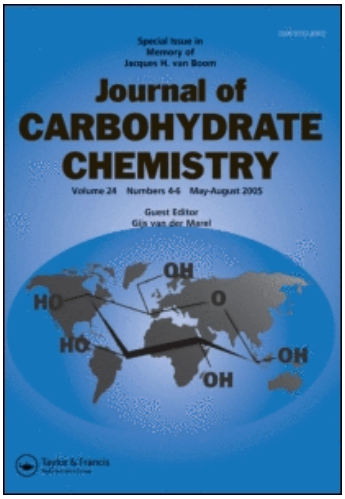


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# The "Reverse Polarity" Approach to Ravidomycin. Aryl C-Aminoglycosides from a Lithiated Aminoglycal

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# The "Reverse Polarity" Approach to Ravidomycin. Aryl C-Aminoglycosides from a Lithiated Aminoglycal

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A three-step sequence affects the regio- and stereospecific elaboration of an aryl C-aminoglycoside from a simple aminoglycal and a quinone. Direct lithiation of the glycal followed by addition of the quinone, reduction of the quinol adduct, and hydroboration gives a product with a trans-trans stereochemical relationship between the substituents at C1′, C2′, and C3′, appropriate for compounds in the ravidomycin series.

**Keywords** Ravidomycin, Aminoglycal, Aryl C-aminoglycosides, Quinone, Quinol, Aromatization, Reverse polarity, Umpolung

Among the aryl C-glycoside antibiotics,[1] the gilvocarcin family (**1**)[2] is one of the major structural classes.[3]

In the gilvocarcins, a single carbohydrate substituent is attached to an extended aglycone at a position para to a phenolic hydroxyl group. The chrysomycins are aryl C-pyranosides, gilvocarcins M, E, and V[4] are aryl C-furanosides, and ravidomycin and its derivatives[5] are 3,6-dideoxy-3-dimethylamino C-pyranosides (Fig. 1).

The development of methodology based on a "reverse polarity" strategy has allowed us to prepare aryl C-glycosides that are models for the

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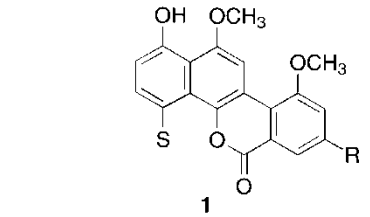

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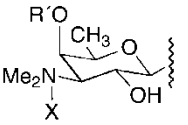
**Ravidomycins** R = $CH{=}CH_2$, S =

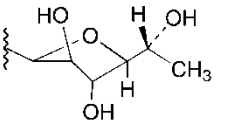


**1a) Ravidomycin** R′= Ac, X = $e^-$ pair

**1b) Deacetylravidomycin** R′= H, X = $e^-$ pair

**1c) Deacetylravidomycin N-oxide** R′= H, X = O

**Gilvocarcins** S =

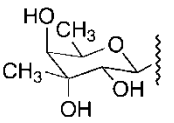


**1d) Gilvocarcin M** R = $CH_3$

**1e) E** R = $CH_2CH_3$

**1f) V** R = $CH{=}CH_2$

**Chrysomycins** S =



**1g) Chrysomycin A** R = $CH{=}CH_2$

**1h) B** R = $CH_3$

**Figure 1:** The gilvocarcin antitumor antibiotics.

gilvocarcins[6] as well as some that are models for other classes of aryl C-glycosides.[7] To date, however, the reaction sequences forthcoming from this approach have been applied only in the context of the preparation of aryl C-pyranosides and -furanosides.[8] We are now pleased to report the extension of this chemistry by the preparation of a lithiated aminoglycal reagent[9] and its use in the synthesis of aryl C-aminoglycosides. Our results support the pursuit of the reverse polarity approach to the preparation of ravidomycins (strategy shown in Fig. 2).

