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Synthesis of Spirocyclic *C*-Arylglycosides and -Ribosides by Ruthenium-Catalyzed Cycloaddition

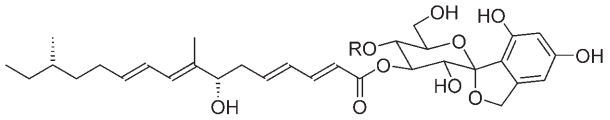
Yoshihiko Yamamoto,*[a] Ken Yamashita,[a] Tomitaka Hotta,[a] Toru Hashimoto,[b] Makoto Kikuchi,[b] and Hisao Nishiyama[b]

Abstract: Spirocyclic *C*-arylglycosides were synthesized from the appropriately protected δ-gluconolactones. Addition of lithium acetylide followed by glycosylation with 3-(trimethylsilyl)propargyl alcohol converted the δ-gluconolactones into silylated diynes. After desilylation, subsequent ruthenium-catalyzed cycloaddition of the resultant diynes with alkynes or chloroacetonitrile gave spirocyclic *C*-arylglycosides in good yields and selectivity. This strategy was also extended to the synthesis of spirocyclic *C*-arylribosides from the known γ-ribonolactone derivative. Moreover, silver-catalyzed iodination of the sugar diynes followed by ruthenium-catalyzed cycloaddition with acetylene delivered spirocyclic *C*-iodophenylglycosides and -ribosides, which were subjected to palladium-catalyzed C–C bond-forming reactions and copper-catalyzed coupling with nitrogen heterocycles to lead to various derivatives.

Keywords: glycosides · copper · cycloaddition · palladium · ruthenium

Introduction

C-Arylglycosides are important synthetic targets and are found in several bioactive natural products such as anthracyclinone *C*-glycosides, gilvocarcins, and kidamycins.[1–4] In striking contrast to the more popular *O*-arylglycosides, *C*-arylglycosides have an aryl ring directly connected to a sugar core, which confers stability toward enzymatic and chemical hydrolysis.[5] Among the *C*-arylglycosides, spirocyclic *C*-arylglycoside motifs have received renewed interest,[6] partly because some members of naturally occurring *C*-arylglycosyl spiroacetal papulacandines were found to be active against *Pneumocystis carinii* pneumonia, the common opportunistic infection in AIDS patients (Scheme 1).[7]



Papulacandin A–C: R = 6-*O*-acyl-β-galactopyranosyl
Papulacandin D: R = H

Scheme 1. Naturally occurring spirocyclic *C*-arylglycoside papulacandins.

C-Arylglycosides are generally synthesized by the direct arylation of appropriate carbohydrate substrates,[8] but the control of regiochemistry is a crucial problem when a multiply substituted aromatic precursor is employed for this purpose. To address this issue, alternative methods of directly constructing a glycosylated-benzene skeleton have recently been developed by exploiting the benzannulation or cycloaddition strategy.[9] In this context, the [2+2+2] cycloaddition of *C*-alkynylglycosides may be a promising approach for obtaining *C*-arylglycosides in a convergent and atom-economical manner.[10] McDonald et al. were the first to realize this method and elegantly applied it to the synthesis of a spirocyclic *C*-arylglycoside relevant to papulacandin D (Scheme 2).[10a] In this example, the cycloaddition of *C*-alkynyl-*O*-propargylglycoside **2**, which was derived from δ-gluconolactone **1a**, with acetylene was conducted in EtOH at room temperature for 16 h in the presence of 10 mol% $[RhCl(PPh_3)_3]$ to afford **3** in 89% yield. Although the desired spirocyclic framework was constructed efficiently, the

[a] Prof. Dr. Y. Yamamoto, K. Yamashita, T. Hotta
Department of Applied Chemistry
Graduate School of Science and Engineering
Tokyo Institute of Technology
O-okayama, Meguro-ku
Tokyo 152-8552 (Japan)
Fax: (+81) 3-5734-3339
E-mail: omyy@apc.titech.ac.jp

[b] T. Hashimoto, Dr. M. Kikuchi, Prof. Dr. H. Nishiyama
Department of Applied Chemistry
Graduate School of Engineering
Nagoya University, Chikusa
Nagoya 464-8603 (Japan)

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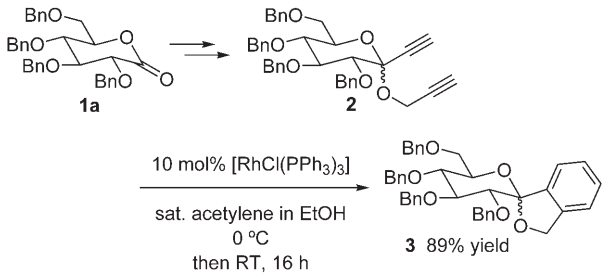
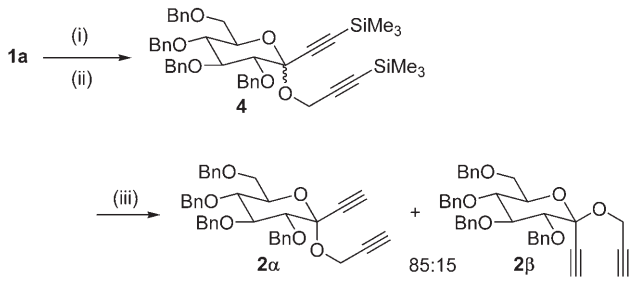


Scheme 2. The McDonald synthesis of spirocyclic *C*-arylglycoside **3** relevant to papulacandins. Bn = benzyl.



Scheme 3. Improved synthesis of **2**. Reagents and conditions: i) LiC≡CSiMe$_3$ (2 equiv), THF, −78 °C, 1.5 h; ii) Me$_3$SiC≡CCH$_2$OH (6 equiv), montmorillonite K10, MS4A, CH$_2$Cl$_2$, room temperature, 4 h; iii) 50 % aq. NaOH, BnNEt$_3$Cl (0.4 equiv), CH$_3$CN/CH$_2$Cl$_2$ (4:1), room temperature, 45 min.

scope of this cycloaddition strategy has remained unexplored. Herein, we report the full details of our study on the ruthenium-catalyzed assembly of spirocyclic *C*-arylglycosides, leading to the significant extension of the [2+2+2] cycloaddition strategy.[11]

Results and Discussion

Modified Synthesis of Diyne 2

Previously, McDonald et al. prepared the diyne substrate **2** from **1a** by the following procedure: 1) addition of 2-(trimethylsilyl)ethynyllithium, 2) acetylation of the resultant hemiacetal, 3) Lewis acid catalyzed glycosylation with propargyl trimethylsilyl ether, and 4) alkaline desilylation. Although they were able to assemble the desired diyne **2** from readily available starting materials by this four-step route, the overall yield was less than 25 %. Thus, prior to the exploration of the ruthenium-catalyzed cycloaddition, we searched for a more efficient route to **2**. From the viewpoint of step economy,[12] a modified method capable of employing the hemiacetal intermediate directly for the glycosylation step is highly desirable. To this end, montmorillonite K10 mediated glycosylation with trimethylsilylpropargyl alcohol is the method of choice.[13] The crude hemiacetal obtained by addition of 2-(trimethylsilyl)ethynyllithium to **1a** was subjected to glycosylation with trimethylsilylpropargyl alcohol in the presence of montmorillonite K10 and MS4A (4-Å molecular sieves), in accordance with the literature, to give bissilylated diyne **4** as an inseparable mixture of isomers (Scheme 3). After alkaline desilylation, purification by silica-gel chromatography separated the desired isomer **2α** as a major product from the minor isomer **2β** (overall yield 53 %, α/β = 85:15). Accordingly, this modified procedure not only doubled the overall yield, but also notably improved the anomeric stereoselectivity up to about 6:1 from 2:1 for the previous Lewis acid catalyzed method.[10a]

Exploratory Study on Ru-Catalyzed Cycloaddition of *C*-Alkynyl-*O*-proargylglycosides

Having established the modified preparative method for the diyne precursor **2**, we applied the ruthenium catalysis to the cycloaddition of **2α** with acetylene (Scheme 4).[14] Under

Scheme 4. Ruthenium-catalyzed cycloaddition of **2α** with acetylene.

acetylene atmosphere (balloon), **2α** was treated with 1 mol % [Cp*RuCl(cod)] (Cp* = η^5-C$_5$Me$_5$, cod = 1,5-cyclooctadiene) in 1,2-dichloroethane (DCE) at room temperature. The cycloaddition reached completion within 30 min to give the desired spirocyclic *C*-arylglycoside **3α** in 86 % yield after chromatographic purification.

