevant analogy to the reduction of dihydropyran **7** to tetrahydropyran **12**. However, these two conversions may not be mechanistically related. See Monti, S. A.; Schmidt, R. R. *Tetrahedron* **1971**, *27*, 3331.

Table 3. Product Distribution as a Function of Hydride Reagent



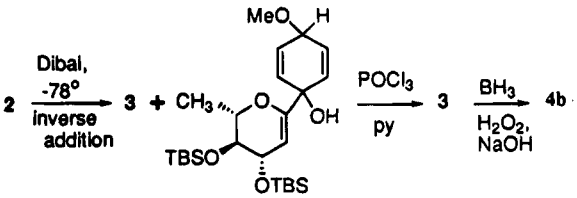
7 8 11 10 13

hydride reagent	T, °C	yield of product 8	11	10	13
4/3 eq $BH_2Br{\cdot}SMe_2$	20	0	0	100	0
4/3 eq 9-BBN	20	0	0	58	0
4/3 eq $(BH_3OTFA^-)\ Na^+$	20	0	0	0	19[11]
5 eq Red-Al	20	0	0	100	0
5 eq DIBAL-H	20	0	0	100	0
5 eq DIBAL-H	−78	0	80	20	0
5 eq DIBAL-H[a]	−78	75	25	0	0

[a] Inverse addition.

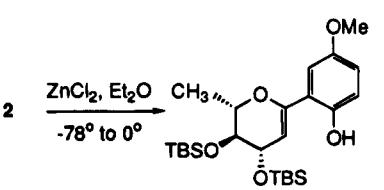
The inverse addition DIBAL-H procedure afforded only ether **11**, the product of simple ketal reduction, and substituted anisole **8**, the product of ketal reduction and dehydration. This procedure was therefore applied in the glycal series.

When glycal substituted quinol ketal **2** was added to a methylene chloride solution of DIBAL-H at −78 °C, a mixture consisting only of **3** and **14** (approximately 2:1 by NMR integration) was isolated. Attempts to complete the dehydration required for efficient conversion of ketal **2** to *C*-aryl glycal **3** were rewarded when it was found that treatment of the mixture with phosphorus oxychloride in pyridine led, exclusively, to the recovery of the key intermediate **3**. Then hydroboration followed by oxidation with basic peroxide, a procedure which has been used previously with *C*-aryl glycals, completed the desired sequence to afford *C*-aryl glycoside **4b**.[12]



14

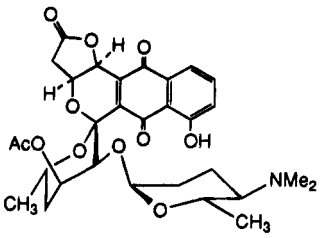
The clean conversion of model substrate **7** to the glycal migration product **10**, a product which has not undergone reduction, by several of the reagents studied in Table 3 led us to examine the effect of a nonreducing Lewis acid on this substrate. Treatment of glycal quinol ketal **2** with zinc chloride in ether gave 96% of the rearranged *C*-aryl glycal **15**.



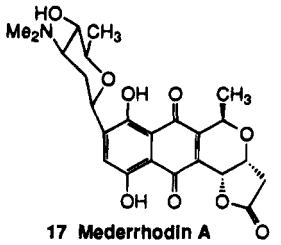
15 (96%)

The substitution pattern of this product is reminiscent of that in the griseusins (e.g. 3′-*O*-α-D-forosaminyl-(+)-

griseusin A, **16**)[13] and in the hybrid mederrhodin antibiotics (e.g. mederrhodin A, **17**).[14]



16 Forosaminyl Griseusin A



17 Mederrhodin A

The glycal-substituted quinol ketals (e.g. **2**), then, can be converted to *C*-aryl glycals with either of two substitution patterns (i.e. **3** by reductive aromatization or **15** by nonreductive aromatization). Thus these readily available intermediates are potential precursors to two of the four classes of naturally occurring *C*-aryl glycosides.[15] Applications of the quinol glycal chemistry to the synthesis of some of these targets is under investigation.

Experimental Section

General. Flash chromatography was performed using E. Merck silica gel 60 (70–230 mesh).

