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Synthesis of a Key Precursor for Orienticin C and Model Study on Ruthenium-Mediated Macrocyclization

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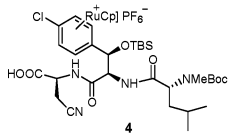

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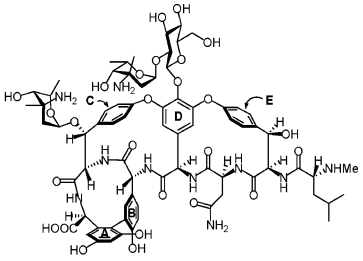
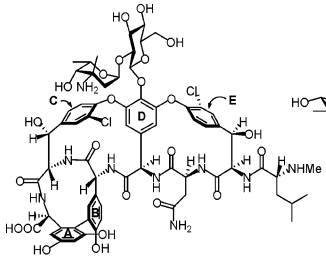


2 Orienticin C

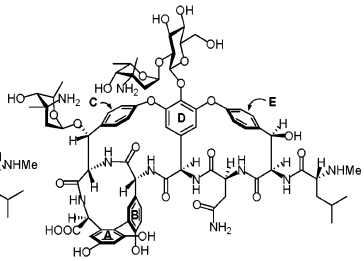
A tripeptido−arene−ruthenium complex was prepared as a key precursor for the projected synthesis of orienticin C, demonstrating that the cyclopentadienylruthenium moiety can be attached to a chloroarene in the presence of multiple functionality. The ruthenium-mediated intramolecular S_NAr reaction for formation of the required diaryl ether linkage was successfully tested on a model system.

Vancomycin-related glycopeptides constitute a large family of clinically important antibiotics, used as drugs of last resort in treating infections caused by methicillin-resistant *Staphylococcus aureus*.[1] However, the frequency of vancomycin resistant pathogens has increased significantly over the past decade,[2] prompting an interest in the development of synthetic and semisynthetic glycopeptides.[3]

Members of the vancomycin family have a complex rigid molecular architecture with a heptapeptide backbone structure, synthetically challenging components, and numerous stereocenters.[4] Orienticin C (**2**) is structurally similar to vancomycin (**1**), having one extra vancosamine unit and lacking the chloro-substituents on the C and E aromatic rings, which gives orienticin C the name bis-dechlorovancomycin, also known as A82846C. A key structural element for the vancomycin-type molecules is the diaryl ether, and a variety of approaches have been developed for construction of this type of linkage.[5] Total syntheses of the aglycones of vancomycin,[6] orienticin C,[7] and the related antibiotics teicoplanin[8] and ristocetin A[9] have been reported, and a total synthesis of the full vancomycin structure has been accomplished.[10]



1 Vancomycin



2 Orienticin C

Our group has investigated ruthenium-mediated S_NAr methodology as a general approach for construction of diaryl ethers, and this methodology was successfully applied for construction of an intermediate **3** representing the ABCD ring system of orienticin C (and ristocetin A).[11] For this to be applied in a synthesis of orienticin C, a chloroarene−ruthenium complex **4**

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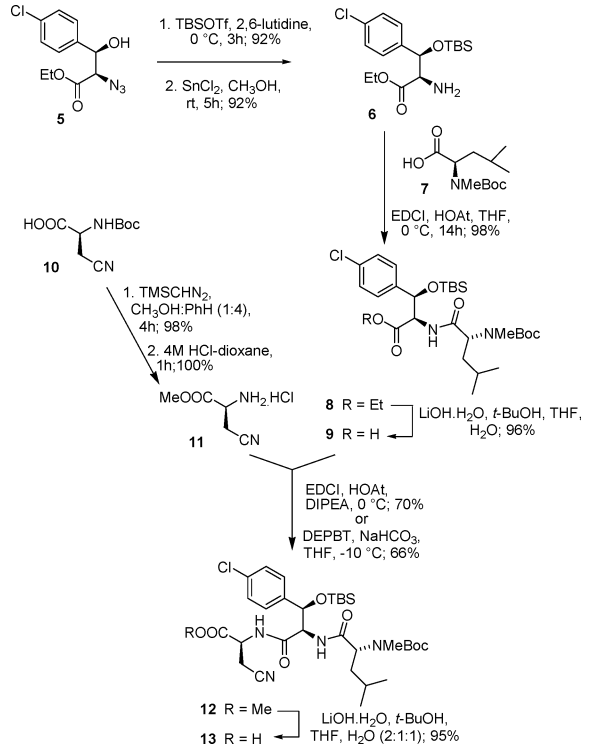
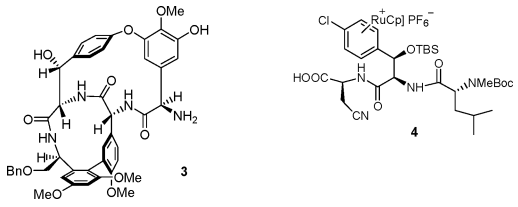
SCHEME 1. Synthesis of Tripeptide Acid 13