Next, we turned our attention to the regioselective cycloaddition of a diyne bearing one internal alkyne. For spectral simplicity, we prepared methyl-protected diyne **6** from δ-gluconolactone **1b** (Scheme 5). Synthetic procedures similar to that for **2** gave **6α** and **6β** after separation by silica-gel chromatography. Although a good overall combined yield of 73 % was obtained, the stereoselectivity (α/β ≈ 3:1) was unfortunately lowered. This ratio is, however, close to that of the parent ethynyl derivatives **5′** (R = H) reported by Tomooka et al. (α/β = 2.6:1).[13a] The stereochemistry of these products was determined by comparison of their ^{1}H NMR spectra with those reported for **5′**[13a] and later ensured by single-crystal X-ray analysis of a cycloadduct (see below).

Abstract in Japanese:

δ-グルコノラクトンより誘導した 1,6-ジインを，ルテニウム触媒存在下にアルキン類やクロロアセトニトリルと反応させることにより，生理活性天然物である papulacandin 類に含まれるスピロ環状 *C*-アリールグリコシド骨格を構築した．更にこの手法をγ-リボノラクトンに適用することにより，スピロ環状 *C*-アリールリボシドを合成した．また，同様にして合成したスピロ環状 *C*-ヨウ化アリールグリコシドおよびリボシドに対しパラジウムおよび銅触媒交差カップリング反応を行うことで，*trans*-スチルベン，ビアリール，ジフェニルアセチレン，ビアリールアミノ酸，および窒素複素環部位を有する種々の誘導体へと変換することができた。

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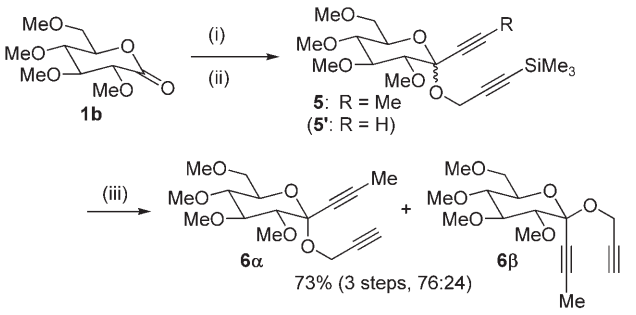
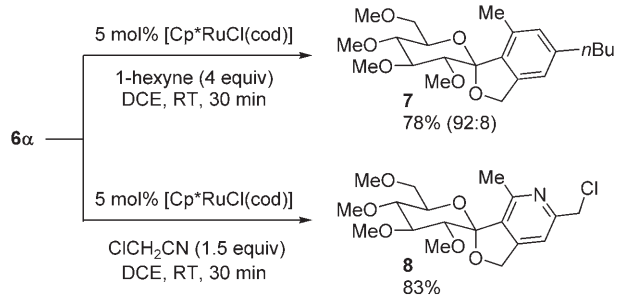


Scheme 5. Synthesis of diyne **6**. Reagents and conditions: i) LiC≡CMe (2 equiv), THF, −78 °C, 1 h; ii) $HOH_2CC{\equiv}CSiMe_3$ (6 equiv), montmorillonite K10, MS4A, CH_2Cl_2, room temperature, 2 h; iii) 50 % aq. NaOH, $BnNEt_3Cl$ (0.2 equiv), CH_3CN/CH_2Cl_2 (4:1), room temperature, 30 min.

In the presence of 5 mol % [Cp*RuCl(cod)], the major isomer **6α** underwent cycloaddition with 1-hexyne (4 equiv) at room temperature for 30 min (Scheme 6). Spirocycle **7**



Scheme 6. Ruthenium-catalyzed cycloaddition of **6α** with 1-hexyne and chloroacetonitrile.

was obtained as the major regioisomer (92:8) in 78 % yield. Similarly, **6α** was allowed to react with chloroacetonitrile (1.5 equiv) to give pyridine-fused spirocycle **8** in 83 % yield as the sole regioisomer.[15a,b] The stereochemistry as well as regiochemistry of pyridine **8** were unambiguously confirmed by single-crystal X-ray diffraction (Figure 1). The anomeric stereochemistry was clearly confirmed as α, and this is in accordance with the ^{1}H NMR spectroscopic analysis of the diyne precursor **6α**. This assignment also shows that the integrity of the anomeric configuration was preserved during the ruthenium-catalyzed cycloaddition.

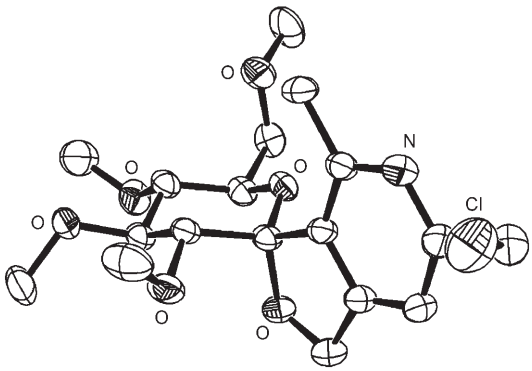
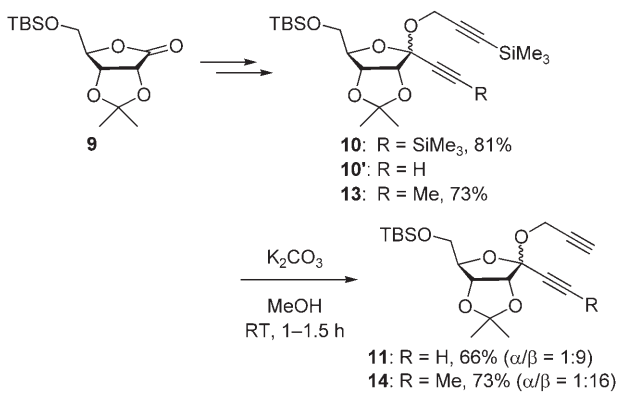


Figure 1. ORTEP diagram of pyridine **8**. Ellipsoids are shown at the 50 % probability level. All hydrogen atoms are omitted for clarity.