4,4-Dimethoxy-1-methyl-2,5-cyclohexadien-1-ol (5a). To a solution of 4,4-dimethoxy-2,5-cyclohexadien-1-one (Aldrich, 98%) (500 mg, 3.2 mmol) in 5 mL of THF at −78 °C was added 3.4 mL (3.22 mmol) of CH_3Li (1.4 M in ether, Aldrich). The solution was stirred for 20 min at −78 °C and then quenched by the addition of 10 mL of brine. The pale yellow solution was extracted with CH_2Cl_2 (5 × 10 mL), dried ($CaSO_4$), and concentrated to leave 494 mg (91%) of a yellow oil: ^1H NMR ($CDCl_3$) δ 1.31 (s, 3H), 3.16 (bs, 1H) 3.22 (s, 3H), 3.27 (s, 3H), 5.80 (d, J = 10.4 Hz, 2H), 6.08 (d, J = 10.4 Hz, 2H); IR (neat) 3448, 1685, 1105 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 138.1, 124.6, 93.1, 65.5, 49.4, 27.4; HRMS calcd for $C_9H_{14}O_3$ (M^+) 170.0943, found 170.0947.

1-n-Butyl-4,4-dimethoxy-2,5-cyclohexadien-1-ol (5b). To a solution of 4,4-dimethoxy-2,5-cyclohexadien-1-one (655 mg, 4.25 mmol) in 7 mL of THF at −78 °C was added 2.7 mL (4.32 mmol) of n-BuLi (1.6 M in hexanes, Aldrich). The resulting blue reaction mixture was stirred for 1 h at −78 °C, quenched with brine (10 mL), extracted with ether (3 × 10 mL), dried ($CaSO_4$), and evaporated to leave 879 mg (91%) of a gold-colored oil: ^1H NMR ($CDCl_3$) δ 0.86 (m, 3H), 1.24 (m, 4H), 1.56 (m, 2H), 2.82 (s, 1H), 3.26 (s, 3H), 3.28 (s, 3H), 5.89 (d, J = 10.5 Hz, 2H), 6.01 (d, J = 10.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 137.1, 125.9, 93.1, 68.3, 49.5, 39.9, 25.7, 22.8, 13.8; IR (neat) 3417, 1681, 1070 cm^{-1}; HRMS calcd for $C_{12}H_{20}O_3$ (M^+) 212.1412, found 212.1401.

4,4-Dimethoxy-1-phenyl-2,5-cyclohexadien-1-ol (5c).[16] To a solution of 4,4-dimethoxy-2,5-cyclohexadien-1-one (500 mg, 3.2 mmol) in 5 mL of THF at −78 °C was added 1.68 mL (3.36 mmol) of phenyllithium (2.0 M in 70/30 cyclohexane/ether, Aldrich). The mixture was quenched with 10 mL of brine after 30 min, the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL) and dried ($CaSO_4$), and the solvent was evaporated to leave 691 mg (92%) of a yellow oil: ^1H NMR ($CDCl_3$) δ 7.60–7.15 (m, 5H), 6.12 (d, J = 10.4 Hz, 2H), 5.97 (d, J = 10.4 Hz, 2H), 3.35 ("s", 6H), 2.80 (s, 1H); IR (neat) 3402 cm^{-1}; HRMS calcd for $C_{14}H_{16}O_3$ (M^+) 232.1189, found 232.1171.

3-Bromo-4,4-dimethoxy-1-methyl-2,5-cyclohexadien-1-ol (5d).[17] To a solution of 3-bromo-4,4-dimethoxy-2,5-cyclohexadien-1-one (605 mg, 2.60 mmol) in 5 mL of THF at −78 °C was added 1.9 mL (2.66 mmol) of CH_3Li (1.4 M in ether, Aldrich). The mixture was stirred for 90 min at −78 °C, quenched with 5 mL of brine, and extracted with CH_2Cl_2 (3 × 15 mL). The organic extracts were washed once each with 10 mL of saturated $NaHCO_3$, H_2O, and brine and then dried over $CaSO_4$. Removal of the solvent left 637 mg (98%) of a solid, mp 89–91 °C (lit. mp 88.5–91 °C).

