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Synthetic Studies of Kinamycin Antibiotics: Stereoselective Synthesis of the Highly Oxygenated D-Ring and Construction of the ABD-Ring System of Kinamycins

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A concise and stereoselective synthesis of the highly oxygenated D-ring of the kinamycin family of antitumor antibiotics was achieved from commercially available 3-methyl-2-cyclohexen-1-one. The key steps included a regioselective isomerization of a *cis*-epoxy alcohol, a regioselective reductive ring opening of a benzylidene ketal, and a stereoselective α-hydroxy-directed ketone reduction. The Ullmann coupling between a bromonaphthaldehyde AB-ring fragment and an α-iodocyclohexenone, which is a versatile D-ring precursor, effected the construction of the functionalized ABD-ring system that may provide access to kinamycin F and its structural analogues.

Introduction

The kinamycins are a family of structurally unique natural products that contain a highly oxygenated cyclohexene ring and an unusual diazobenzo[*b*]fluorene moiety (see Figure 1).[1] Four kinamycin antibiotics, namely, A–D, were isolated in 1970 from the culture broth of *Streptomyces murayamaensis* and display a strong inhibition of Gram-positive bacteria.[2] Kinamycin C exhibits cell growth inhibitory effects in the 60-cancer cell line panel of the National Cancer Institute (NCI). It was proposed that fully deacetylated kinamycin F, which is detected as a metabolite in the culture broths of *Streptomyces murayamaensis*,[3] may be generated in cells by esterase activity on the *O*-acetylated forms of kinamycin. It may also represent the active metabolite that is responsible for the observed inhibition of cancer cell growth.[4,5] The potential of the kinamycins as new anticancer agents was realized only recently with the isolation of lomaiviticin A, a potent antitumor antibiotic that contains unique dimeric diazobenzofluorene glycoside structures.[6] The biological activity of the kinamycins and lomaiviticin is thought to arise from the reductive cleavage[6,7] of DNA in which the diazonapthoquinone function is involved.[8] These molecules have become attractive synthetic targets, and several total syntheses of the kinamycins[9] as well as the synthesis of the dimeric unit of the lomaiviticin aglycon[10] have been reported.

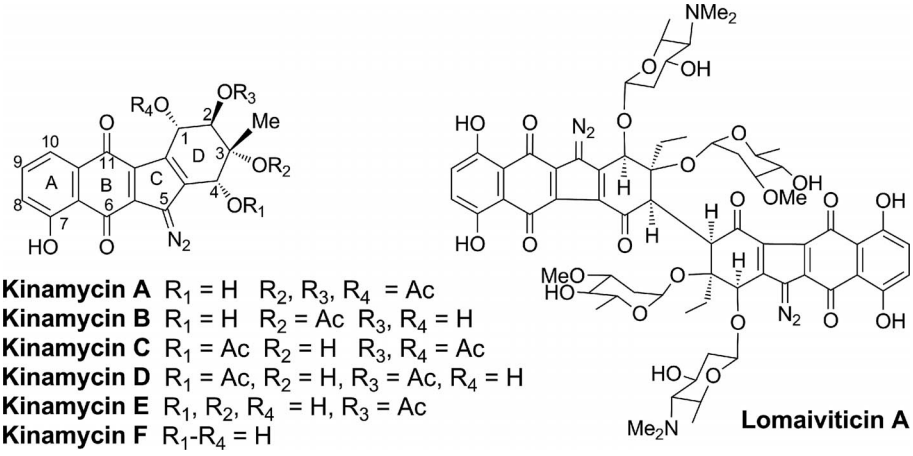

Figure 1. The family of diazobenzo[*b*]fluorene antitumor antibiotics.

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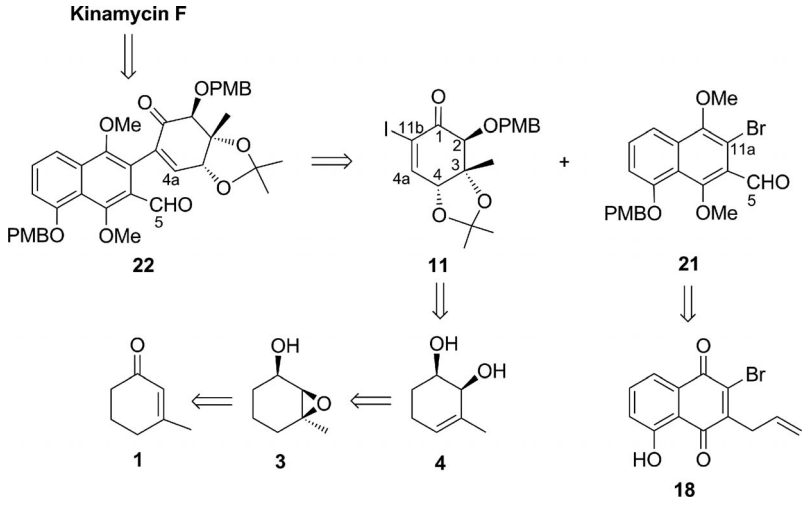
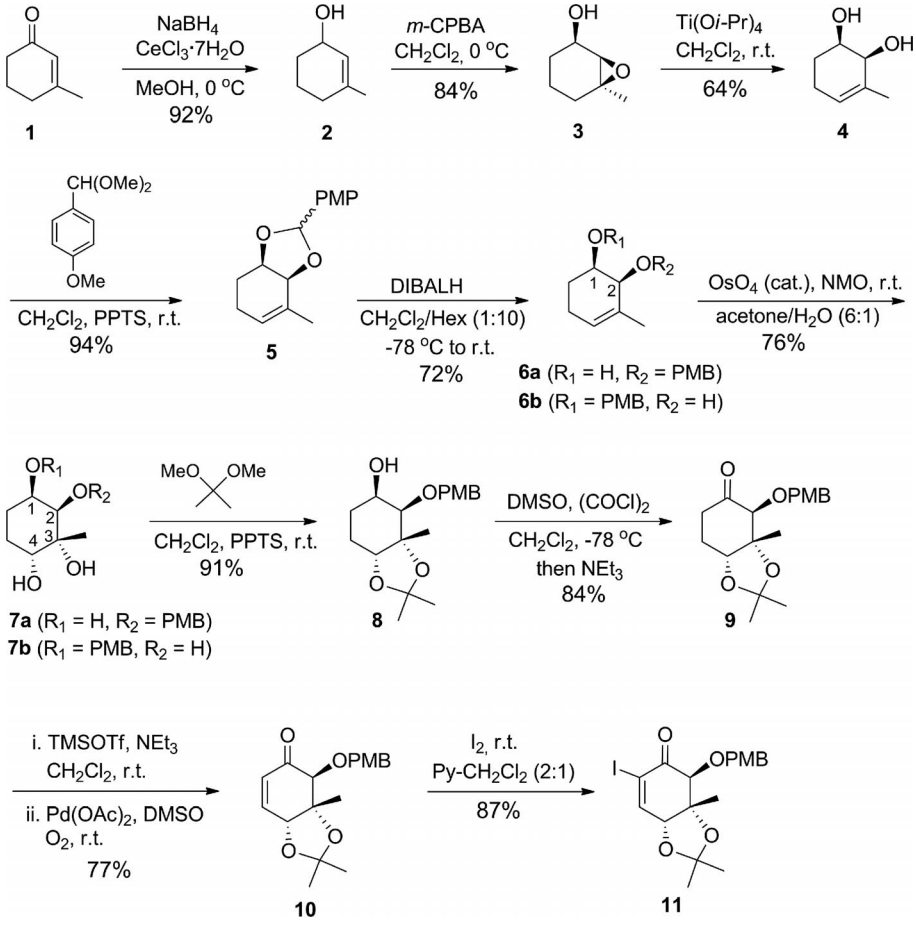
In the search of a convergent entry to kinamycin F and its structural analogs, we surmised that access was possible from α-naphthylcyclohexenone **22**, which is the product of a metal-catalyzed coupling between α-iodocyclohexenone **11** and bromonaphthaldehyde **21** (see Scheme 1). AB-ring fragment **21** could be prepared from naphthoquinone **18**. Cyclohexenone **11**, which is a highly oxygenated D-ring precursor that has in place the latent C-2, C-3, and C-4 kinamycin chiral centers,[11] could result from cyclohexenediol **4**, which is the product of a regioselective isomerization of epoxy alcohol **3**. Entry to **3** could, in turn, be achieved from commercially available 3-methyl-2-cyclohexenone (**1**).