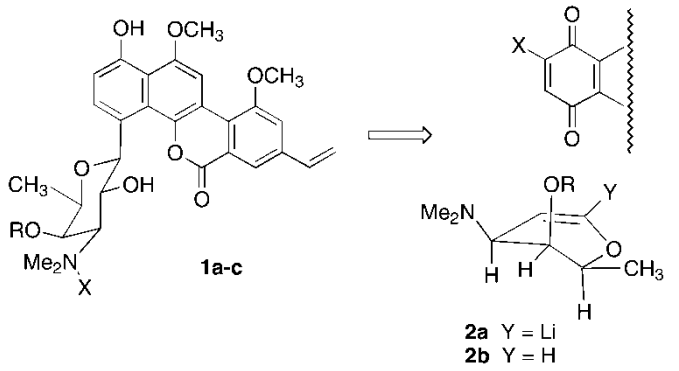
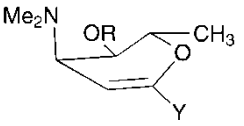



**Figure 2:** The ravidomycin restrosynthetic analysis.



## SYNTHESIS OF AMINOGLYCAL 3

Aminoglycal **2b** would be an appropriate precursor to the lithiated reagent **2a**. However, this glycal is relatively difficult to obtain. Therefore, for our feasibilitiy studies, we chose to work with reagent **3a**, to be derived from the direct lithiation of aminoglycal **3b**. We postulated that this compound would be obtained by modification of oxazolidone **7**, presumably available in four steps from rhamnal (Sch. 1) by modification of the chemistry of Danishefsky.[10]

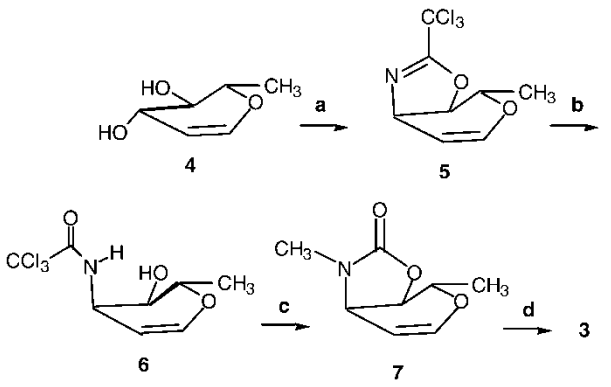



**3a** Y = Li, R = TBDPS
**3b** Y = H, R = TBDPS

Indeed, oxazolidinone **7** was obtained (Sch. 1) by a route parallel to that cited. Rhamnal (**4**), when treated with sodium hydride and trichloroacetonitrile followed by $BF_3 \cdot OEt_2$, delivered oxazoline **5**, in which the stereochemistry at C-3 had been inverted. Hydrolytic ring opening then afforded the hydroxy trichloroacetamide **6**, and adaptation of the literature procedure for cyclization/alkylation provided the desired **7**.

Lithium aluminum hydride reduction of intermediate **7** proceeded at 0°C to give the *surprisingly volatile* dimethylamino glycal intermediate, which was protected without purification as the *t*-butyldiphenyl silyl ether.[a] Multigram quantities of aminoglycal **3** were prepared by this method.

[a]This dimethylamino glycal was also protected as the *t*-butyldimethyl silyl ether. However, the product, which could not be separated from the byproduct TBDMSOH, was unsuitable for lithiation.



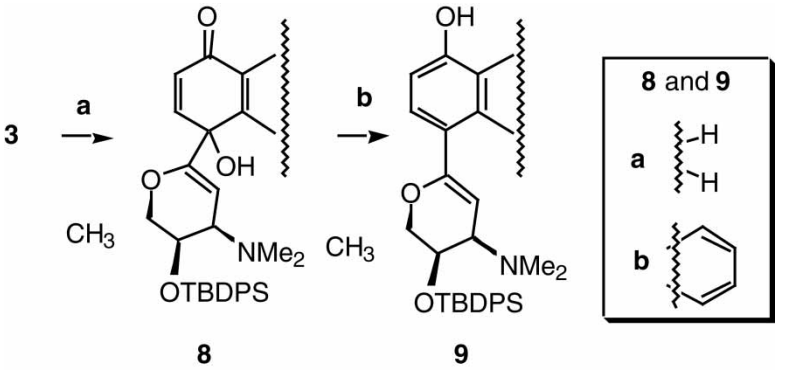

**Scheme 1:** Key: (a) NaH, trichloroacetonitrile, then $BF_3 \cdot OEt_2$, 42%, (b) TsOH, aq. py, 61%, (c) NaH, $Me_2SO_4$, 96%, (d) $LiAlH_4$, then TBDPSCl, 79%.