1-Methyl-3,4,4,5-tetramethoxy-2,5-cyclohexadien-1-ol (5e). To a solution of 3,4,4,5-tetramethoxy-2,5-cyclohexadien-1-one[18] (428 mg, 2.0 mmol) in 35 mL of THF at −78 °C was slowly added 2.1 mL (1.4 M, Aldrich) of CH_3Li. The mixture gradually became dark orange and was stirred at −78 °C for 90 min before it was diluted with ether (100 mL) and quenched with brine (50 mL). The resulting yellow solution was extracted with ether (3 × 25 mL), dried ($CaSO_4$), and concentrated to leave 349 mg (76%) of a yellow oil which was used immediately without further purification: ^1H NMR ($CDCl_3$) δ 1.47 (s, 3H), 3.15 (s, 3H), 3.23 (s, 3H), 3.64 (s, 6H), 5.23 (s, 2H); IR (neat) 3458, 1651, 1128 cm^{-1}; HRMS calcd for $C_{11}H_{18}O_5$ (M^+) 230.1154, found 230.1169.

Reductive Aromatizations of Quinol Ketals 5a–e. The procedure described for the reductive aromatization of ketal **5a** was applied in the reduction of ketals **5b–e**. In these cases, only the following information is given: milligrams (mmol), solvent, time, and yield. All compounds exhibit physical properties consistent with the known data.

4-Methylanisole (6a).[19] To a solution of ketal **5a** (1.4 g, 8.2 mmol) in 7.3 mL of CH_2Cl_2 was added dropwise 1.3 equiv (1.0 mL, 10.0 mmol) of BH_3·SMe_2 (10 M in CH_2Cl_2, Aldrich) at 23 °C. After 90 min, the mixture was quenched with 1 mL of brine and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic solution was washed with cold H_2O (2 × 5 mL), dried ($CaSO_4$), and concentrated to give 960 mg (96%) of **6a**.

4-Butylanisole (6b):[20] 295 mg (1.39 mmol); THF (3.0 mL); 4.5 h; 187 mg (88%).

4-Phenylanisole (6c):[21] 383 mg (1.65 mmol); THF (10 mL); 4.5 h; 261 mg (86%).

2-Bromo-4-methylanisole (6d):[22] 204 mg (0.82 mmol); CD_2Cl_2 (1.0 mL); 15 min; 140 mg (85%).

3,4,5-Trimethoxytoluene (6e):[23] 549 mg (2.38 mmol); CD_2Cl_2 (2.0 mL); 6 min, 355 mg (82%).

1-[2-(5,6-Dihydro-4*H*-pyranyl)]-4,4-dimethoxy-2,5-cyclohexadien-1-ol (7). To a solution of 5.92 mL (5.46 g, 65.0 mmol) of dihydropyran in 15 mL of THF at −78 °C was added 28.7 mL (48.8 mmol) of t-BuLi (1.7 M in pentane, Aldrich). After stirring for 10 min the solution was warmed to 0 °C and stirred for an additional 30 min. The pale yellow lithio DHP solution was recooled to −78 °C and added via cannula to a −100 °C solution of 5.0 g (32.5 mmol) of 4,4-dimethoxy-2,5-cyclohexadien-1-one in 50 mL of ether. After 80 min the reaction was quenched by pouring into 100 mL of H_2O and then extracted with ether (3 × 50 mL). The organic extracts were washed with $NaHCO_3$ (3 × 30 mL), water (2 × 20 mL), and then brine (1 × 50 mL) and dried over $CaSO_4$. Removal of the solvent left 7.64 g (99%) of a yellow oil: ^1H NMR ($CDCl_3$) δ 1.79 (m, 2H), 2.00 (m, 2H), 3.00 (s, 1H), 3.29 (s, 3H), 3.30 (s, 3H), 4.02 (t, J = 5.1 Hz, 2H), 4.86 (t, J = 3.8 Hz, 1H), 5.93 (d, J = 10.4 Hz, 2H), 6.18 (d, J = 10.4 Hz, 2H); IR (neat) 3396, 1666 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 153.5, 134.8, 126.7, 96.5, 93.4, 68.0, 66.6, 49.9, 22.0, 19.8; HRMS calcd for $C_{13}H_{18}O_4$ (M^+) 238.1205, found 238.1222.

Reaction of Ketal 7 with Borane Methyl Sulfide, Table 2. The procedure outlined for the reductive aromatization of ketal **7** (entry 3, Table 2) is applicable to the other entries. For the other entries, the only change in the procedure is the number of mole equivalents of BH_3–SMe_2 employed.