Scheme 1. Proposed strategy for the synthesis of kinamycin F.



Scheme 2. Stereoselective synthesis of the highly oxygenated D-ring cyclohexenone **11** (PPTS = pyridinium *p*-toluenesulfonate, NMO = *N*-methylmorpholine *N*-oxide, DMSO = dimethyl sulfoxide).

Furthermore, the stereoselective reduction of cyclohexenone **11** to the corresponding cyclohexenol with the desired *trans* stereochemistry between the C-1 and C-2 chiral centers would establish the D-ring of the kinamycins. Herein, we wish to report the results of our studies pertaining to the regio- and stereoselective synthesis of the highly oxygenated D-ring[12] of the kinamycins. Our investigation involves the preparation of cyclohexenone **11** (see Scheme 2) and cyclohexene **15** (see Scheme 4) as well as the assembly of the kinamycin ABD-ring intermediate **22** (see Scheme 6).

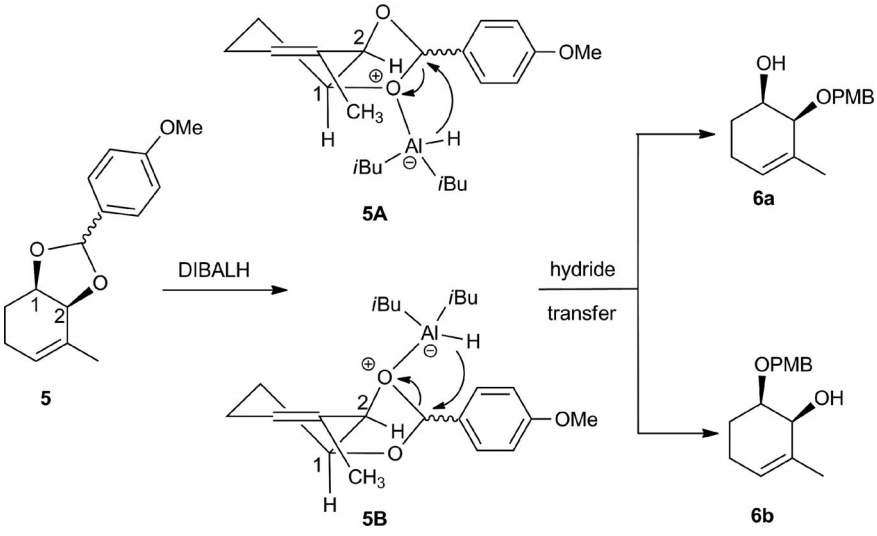
Results and Discussion

The synthesis commenced with the Luche reduction of cyclohexenone **1** to cyclohexenol **2**,[13] which was directly epoxidized with *meta*-chloroperoxybenzoic acid (*m*-CPBA) to generate epoxy alcohol **3**[14] (see Scheme 2). Compound **3** underwent a $Ti(OiPr)_4$ mediated regioselective isomerization to produce *cis*-diol **4** in 64% yield.[15] The protection of **4** with *p*-methoxybenzaldehyde dimethyl acetal afforded benzylidene ketal **5** (PMP = *p*-methoxyphenyl) in 94% yield as a mixture of diastereomers. The reductive ring opening of ketal **5** with diisobutylaluminum hydride (DIBALH)[16] in a mixture of CH_2Cl_2/hexane (1:10) at –78 °C proceeded from the less-hindered site and gave an inseparable mixture of alcohols **6a** and **6b** in 72% yield, in which the desired regioisomer **6a** (PMB = *p*-methoxybenzyl) was the major product (**6a**/**6b** = 5:1).[17] However, alcohols **6a** and **6b** were obtained as a 1:1 mixture when CH_2Cl_2 was utilized as the sole reaction solvent.

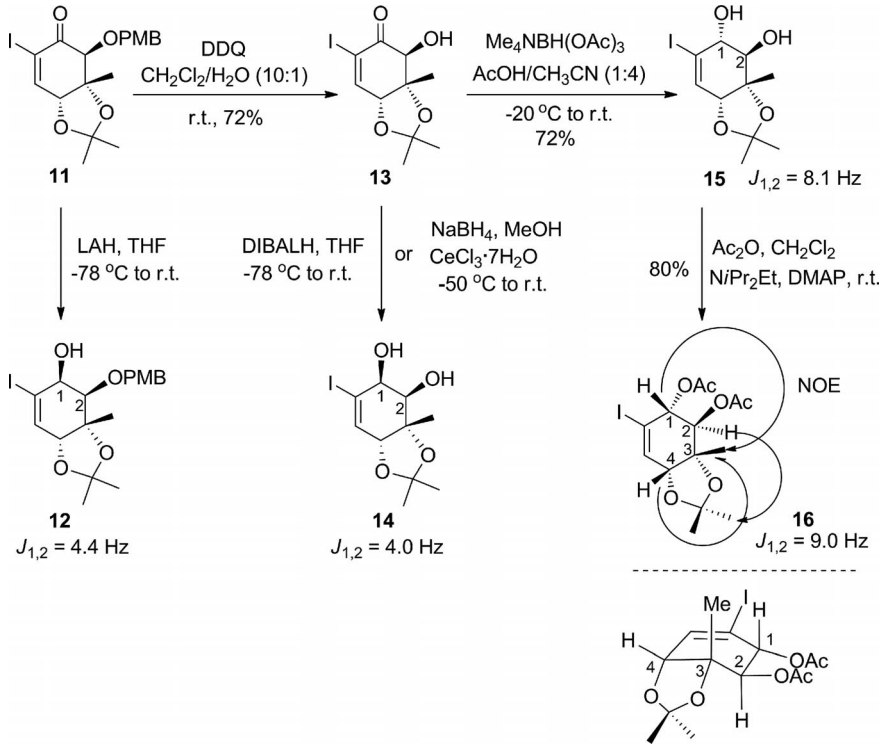
The regioselective reductive ring opening of ketal **5** to give **6a** in CH_2Cl_2/hexane (1:10) may presumably involve the association of DIBALH at the less sterically hindered site of the ketal, that is, the O-1 atom could form aluminum complex **5A**, which could then undergo a hydride transfer through a four-centered transition state or an oxocarbenium ion.[18] Apart from steric factors that may favor the kinetic and thermodynamic formation of complex **5A** over **5B**, in which aluminum complexation occurs at the more sterically hindered ketal O-2 atom, electronic factors should be considered as well. For example, the presence of nonpolar hexane in the solvent system may increase the Lewis acid character of the aluminum and, thus, enhance its complexation with the more nucleophilic ketal O-1 atom and lead to the predominant formation of complex **5A**. On the contrary, the use of the more polar CH_2Cl_2 as the sole reaction solvent most likely enables the equal coordination of DIBALH at both ketal oxygens to give aluminum complexes **5A** and **5B** and result in a 1:1 mixture of **6a** and **6b**, respectively (see Scheme 3).