Synthesis of Spirocyclic *C*-Arylribosides

Recently, *C*-arylnucleosides have received much attention as they are expected to be the stable isosteres of natural nucleosides.[16] Moreover, many natural *C*-arylnucleosides also exhibit antibiotic, anticancer, or antiviral activity.[16] The cyclotrimerization strategy again was yet to be explored in the synthesis of *C*-arylnucleosides. We and others previously reported the synthesis of *C*-aryldeoxyribosides by transition-metal-catalyzed cycloaddition of *C*-alkynyldeoxyribosides with 1,6-diynes.[10b–d] No spirocyclic analogues relevant to papulacandines have been synthesized to date, although they are interesting as conformationally constrained *C*-arylnucleosides. Toward this aim, we prepared ribose-derived diynes **11** and **14** from γ-ribonolactone derivative **9** (Scheme 7). In a manner similar to the synthesis of the glu-



Scheme 7. Synthesis of ribose-derived diynes **11** and **14**. TBS = *tert*-butyldimethylsilyl.

cose derivatives, acetylide addition followed by montmorillonite K10 mediated glycosylation delivered silylated diynes **10** or **13**, which were treated with K_2CO_3 in MeOH at ambient temperature to give desilylated diynes **11** and **14**, respectively. Unfortunately, these diynes were obtained as an anomer mixture inseparable by silica-gel chromatography, although one of the stereoisomers was selectively formed with ratios of 1:9 and 1:16, respectively. The anomeric stereochemistry for the major isomers was determined as β by comparison of their ^{1}H NMR spectra with that of the closely related β-**10′** reported by Tomooka et al.[13a]

With the ribose-derived diynes in hand, the ruthenium-catalyzed cycloadditions with alkynes were examined (Scheme 8). Under acetylene atmosphere, **11** was treated with 1 mol % [Cp*RuCl(cod)] at room temperature. Compared to the case of **2α**, a longer reaction time of 1.5 h was required for the complete conversion of **11**. Separation with

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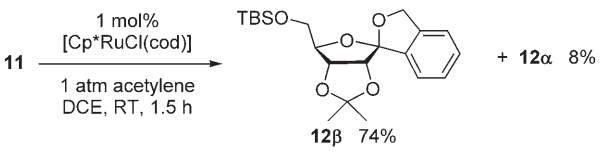
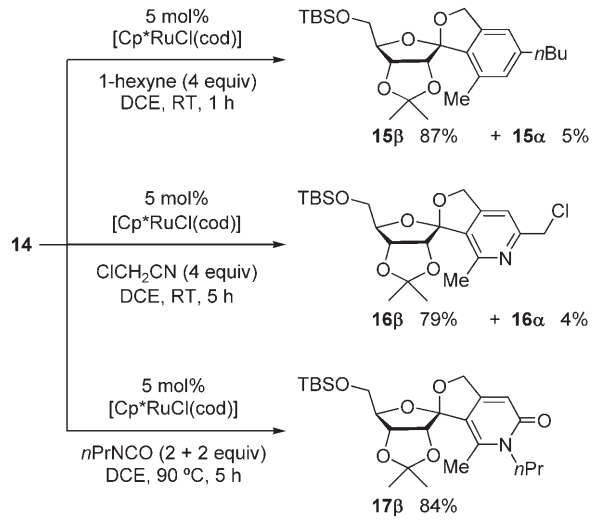


Scheme 8. Ruthenium-catalyzed cycloaddition of **11** with acetylene.

silica-gel chromatography gave cycloadducts **12β** and **12α** in 74 and 8% yield, respectively.

Next, regioselectivity for the cycloaddition of unsymmetrical diyne **14** was examined (Scheme 9). With a catalyst load-



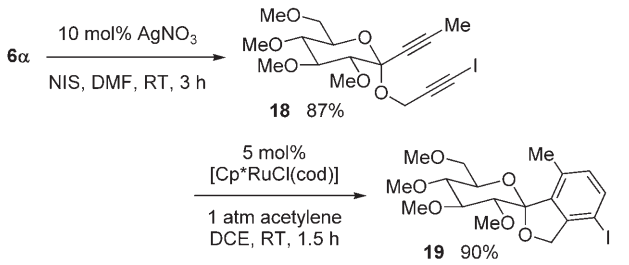
Scheme 9. Ruthenium-catalyzed regioselective cycloaddition of **14** with 1-hexyne, chloroacetonitrile, and *n*-propylisocyanate.

ing of 5 mol%, **14** was allowed to react with 1-hexyne (4 equiv) at room temperature for 1 h. Notably, anomers **15β** and **15α** were obtained as single regioisomers in 87 and 5% yield, respectively. Similarly, **14** was treated with 5 mol% [Cp*RuCl(cod)] in the presence of 1.5 equivalents of chloroacetonitrile at room temperature to give the desired pyridines as well as small amounts of the dimer of **14**. To suppress the dimerization of **14**, an increased amount of the nitrile (4 equiv) was employed to result in almost exclusive formation of pyridines **16β** and **16α** in 79 and 4% yield, respectively.

Yokoyama and co-workers introduced pyridin-2-one as a pyrimidine analogue that is complementary in shape to non-natural purine nucleobases that bear bulky *N*,*N*-dimethylamine or 2-thienyl groups at their 6-positions.[17] We therefore attempted to synthesize a pyridone analogue of the spiro *C*-arylribosides. According to our previous report,[15c] diyne **14** was allowed to react with excess *n*-propylisocyanate in DCE under reflux for 5 h to obtain the desired pyridone **17β** in 84% yield as the exclusive product.

Sequential Ag-Catalyzed C(sp)–H Iodination/Ru-Catalyzed Cycloaddition/Pd-Catalyzed Cross-Coupling Process

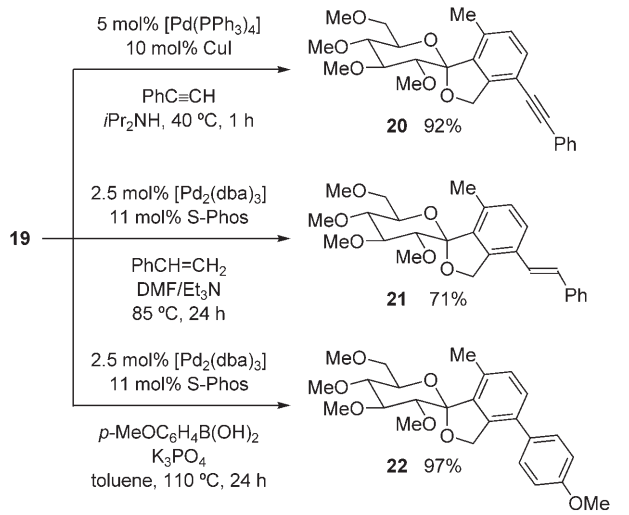
Lately, complexity-generating, multicomponent coupling processes have become increasingly important in terms of diversity-oriented synthesis toward the construction of small molecular libraries.[18] In this context, we recently developed the sequential silver-catalyzed C(sp)–H iodination/ruthenium-catalyzed cycloaddition/palladium-catalyzed cross-coupling process.[19] This novel strategy would significantly expand product diversity in the present spirocyclic sugar synthesis. Toward this aim, we next attempted the synthesis of iodobenzene platform **19** (Scheme 10).[20] Upon treatment



Scheme 10. Synthesis of iododiyne **18** and its ruthenium-catalyzed cycloaddition with acetylene. DMF = *N*,*N*-dimethylformamide.

with 10 mol% $AgNO_3$ and 2 equivalents of *N*-iodosuccinimide (NIS),[21] **6α** was converted into iododiyne **18** in 87% yield. Iododiyne **18** was thereafter treated with 5 mol% [Cp*RuCl(cod)] in DCE under acetylene atmosphere at ambient temperature to deliver the desired **19** in 90% yield.