## ELABORATION OF AMINOGLYCAL 3 TO ARYL C-AMINOGLYCOSIDES

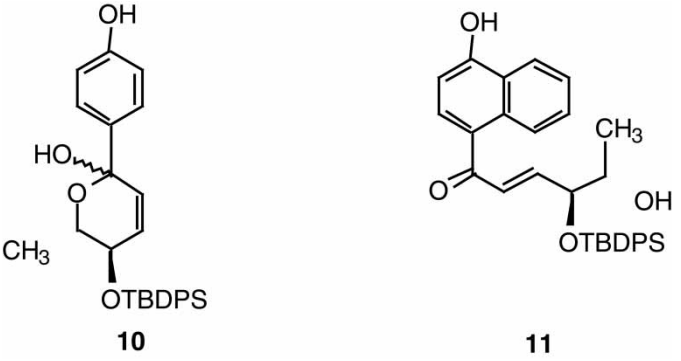
Lithiation of aminoglycal **3b** by the standard protocol was straight-forward. Addition of the resulting reagent to benzoquinone gave aminoglycal-substituted quinol **8a**, and addition to naphthoquinone gave naphthoquinol **8b** (Sch. 2).

Although neither quinol **8a** nor **8b** was reduced by $Na_2S_2O_4$, reduction of both substrates proceeded readily with aluminum amalgam.[6b] The crude product of each of these reductions (**9**) suffered hydrolytic Ferrier rearrangement when subjected to preparative TLC. Thus, from the attempted purification of aryl C-glycal **9a**, we isolated hexenopyranose **10**. From attempted




**Scheme 2:** Key: (a) *t*-BuLi, then benzoquinone → **8a**, 85% (80% conversion) or *t*-BuLi, then naphthoquinone → **8b**, 81%, (b) Al/Hg (see text).

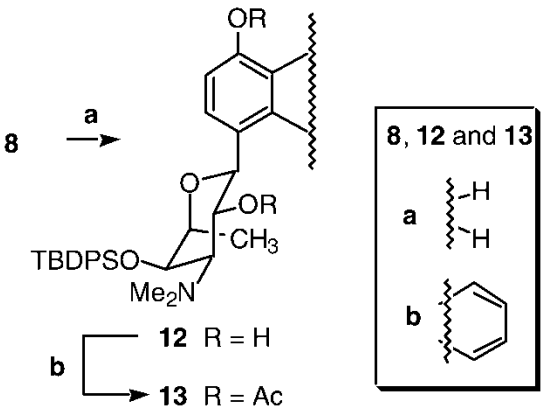
purification of glycal **9b**, we isolated the hydroxy enone **11**, the ring-opened isomer of the corresponding naphthyl hexenopyranose.






A procedure in which the adduct **8a** was treated with Al/Hg followed by $BH_3 \cdot THF$ at room temperature and stirring of the resulting mixture with basic hydrogen peroxide afforded the glycoside **12a** in which both reductive aromatization and anti-Markovnikov hydration had taken place (Sch. 3). A similar procedure applied to adduct **8b** gave glycoside **12b**. Each *p*-hydroxy aryl C-glycoside was characterized as its diacetate, **13a** and **13b**, respectively.

The stereochemistry of the aryl C-aminoglycosides **13a** and **13b** was determined by analysis of the coupling constants of the protons in the amino sugar moiety (e.g., in diacetate **13a**, $J\ H^1-H^2 = 9.2\,Hz$, $J\ H^2-H^3 = 10.7\,Hz$, and $J\ H^3-H^4 = 2.6\,Hz$). Hydroboration of the double bond in the 3′-deoxy-3′-dimethylamino glycals occurs from the side opposite the 3′-amino substituent, a preference that is most likely the result of a simple steric effect. The hydroboration thus completes the construction of an aryl C-aminoglycoside moiety




**Scheme 3:** Key: (a) Al/Hg, then $BH_3$, $H_2O_2$, NaOH, (b) $Ac_2O$: **13a**, 60% from **8a**; **13b**, 46% from **8b**.

with the C-1′, C-2′, and C-3′ trans-trans stereochemical relationship required for the projected synthesis of ravidomycin. In fact, compounds **12** and **13** bear the stereochemical array of the structure originally assigned to ravidomycin and now designated 5′-epi ravidomycin.[5]

The preparation of the model aryl C-aminoglycosides **12** and **13** provides the first examples of the generation and use of a lithiated aminoglycal. In the following paper, we show further applications of this class of highly functionalized reagents.