(10) The following reagents (1.3 equiv) did not react with substrate **7** at 20 °C: $NaBH_3CN$, $LiBEt_3H$, and $KB(iBu)_3H$.

(11) A 76% yield of 5-hydroxy-1-(4-methoxyphenyl)-1-pentanone was also obtained in this reaction.

(12) Friesen and Daljeett have shown that, in the hydroboration/oxidation of *C*-aryl glycals, silyl migration is pH dependent and can be avoided by the use of buffer. See Friesen, R. W.; Daljeet, A. K. *Tetrahedron Lett.* **1990**, *31*, 6133.

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(19) Aldrich Chemical Co., No. 14, 809-1.

(20) Dewar, M. J. S.; Puttnam, N. A. *J. Chem. Soc.* **1959**, 4080.

(21) Lancaster Synthesis No. 1260.

(22) Trans World Chemicals, No. B2945.

(23) Aldrich Chemical Co., No. 22,771-4.

Entry 3. To a solution of 1.50 g (6.3 mmol) of ketal **7** in 20 mL of THF was added dropwise 0.82 mL (8.2 mmol) of BH_3·SMe_2 (10 M) over a 5 min period. The colorless reaction mixture was stirred at 23 °C for 14 h and then quenched by the addition of 10 mL of MeOH. A 1:1 solution (40 mL) of 3 N NaOH and 30% H_2O_2 was added and after effervescence was heated at 45 °C for 3 h. The reaction was poured into ether (3 × 50 mL), and the organic extracts were washed with brine (2 × 30 mL), dried ($CaSO_4$), and chromatographed to leave 399 mg (36%) of **9**, 562 mg (47%) of **8**, and 221 mg (17%) of **10**.

4-[2-(5,6-Dihydro-4*H*-pyranyl)]anisole (8): ^1H NMR ($CDCl_3$) δ 7.36 (d, J = 6.8 Hz, 2H), 6.74 (d, J = 6.8 Hz, 2H), 5.10 (t, J = 4.0 Hz, 1H), 4.05 (t, J = 5.0 Hz, 2H), 3.75 (s, 3H), 2.07 (m, 2H), 1.80 (m, 2H); IR (neat) 2942, 2851, 1651, 1609, 1510, 1464, 1344, 1248, 1174 cm^{-1}; HRMS calcd for $C_{12}H_{14}O_2$ (M^+) 190.0994, found 190.0989.

***trans*-3-Hydroxy-2-(4-methoxyphenyl)tetrahydropyran (9):** ^1H NMR ($CDCl_3$) δ 1.47 (m, 1H), 1.83 (m, 2H), 2.23 (m, 1H), 3.55 (m, 2H), 3.81 (s, 3H), 3.92 (d, J = 9 Hz, 1H), 4.04 (m, 1H), 6.91 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 25.7, 31.8, 55.3, 68.3, 71.5, 85.1, 114.1, 127.8, 128.7, 131.4, 159.7; IR (neat) 3397, 1613 cm^{-1}; HRMS calcd for $C_{12}H_{16}O_3$ (M^+) 208.1099, found 208.1080.

2-[2-(5,6-Dihydro-4*H*-pyranyl)]-4-methoxyphenol (10): ^1H NMR ($CDCl_3$) δ 7.63 (s, 1H), 6.80 (m, 1H), 6.76 (m, 2H), 5.21 (t, J = 4.0 Hz, 1H), 4.20 (t, J = 5.0 Hz, 2H), 3.73 (s, 3H), 2.20 (m, 2H), 1.85 (m, 2H); IR (neat) 3360, 2949, 1669, 1495, 1066 cm^{-1}; HRMS calcd for $C_{12}H_{14}O_3$ (M^+) 206.0943, found 206.0951.

2-(4-Methoxyphenyl)tetrahydropyran (12): ^1H NMR ($CDCl_3$) δ 7.26 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 4.63 (t, J = 6.6 Hz, 1 H), 3.80 (s, 3 H), 3.63 (t, J = 6.4 Hz, 2 H), 1.83 (m, 1 H), 1.72 (m, 1 H), 1.58 (m, 2 H + imp), 1.41 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 22.1, 32.5, 38.6, 55.3, 62.8, 74.2, 113.9, 127.1, 136.9, 159.1; IR (neat) 3346 (imp), 2938, 1612 cm^{-1}; HRMS calcd for $C_{12}H_{16}O_2$ (M^+) 192.1150, found 192.1151.