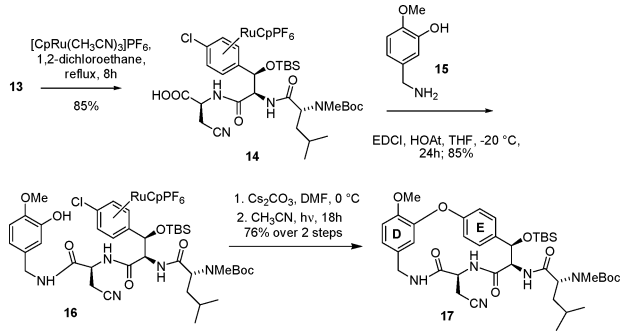


is required. Connecting **3** and **4** and further elaboration would afford the orienticin C core structure. However, ruthenium attachment to an advanced polyfunctional peptido-arene of this type has not yet been investigated. Here we describe the synthesis of **4** as well as a model study on its use in macrocyclization that is needed for the orienticin C synthesis. This approach offers maximum recycling potential for the use of ruthenium, because the metal moiety is not carried through a multistep sequence. The cyclopentadienyl-ruthenium moiety is attached to and removed from the aromatic ring under noninvasive conditions and provides a convenient temporary activator for the S_NAr chemistry that is required for aryl ether construction.



Construction of **4** involves elaboration of a tripeptide from the corresponding amino acids via standard peptide coupling reactions. One of the required amino acids is the arylserine derivative **6**, which was obtained from the azide **5** already prepared in our laboratory (Scheme 1).[12] Protection of the free alcohol **5**, as its TBS derivative, followed by reduction of the azide functional group[13] furnished the desired amine **6** in 92% overall yield. Coupling **6** with D-*N*-Boc-*N*-methylleucine (**7**), using EDCI and HOAt as coupling reagents at 0 °C, afforded

SCHEME 2. Synthesis of 16-Membered Macrocycle



the dipeptide **8** in nearly quantitative yield with no detectable epimerization at the chiral centers. Hydrolysis of the ethyl ester dipeptide **8** provided subunit **9** with minimal epimerization (ca. 5% by NMR).

The third amino acid needed is an asparagine derivative, *N*-Boc-*β*-cyanoalanine, obtained from commercially available L-*N*-Boc-asparagine via amide dehydration, following a known procedure.[14] Evans[15] has used the nitrile as a latent carboxamide of asparagine in his studies toward the vancomycin family of glycopeptides, and also, Boger[6c] has exploited the same protected asparagine in his total synthesis of vancomycin aglycone. Carboxylic acid **10** was protected as its methyl ester derivative by treatment with $TMSCHN_2$ in methanol−benzene mixture (1:4) at room temperature.[14] Removal of the Boc protecting group, using 4 M HCl in dioxane at room temperature, furnished the desired building block **11** in quantitative yield. Coupling this intermediate with dipeptide **9** was then investigated. After screening different reaction conditions, the best result was obtained by using EDCI and HOAt as coupling reagents, and DIPEA as a base, to afford **12**, which was then hydrolyzed to carboxylic acid **13** under standard conditions.