Iodobenzene **19** was subsequently subjected to a range of palladium-catalyzed C–C bond-forming reactions (Scheme 11). Sonogashira reaction with phenylacetylene under conventional conditions gave diphenylacetylene analogue **20** in 92% yield. Mizoroki–Heck reaction with styrene



Scheme 11. Palladium-catalyzed coupling of **19**, leading to spirocyclic *C*-arylglycosides **20**–**22**.

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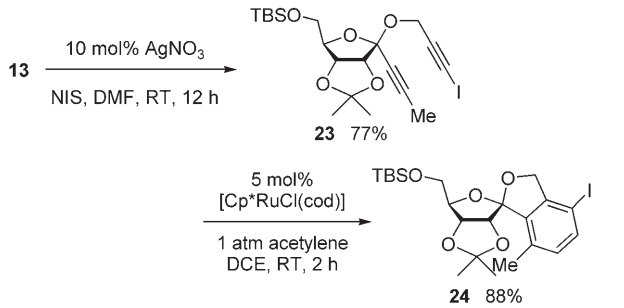
was carried out by using a catalyst system derived from 2.5 mol% $[Pd_2(dba)_3]$ (dba = dibenzylideneacetone) and 11 mol% Buchwald S-Phos[22] (2-dicyclohexylphosphanyl-2′,6′-dimethoxybiphenyl) to afford *trans*-stilbene derivative **21** in 71% yield. Suzuki–Miyaura coupling with *p*-methoxyphenylboronic acid proceeded successfully with the $[Pd_2(dba)_3]$/S-Phos catalyst system to furnish biphenyl derivative **22** in 97% yield.

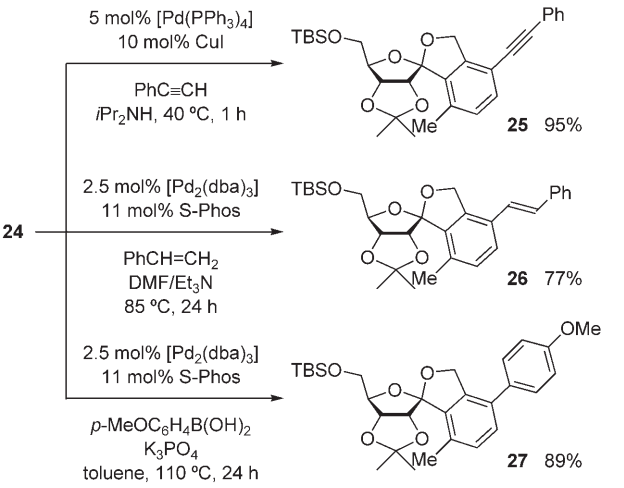
The ribose series was also examined in a similar way (Scheme 12). Because the anomers of diyne **14** were insepa-



Scheme 12. Direct iodination of silyldiyne **13** and ruthenium-catalyzed cycloaddition of the resultant iododiyne **23**.

rable, silylated precursor **13** was directly subjected to silver-catalyzed iodination as reported by Nishikawa, Isobe, and co-workers.[23] Silyldiyne **13** was treated with 10 mol% $AgNO_3$ and 1.5 equivalents of NIS to give iododiyne **23** without affecting the TBS ether moiety. Gratifyingly, **23** was isolated as a single anomer in 77% yield. The subsequent ruthenium-catalyzed cycloaddition of **23** successfully delivered the desired iodobenzene platform **24** in 88% yield.

The Sonogashira reaction, the Mizoroki–Heck reaction, and the Suzuki–Miyaura coupling of **24** were carried out in the same manner as with **19**. Consequently, spirocyclic *C*-arylribosides **25**–**27** were obtained in 95, 77, and 89% yield, respectively (Scheme 13).

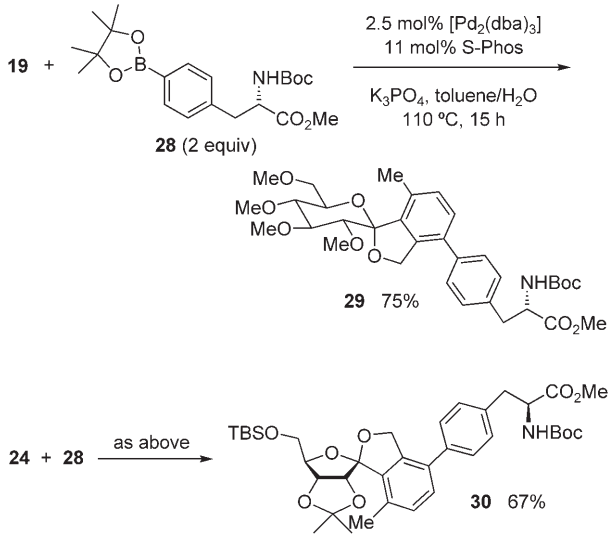


Scheme 13. Palladium-catalyzed coupling of **24**, leading to spirocyclic *C*-arylribosides **25**–**27**.

Synthesis of Spiro Suger–Amino Acid Conjugates

Artificial sugar–amino acid conjugate molecules have received increasing attention as mimics of the natural counterparts found in glycopeptides.[24] In particular, sugar amino acids, in which the sugar unit is connected to the amino acid moiety by an all-carbon tether, are of significance because they are metabolically resistant analogues of natural sugar amino acids that exhibit inhibitory activity toward glycosidases. Along this line, Kotha reported the [2+2+2] cycloaddition of amino acid tethered diyne derivatives with monoalkynes by means of rhodium and cobalt catalysis, which leads to constrained phenylalanine analogues.[25] We also accomplished the synthesis of sugar amino acids through the [2+2+2] cycloaddition of diynes that contain an amino acid moiety with *C*-alkynylglycosides.[10b,c] Recently, the syntheses of a naturally occurring *C*-glycosylamino acid, *C*-mannosyl tryptophan, and its derivatives were reported independently by Nishikawa, Isobe, and co-workers and Ito and co-workers.[26] In this section, we describe the synthesis of novel spiro sugar–amino acid conjugate molecules by our ruthenium-catalyzed cycloaddition/palladium-catalyzed cross-coupling strategy.

Recently, Suzuki–Miyaura coupling with phenylalanine-derived arylboronic acids was successfully applied to the synthesis of adenine and purine nucleosides that bear an amino acid moiety.[27] We assumed that Suzuki–Miyaura coupling of the iodobenzene platforms **19** and **24** with known boronate **28** would give rise to the spirocyclic glycoside and riboside with a biphenyl-tethered amino acid moiety (Scheme 14). Such a biaryl amino acid is also an interesting structural motif found in naturally occurring compounds.[28] The Suzuki–Miyaura coupling of **19** and 2 equivalents of **28** was carried out under aqueous conditions, and the starting material **19** was completely consumed after 15 h. Chromatographic purification afforded the desired coupling



Scheme 14. Synthesis of spirocyclic *C*-arylglycoside–amino acid conjugate molecules **29** and **30**.

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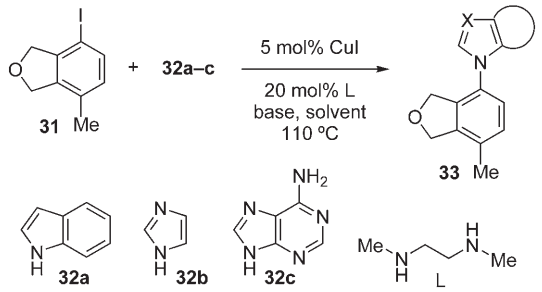
product **29** in 75% yield. In a similar manner, the spirocyclic *C*-riboside analogue **30** was obtained in 67% yield.