1-[2-(5,6-Dihydro-4*H*-pyranyl)]-4-methoxy-2,5-cyclohexadien-1-ol (11). To a solution of 238 mg (1.0 mmol) of ketal **7** in 1.0 mL of CH_2Cl_2 at −78 °C was added 5.0 mL (5.0 mmol) of DIBAL-H (1 M in CH_2Cl_2). After 1 h, the temperature was warmed to 0 °C where the solution was stirred for an additional 1h and warmed to room temperature. The reaction mixture was poured into 10 mL of 2 N NaOH and extracted with ether. Drying (Na_2SO_4) gave 208 mg of a 4:1 mixture of **11** and **10**. Data for **11**: ^1H NMR ($CDCl_3$) δ 6.00 (m, 4 H), 4.82 (t, J = 3.8 Hz, 1 H), 4.32 (t, J = 1.5 Hz, 1 H), 4.03 (t, J = 5.1 Hz, 2 H), 3.32 (s, 3 H), 2.63 (s, 1 H), 2.02 (m, 2 H), 1.80 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 154.6, 132.4, 127.4, 96.3, 69.5, 68.2, 66.8, 53.9, 22.2, 19.9; IR (neat) 3397, 2928, 1665, 1065 cm^{-1}.

Ketal 2.[6] To a solution of 1.79 g (5.0 mmol) of L-rhamnal di-TBS ether[24] in 1.6 mL of THF at −78 °C was added 5.85 mL (10.0 mmol) of t-BuLi (1.7 M in pentane, Aldrich). After 15 min at −78 °C the solution was warmed to 0 °C. After 2 h, the lithiated glycal was recooled to −78 °C and added *via* cannula to a solution of 4,4-dimethoxy-2,5-cyclohexadien-1-one (1.05 g, 4.5 mmol) in 7.5 mL of THF at −99 °C over a 15 min period. The resulting blue solution was allowed to slowly warm to room temperature over 6 h, quenched with 50 mL of brine, extracted with CH_2Cl_2 (3 × 20 mL), and dried ($CaSO_4$). Column chromatography (50% EtOAc/Hex) left 1.26 g (55%) of a colorless oil: ^1H NMR ($CDCl_3$) δ 0.07 (m, 12H), 0.88 (m, 18H), 1.30 (d, J = 6.8 Hz, 3H), 2.72 (s, 1H), 3.26 (s, 3H), 3.30 (s, 3H), 3.54 (m, 1H), 4.02 (m, 2H), 4.86 (d, J = 3.6 Hz, 1H), 5.93 (m, 2H), 6.14 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 152.6, 134.8, 134.6, 127.6, 127.3, 98.3, 93.7, 76.1, 74.1, 69.2, 67.9, 50.3, 50.2, 25.9, 25.8, 18.0, 17.9, 16.7, −3.9, −4.1, −4.2, −4.4; IR (neat) 3418, 1668 cm^{-1}; HRMS calcd for $C_{26}H_{48}O_6Si_2$ (M^+) 512.2989, found 512.2957.

(24) Paquette, L. A.; Oplinger, J. A. *Tetrahedron* **1989**, 45, 107.

***C*-Aryl Glycal 3.**[6] To a solution of 5 mL (5.0 mmol) of DIBAL-H in CH_2Cl_2 (1 M, Aldrich) at −78 °C was added dropwise 512 mg (1.0 mmol) of ketal **2** in 2 mL of CH_2Cl_2. After 1 h at this temperature the solution was allowed to warm slowly to room temperature over 1.5 h. The reaction mixture was quenched by the dropwise addition of 50% methanolic CH_2Cl_2 until effervescence ceased. 2 N NaOH (2.5 mL) was added, and the mixture was stirred rapidly for 30 min, filtered through Celite, extracted with brine (2 × 2 mL), and dried (Na_2SO_4). ^1H NMR showed a 2:1 mixture of **3** and **14**. This mixture was immediately dissolved in 3 mL of pyridine and treated with 0.5 mL (822 mg, 5.3 mmol) of $POCl_3$ for 1 h at room temperature. The reaction was diluted with 10 mL of Et_2O and washed with 1 N NaOH (2 × 1 mL), H_2O (2 × 2 mL), $CuSO_4$ (2 × 2 mL), and then brine (1 × 3 mL). Drying (Na_2SO_4) and removal of the solvent left 436 mg (94%) of **3** as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.50 (d, J = 8.9 Hz, 2H), 6.88 (d, J = 8.9 Hz, 2H), 5.11 (d, J = 3.2 Hz, 1H), 4.30 (m, 1H), 4.07 (m, 1H), 3.78 (s, 3H), 3.62 (m, 1H), 1.40 (d, J = 7.0 Hz), 0.9 (m, 18H), 0.15 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 160.0, 150.9, 127.0, 126.5, 113.5, 97.9, 75.6, 75.2, 71.2, 55.3, 26.3, 26.2, 26.1, 25.9, 17.4, −3.5, −3.6, −3.9, −4.2; IR (neat) 1653, 1255 cm^{-1}; HRMS calcd for $C_{25}H_{44}O_4Si_2$ (M^+) 464.2778, found 464.2740.