Hydroxylation of the mixture of cyclohexenols **6a** and **6b** with catalytic OsO_4 occurred from the opposite face of the allylic oxygen[19] to produce triols **7a** and **7b**, which established the stereochemistry at the C-2, C-3, and C-4 chiral centers. The separation of the resulting mixture by flash chromatography enabled the isolation of the desired triol **7a** in 76% yield. Protection of the *cis*-diol moiety in **7a** as an acetonide gave alcohol **8** in 91% yield, which underwent a Swern[20] oxidation to generate ketone **9** in 84% yield. Treatment of **9** with trimethylsilyl trifluoromethanesulfonate (TMSOTf) and NEt_3 resulted in the intermediate trimethylsilyl enol ether, which underwent a Saegusa–Ito[21] oxidation of afford enone **10** in 77% yield. The clean formation of the desired trimethylsilyl enol ether of ketone **9** was also observed upon treatment of the ketone with lithium hexamethyldisilazide (LHMDS) in tetrahydrofuran (THF) followed by the addition of TMSCl. Finally, iodination[22] of **10** by treatment with iodine and pyridine under Baylis–Hillman conditions,[23] produced the desired α-iodocyclohexenone **11** in 87% yield (see Scheme 2).

Attempts to stereoselectively reduce iodoenone **11** with lithium aluminum hydride (LAH) to the corresponding D-ring cyclohexenol were not fruitful, and *cis*-alcohol **12** ($J_{1,2}$ = 4.4 Hz in $CDCl_3$) was formed as the sole product (see Scheme 4). In the hope to achieve the desired stereochemis-



Scheme 3. Likely mechanism for the observed regioselectivity in the reductive ring opening of ketal **5**.



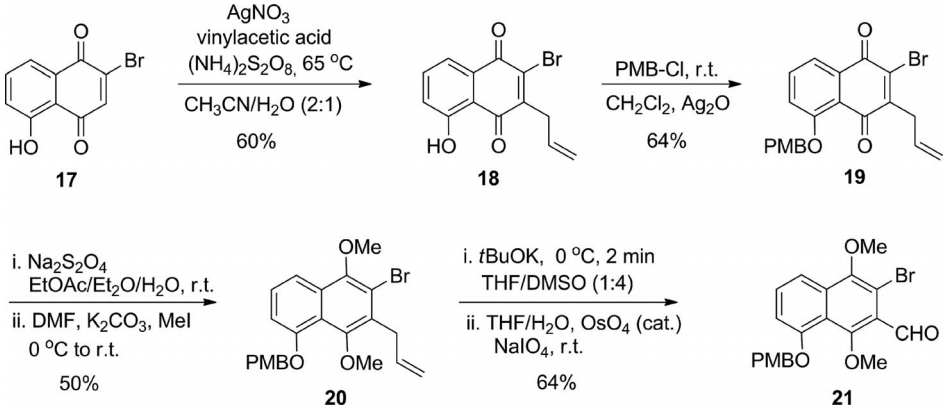
Scheme 4. Entry to the D-ring of kinamycins through an α-hydroxy-directed ketone reduction [DMAP = 4-(*N*,*N*-dimethylamino)pyridine].

try through an α-hydroxy-directed ketone reduction, enone **11** was converted into hydroxyketone **13** upon treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). However, the reduction of **13** with a series of reducing agents such as $NaBH_4/CeCl_3·7H_2O$ or DIBALH, resulted in *cis*-diol **14** ($J_{1,2}$ = 4.0 Hz in $CDCl_3$). On the contrary, compound **13** underwent a facile α-hydroxy-directed ketone reduction with $Me_4NBH(OAc)_3$[24] to yield *trans*-diol **15** ($J_{1,2}$ = 8.1 Hz in $CDCl_3$). The conversion of **15** into diacetate **16** clearly confirmed the desired *trans* stereochemistry ($J_{1,2}$ = 9.0 Hz in $CDCl_3$). The observed coupling constants are consistent with the half-chair being the predominant conformation in which the C-1 and C-2 hydroxy or acetoxy groups are in pseudoequatorial orientations and are comparable to the $J_{1,2}$ values reported for kinamycins A, C, D, E, and J.[25] Nuclear Overhauser effect spectroscopy (^1H-^1H NOESY) of diacetate **16** revealed contacts between H-1 and the C-3 methyl, H-4 and the C-3 methyl, and between H-2 and the α-methyl of the acetonide, which confirmed the assigned structure of D-ring cyclohexene **16**.

Iodocyclohexenes **15** and **16** are ideal candidates to participate in a Suzuki or Stille reaction with an appropriate AB-ring fragment to assemble the ABD-ring system of the kinamycins. However, their precursor α-iodocyclohexenone **11** appeared to be an attractive candidate for an Ullmann[26] reaction with bromonaphthaldehyde **21**. This direct coupling would obviate the preparation of the boronated and stannylated AB-ring fragments.