Ruthenium complexation of **13** followed the standard reaction procedure, wherein the tripeptide acid was treated with $[CpRu(CH_3CN)_3]PF_6$ in 1,2-dichloroethane under reflux conditions for 8 h to afford complex **14** in 85% yield (Scheme 2). Importantly, this demonstrates that the complexation reaction is not compromised by the multiple functionality of this molecule. With this complex in hand, we tested the ruthenium-mediated S_NAr reaction for construction of the biaryl ether linkage on a model system **16**, whose synthesis is shown in Scheme 2. The ruthenium tripeptide **14** was treated with the amine **15** and the peptide coupling reagents EDCI and HOAt to afford the pseudotetrapeptide ruthenium complex **16** in 85% yield. According to NMR analysis, a demetalated pseudotetrapeptide was formed as a byproduct in this reaction but only in 5% yield, and this is consistent with TLC observation, which showed formation of a less polar product. It could be formed by in situ demetalation of the ruthenium pseudotetrapeptide **16** and/or demetalation of ruthenium tripeptide acid **14** that then underwent peptide coupling. The macrocyclization proceeded smoothly in the presence of Cs_2CO_3 as base, and demetalation of the product was achieved by irradiating an acetonitrile solution of the ruthenium complex with UV light (Rayonet apparatus) for 18

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h. The desired product **17** was obtained in 76% yield over two steps and was easily characterized by ^{1}H NMR, which shows a characteristic pattern where one of the D-ring aromatic protons is shifted upfield relative to the others due to the shielding effect of the neighboring E-phenyl ring.[16] The minor product present in the reaction mixture was uncyclized demetalated starting material.

In conclusion, an arene−tripeptide complex was prepared as a key building block for the synthesis of orienticin C, followed by further conversion to a ruthenium complex on which the metal-driven S_NAr reaction was applied to afford the diaryl ether linkage, thus demonstrating the feasibility of using this methodology for synthesis of orienticin C, a member of the vancomycin class of antibiotics.

Experimental Section

Dipeptide (8). A solution of **6** (189.1 mg, 0.532 mmol, 1.0 equiv) and D-*N*-Boc-*N*-methylleucine (**7**) (130.7 mg, 0.532 mmol, 1.0 equiv) in anhydrous THF (10 mL) was cooled to 0 °C. HOAt (343.9 mg, 1.758 mmol, 3.3 equiv) and EDCI (221.9 mg, 1.598 mmol, 3.0 equiv) were added, and the resulting mixture was stirred vigorously for 14 h. H_2O (5 mL) was added at 0 °C, and after 15 min, the aqueous phase was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with aqueous saturated $NaHCO_3$ solution (3 × 3 mL), H_2O (5 mL), brine (5 mL), dried (Na_2SO_4), and concentrated, and the residue was purified by flash column chromatography (15% EtOAc/hexanes) to give the product **8** (306 mg) as a pale-yellow foam, (98% yield). R_f = 0.35 (15% EtOAc/hexanes). $[\alpha]^{25}_D$ +22 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35−7.30 (4H), 5.20−4.96 (br, 1H), 4.69 (d, 1H, J = 7.6 Hz), 4.59 (br, 1H), 4.17 (q, 2H, J = 7.2 Hz), 2.60−2.40 (br, 3H), 1.60−1.30 (br, 12H), 1.26 (t, 3H, J = 7.2 Hz), 0.91 (dd, 6H, J = 8.4, 6.4 Hz), 0.85 (s, 9H), 0.05 (s, 3H), −0.18 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.4, 171.2, 157.6, 140.5, 134.8, 129.7, 129.3, 81.5, 75.5, 62.4, 60.0, 56.7, 38.1, 30.0, 28.7, 26.3, 26.1, 25.8, 23.4, 22.1, 18.8, 14.4, −4.4, −4.9. FABHRMS (*m*/*z*) [M H$^+$] calcd for ($C_{29}H_{50}ClN_2O_6Si$) 585.3127, found 585.3107.