***C*-Aryl Glycoside 4b.**[6] To a solution of glycal **3** (172 mg, 0.37 mmol) in 2 mL of THF was added 0.92 mL (2.5 equiv) of BH_3·THF (1 M in THF, Aldrich). After stirring at 23 °C for 16 h, excess borane was quenched by the addition of CH_3OH and 1 mL of a 1:1 mixture of 30% H_2O_2 and 3 N NaOH was added. The reaction mixture was stirred at 23 °C for 48 h, diluted with 10 mL of Et_2O, washed with H_2O (3 × 2 mL), dried (Na_2SO_4), and concentrated to leave 91 mg (51%) of a colorless oil: ^1H NMR ($CDCl_3$) δ 7.26 (d, J = 8.3 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 4.05 (d, J = 8.2 Hz, 1H), 3.79 (s, 3H), 3.50 (m, 2H), 3.41 (m, 1H), 3.29 (m, 1H), 2.06 (s, 1H), 1.27 (d, J = 6.1 Hz, 3H), 0.92 (s, 9H), 0.70 (s, 9H), 0.18 (s, 3H), 0.13 (s, 3H), 0.05 (s, 3H), −0.63 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 159.6, 131.9, 129.3, 127.8, 113.7, 113.2, 82.4, 79.7, 76.6, 76.5, 55.4, 29.7, 26.0, 25.9, 25.8, 18.7, 18.2, 18.0, −3.5, −4.2, −4.4, −5.6; IR (neat) 3405 cm^{-1}; HRMS calcd for $C_{25}H_{46}O_5Si_2$ (M^+) 482.2883, found 482.2881.

Rearranged *C*-Aryl Glycal 15. To a solution of 54 mg (0.105 mmol) of ketal **2** in 3 mL of ether at −78 °C was added 0.32 mL (0.32 mmol, 3.0 equiv) of 1 M $ZnCl_2$ in ether. After 75 min the solution was allowed to warm to 0 °C and then stirred for an additional 45 min. The mixture was poured into 5 mL of saturated $NaHCO_3$, filtered through Celite and then extracted with ether. The combined extracts were washed with brine and dried over Na_2SO_4. Column chromatography (1:1 EtOAc/Hexanes) gave 48.6 mg (96%) of a yellow oil: ^1H NMR (acetone-d_6) δ 7.93 (s, 1H), 6.99 (dd, J = 1.3, 2.2 Hz, 1 H), 6.78 (m, 2H), 5.61 (d, J = 3.7 Hz, 1H), 4.31 (m, 1H), 4.22 (m, 1H), 3.74 (m, 1H), 3.71 (s, 3H), 1.45 (d, J = 6.7 Hz, 3H), 0.92 ("s", 18H), 0.18 ("s", 12H); ^{13}C NMR (acetone-d_6) δ 153.7, 149.9, 122.2, 118.1, 116.2, 113.3, 103.6, 76.6, 75.3, 71.2, 55.9, 26.4, 26.3, 18.8, 18.6, 17.5, −3.5, −3.7, −3.8, −4.1; IR (neat) 3433, 1657 cm^{-1}; HRMS calcd for $C_{25}H_{44}O_5Si_2Na$ (M + Na) 503.2625, found 503.2636.

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Supplementary Material Available: Copies of ^1H NMR spectra for compounds **7**−**15** (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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