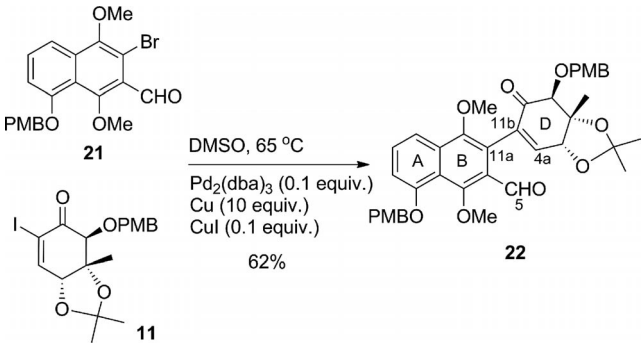
The synthesis of compound **21** commenced from readily available bromojuglone **17**[27] by employing a modified version of the protocol that was used by Nicolaou[9b] to prepare a similar substrate (see Scheme 5). The allylation of **17** with vinyl acetic acid in the presence of silver nitrate and ammonium persulfate[28] afforded naphthalenedione **18**,[9b] which was converted into substrate **19** upon treatment with PMB-Cl and freshly prepared Ag_2O. The reduction of quinone **19** with $Na_2S_2O_4$ gave the intermediate hydroquinone, which was successfully methylated with MeI and K_2CO_3 to provide bromonaphthalene derivative **20**. Attempts to isomerize the allyl group in **20** by treatment with *t*BuOK in THF as the solvent by employing existing literature protocols, described for the syntheses of similar systems,[9b,28b,28c] were not fruitful, and starting material was recovered. However, dropwise addition of a solution of **20** in DMSO to a solution of *t*BuOK in THF effected the successful isomerization of **20** to provide an internal olefin, which underwent a Lemieux–Johnson oxidation to afford aldehyde **21**.

Initial attempts to construct adduct **22** by applying Ullmann conditions as described in the literature[9b,26] for the coupling of similar substrates were not very successful. Iodoenone **11** and bromonaphthaldehyde **21** were dissolved in DMSO followed by the addition of the metal catalysts and heating at 65 °C to afford low yields (ca. 20–30%) of the desired compound **22** as well as other dimerization byproducts. However, after careful experimentation, iodoenone **11** and bromonaphthaldehyde **21** underwent a facile Ullmann coupling reaction to form the latent C-11a–C-11b kinamycin bond and generate α-naphthylcyclohexenone **22** in 62% yield (see Scheme 6). Indeed, the dropwise addition of a solution of **21** to a mixture of iodoenone **11**, $Pd_2(dba)_3$, copper, and CuI in DMSO followed by heating the reaction mixture at 65 °C for 2 h was required to minimize the di-

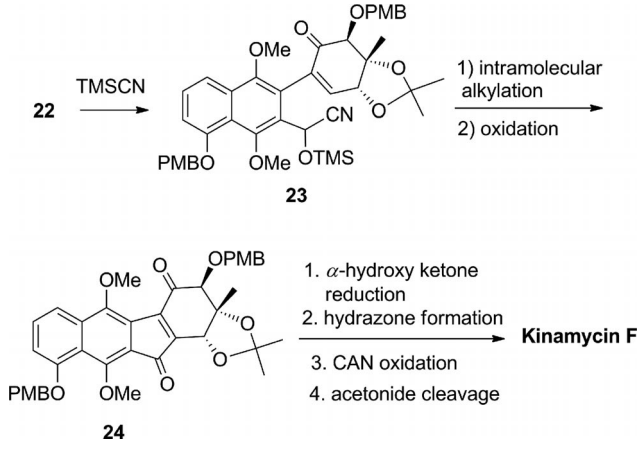


Scheme 5. Synthesis of the AB-ring fragment **21** (DMF = *N*,*N*-dimethylformamide).

merization of bromonaphthaldehyde **21** and enone **11** and ensure the formation of the product.[29] Compound **22** incorporates the ABD-ring system of the kinamycins and contains the appropriate functionality to enable the C-ring closure by a C-4a–C-5 bond connection. For example, the cyanation of the aldehyde group in **22** should render the corresponding cyanohydrin silyl ether **23** an appropriate substrate for an intramolecular cyanohydrin anion alkylation to synthesize benzofluorenone **24**, which is an advanced tetracyclic intermediate that could be converted into kinamycin F through a series of known transformations (see Scheme 7).



Scheme 6. Construction of the kinamycin ABD-ring system through an Ullmann-type coupling reaction.



Scheme 7. Proposed strategy for the conversion of **22** to kinamycin F (CAN = cerium ammonium nitrate).

Conclusions

In summary, this study established an efficient method for the regio- and stereoselective synthesis of the highly oxygenated D-ring of the kinamycins by employing cyclohexenone **11** and cyclohexene **15**, which were prepared from commercially available cyclohexenone **1** in 10 and 12 steps, respectively. This study also achieved the construction of α-naphthylcyclohexenone **22**, a highly functionalized intermediate that could provide access to the tetracyclic ring system of the kinamycins. Furthermore, the chemistry that was developed here may be amenable to asymmetric synthesis given that access to optically active material can be achieved by either the enzymatic resolution[30] of racemic allylic alcohol **2** or the chiral reduction[31] of cyclohexenone **1**. Studies toward the conversion of **22** into benzofluorenone **24** and kinamycin F are currently in progress.

Experimental Section

General Methods: All commercially available chemicals were used without further purification. All reactions were performed under argon with dry solvents under anhydrous conditions, unless otherwise noted. Tetrahydrofuran, diethyl ether (Et_2O), dichloromethane (CH_2Cl_2), acetonitrile (CH_3CN), dimethylformamide, and dimethyl sulfoxide were purchased in anhydrous form and used without further purification. Air- and moisture-sensitive liquids were transferred with a syringe. Organic solutions were concentrated by rotary evaporation at 40 °C. Flash column chromatography was performed with silica gel 60 (230–400 mesh) as described by Still et al.[32] Thin layer chromatography was performed with precoated silica gel 60 F254 plates, and the eluent is reported in parenthesis. TLC plates were visualized by exposure to ultraviolet light (UV) and/or submersion into aqueous potassium permanganate solution ($KMnO_4/H_2SO_4$) followed by heating. Infrared spectra were recorded with a Shimadzu 8400S FTIR spectrometer. The ^1H NMR spectroscopic data were recorded with a 250 or 400 MHz Bruker Avance FT-NMR spectrometer. The ^{13}C NMR spectroscopic data

were recorded at 62.9 MHz. Distortionless enhancement by polarization transfer spectra [DEPT (135)] were recorded at 62.9 MHz. The ^{13}C NMR and the DEPT (135) data are combined and represented in the order of chemical shift, carbon type obtained from DEPT (135) experiments. The ^{1}H-^{1}H NOESY spectroscopic data were recorded with a 500 MHz Bruker Avance FT-NMR spectrometer. Chemical shifts are reported in ppm relative to the solvent signal. Multiplicity is indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br. (broad), dd (doublet of doublets), and ddd (doublet of doublets of doublets). ESI (electrospray ionization) mass spectra were recorded with an Agilent 1100 Series LC/MSD instrument. High resolution mass spectra were obtained under electrospray ionization conditions with a Thermo Scientific LC–MS/linear trap quadrupole (LTQ)-Orbitrap mass spectrometer.