Dipeptide Acid (9). A solution of ethyl ester **8** (276 mg, 0.472 mmol, 1.0 equiv) in THF (1.2 mL) was cooled to 0 °C, and then a mixture of 2:1 *t*-BuOH:H_2O (2.4 mL *t*-BuOH, 1.2 mL H_2O) was added. This solution was treated with LiOH·H_2O (70.6 mg, 0.943 mmol, 2.0 equiv) and stirred for 10 h. When the reaction was complete, the pH of the solution was adjusted to 3 by the dropwise addition of 6 N HCl solution, the reaction mixture was diluted with EtOAc (5 mL), and the layers were separated. The resulting aqueous phase was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (3 × 3 mL), H_2O (5 mL), brine (10 mL), dried (Na_2SO_4), and then concentrated *in vacuo*. Flash chromatography (5% MeOH and 1% AcOH in CH_2Cl_2) afforded **9** (252.2 mg) as a white foam (96% yield). R_f = 0.3 (5% MeOH and 1% AcOH in CH_2Cl_2). $[\alpha]^{25}_D$ +20 (*c* 0.88, $CHCl_3$). ^{1}H NMR (CD_3OD, 400 MHz) δ 7.35−7.29 (4H), 5.30−5.15 (br, 1H), 4.78−4.70 (br, 1H), 4.70−4.58 (br, 1H), 2.80−2.60 (br, 3H), 1.78−1.44 (br, 12H), 0.94−0.87 (6H), 0.86 (s, 9H), 0.09 (s, 3H), −0.08 (s, 3H). ^{13}C NMR (CD_3OD, 100 MHz) δ 173.7, 172.5, 157.6, 140.6, 134.7, 129.7, 129.2, 82.09, 81.5, 75.5, 69.4, 60.4, 58.2, 56.9, 38.0, 31.1, 30.1, 28.6, 26.2, 25.8, 23.5, 22.0, 18.9, −4.6, −4.9. FABHRMS (*m*/*z*) [M H$^+$] calcd for ($C_{27}H_{46}ClN_2O_6Si$) 557.2814, found 557.2824.

Methyl β-Cyanoalanate Hydrochloride (11). To a solution of L-*N*-Boc-β-cyanoalanine (**10**) (658 mg, 3.07 mmol, 1.0 equiv) in benzene-CH_3OH (4:1, 15 mL) at room temperature was slowly added a solution of (trimethylsilyl)diazomethane (2.0 M in hexane, 2 mL, 4.0 mmol, 1.3 equiv), and the mixture was stirred at this temperature for 4 h. The reaction was quenched by adding glacial acetic acid (2 mL). The volatiles were removed *in vacuo*, and the residue was dissolved in CH_2Cl_2 (15 mL), washed with saturated aqueous $NaHCO_3$ (3 × 4 mL), H_2O (10 mL), brine (10 mL), dried (Na_2SO_4), and then concentrated *in vacuo*. Flash chromatography (40% EtOAc/hexanes) afforded the methyl ester (687 mg) as a white solid (98% yield). R_f = 0.35 (40% EtOAc/hexanes): mp = 80−82 °C; $[\alpha]^{25}_D$ +36 (*c* 1.7, $CHCl_3$). ^{1}H NMR (CD_3OD, 400 MHz) δ 4.46 (dd, 1H, J = 8.4, 5.2 Hz), 3.76 (s, 3H), 3.01 (dd, 1H, J_{AB} = 17.0, J_{AX} = 5.2 Hz), 2.90 (dd, 1H, J_{AB} = 17.0, J_{BX} = 8.4 Hz), 1.46 (s, 9H). ^{13}C NMR (CD_3OD, 100 MHz) δ 171.4, 157.5, 118.2, 81.1, 53.2, 51.5, 28.5, 21.1. FABHRMS (*m*/*z*) [MH$^+$] calcd for ($C_{10}H_{17}N_2O_4$) 229.1188, found 229.1191.

A solution of *N*-Boc-β-cyanoalanine methyl ester (687 mg, 3 mmol) in 4 M HCl−dioxane (30 mL) was stirred at room temperature for 1 h. The solvent is removed *in vacuo* to provide the product (498 mg, 100%) as a yellow oil. ^{1}H NMR (CD_3OD, 400 MHz) δ 4.51 (t, 1H, J = 6.0 Hz), 3.91 (s, 3H), 3.22 (ABX, 2H, J = 6.0, 4.0, 18.0 Hz). ^{13}C NMR (CD_3OD, 100 MHz) δ 168.2, 116.0, 54.5, 50.2, 19.7. FABHRMS (*m*/*z*) [MH$^+$] calcd for ($C_5H_{10}N_2O_2Cl$) 165.0431, found 165.0444.