## EXPERIMENTAL SECTION

Solvents were dried and purified by standard methods before use. Ether refers to diethyl ether. Flash chromatography was performed with silica gel (200–425 mesh).



**Oxazoline 5.** To a solution of 430 mg (3.31 mmol) of dihydroxy glycal **4** in 33 mL of $CH_2Cl_2$ at 0°C was added 213 mg (8.88 mmol) of NaH. After 10 min, 7.5 mL (7.5 mmol) of $CCl_3CN$ was added dropwise over 15 min. The reaction mixture was stirred at rt for 2 hr, then cooled to −78°C. To this solution was added 2 mL of $BF_3 \cdot OEt_2$ (16.2 mmol). The resulting solution was stirred at −78°C for 1 hr, then quenched with 20 mL of $H_2O$, and extracted with $CH_2Cl_2$ (4 × 15 mL). The combined organic solution was dried over $Na_2SO_4$ and concentrated. Flash column chromatography (hexane/EtOAc 3 : 1) gave 356 mg (42%) of light yellow oil: $^1$H NMR ($CDCl_3$): $\delta$ 6.59 (dd, $J$ = 6.0, 1.1 Hz, 1H), 5.27 (dd, $J$ = 3.9, 1.3 Hz, 1H), 4.63 (m, 2H), 3.55 (m, 1H), 1.35 (d, $J$ = 6.3 Hz, 3H); $^{13}$C NMR ($CDCl_3$): $\delta$ 162.0, 147.2, 100.3, 86.6, 83.2, 69.3, 61.3, 17.6; FTIR ($CDCl_3$): 1725, 1659 cm$^{-1}$; HRMS (EI): calcd. 256.9591, found: 256.9583 ($^{35}Cl_2^{37}Cl$).

**Trichloroacetamide 6.** To a solution of 434 mg (1.69 mmol) of oxazoline **5** in 17 mL pyridine/$H_2O$ (1 : 1) at 80°C was added 321 mg of TsOH (1.69 mmol). The reaction solution was stirred at 80°C for 2 hr and 15 min and then cooled down to rt and quenched with 20 mL of $H_2O$. The resulting solution was extracted with $CH_2Cl_2$ (3 × 20 mL) and EtOAc (3 × 20 mL). The combined organic solution was dried over $Na_2SO_4$ and concentrated. Flash column chromatography (hexane/EtOAc 3 : 1) gave 283 mg (61%) of a light yellow oil: $^1$H NMR ($CDCl_3$): $\delta$ 6.94 (s, 1H), 6.42 (dd, $J$ = 6.1, 1.5 Hz, 1H), 4.72 (dd, $J$ = 6.1, 4.0 Hz, 1H), 4.52 (m, 1H), 3.99 (q, $J$ = 6.5 Hz, 1H), 3.79 (dd, $J$ = 6.0, 8.7 Hz, 1H), 2.38 (d, $J$ = 6.0 Hz, 1H), 1.35 (d, $J$ = 6.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$): $\delta$ 162.8, 145.7, 97.1, 92.3, 72.7, 69.5, 45.8, 16.5; FTIR (neat): 3372, 1694, 1651 cm$^{-1}$; HRMS (EI): calcd. 256.9591, found: 256.9597 (M-$H_2O$, $^{35}Cl_2^{37}Cl$).