Diol 4: A solution of epoxy alcohol **3** (5.4 g, 42.0 mmol) in CH_2Cl_2 (90 mL) was treated with $Ti(OiPr)_4$ (22.5 mL, 75.6 mmol), and the reaction mixture was stirred at room temperature overnight. The solvent was evaporated under reduced pressure, and the resulting residue was dissolved in Et_2O (80 mL) followed by the addition of water (50 mL). A white precipitate was formed, which was treated in an ice bath with concentrated HCl dropwise until it gradually dissolved, resulting in two clear phases. The ether phase was separated, and the remaining aqueous phase was extracted with EtOAc (3 × 60 mL). The combined organic phases were washed with brine (60 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, from 1:4 to 1:2) afforded diol **4** (3.44 g, 64%) as a pale yellow oil; R_f = 0.28 (hexane/EtOAc, 1:1; $KMnO_4$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.56 (m, 1 H), 3.93 (d, J = 3.6 Hz, 1 H), 3.76 (m, 1 H), 2.20–1.95 (br. s, 4 H), 1.81 (d, J = 1.7 Hz, 3 H), 1.70 (m, 2 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 133.7 (C), 125.7 (CH), 70.3 (CH), 69.8 (CH), 25.6 (CH_2), 24.0 (CH_2), 20.9 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 3369, 3032, 2937, 2914, 2881, 2839, 1647, 1444 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_7H_{12}O_2Na$ $[M + Na]^+$ 151.0730; found 151.0721.

Ketal 5: To a solution of diol **4** (467 mg, 3.64 mmol) in CH_2Cl_2 (15 mL) were added 4-methoxybenzaldehyde dimethyl acetal (1.2 mL, 7.2 mmol) and pyridinium *p*-toluenesulfonate (92 mg, 0.37 mmol). The reaction mixture was stirred at room temperature for 1 h and then diluted with water (10 mL). The resulting solution was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:4) afforded ketal **5** (833 mg, 94%) as a colorless oil; R_f = 0.58 (hexane/EtOAc, 4:1; UV, $KMnO_4$). ^{1}H NMR (250 MHz, CD_3OD, mixture of diastereomers): δ = 7.39 (d, J = 8.7 Hz, 2 H), 6.93 (d, J = 8.8 Hz, 2 H), 5.82 (s, 0.3 H), 5.79 (s, 0.7 H), 4.59–4.31 (m, 2 H), 3.81 (s, 3 H), 2.31–1.85 (m, 4 H), 1.80 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, CD_3OD, mixture of diastereomers): δ = 162.0 (C), 161.9 (C), 133.1 (C), 132.3 (C), 132.0 (C), 131.5 (C), 129.6 (CH), 129.1 (CH), 128.4 (CH), 126.7 (CH), 114.6 (CH), 104.8 (CH), 104.7 (CH), 103.4 (CH), 77.3 (CH), 77.0 (CH), 76.0 (CH), 75.5 (CH), 55.7 (CH_3), 53.1 (CH_3), 26.9 (CH_2), 26.4 (CH_2), 22.0 (CH_2), 21.4 (CH_2), 20.7 (CH_3), 20.3 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 3005, 2934, 2918, 2839, 1643, 1614, 1589, 1516 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{15}H_{18}O_3Na$ $[M + Na]^+$ 269.1148; found 269.1148.

Cyclohexenols 6a and 6b: A solution of ketal **5** (3.22 g, 13.0 mmol) in CH_2Cl_2/hexane (1:10, 90 mL) at –78 °C was treated dropwise with diisobutylaluminium hydride (1.0 M in hexanes, 78 mL, 78.0 mmol). The reaction mixture was gradually warmed to 0 °C over a period of 2 h and then carefully quenched with acetone (10 mL) and methanol (10 mL). The resulting mixture was stirred vigorously at room temperature and then filtered through a Celite pad. The filtrate was concentrated under reduced pressure, and the resulting oil was dissolved in EtOAc (80 mL). The resulting solution was then washed with water (70 mL). The aqueous phase was extracted with EtOAc (4 × 60 mL), and the combined organic layers were washed with brine (70 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:6) afforded an inseparable mixture of regioisomeric alcohols **6a** and **6b** (**6a/6b**, 5:1; 2.32 g, 72%) as a colorless oil; R_f = 0.38 (hexane/EtOAc, 4:1; UV, $KMnO_4$). Data for alcohol **6a**: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.30 (d, J = 8.5 Hz, 2 H), 6.89 (d, J = 8.6 Hz, 2 H), 5.55 (s, 1 H), 4.65 (ABq, J = 11.2 Hz, 2 H), 3.93 (br. s, 1 H), 3.81 (s, 4 H), 2.34 (br. s, 1 H), 2.16 (br. s, 1 H), 2.04–1.83 (m, 1 H), 1.73 (s, 3 H), 1.68–1.59 (m, 2 H) ppm. IR (film): $\tilde{\nu}_{max}$ = 3421, 3036, 2999, 2934, 2914, 2876, 2842, 1639, 1612, 1585, 1514 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{15}H_{20}O_3Na$ $[M + Na]^+$ 271.1305; found 271.1303.

Triol 7a: To a solution of alcohols **6a** and **6b** (1.31 g, 5.3 mmol) in acetone/H_2O (6:1, 40 mL) were added *N*-methylmorpholine-*N*-oxide (931 mg, 7.94 mmol) and 4% aqueous OsO_4 (1.65 mL, 0.2 mmol). The reaction mixture was stirred at room temperature for 18 h and then concentrated to a reduced volume (10 mL), which was diluted with water (15 mL). The resulting solution was then extracted with EtOAc (4 × 40 mL). The combined organic layers were washed with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 3:1) afforded the desired triol **7a** (1.14 g, 76%) as a white solid; R_f = 0.23 (hexane/EtOAc, 1:3; UV, $KMnO_4$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.28 (d, J = 8.9 Hz, 2 H), 6.90 (d, J = 8.6 Hz, 2 H), 4.62 (ABq, J = 11.3 Hz, 2 H), 4.12 (m, 1 H), 3.81 (s, 3 H), 3.72 (m, 1 H), 3.58 (d, J = 3.3 Hz, 1 H), 2.13–1.99 (br. s, 3 H), 1.87–1.76 (m, 2 H), 1.74–1.58 (m, 2 H), 1.36 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 159.5 (C), 130.5 (C), 129.4 (CH), 114.1 (CH), 82.7 (CH), 74.8 (C), 73.5 (CH), 73.4 (CH_2), 67.6 (CH), 55.4 (CH_3), 25.4 (CH_2), 25.1 (CH_2), 23.1 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 3412, 2951, 2932, 2870, 1643, 1614, 1587, 1514 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{15}H_{22}O_5Na$ $[M + Na]^+$ 305.1359; found 305.1359.