Tripeptide (12). A solution of carboxylic acid **9** (338.3 mg, 0.607 mmol, 1.0 equiv) and amine hydrochloride **11** (100 mg, 0.607 mmol, 1.0 equiv) in THF (10 mL) was cooled to 0 °C, and after 15 min, DIPEA (0.22 mL, 1.214 mmol, 2.0 equiv) was added and the reaction mixture was stirred for 10 min. HOAt (276.8 mg, 2.003 mmol, 3.3 equiv) and EDCI (350.8 mg, 1.821 mmol, 3.0 equiv) were added, and the resulting mixture was stirred vigorously for 24 h. H_2O (5 mL) was added at 0 °C, and after 15 min, the aqueous phase was extracted with EtOAc (3 × 6 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (3 × 4 mL), H_2O (12 mL), brine (15 mL), dried (Na_2SO_4), and concentrated to give 283 mg (70% combined yield) of a mixture of two diastereomers (8:1 ratio by NMR analysis), which was further separated by flash column chromatography (30% EtOAc/hexanes): 252 mg of **12** (major product), as a yellowish foam and 31 mg of its epimer as a white foam. For the major isomer: R_f = 0.35 (30% EtOAc/hexanes). $[\alpha]^{25}_D$ + 31.3 (*c* 2.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36−7.31 (4H), 5.04 (d, 1H, J = 8 Hz), 4.70 (t, 2H, J = 6.4 Hz), 4.62−4.46 (br, 1H), 3.76 (s, 3H), 2.99 (d, 2H, J = 6.4 Hz), 2.50−2.40 (br, 3H), 1.54−1.40 (br, 12H), 0.90 (dd, 6H, J = 8.4, 6.4 Hz), 0.84 (s, 9H), 0.04 (s, 3H), −0.15 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.6, 171.7, 170.4, 140.5, 134.7, 130.0, 129.3, 129.1, 117.7, 75.0, 61.3, 59.8, 53.5, 50.3, 37.9, 29.9, 28.6, 26.2, 25.6, 23.5, 21.8, 20.9, 20.6, 18.8, 14.5, −4.4, −4.7. FABHRMS (*m*/*z*) [MH$^+$] calcd for ($C_{32}H_{52}ClN_4O_7Si$) 667.3294, found 667.3305. The minor product results from epimerization at the phenylalanine α-center (evident from the ^{1}H NMR *J* couplings) during the coupling reaction and was not fully characterized.

Tripeptide Acid (13). A solution of methyl ester **12** (159.3 mg, 0.238 mmol, 1.0 equiv) in THF (1.5 mL) was cooled to 0 °C, and a mixture of *t*-BuOH/H_2O (2:1, 4.5 mL) was added. This solution was treated with LiOH·H_2O (36 mg, 0.477 mmol) and stirred for 10 h. Upon completion, the pH of the solution was adjusted to 3 by the dropwise addition of 6 N HCl solution. EtOAc (6 mL) was added to the reaction mixture, and the layers were separated. The resulting aqueous phase was further extracted with EtOAc (3 × 3 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (3 × 3 mL), H_2O (6 mL), brine (10 mL), dried (Na_2SO_4), and then concentrated *in vacuo*. Flash chromatography (10% MeOH in CH_2Cl_2) afforded **13** (148 mg) as a white foam (95% yield). R_f = 0.3 (8% MeOH in CH_2Cl_2). $[\alpha]^{25}_D$ +47 (*c* 0.58, $CHCl_3$). ^{1}H NMR (CD_3OD, 400 MHz) δ 7.38−7.31 (4H), 5.09 (d, 1H, J = 7.2 Hz), 4.72 (d, 1H, J = 8 Hz), 4.64−4.58 (br, 1H), 4.51 (t, 1H, J = 5.6 Hz), 2.99 (d, 2H, J = 5.2 Hz), 2.58−2.42 (br, 3H),

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(17) Yoshikawa, S. Patent: JP11130739 A2, Jpn. Kokai Tokkyo Koho, 1999.