Cu-Catalyzed Coupling of Spiro *C*-Iodoarylriboside with Nitrogen Heterocycles

Nucleosides with a five-membered nitrogen heterocycle have been known to exhibit a broad range of significant biological activities such as antiviral, antitumor, anti-HIV, antiproliferative, and inosine monophosphate dehydrogenase inhibitory activities.[29] Among them, 5-amino-1-(β-D-ribofuranosyl)imidazole-4-carboxamide (AICA ribonucleoside) is the oldest known imidazole derivative,[30] and its 4-hydroxy analogue bredinin shows cytotoxic and immunosuppressant activities.[31] On the other hand, substituted indoles have been used as isosteres of purine nucleobases for studies on the recognition of nonpolar nucleosides in DNA.[32] Moreover, chlorinated indole nucleosides were recently reported as potent inhibitors of human cytomegalovirus in vitro.[33]

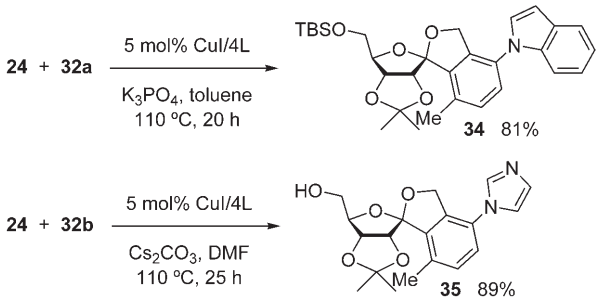
In this context, recent advances in Cu-catalyzed C(aryl)–heteroatom bond formation offers us a good opportunity to create novel N-heterocyclic ribosides extended by the spiro phthalan spacer through cross-coupling of iodoarene scaffold **24** with five-membered nitrogen heterocycles.[34] To this end, we first examined the coupling of model iodophthalan **31**[19] with heterocycles **32a–c** (Scheme 15). According to



Scheme 15. Optimization study on Cu-catalyzed coupling of **31** with N-heterocycles **32a–c**.

Buchwald and co-workers,[35] *N*,*N*′-dimethylethylenediamine (L) was used as a ligand for CuI with a Cu/L ratio of 1:4. In the presence of 2.1 equivalents of K_3PO_4, **31** and 1.2 equivalents of indole **32a** were treated with 5 mol% of the copper catalyst in toluene at 110°C for 20 h. As a result, the desired coupling product **33a** was formed in 95% yield. As opposed to **32a**, imidazole **32b** gave the corresponding coupling adduct **33b** in only moderate yield (47%) along with recovery of **31** (46%). The use of DMF as a solvent improved the conversion to afford **33b** in 70% yield. The yield was raised to 82% when the reaction was performed with an increased loading of imidazole (2 equiv) in DMF for 25 h. The highest yield of 93% was achieved by using Cs_2CO_3 in place of K_3PO_4 under otherwise identical conditions. The optimal conditions for **32b**, however, proved to be totally ineffective for adenine **32c**; it resulted in 93% recovery of **31**.

Under optimal conditions, the coupling of **24** and indole **32a** was carried out to obtain the desired **34** in 81% yield (Scheme 16). In the case of imidazole **32b**, the modified pro-



Scheme 16. Synthesis of N-heterocycle ribosides **34** and **35** with phthalan spacer.

cedure with Cs_2CO_3 in DMF was applied to **24**; however, ^{1}H NMR spectroscopic analysis of the crude reaction mixture showed that the TBS group was removed during the reaction. Chromatographic separation furnished **35** in 89% yield as colorless crystals. The β anomeric stereochemistry was unambiguously confirmed by X-ray diffraction analysis (Figure 2).[36] This shows that the integrity of the anomeric configuration was preserved during the ruthenium-catalyzed cycloaddition and copper-catalyzed coupling.

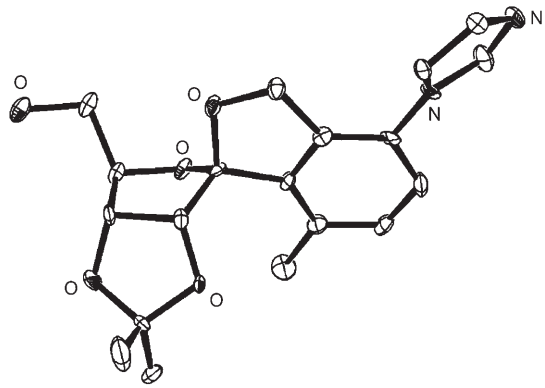


Figure 2. ORTEP diagram of imidazole **35**. Ellipsoids are shown at the 50% probability level. All hydrogen atoms are omitted for clarity.

Conclusions

We have successfully developed a convergent route to spirocyclic *C*-arylglycosides with structures related to the natural products, papulacandins. The starting glucose-derived diynes were efficiently obtained from the known δ-gluconolactone derivative by acetylide addition/stereoselective glycosylation with montmorillonite K10 clay. Cycloadditions of the obtained diyne with acetylene, 1-hexyne, and chloroacetonitrile were carried out under ruthenium catalysis to deliver the

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corresponding benzene and pyridine products in good yields and with excellent selectivity. This method could be applied to the synthesis of spirocyclic *C*-arylribosides from a known γ-ribonolactone.

Furthermore, silver-catalyzed iodination of the sugar diynes delivered the corresponding iododiynes, which were converted into iodinated spiro sugars by ruthenium-catalyzed cycloaddition with acetylene. The iodobenzene platforms thus synthesized were then subjected to Sonogashira reaction with phenylacetylene, Mizoroki–Heck reaction with styrene, and Suzuki–Miyaura coupling with *p*-methoxyphenylboronic acid to deliver various spirocyclic *C*-arylglycosides and *C*-arylribosides effectively. This sequential process was successfully applied to the synthesis of spiro sugar–amino acid conjugate molecules, in which the sugar and amino acid moieties are connected by the biaryl spacer. Moreover, application of copper-catalyzed coupling with nitrogen heterocycles to the spiro *C*-iodoarylriboside scaffold provided access to novel N-heterocycle ribosides with the spiro phthalan spacer.

Experimental Section

General

Flash column chromatography was performed on silica gel (Cica silica gel 60N) with mixed solvents (hexane/ethyl acetate). ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 or Gemini 2000 NMR spectrometer in $CDCl_3$ at 25 °C. ^{1}H NMR chemical shifts are reported in ppm relative to the singlet at $\delta = 7.26$ ppm for chloroform. Splitting patterns are designated as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, m = multiplet. Coupling constants are reported in Hz. ^{13}C NMR spectra are fully decoupled and are reported in ppm relative to the triplet at $\delta = 77.0$ ppm for $CDCl_3$. EI and ESI mass spectra were recorded on a JEOL JMS700 and JMS-T100CS mass spectrometer, respectively. Elemental analysis was performed with a Perkin–Elmer 2400II CHNS/O elemental analyzer. Melting points were obtained by a Büchi B-540 or a Yamato MP-12 melting-point apparatus and are uncorrected. Dichloromethane, DCE, and toluene were distilled from CaH_2 and degassed before use. Dry THF and DMF were purchased and used as received. The preparation of [Cp*RuCl(cod)], lactones **1b** and **9**, and boronate **28** is reported in the literature.[37–40]