Alcohol 8: A solution of triol **7a** (847 mg, 3.0 mmol) in CH_2Cl_2 (35 mL) was treated with 2,2-dimethoxypropane (737 μL, 6.0 mmol) and a catalytic amount of pyridinium *p*-toluenesulfonate (37 mg, 0.15 mmol). The reaction mixture was stirred at room temperature for 7 h and then quenched with water (10 mL). The resulting solution was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (20 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:6) afforded alcohol **8** (880 mg, 91%) as a pale yellow oil; R_f = 0.28 (hexane/EtOAc, 4:1; UV, $KMnO_4$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.30 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 4.78 (d, J = 11.6 Hz, 1 H), 4.58 (d, J = 11.6 Hz, 1 H), 4.04 (q, J = 3.0 Hz, 1 H), 3.99 (t, J = 2.8 Hz, 1 H), 3.81 (s, 3 H), 3.52 (d, J = 3.1 Hz, 1 H), 2.15–1.95 (m, 2 H), 1.90–1.80 (m, 1 H), 1.79–1.70 (m, 2 H), 1.42 (s, 3 H), 1.40 (s, 3 H), 1.38 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 159.4 (C), 130.8 (C), 129.5 (CH), 113.9 (CH), 107.5 (C), 82.8 (C), 81.7 (CH), 80.5 (CH), 72.2 (CH_2), 68.5 (CH), 55.4 (CH_3), 28.4 (CH_3), 27.4 (CH_3), 24.5 (CH_2), 20.5 (CH_3), 20.0 (CH_2) ppm. IR (film): $\tilde{\nu}_{max}$ = 3418, 2935, 1639 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{18}H_{26}O_5Na$ $[M + Na]^+$ 345.1672; found 345.1665.

Ketone 9: A solution of oxalyl chloride (1.1 mL, 9.9 mmol) in CH_2Cl_2 (20 mL) at –78 °C under argon was treated dropwise with DMSO (1.4 mL, 19.8 mmol) and then with alcohol **8** (800 mg, 2.48 mmol) as a solution (15 mL) in CH_2Cl_2/DMSO (3:1). After stirring at –78 °C for 15 min, the reaction mixture was treated with Et_3N (6.2 mL, 44.6 mmol) and gradually warmed to 0 °C over a period of 2 h. It was then quenched with water (20 mL), and the resulting solution was extracted with CH_2Cl_2 (3× 50 mL). The combined organic layers were washed with brine (20 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:8) afforded ketone **9** (670 mg, 84%) as a colorless oil; R_f = 0.33 (hexane/EtOAc, 4:1; UV, $KMnO_4$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.26 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 4.62 (d, J = 11.8 Hz, 1 H), 4.42 (d, J = 11.8 Hz, 1 H), 4.09 (t, J = 3.0 Hz, 1 H), 3.80 (s, 3 H), 3.76 (s, 1 H), 2.63–2.47 (m, 1 H), 2.36–2.16 (m, 3 H), 1.37 (s, 3 H), 1.33 (s, 3 H), 1.30 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 208.8 (C), 159.6 (C), 129.8 (CH), 129.5 (C), 113.9 (CH), 108.7 (C), 85.6 (C), 84.5 (CH), 79.0 (CH), 72.3 (CH_2), 55.4 (CH_3), 33.1 (CH_2), 27.5 (CH_3), 26.6 (CH_3), 23.3 (CH_2), 20.8 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 2984, 2934, 2880, 2837, 1724, 1637, 1612, 1585, 1514 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{18}H_{24}O_5Na$ $[M + Na]^+$ 343.1516; found 343.1516.

Cyclohexenone 10: A solution of ketone **9** (200 mg, 0.62 mmol) in CH_2Cl_2 (15 mL) was treated with Et_3N (522 µL, 3.7 mmol) and TMSOTf (340 µL, 1.9 mmol). The reaction mixture was stirred at room temperature for 1 h and then diluted with water (10 mL). The resulting solution was then extracted with CH_2Cl_2 (3× 20 mL). The combined organic layers were washed with brine (20 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude trimethylsilyl enol ether. The resulting enol ether was dissolved in DMSO (2 mL), and the solution was treated with $Pd(OAc)_2$ (14 mg, 0.06 mmol). The reaction mixture was degassed under vacuum and stirred at room temperature for 48 h under oxygen (balloon). It was then quenched with water (10 mL), and the solution was extracted with EtOAc (3× 10 mL). The combined organic layers were washed with brine (20 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:6) afforded cyclohexenone **10** (147 mg, 77%) as a colorless oil; R_f = 0.23 (hexane/EtOAc, 4:1; UV, $KMnO_4$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.31 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 6.76 (dd, J = 10.2, 4.4 Hz, 1 H), 6.12 (d, J = 10.2 Hz, 1 H), 4.83 (d, J = 11.9 Hz, 1 H), 4.63 (d, J = 11.9 Hz, 1 H), 4.45 (d, J = 4.5 Hz, 1 H), 4.16 (s, 1 H), 3.79 (s, 3 H), 1.42 (s, 3 H), 1.35 (s, 3 H), 1.29 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 197.4 (C), 159.6 (C), 140.1 (CH), 130.7 (CH), 130.1 (CH), 129.6 (C), 113.9 (CH), 110.8 (C), 83.7 (C), 82.2 (CH), 78.0 (CH), 73.0 (CH_2), 55.4 (CH_3), 28.0 (CH_3), 27.6 (CH_3), 19.6 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 3047, 2986, 2935, 2868, 2837, 1703, 1637, 1612, 1593, 1514 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{18}H_{22}O_5Na$ $[M + Na]^+$ 341.1359; found 341.1361.

Iodocyclohexenone 11: A solution of cyclohexenone **10** (140 mg, 0.44 mmol) in CH_2Cl_2 (2 mL) and pyridine (4 mL) was treated with I_2 (335 mg, 1.32 mmol). After stirring at room temperature for 18 h, the reaction mixture was quenched with water (4 mL) and aqueous $Na_2S_2O_3$ (3 mL), and the resulting mixture was then extracted with EtOAc (3× 20 mL). The combined organic layers were washed with brine (7 mL), dried with Na_2SO_4, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:6) afforded iodocyclohexenone **11** (170 mg, 87%) as a colorless oil; R_f = 0.40 (hexane/EtOAc, 4:1; UV, $KMnO_4$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.46 (d, J = 4.6 Hz, 1 H), 7.28 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.75 (d, J = 11.7 Hz, 1 H), 4.51 (d, J = 11.7 Hz, 1 H) 4.37 (d, J = 4.6 Hz, 1 H), 4.17 (s, 1 H), 3.79 (s, 3 H), 1.42 (s, 3 H), 1.37 (s, 3 H), 1.26 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 191.4 (C), 159.7 (C), 149.5 (CH), 130.2 (CH), 129.0 (C), 114.0 (CH), 111.4 (C), 105.0 (C), 83.5 (C), 81.0 (CH), 79.6 (CH), 73.0 (CH_2), 55.4 (CH_3), 28.0 (CH_3), 27.9 (CH_3), 20.2 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 3038, 2986, 2934, 2868, 2835, 1711, 1612, 1585, 1514 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{18}H_{20}IO_5$ $[M – H]^+$ 443.0361; found 443.0364.