1.58−1.40 (br, 12H), 0.89 (dd, 6H, J = 4.8, 6.8 Hz), 0.84 (s, 9H), 0.05 (s, 3H), −0.15 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.6, 171.5, 157.6, 157.0, 140.6, 134.8, 130.1, 129.4, 118.3, 81.9, 81.5, 75.1, 60.3, 58.1, 56.9, 51.2, 37.9, 31.1, 29.9, 28.6, 26.3, 26.2, 25.7, 23.5, 21.4, 18.9, −4.5, −4.7. FABHRMS (m/z) [(M − H)Na_2^+] calcd for ($C_{31}H_{48}ClN_4O_7SiNa_2^+$) 697.2777, found 697.2784.

Ruthenium−Tripeptide Acid Complex (14). A solution of tripeptide acid **13** (94.2 mg, 0.144 mmol, 1.05 equiv) in dry 1,2-dichloroethane (20 mL) was degassed with argon at 60 °C for 1 h. [CpRu(CH_3CN)$_3$]PF_6 (62.62 mg, 0.137 mmol, 1.0 equiv) was added to the cooled solution, which was then heated under reflux (90 °C) for 8 h. The solution was cooled, and the solvent was removed under reduced pressure. The resulting solid was dried *in vacuo* to give the crude ruthenium complex, which was purified by flash chromatography (5−30% MeOH in CH_2Cl_2 gradient elution) to afford **14** (118 mg, 85%) as a white solid. $[\alpha]^{25}_D$ +2.6 (*c* 0.65, $CHCl_3$). ^{1}H NMR (CD_3OD, 400 MHz) δ 6.80 (d, 1H, J = 6.4 Hz), 6.69 (d, 1H, J = 6.0 Hz), 6.46 (d, 1H, J = 6.0 Hz), 6.32 (d, 1H, J = 5.2 Hz), 5.50 (s, 5H), 5.38−5.30 (br, 1H), 5.12−5.06 (br, 1H), 4.70 (dd, 2H, J = 5.2, 10.4 Hz), 4.44 (t, 1H, J = 5.6 Hz), 3.16−2.96 (2H), 2.85 (s, 3H), 1.44 (3H overlapped with s, 9H), 0.88 (6H overlapped with s, 9H), 0.35 (s, 3H), 0.20 (s, 3H). ^{13}C NMR (CD_3OD, 125 MHz) δ 174.1, 169.4, 157.7, 119.2, 118.9, 107.0, 106.5, 87.8, 85.3, 83.7, 81.3, 72.8, 60.2, 58.2, 57.1, 52.6, 52.1, 38.4, 30.7, 28.8, 26.5, 26.1, 23.4, 22.0, 21.8, 18.8, −3.8, −4.7. FABMS (m/z) [M − PF_6]$^+$ calcd for ($C_{36}H_{54}ClN_4O_7SiRu$) 819.2494, found 819.2500.