Syntheses

2 from **1a**: A solution of trimethylsilylethynyllithium, freshly prepared from trimethylsilylacetylene (0.626 g, 6.37 mmol) and *n*BuLi (1.6 M in hexane, 3.9 mL, 6.24 mmol), in dry THF (15 mL) was added to a solution of **1a** (1.66 g, 3.08 mmol) in dry THF (8 mL) at −78 °C. The solution was stirred for 1.5 h at this temperature, and the reaction was quenched with saturated NH_4Cl (10 mL). The reaction mixture was extracted with diethyl ether (3 × 20 mL). The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue (1.78 g) was used directly in the next step. A solution of the crude alcohol obtained above (205.6 mg, 0.323 mol) in dry CH_2Cl_2 (2 mL) was added to MS4A (699 mg). 3-(Trimethylsilyl)propargyl alcohol (41.4 mg, 0.32 mmol) was added to this solution, followed by predried montmorillonite K10 (41.9 mg) at ambient temperature. The reaction mixture was stirred at room temperature for 4 h, filtered through a glass frit, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 15:1) to afford **4** (183.0 mg, 76 %) as a colorless oil. Diyne **4** (149.5 mg, 0.200 mmol) and $BnNEt_3Cl$ (18.3 mg, 0.08 mmol) were dissolved in CH_3CN/CH_2Cl_2 (5 mL, 4:1). Aqueous NaOH (50 %, 41 mL) was added to this solution at 0 °C, and the solution was stirred at room temperature for 45 min. The reaction mixture was diluted with diethyl ether (10 mL) and washed with H_2O (3 × 5 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 10:1) to afford **2β** (13.8 mg, 11 %) as a colorless oil. Further elution (hexane/EtOAc = 5:1) gave **2α** (79.1 mg, 65 %) as a colorless oil. Their spectral data are in good agreement with those reported in the literature.[10a]

6 from **1b**: A solution of **1b** (1.00 g, 4.27 mmol) in dry THF (15 mL) was added to a solution of propynyllithium, freshly prepared from 1-bromopropene (1.39 g, 11.5 mmol) and *n*BuLi (1.6 M in hexane, 10.8 mL, 17.1 mmol), in dry THF (25 mL) at −78 °C. The solution was stirred for 1 h at this temperature, and the reaction was quenched with saturated NH_4Cl (15 mL). The reaction mixture was extracted with diethyl ether (3 × 30 mL). The combined organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue (1.17 g) was used directly in the next step. A solution of the crude alcohol obtained above in dry CH_2Cl_2 (40 mL) was added to MS4A (9 g). 3-(Trimethylsilyl)propargyl alcohol (3.28 g, 25.6 mmol) was added to this solution, followed by predried montmorillonite K10 (5.51 g) at ambient temperature. The reaction mixture was stirred at room temperature for 2 h, filtered through a glass frit, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 25:1–10:1) to afford **5** (1.33 g) as a colorless oil. Diyne **5** (1.33 g, 3.46 mmol) and $BnNEt_3Cl$ (157.5 mg, 0.69 mmol) were dissolved in CH_3CN/CH_2Cl_2 (80 mL, 4:1). Aqueous NaOH (50 %, 0.36 mL) was added to this solution at 0 °C, and the solution was stirred at room temperature for 30 min. The reaction mixture was diluted with diethyl ether (100 mL) and washed with H_2O (3 × 20 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (silica gel, hexane/EtOAc = 15:1) to afford **6** (972.3 mg, 73 % over 3 steps) as a colorless oil. Major α isomer: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 1.88$ (s, 3 H), 2.36 (t, $J = 2.4$ Hz, 1 H), 3.21 (dd, $J = 10.2$, 9.0 Hz, 1 H), 3.23 (d, $J = 9.6$ Hz, 1 H), 3.38 (s, 3 H), 3.51 (dd, $J = 9.6$, 9.0 Hz, 1 H), 3.53 (s, 3 H), 3.56 (d, $J = 3.0$ Hz, 2 H), 3.63 (s, 3 H), 3.66 (s, 3 H), 3.67 (dt, $J = 10.2$, 3.0 Hz, 1 H), 4.33 (dd, $J = 15.6$, 2.4 Hz, 1 H), 4.40 ppm (dd, $J = 15.6$, 2.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 3.8$, 51.9, 59.1, 60.4, 60.9, 61.6, 70.6, 71.6, 74.0, 74.7, 79.2, 79.6, 83.2, 83.8, 85.9, 96.2 ppm; MS (EI): *m*/*z* (%) = 312 (1) $[M]^+$, 257 (34) $[M-OCH_2C{\equiv}CH]^+$, 225 (100) $[M-OCH_2C{\equiv}CH-HOMe]^+$; elemental analysis: calcd (%) for $C_{16}H_{24}O_6$ (312.36): C 61.52, H 7.74; found: C 61.48, H 7.78. Minor β isomer: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 1.94$ (s, 3 H), 2.38 (t, $J = 2.4$ Hz, 1 H), 3.07 (d, $J = 9.3$ Hz, 1 H), 3.15 (dd, $J = 9.9$, 9.0 Hz, 1 H), 3.33 (dd, $J = 9.3$, 9.0 Hz, 1 H), 3.38 (s, 3 H), 3.53 (s, 3 H), 3.59 (d, $J = 3.6$ Hz, 1 H), 3.61 (s, 3 H), 3.62 (s, 3 H), 3.62–3.68 (m, 1 H), 4.39 (dd, $J = 15.0$, 2.4 Hz, 1 H), 4.49 ppm (dd, $J = 15.0$, 2.4 Hz, 1 H).

Representative procedure for the preparation of ribose-derived diynes: **11** from **9**: A solution of 2-(trimethylsilyl)ethynyllithium, freshly prepared from trimethylsilylacetylene (982 mg, 10.0 mmol) and *n*BuLi (1.6 M in hexane, 6.36 mL, 10 mmol), in dry THF (30 mL) was added to a solution of 5-*O*-*tert*-butyldimethylsilyl-2,3-*O*,*O*-isopropylidene-γ-ribonolactone (**9**; 1.51 g, 5.0 mmol) in dry THF (20 mL) at −78 °C. The solution was stirred for 40 min at this temperature, and the reaction was quenched with saturated NH_4Cl (20 mL). The reaction mixture was diluted with water (100 mL) and extracted with diethyl ether (3 × 80 mL). The combined organic layer was washed with brine (3 × 80 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was used directly in the next step. A solution of the crude alcohol obtained above in dry CH_2Cl_2 (40 mL) was added to MS4A (10 g). 3-(Trimethylsilyl)propargyl alcohol (3.85 g, 30.0 mmol) was added to this solution, followed by predried montmorillonite K10 (6.45 g) at ambient temperature. The reaction mixture was stirred at room temperature for 1 h, filtered through a glass frit, and the filtrate was concentrated in vacuo. The residue was purified by short column chromatography (silica gel, hexane/EtOAc = 30:1) to afford **10** (2.48 g) as a colorless oil. K_2CO_3 (1.11 g, 8.0 mmol) was added to a solution of **10** (2.03 g, 4.08 mmol) in dry MeOH (30 mL), and the reaction mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated NH_4Cl (80 mL), and the mixture was extracted with diethyl ether (6 × 50 mL). The combined organic layer was washed with brine (2 × 30 mL), dried over $MgSO_4$, and concentrated in vacuo.