**Oxazolidinone 7.** To a solution of 183 mg (0.67 mmol) of amide **6** in 7 mL of $CH_2Cl_2$ at 0°C was added 90 mg of NaH (5.60 mmol). After addition of NaH, the ice-bath was removed and the solution was stirred at rt for 1 hr. Then it was cooled down to 0°C and another portion of 93 mg of NaH (5.78 mmol) was added. The mixture was stirred at rt for 30 min and then treated with 0.32 mL of $Me_2SO_4$ (3.37 mmol). After 3 hr and 30 min, the reaction was cooled to 0°C, quenched with 10 mL of $H_2O$, and extracted with $CH_2Cl_2$ (1 × 30 mL) and EtOAc (3 × 20 mL). The combined organic solution was dried over $Na_2SO_4$. Removal of solvent left 109 mg (96%) of a colorless oil: $^1$H NMR ($CDCl_3$): $\delta$ 6.62 (d, $J = 6.2$ Hz, 1H), 4.95 (dd, $J = 6.1$, 4.1 Hz, 1H), 4.21 (dd, $J = 9.2$, 7.1 Hz, 1H), 4.02 (ddd, $J = 7.7$, 4.2, 1.3 Hz, 1H), 3.66 (m, 1H), 2.82 (s, 3H), 1.41 (d, $J = 6.3$ Hz, 3H); $^{13}$C NMR ($CDCl_3$): $\delta$ 157.2, 148.3, 96.7, 73.6, 70.3, 51.3, 28.6, 17.2; FTIR (neat): 1745, 1651 cm$^{-1}$; HRMS (EI): calcd. 169.0739, found: 169.0731.



**Aminoglycal 3.** To a solution of 700 mg (4.14 mmol) of oxazolidinone **7** in 50 mL of ether at 0°C was added 800 mg (21.05 mmol) of LAH. The reaction mixture was stirred at 0°C for 2 hr, quenched with 50 mL of $H_2O$, and extracted with ether (4 × 50 mL). The ether solution was washed with brine (2 × 100 mL), dried with $MgSO_4$, and concentrated. To a solution of this crude product in 50 mL of DMF was added 53 mg (0.43 mmol) of DMAP, 1.51 g (22 mmol) of imidazole, and 2.3 mL (8.7 mmol) of TBDPSCl. The reaction mixture was stirred for 15 hr and then 50 mL of ether was added. The solution was poured into 50 mL of $H_2O$, and the resulting mixture was extracted with ether (4 × 30 mL). The combined ether solution was washed with $H_2O$ (3 × 50 mL), dried with $MgSO_4$, and concentrated. Flash column chromatography (hexanes/EtOAc, 1 : 4, then with 1% $Et_3N$ in hexanes/EtOAc, 1 : 4, and finally with 1% $Et_3N$ in EtOAc) gave 1.30 g (79% for two steps) of light yellow oil: $^1$H NMR ($CDCl_3$): $\delta$ 7.80 (dd, $J = 7.7$, 1.3 Hz, 2H), 7.70 (dd, $J = 7.6$, 1.5 Hz, 2H), 7.38 (m, 6H), 6.35 (dd, $J = 6.3$, 1.6 Hz, 1H), 4.60 (dd, $J = 6.2$, 3.8 Hz, 1H), 3.96 (q, $J = 7.0$ Hz, 1H), 3.81 (dd, $J = 7.3$, 5.5 Hz, 1H), 2.81 (q, $J = 2.2$ Hz, 1H), 2.21 (s, 6H), 1.08 (s, 9H), 1.05 (d, $J = 6.4$ Hz, 3H); $^{13}$C NMR ($CDCl_3$): $\delta$ 144.1, 136.3, 136.1, 134.4, 134.3, 129.6, 129.4, 127.4, 127.3, 96.5, 73.1, 56.8, 43.0, 27.1, 19.5, 18.2; FTIR (neat): 1646 cm$^{-1}$; HRMS (FAB, NaI): calcd. 418.2178, found: 418.2182 (M + Na).

**Aminoglycal-substituted Quinol 8a.** To a solution of 65 mg (0.16 mmol) of aminoglycal **3** in 2 mL of THF at −78°C was added 0.7 mL (0.83 mmol) of *t*-BuLi (1.2 M in pentane). After stirring at −78°C for 5 min and at 0°C for 1 hr, the solution was cooled to −78°C and added dropwise by cannula to a solution of 29 mg (0.27 mmol) of benzoquinone in 2 mL of THF at −78°C. The blue reaction mixture was stirred at −78°C for 4 hr, then quenched with 20 mL of $H_2O$ and extracted with EtOAc (4 × 15 mL). The