Hydroxy Ketone 13: A biphasic solution of iodocyclohexenone **11** (25 mg, 0.056 mmol) in CH_2Cl_2/H_2O (10:1, 3 mL) was treated with DDQ (19 mg, 0.08 mmol). The reaction mixture was stirred at room temperature for 18 h and then diluted with water (10 mL). The resulting solution was then extracted with CH_2Cl_2 (3× 10 mL). The combined organic layers were washed with aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:8) afforded hydroxyketone **13** (13 mg, 72%) as a pale yellow oil; R_f = 0.20 (hexane/EtOAc, 4:1; UV, $KMnO_4$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.61 (d, J = 5.2 Hz, 1 H), 4.66 (s, 1 H), 4.41 (d, J = 5.2 Hz, 1 H), 3.26 (br. s, 1 H), 1.58 (s, 3 H), 1.45 (s, 3 H), 1.26 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 193.6 (C), 148.8 (CH), 111.8 (C), 103.1 (C), 83.8 (C), 79.8 (CH), 77.4 (CH), 28.2 (CH_3), 27.3 (CH_3), 18.0 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 3582, 1703, 1601, 1551 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{10}H_{13}IO_4Na$ $[M + Na]^+$ 346.9751; found 346.9746.

Cyclohexene-*trans*-diol 15: A solution of hydroxyketone **13** (18 mg, 0.055 mmol) and $Me_4NBH(OAc)_3$ (71 mg, 0.27 mmol) in CH_3CN (2 mL) at –20 °C was treated with acetic acid (500 µL). The reaction mixture was gradually warmed and stirred at room temperature overnight. It was then quenched with aqueous $NaHCO_3$ (5 mL), and the resulting mixture was extracted with CH_2Cl_2 (3× 15 mL). The combined organic layers were washed with brine (10 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:3) afforded diol **15** (13 mg, 72%) as a colorless oil; R_f = 0.18 (hexane/EtOAc, 2:1; UV, $KMnO_4$). ^1H NMR (250 MHz, $CDCl_3$): δ = 6.56 (dd, J = 4.7, 1.2 Hz, 1 H), 4.14 (d, J = 4.6 Hz, 1 H), 3.93 (d, J = 8.2 Hz, 1 H), 3.87 (d, J = 8.1 Hz, 1 H), 2.71 (br. s, 2 H), 1.49 (s, 3 H), 1.41 (s, 3 H), 1.32 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 133.9 (CH), 110.8 (C), 109.2 (C), 81.4 (C), 80.0 (CH), 75.7 (CH), 74.7 (CH), 28.7 (CH_3), 27.3 (CH_3), 18.0 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 3418, 2933, 1643, 1637, 1439, 1379 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{10}H_{15}IO_4Na$ $[M + Na]^+$ 348.9907; found 348.9903.

Diacetate 16: A solution of diol **15** (8 mg, 0.025 mmol), N*i*Pr_2Et (9 µL, 0.05 mmol), acetic anhydride (12 µL, 0.125 mmol), and a catalytic amount of DMAP in CH_2Cl_2 (1 mL) was stirred at room temperature overnight. The reaction mixture was diluted with water (3 mL) and a few drops of HCl (1 N solution), and the resulting solution was then extracted with CH_2Cl_2 (3× 10 mL). The combined organic layers were washed with brine (10 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:6) afforded diacetate **16** (8.2 mg, 80%) as a colorless oil; R_f = 0.33 (hexane/EtOAc, 4:1; UV, $KMnO_4$). ^1H NMR (250 MHz, $CDCl_3$): δ = 6.67 (dd, J = 5.3, 1.8 Hz, 1 H), 5.48 (ddd, J = 9.0, 1.8, 0.8 Hz, 1 H), 5.42 (d, J = 9.0 Hz, 1 H), 4.12 (dd,

J = 5.3, 0.8 Hz, 1 H), 2.13 (s, 3 H), 2.08 (s, 3 H), 1.51 (s, 3 H), 1.38 (s, 6 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 169.9 (C), 169.8 (C), 135.4 (CH), 111.2 (C), 103.2 (C), 80.1 (CH), 79.9 (C), 73.5 (CH), 73.2 (CH), 28.0 (CH_3), 27.2 (CH_3), 21.1 (CH_3), 21.0 (CH_3), 18.1 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 2982, 2935, 2866, 1755, 1634, 1454, 1435, 1377, 1232, 1215 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{14}H_{19}IO_6Na$ [M + Na]$^+$ 433.0119; found 433.0123.

Benzyloxynaphthoquinone 19: To a solution of hydroxynaphthoquinone **18** (258 mg, 0.88 mmol) in CH_2Cl_2 (12 mL) were added *p*-methoxybenzyl chloride (239 μL, 1.76 mmol) and freshly prepared Ag_2O[33] (204 mg, 0.88 mmol). After stirring at room temperature overnight, the reaction mixture was filtered through a Celite pad, and the resulting filtrate was concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:5) afforded naphthoquinone **19** (233 mg, 64%) as a yellow oil; R_f = 0.35 (hexane/EtOAc, 4:1; UV). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.81 (d, J = 7.5 Hz, 1 H), 7.60 (t, J = 8.3, 7.8 Hz, 1 H), 7.46 (d, J = 8.5 Hz, 2 H), 7.33 (d, J = 8.5 Hz, 1 H), 6.94 (d, J = 8.5 Hz, 2 H), 5.87 (m, 1 H), 5.26 (dd, J = 14.5, 1.5 Hz, 1 H), 5.23 (s, 2 H), 5.13 (dd, J = 10.0, 1.5 Hz, 1 H), 3.82 (s, 3 H), 3.62 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 180.1 (C), 178.3 (C), 159.6 (C), 159.2 (C), 150.8 (C), 136.8 (C), 134.8 (CH), 133.5 (C), 132.0 (CH), 130.2 (C), 128.6 (CH), 128.0 (C), 120.7 (CH), 120.3 (CH), 118.2 (CH_2), 114.3 (CH), 71.1 (CH_2), 55.4 (CH_3), 35.8 (CH_2) ppm. IR (film): $\tilde{\nu}_{max}$ = 1672, 1607, 1585, 1550, 1514 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{21}H_{17}{}^{79/81}BrO_4Na$ [M + Na]$^+$ 435.0202/437.0182; found 435.0207/437.0187.