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The residue was purified by flash silica-gel column chromatography (hexane/Et_2O=20:1) to afford **11** (994 mg, 66%) as a colorless oil. Major β isomer: ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=0.07 (s, 6H), 0.90 (s, 9H), 1.36 (s, 3H), 1.55 (s, 3H), 2.42 (t, J=2.4 Hz, 1H), 2.78 (s, 1H), 3.63 (dd, J=10.2, 8.7 Hz, 1H), 3.68 (dd, J=10.2, 6.6 Hz, 1H), 4.26 (ddd, J=8.7, 6.6, 1.2 Hz, 1H), 4.29 (dd, J=14.7, 2.4 Hz, 1H), 4.40 (dd, J=14.7, 2.4 Hz, 1H), 4.65 (d, J=5.7 Hz, 1H), 4.76 ppm (dd, J=5.7, 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=−5.3, −5.2, 18.4, 25.6, 26.0, 26.6, 51.7, 63.6, 74.2, 76.0, 76.4, 79.1, 82.0, 87.0, 87.3, 104.6, 113.3 ppm; MS (EI): m/z (%)=366 (100) $[M]^+$, 351 (30) $[M-CH_3]^+$; elemental analysis: calcd (%) for $C_{19}H_{30}O_5Si$ (366.52): C 62.26, H 8.25; found: C 62.37, H 8.33.

13 and **14** from **9**: In a similar manner to **10**, **9** (2.42 g, 8.00 mmol) gave **13** (2.65 g, 73%) as a colorless oil. Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=0.08 (s, 6H), 0.17 (s, 9H), 0.90 (s, 9H), 1.36 (s, 3H), 1.54 (s, 3H), 1.93 (s, 3H), 3.63 (dd, J=10.2, 8.2 Hz, 1H), 3.66 (dd, J=10.2, 7.0 Hz, 1H), 4.21 (ddd, J=8.2, 7.0, 1.2 Hz, 1H), 4.24 (d, J=15.0 Hz, 1H), 4.41 (d, J=15.0 Hz, 1H), 4.63 (d, J=5.7 Hz, 1H), 4.73 ppm (dd, J=5.7, 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=−5.3, −5.2, −0.1, 3.9, 18.4, 25.6, 26.0, 26.6, 52.1, 63.7, 72.0, 82.1, 85.3, 86.8, 86.9, 90.6, 101.1, 104.8, 112.9 ppm; MS (EI): m/z (%)=452 (3) $[M]^+$, 437 (44) $[M-CH_3]^+$, 395 (100) $[M-C(CH_3)_3]^+$, 337 (63) $[M-SiMe_2tBu]^+$; elemental analysis: calcd (%) for $C_{23}H_{40}O_5Si_2$ (452.73): C 61.02, H 8.91; found: C 60.86, H 9.13. Desilylation of **13** (3.35 g, 7.40 mmol) afforded **14** (2.45 g, 73%) as a colorless oil. Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=0.07 (s, 6H), 0.90 (s, 9H), 1.36 (s, 3H), 1.54 (s, 3H), 1.94 (s, 3H), 2.40 (t, J=2.4 Hz, 1H), 3.63 (dd, J=10.2, 8.2 Hz, 1H), 3.67 (dd, J=10.2, 6.8 Hz, 1H), 4.22 (ddd, J=8.2, 6.8, 1.2 Hz, 1H), 4.25 (dd, J=15.3, 2.4 Hz, 1H), 4.39 (dd, J=15.3, 2.4 Hz, 1H), 4.62 (d, J=6.0 Hz, 1H), 4.73 ppm (dd, J=6.0, 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=−5.3, −5.2, 3.9, 18.4, 25.6, 26.0, 26.6, 51.4, 63.7, 72.0, 73.8, 79.6, 82.1, 85.5, 86.8, 86.9, 104.9, 113.0 ppm; MS (EI): m/z (%)=365 (60) $[M-CH_3]^+$, 323 (100) $[M-C(CH_3)_3]^+$, 309 (20) $[M-CH_3-C(CH_3)_3]^+$, 265 (52) $[M-SiMe_2tBu]^+$ (no molecular ion); elemental analysis: calcd (%) for $C_{20}H_{32}O_5Si$ (380.55): C 63.12, H 8.48; found: C 62.92, H 8.68.

Representative procedure for silver-catalyzed iodination of diynes: **18** from **6a**: A solution of **6a** (197.6 mg, 0.633 mmol), NIS (288.5 mg, 1.28 mmol), and $AgNO_3$ (11.3 mg, 0.066 mmol) in dry DMF (3.8 mL) was stirred for 3 h at room temperature in the dark. The reaction mixture was diluted with EtOAc (30 mL), the reaction was quenched with saturated $Na_2S_2O_3$ (6 mL), and the mixture was extracted with EtOAc (3×30 mL). The combined organic layer was washed with brine (2×60 mL) and dried with $MgSO_4$. The solvent was removed in vacuo, and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt=5:1) to give **18** (241 mg, 87%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=1.88 (s, 3H), 3.23 (dt, J=9.6, 4.5 Hz, 2H), 3.39 (s, 3H), 3.49 (d, J=9.0 Hz, 1H), 3.54 (s, 3H), 3.56–3.57 (m, 2H), 3.61–3.65 (m, 1H), 3.64 (s, 3H), 3.66 (s, 3H), 4.50 (d, J=15.6 Hz, 1H), 4.56 ppm (d, J=15.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=2.7, 3.5, 53.5, 59.1, 60.3, 60.8, 61.6, 70.7, 71.8, 74.8, 79.3, 83.5, 83.8, 86.1, 90.1, 96.4 ppm; MS (ESI): m/z=461 $[M-Na]^+$; elemental analysis: calcd (%) for $C_{16}H_{23}IO_6$ (438.25): C 43.85, H 5.29; found: C 43.64, H 5.44.

23 from **13**: In a similar manner to the synthesis of **18**, Ag-catalyzed iodination of **13** gave **23** (775 mg, 77%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=0.08 (s, 6H), 0.90 (s, 9H), 1.36 (s, 3H), 1.53 (s, 3H), 1.93 (s, 3H), 3.61 (dd, J=10.2, 8.2 Hz, 1H), 3.65 (dd, J=10.2, 6.6 Hz, 1H), 4.21 (ddd, J=8.2, 6.6, 1.2 Hz, 1H), 4.41 (d, J=15.0 Hz, 1H), 4.53 (d, J=15.0 Hz, 1H), 4.59 (d, J=6.0 Hz, 1H), 4.72 ppm (dd, J=6.0, 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=−5.2, −5.1, 2.3, 3.9, 18.4, 25.6, 26.0, 26.6, 53.0, 63.7, 71.9, 82.1, 85.6, 86.8, 86.9, 89.9, 104.9, 113.0 ppm; MS (EI): m/z (%)=506 (17) $[M]^+$, 492 (27) $[MH-CH_3]^+$, 449 (100) $[M-C(CH_3)_3]^+$; elemental analysis: calcd (%) for $C_{20}H_{31}IO_5Si$ (506.45): C 47.43, H 6.17; found: C 47.30, H 6.30.

Representative procedure for ruthenium-catalyzed cycloaddition of diynes with acetylene: **3α** from **2α**: A solution of **2α** (66.2 mg, 0.11 mmol) in dry degassed DCE (2 mL) was added to a solution of [Cp*RuCl(cod)] (0.43 mg, 1.09 mmol) in dry degassed DCE (1 mL) over 15 min at room temperature under acetylene atmosphere, and the mixture was stirred for 0.5 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc=10:1) to give **3α** (59.7 mg, 86%) as a colorless oil. Its spectral data are in good agreement with those reported in the literature.[10a] Cycloadditions of **11**, **18**, and **23** were carried out in a similar manner.