combined EtOAc solution was dried over $MgSO_4$ and concentrated. Preparative TLC (hexanes/EtOAc, 1 : 4) gave 13 mg of aminoglycal **3** (20% recovery) and 56 mg (85% based on unrecovered starting material) of a yellow oil: $^1$H NMR ($CDCl_3$): $\delta$ 7.73 (ddd, $J = 9.5$, 5.5, 1.6 Hz, 4H), 7.39 (m, 6H), 6.80 (td, $J = 10.3$, 3.1 Hz, 2H), 6.19 (dt, $J = 7.4$, 2.9 Hz, 2H), 4.95 (dd, $J = 3.0$, 0.7 Hz, 1H), 4.00 (q, $J = 5.6$ Hz, 1H), 3.78 (t, $J = 5.0$ Hz, 1H), 2.81 (dd, $J = 4.9$, 3.1 Hz, 1H), 2.21 (s, 6H), 1.05 (s, 9H), 0.98 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR ($CDCl_3$): $\delta$ 185.4, 150.4, 148.1, 136.1, 136.0, 134.3, 133.7, 129.8, 129.7, 128.5, 128.4, 127.5, 127.4, 94.1, 75.4, 71.4, 57.1, 43.1, 27.0, 19.5, 17.5; FTIR (neat): 3319, 1666 cm$^{-1}$; HRMS (FAB, NaI): calc. 526.2389, found: 526.2393 (M + Na).

**Aminoglycal-substituted Quinol 8b.** To a solution of 121 mg (0.31 mmol) of aminoglycal **3** in 3 mL of THF at $-78^\circ$C was added 0.8 mL (0.94 mmol) of *t*-BuLi (1.2 M in pentane). The resulting solution was stirred at $-78^\circ$C for 5 min and at 0°C for 1 hr, then cooled to $-78^\circ$C and added dropwise by cannula to a solution of 61 mg (0.39 mmol) of naphthoquinone in 3 mL of THF at $-78^\circ$C. The blue reaction mixture was stirred at $-78^\circ$C for 4 hr and 30 min, then diluted with 20 mL of ether and poured into 20 mL of $H_2O$. The resulting mixture was extracted with ether (4 × 20 mL), and the combined ether solution was dried over $MgSO_4$ and concentrated. Preparative TLC (hexanes/EtOAc, 1 : 4) gave 140 mg (81%) of a brown oil: $^1$H NMR ($CDCl_3$): $\delta$ 8.11 (dd, $J = 1.3$, 7.7 Hz, 1H), 7.75 (dd, $J = 1.0$, 7.9 Hz, 1H), 7.65 (dd, $J = 1.6$, 8.9 Hz, 2H), 7.42 (m, 8H), 7.14 (d, $J = 7.1$ Hz, 2H), 6.84 (d, $J = 10.2$, 1H), 6.37 (d, $J = 10.1$, 1H), 5.22 (t, $J = 1.1$ Hz, 1H), 3.80 (dd, $J = 4.3$, 6.7 Hz, 1H), 3.62 (t, $J = 3.6$ Hz, 1H), 2.78 (dd, $J = 2.3$, 4.4 Hz, 1H), 2.12 (s, 6H), 0.96 (s, 9H), 0.83 (d, $J = 6.7$ Hz, 3H); $^{13}$C NMR ($CDCl_3$): $\delta$ 184.9, 152.3, 149.7, 144.4, 136.2, 135.8, 134.2, 133.3, 133.1, 130.7, 129.7, 129.5, 128.6, 128.3, 127.5, 127.3, 127.2, 126.1, 93.4, 75.1, 70.6, 57.0, 42.8, 27.0, 19.3, 16.9; FTIR (neat): 3380, 1666, 1600 cm$^{-1}$; HRMS (FAB, NaI): calcd. 576.2546, found: 576.2543 (M + Na).