Bromonaphthalene 20: To a solution of naphthoquinone **19** (122 mg, 0.29 mmol) in EtOAc (3 mL) and Et_2O (8 mL) was added $Na_2S_2O_4$ (308 mg, 1.77 mmol) in water (10 mL). After stirring at room temperature for 30 min, the biphasic reaction mixture was extracted with EtOAc (3× 20 mL). The combined organic layers were washed with brine (15 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude hydroquinone as a yellow oil. A solution of the resulting hydroquinone in DMF (4 mL) was treated with K_2CO_3 (269 mg, 1.95 mmol) followed by the addition of MeI (110 μL, 1.77 mmol). The reaction mixture was stirred at room temperature overnight and then diluted with water (10 mL). The resulting solution was then extracted with EtOAc (3× 15 mL). The combined organic layers were washed with brine (15 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:20) afforded bromonaphthalene **20** (64 mg, 50%) as a yellow oil; R_f = 0.60 (hexane/EtOAc, 4:1; UV). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.73 (d, J = 8.3 Hz, 1 H), 7.47 (d, J = 8.5 Hz, 2 H), 7.39 (t, J = 8.1 Hz, 1 H), 6.99 (d, J = 7.8 Hz, 1 H), 6.95 (d, J = 8.5 Hz, 2 H), 6.06 (m, 1 H), 5.13 (s, 2 H), 5.11 (dd, J = 11.0, 1.0 Hz, 1 H), 5.02 (dd, J = 17.0, 1.3 Hz, 1 H), 3.95 (s, 3 H), 3.84 (s, 3 H), 3.79 (d, J = 5.7 Hz, 2 H), 3.66 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 159.6 (C), 155.5 (C), 151.6 (C), 149.8 (C), 136.5 (CH), 130.7 (C), 129.9 (C), 129.6 (CH), 129.1 (C), 126.8 (CH), 120.7 (C), 117.7 (C), 115.8 (CH_2), 115.5 (CH), 114.1 (CH), 109.0 (CH), 71.6 (CH_2), 63.3 (CH_3), 61.3 (CH_3), 55.4 (CH_3), 34.5 (CH_2) ppm. IR (film): $\tilde{\nu}_{max}$ = 3011, 2961, 2930, 1637, 1560, 1515 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{23}H_{24}{}^{79/81}BrO_4$ [M + H]$^+$ 443.0852/445.0832; found 443.0863/445.0845.

Bromonaphthaldehyde 21: A solution of *t*BuOK (1.0 M in THF, 190 μL, 0.19 mmol) in THF (500 μL) at 0 °C was treated dropwise with a solution (2 mL) of bromonaphthalene **20** (42 mg, 0.095 mmol) in THF/DMSO (1:8). After stirring for 2 min, the reaction mixture was diluted with water (4 mL), and the resulting solution was extracted with EtOAc (3× 10 mL). The combined organic layers were washed with brine (10 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude isomerized bromonaphthalene, which was used directly without any further purification. A solution of the resulting bromonaphthalene in THF/H_2O (2:1, 3 mL) was treated with 4% aqueous OsO_4 (0.16 M solution, 6 μL, 0.001 mmol) and $NaIO_4$ (49 mg, 0.23 mmol). The reaction mixture was stirred at room temperature overnight and then diluted with water (4 mL). The resulting solution was then extracted with EtOAc (3× 15 mL). The combined organic layers were washed with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, 1:8) afforded bromonaphthaldehyde **21** (26 mg, 64%) as a pale yellow oil; R_f = 0.33 (hexane/EtOAc, 4:1; UV). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 10.5 (s, 1 H), 7.75 (d, J = 8.4 Hz, 1 H), 7.58 (t, J = 8.1 Hz, 1 H), 7.46 (d, J = 8.6 Hz, 2 H), 7.07 (d, J = 7.8 Hz, 1 H), 6.96 (d, J = 8.6 Hz, 2 H), 5.16 (s, 2 H), 3.96 (s, 3 H), 3.84 (s, 3 H), 3.28 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 190.9 (CH), 159.8 (C), 159.1 (C), 157.1 (C), 150.6 (C), 134.1 (C), 130.5 (CH), 129.6 (CH), 128.4 (C), 125.2 (C), 120.3 (C), 115.5 (CH), 114.2 (CH), 111.4 (C), 109.2 (CH), 71.5 (CH_2), 65.5 (CH_3), 61.4 (CH_3), 55.5 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 3005, 2934, 2839, 1691, 1645, 1612, 1551, 1514, 1441, 1366, 1250, 1047 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{21}H_{19}{}^{79/81}BrO_5Na$ [M + Na]$^+$ 453.0308/455.0288; found 453.0302/455.0279.

α-Naphthylcyclohexenone 22: A solution of iodocyclohexenone **11** (14 mg, 0.032 mmol) in DMSO (500 μL) at room temperature was treated with CuI (2.3 mg, 0.012 mmol), $Pd_2(dba)_3$ (2.8 mg, 0.003 mmol), and Cu (20 mg, 0.31 mmol) followed by the dropwise addition of a solution of bromonaphthaldehyde **21** (20 mg, 0.046 mmol) in DMSO (500 μL). The reaction mixture was heated at 65 °C for 2 h and then filtered through a Celite pad. The resulting filtrate was diluted with EtOAc (10 mL), and the resulting solution was washed with water (10 mL). The organic phase was separated, and the aqueous phase was extracted with EtOAc (3× 10 mL). The combined organic layers were washed with brine (10 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product. Purification by flash chromatography on silica gel (EtOAc/hexane, from 1:10 to 1:2) afforded compound **22** (13 mg, 62%) as a yellow oil; R_f = 0.28 (hexane/EtOAc, 2:1; UV). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.47 (s, 1 H), 7.78 (d, J = 8.2 Hz, 1 H), 7.60 (t, J = 8.1, 8.2 Hz, 1 H), 7.53 (d, J = 8.6 Hz, 2 H), 7.48 (d, J = 8.6 Hz, 2 H), 7.09 (d, J = 7.8 Hz, 1 H), 6.97 (d, J = 8.6 Hz, 2 H), 6.89 (d, J = 8.6 Hz, 2 H), 6.56 (d, J = 4.7 Hz, 1 H), 5.19 (s, 2 H), 5.05 (s, 1 H), 4.92 (d, J = 11.8 Hz, 1 H), 4.63 (d, J = 4.9 Hz, 1 H), 4.62 (d, J = 11.8 Hz, 1 H), 3.85 (s, 3 H), 3.80 (s, 6 H), 3.67 (s, 3 H), 1.44 (s, 3 H), 1.43 (s, 3 H), 1.26 (s, 3 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 198.0 (C), 190.8 (CH), 161.5 (C), 159.8 (C), 159.4 (C), 156.9 (C), 151.7 (C), 138.9 (C), 135.0 (C), 133.4 (CH), 130.7 (CH), 130.6 (CH), 130.5 (C), 129.6 (CH), 128.4 (C), 124.3 (C), 123.2 (C), 120.9 (C), 115.9 (CH), 114.2 (CH), 113.8 (CH), 110.5 (C), 109.6 (CH), 83.1 (CH), 78.8 (CH), 78.1 (C), 72.7 (CH_2), 71.5 (CH_2), 66.0 (CH_3), 62.0 (CH_3), 55.5 (CH_3), 27.7 (CH_3), 27.1 (CH_3), 19.1 (CH_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 2993, 2934, 2839, 1709, 1674, 1610, 1570, 1551, 1514 cm^{-1}. HRMS (ESI-LTQ): calcd. for $C_{39}H_{40}O_{10}Na$ [M + Na]$^+$ 691.2514; found 691.2513.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra for all new compounds (**4–11**, **13**, **15**, **16**, and **19–22**) and NOESY spectrum for **16**.

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