Pseudotetrapeptide (16). A solution of ruthenium complex **14** (18.5 mg, 0.019 mmol, 1.0 equiv) and amine **15**[16] (2.9 mg, 0.019 mmol) in THF (1.4 mL) was cooled to −20 °C. HOAt (8.7 mg, 0.063 mmol, 3.3 equiv) was added, and the reaction mixture was stirred for 30 min at this temperature. EDCI (11.11 mg, 0.0575 mmol, 3 equiv) was then added, and the reaction was run for 24 h. H_2O (2 mL) and CH_2Cl_2 (5 mL) were added at 0 °C, and after 10 min, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated, and the residue was first washed with diethyl ether in order to remove the organic material and purified by preparative TLC (25% MeOH in EtOAc) affording **16** (17.8 mg, 85%) as a white film. R_f = 0.3 (25% MeOH in EtOAc). $[\alpha]^{25}_D$ +10.4 (*c* 0.24, $CHCl_3$). ^{1}H NMR (CD_3OD, 400 MHz) δ 6.98−6.89 (3H), 6.72 (d, 1H, J = 5.6 Hz), 6.42 (dd, 2H, J = 5.6, 7.2 Hz), 5.49 (s, 5H), 5.15 (s, 2H), 5.08−5.02 (br, 1H), 4.84−4.76 (br, 1H), 4.70 (dd, 2H, J = 5.2, 10.4 Hz), 4.64−4.60 (br, 1H), 3.87 (s, 3H), 3.11 (dd, 1H, J_{AB} = 17.2, J_{AX} = 5.2 Hz), 3.01 (dd, 1H, J_{AB} = 17.2, J_{BX} = 8.0 Hz), 2.83 (s, 3H), 1.78 (t, 1H, 6.2 Hz) 1.49 (s, 9H), 0.94 (6H overlapped with s, 9H), 0.30 (s, 3H), 0.16 (s, 3H). ^{13}C NMR (CD_3OD, 125 MHz) δ 174.2, 170.6, 170.0, 158.0, 148.4, 147.5, 142.2, 135.6, 119.5, 118.1, 115.4, 112.5, 116.9, 87.7, 87.5, 85.4, 85.2, 83.9, 81.6, 72.6, 65.0, 60.6, 57.3, 56.4, 38.4, 30.9, 30.7, 28.7, 26.4, 26.1, 23.5, 21.7, 20.8, 18.9, −3.8, −4.6. FAB-HRMS (m/z) [MH − PF_6]$^+$ ($C_{44}H_{64}ClN_5O_8SiRu$) 955.3265, found 955.3250.

Diaryl Ether Macrocycle (17). To a solution of **16** (10 mg, 0.009 mmol, 1.0 equiv) in DMF (1.8 mL) at 0 °C was added Cs_2CO_3 (14.6 mg, 0.045 mmol, 5.0 equiv). The reaction mixture was stirred for 8 h at 0 °C and then at rt for 24 h. The mixture was then diluted with CH_2Cl_2 (5 mL), and the organic layer was washed with H_2O (3 mL), brine (5 mL), dried (Na_2SO_4), and concentrated. The residue was dissolved in CH_3CN (4.5 mL) and degassed for 1 h. The solution was photolyzed for 18 h in a Rayonet photoreactor (350 nm). The reaction mixture was filtered through a Celite pad and purified by PTLC (0.5 mm, 40% EtOAc/hexanes) to afford 5.2 mg of **17** (76% yield over two steps). R_f = 0.3 (40% EtOAc/hexanes); $[\alpha]^{25}_D$ + 15.2 (*c* 0.6, $CHCl_3$) ^{1}H NMR (CD_3OD, 400 MHz) δ 7.36−7.18 (2H), 7.12−6.99 (1H), 6.92−6.78 (2H), 6.01 (d, 1H, J = 2.0 Hz), 5.57 (d, 1H, J = 4.4 Hz), 5.12 (d, 1H, J = 5.6 Hz), 5.16 (d, 1H, J = 7.2 Hz), 5.01 (d, 1H, J = 4.8 Hz), 4.70 (d, 1H, J = 6.6 Hz), 4.52 (s, 2H), 3.93 (s, 3H), 2.97 (d, 2H, J = 6.4 Hz), 2.88 (s, 3H), 1.56−1.48 (3H), 1.45 (s, 9H), 0.92 (6H, overlapping s, 9H,), 0.13 (s, 3H), 0.10 (s, 3H). ^{13}C NMR (CD_3OD, 100 MHz) δ 179.5, 174.3, 172.0, 171.5, 157.8, 150.2, 142.7, 140.6, 134.8, 129.3, 120.9, 118.3, 114.5, 81.9, 81.5, 75.1, 68.5, 62.3, 60.3, 58.1, 56.9, 51.2, 37.9, 31.1, 29.6, 28.6, 26.3, 26.2, 25.7, 23.5, 21.8, 21.4, 18.9, −4.4, −4.7. HRMS was not determined (the compound appears to be unexpectedly unstable and undergoes considerable degradation on standing in CD_3OD solution).

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Supporting Information Available: Copies of NMR spectra for all new compounds and details for the preparation of **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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