**Ferrier-rearrangement Product 10.** To a solution of 17 mg (0.034 mmol) of glycal-substituted quinol **8a** in 1 mL of THF/$H_2O$ (9/1) was added 7.7 mg (0.29 mmol) of amalgamated aluminum foil (formed by immersion in 2% aqueous $HgCl_2$, washing with EtOH, then $Et_2O$).[11] The solution was stirred at rt for 2 hr, filtered through a pad of Celite, and concentrated. Preparative TLC (MeOH/$CHCl_3$, 1 : 9) gave 10 mg (67%) of a yellow oil: $^1$H NMR ($CDCl_3$): $\delta$ 7.53 (m, 4H), 7.25 (m, 8H), 6.77 (dd, $J = 2.0$, 6.8 Hz, 2H), 6.63 (d, $J = 11.8$ Hz, 1H), 6.16 (dd, $J = 8.6$, 10.8 Hz, 1H), 4.96 (dd, $J = 3.5$, 8.5 Hz, 1H), 3.90 (m, 1H), 3.39 (m, 1H), 1.23 (d, $J = 6.3$ Hz, 3H), 1.04 (s, 9H); $^{13}$C NMR ($CDCl_3$): $\delta$ 147.0, 135.8, 135.7, 131.3, 129.7, 129.6, 127.6, 127.5, 125.5, 115.2, 74.6, 71.1, 27.0, 19.3, 19.1; FTIR (neat): 3252, 1591 cm$^{-1}$; HRMS (FAB, NaI): calcd. 483.1967, found: 483.1957 (M + Na).

**Ring-opened Ferrier Product 11.** To a solution of 25 mg (0.045 mmol) of aminoglycal-substituted naphthoquinol **9b** in 1 mL of THF/$H_2O$ (9/1) was added 6.0 mg (0.22 mmol) of amalgamated aluminum foil (formed by immersing in 2% aqueous $HgCl_2$, washing with EtOH, then $Et_2O$).[11] The solution was stirred at rt for 1 hr, and 10 min, filtered through a pad of Celite, and concentrated. Preparative TLC (hexanes/EtOAc, 1/1) gave 16 mg (70%) of a yellow oil: $^1$H NMR ($CDCl_3$): $\delta$ 8.77 (dd, $J = 0.8$, 8.5 Hz, 1H), 8.32 (dd, $J = 1.3$, 7.6 Hz, 1H), 7.68 (m, 4H), 7.55 (dt, $J = 1.6$, 8.3 Hz, 2H), 7.44 (m, 6H), 6.83 (dd, $J = 1.6$, 10.3 Hz, 1H), 6.43 (d, $J = 10.3$ Hz, 1H), 6.21 (dd, $J = 2.4$, 9.5 Hz, 1H), 4.33 (m, 2H), 1.46 (d, $J = 6.0$ Hz, 3H), 1.09 (s, 9H); $^{13}$C NMR ($CDCl_3$): $\delta$ 184.4, 158.4, 138.4, 138.2, 137.9, 135.8, 134.5, 133.3, 132.7, 131.8, 131.5, 130.2, 130.1, 128.5, 128.0, 127.9, 127.2, 126.7, 123.9, 119.1, 112.0, 78.2, 69.2, 26.9, 19.3, 18.2; FTIR (neat): 3310, 1635 $cm^{-1}$; HRMS (FAB, NaI): calcd. 533.2124, found: 533.2115 (M + Na).



**Diacetate 13a.** To a solution of 21 mg (0.042 mmol) of quinol glycal **8a** in 1 mL of THF/$H_2O$ (10/1) was added 6 mg (0.22 mmol) of amalgamated aluminum foil (formed by immersing in 2% aqueous $HgCl_2$, washing with EtOH, then $Et_2O$).[11] The solution was stirred at rt for 1 hr, filtered through a pad of Celite, and concentrated. To a solution of this crude product in 1 mL of THF at 0°C was added 0.25 mL (0.25 mmol) of $BH_3 \cdot$ THF over 5 min. The reaction mixture was stirred at rt for 4 hr and then quenched with 1 mL of MeOH and 1 mL of 3 N NaOH/$H_2O_2$ (1 : 1). The resulting solution was stirred at rt for 4 hr and then partitioned between $H_2O$ and ether (4 × 15 mL). The combined ether solution was dried with $MgSO_4$ and concentrated. To a solution of this crude product in 1 mL of pyridine was added a catalytic amount of DMAP and 0.2 mL of $Ac_2O$. The reaction mixture was stirred at rt overnight, quenched with 10 mL of $H_2O$, and extracted with ether (4 × 15 mL). The organic layer was dried with $MgSO_4$ and concentrated. Preparative TLC (hexanes/EtOAc, 1 : 1) gave 15 mg (60%) of a light yellow oil: $^1$H NMR ($CDCl_3$): $\delta$ 7.80 (m, 4H), 7.36 (m, 8H), 7.07 (dd, $J = 1.9$, 6.7 Hz, 2H), 5.56 (dd, $J = 10.7$, 9.3 Hz, 1H), 4.39, (d, $J = 9.2$ Hz, 1H), 4.08 (t, $J = 1.6$ Hz, 1H), 3.81 (q, $J = 6.5$ Hz, 1H), 2.98 (dd, $J = 11.0$, 2.6 Hz, 1H), 2.47, (s, 6H), 2.26 (s, 3H), 1.81 (s, 3H), 1.09 (s, 9H), 0.90 (d, $J = 7.1$ Hz, 3H); $^{13}$C NMR ($CDCl_3$): $\delta$ 169.1, 168.8, 150.6, 136.3, 136.0, 136.0, 134.5, 133.4, 129.7, 129.6, 128.6, 127.6, 127.5, 121.2, 77.2, 76.5, 75.0, 74.9, 71.7, 62.5, 43.5, 27.2, 21.2, 21.1, 19.4, 14.8; FTIR ($CDCl_3$): 1758 $cm^{-1}$; HRMS (FAB, NaI): calcd. 612.2757, found: 612.2767 (M + Na).

**Diacetate 13b.** To a solution of 40 mg (0.072 mmol) of quinol glycal **8b** in 1 mL of THF/$H_2O$ (10/1) was added 12 mg (0.43 mmol) of amalgamated aluminum foil (formed by immersing in 2% aqueous $HgCl_2$, washing with EtOH, then $Et_2O$).[11] The solution was stirred at rt for 1 hr, filtered through a

pad of Celite, and concentrated. To a solution of this crude product in 1 mL of THF at 0°C was added 0.36 mL (0.36 mmol) of $BH_3 \cdot THF$ over 5 min. The reaction mixture was stirred at rt for 12 hr and then quenched with 1 mL of MeOH and 1 mL of 3 N $NaOH/H_2O_2$ (1 : 1). The resulting solution was stirred at rt for 4 hr, quenched with 10 mL of $H_2O$ and 20 mL of sat. $NaHCO_3$, and extracted with ether (4 × 15 mL). The combined ether solution was dried over $MgSO_4$ and concentrated. To a solution of this crude product in 1 mL of pyridine was added a catalytic amount of DMAP and 0.5 mL of $Ac_2O$. The reaction mixture was stirred at rt overnight, quenched with 10 mL of $H_2O$, and extracted with ether (4 × 15 mL). The organic solution was dried with $MgSO_4$ and concentrated. Preparative TLC (hexanes/EtOAc, 1 : 1) gave 21 mg (46%) of a light yellow oil: $^1$H NMR ($CDCl_3$): $\delta$ 8.50 (bd, 1H) 7.87 (m, 4H), 7.67 (m, 1H), 7.46 (m, 8H), 7.29 (m, 2H), 5.91 (dd, $J = 10.0$, 9.5 Hz, 1H), 5.08, (d, $J = 7.8$ Hz, 1H), 4.15 (bs, 1H), 4.00 (d, $J = 7.0$ Hz, 1H), 3.17 (d, $J = 10.0$ Hz, 1H), 2.44 (2s, 9H), 1.50 (s, 3H), 1.13 (s, 9H), 0.95 (d, $J = 7.1$ Hz, 3H); $^{13}$C NMR ($CDCl_3$): $\delta$ 169.0, 168.6, 147.0, 136.2, 136.1, 134.4, 133.2, 132.7, 129.8, 127.6, 126.9, 126.3, 125.9, 121.7, 117.3, 76.0, 75.1, 71.2, 62.7, 43.1, 27.3, 21.1, 20.8, 19.4, 14.7; FTIR ($CDCl_3$): 1767, 1743 $cm^{-1}$; HRMS (FAB, NaI): calcd. 662.2914, found: 662.2925 (M + Na).



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