12β: Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=0.08 (s, 3H), 0.09 (s, 3H), 0.92 (s, 9H), 1.36 (s, 3H), 1.65 (s, 3H), 2.48 (s, 3H), 2.56 (t, J=7.8 Hz, 2H), 3.75 (dd, J=10.2, 8.1 Hz, 1H), 3.79 (dd, J=10.2, 6.9 Hz, 1H), 4.24 (ddd, J=8.1, 6.9, 1.2 Hz, 1H), 4.71 (d, J=6.0 Hz, 1H), 4.91 (dd, J=6.0, 1.2 Hz, 1H), 4.98 (d, J=12.6 Hz, 1H), 5.13 (d, J=12.6 Hz, 1H), 7.21–7.24 (m, 1H), 7.31–7.40 (m, 2H), 7.61–7.64 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C) δ=−5.2, −5.1, 18.5, 24.9, 26.0, 26.6, 64.2, 71.7, 82.9, 85.7, 86.4, 112.5, 117.1, 120.4, 125.9, 127.4, 129.4, 135.6, 140.3 ppm; MS (EI): m/z (%)=393 (8) $[MH]^+$, 377 (53) $[M-CH_3]^+$, 335 (100) $[M-C(CH_3)_3]^+$, 277 (100) $[M-SiMe_2tBu]^+$; elemental analysis: calcd (%) for $C_{21}H_{32}O_5Si$ (392.56): C 64.25, H 8.22; found: C 64.17, H 8.30.

19: Colorless solid. M.p.: 94.0–94.6°C; ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=2.04 (s, 3H), 3.15 (s, 3H), 3.30 (dd, J=10.2, 8.7 Hz, 1H), 3.36 (s, 3H), 3.52 (dd, J=11.2, 2.1 Hz, 1H), 3.58 (d, J=8.7 Hz, 1H), 3.58 (s, 3H), 3.63 (d, J=8.7 Hz, 1H), 3.65 (dd, J=11.1, 4.5 Hz, 1H), 3.68 (s, 3H), 3.90 (ddd, J=10.2, 4.5, 2.1 Hz, 1H), 4.97 (d, J=13.0 Hz, 1H), 5.01 (d, J=13.0 Hz, 1H), 6.82 (d, J=7.8 Hz, 1H), 7.57 ppm (d, J=7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=17.2, 59.2, 60.1, 60.2, 60.8, 71.3, 72.7, 76.9, 79.6, 83.7, 83.8, 84.9, 111.7, 132.0, 133.4, 137.0, 138.2, 145.0 ppm; MS (ESI): m/z=487 $[M+Na]^+$; elemental analysis: calcd (%) for $C_{18}H_{25}IO_6$ (464.29): C 46.56, H 5.43; found: C 46.81, H 5.30.

24: Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=0.09 (s, 3H), 0.09 (s, 3H), 0.92 (s, 9H), 1.30 (s, 3H), 1.56 (s, 3H), 2.46 (s, 3H), 3.74 (dd, J=10.2, 8.7 Hz, 1H), 3.79 (dd, J=10.2, 6.0 Hz, 1H), 4.33 (ddd, J=8.7, 6.0, 1.8 Hz, 1H), 4.69 (d, J=6.0 Hz, 1H), 4.76 (d, J=13.5 Hz, 1H), 4.85 (dd, J=6.0, 1.8 Hz, 1H), 4.88 (d, J=13.5 Hz, 1H), 6.86 (d, J=8.0 Hz, 1H), 7.57 ppm (d, J=8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=−5.2, −5.1, 18.5, 18.8, 24.2, 26.1, 64.3, 74.5, 82.2, 83.6, 85.9, 87.2, 112.8, 119.5, 132.2, 134.6, 136.8, 138.1, 144.5 ppm; MS (EI): m/z (%)=531 (4) $[M-H]^+$, 517 (30) $[M-CH_3]^+$, 475 (100) $[M-C(CH_3)_3]^+$, 457 (30) $[M-CH_3-C(CH_3)_3]^+$, 417 (100) $[M-SiMe_2tBu]^+$; elemental analysis: calcd (%) for $C_{22}H_{33}IO_5Si$ (532.48): C 49.62, H 6.25; found: C 49.63, H 6.39.

Representative procedure for ruthenium-catalyzed cycloaddition of diynes with 1-hexyne: **7** from **6α**: A solution of **6α** (93.7 mg, 0.30 mmol) in dry degassed DCE (2 mL) was added to a solution of [Cp*RuCl(cod)] (5.7 mg, 0.015 mmol) and 1-hexyne (98.6 mg, 1.2 mmol) in dry degassed DCE (1 mL) over 15 min at room temperature under argon atmosphere, and the solution was stirred for 0.5 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc=8:1) to give **7** (91.8 mg, 78%) as a pale-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=0.92 (t, J=7.2 Hz, 3H), 1.34 (sext, J=7.5 Hz, 2H), 1.51–1.61 (m, 2H), 2.42 (s, 3H), 2.57 (t, J=7.5 Hz, 2H), 3.12 (s, 3H), 3.32 (ddd, J=9.9, 6.0, 3.0 Hz, 1H), 3.36 (s, 3H), 3.52 (dd, J=10.8, 1.8 Hz, 1H), 3.58 (dd, J=12.0, 3.6 Hz, 1H), 3.59 (s, 3H), 3.63 (d, J=3.6 Hz, 1H), 3.64 (dd, J=7.2, 4.5 Hz, 1H), 3.68 (s, 3H), 3.90 (ddd, J=10.2, 4.2, 1.8 Hz, 1H), 5.10 (s, 1H), 6.84 (s, 1H), 6.87 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=14.0, 17.9, 22.4, 33.7, 35.5, 59.3, 60.1, 60.4, 60.9, 71.4, 72.6, 72.9, 79.7, 83.7, 85.2, 110.0, 118.1, 130.1, 132.7, 133.2, 140.7, 144.3 ppm; MS (EI): m/z (%)=394 (100) $[M]^+$, 349 (72) $[M-3CH_3]^+$; elemental analysis: calcd (%) for $C_{22}H_{34}O_6$ (394.24): C 66.98, H 8.69; found: C 66.90, H 8.75.

15β: Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=0.08 (s, 3H), 0.09 (s, 3H), 0.91 (t, J=7.2 Hz, 3H), 0.92 (s, 9H), 1.30 (s, 3H), 1.34 (sext, J=7.8 Hz, 2H), 1.51–1.62 (m, 2H), 1.57 (s, 3H), 2.48 (s, 3H), 2.56 (t, J=7.8 Hz, 2H), 3.75 (dd, J=10.2, 9.0 Hz, 1H), 3.79 (dd, J=10.2, 6.0 Hz, 1H), 4.31 (ddd, J=9.0, 6.0, 1.5 Hz, 1H), 4.68 (d, J=6.0 Hz, 1H), 4.85 (dd, J=6.0, 1.5 Hz, 1H), 4.88 (d, J=12.0 Hz, 1H), 4.98 (d, J=12.0 Hz, 1H), 6.81 (s, 1H), 6.92 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): δ=−5.1, −5.0, 14.1, 18.5, 19.2, 22.5, 24.2, 26.1, 26.2, 33.6, 35.5, 64.4, 70.5, 82.4, 85.8, 112.6, 117.8, 118.3, 126.5, 130.5, 136.1, 140.8, 144.4 ppm; MS (EI): m/z (%)=461 (29) $[M-H]^+$, 447 (7) $[M-CH_3]^+$, 419 (100)

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$[M-CH_2{=}CHCH_3]^+$, 405 (95) $[M-CH_2{=}CHCH_2CH_3]^+$; elemental analysis: calcd (%) for $C_{26}H_{42}O_5Si$ (462.69): C 67.49, H 9.15; found: C 67.36, H 9.28.

Representative procedure for ruthenium-catalyzed cycloaddition of diynes with chloroacetonitrile: **8** from **6α**: A solution of **6α** (93.7 mg, 0.30 mmol) in dry degassed DCE (2 mL) was added to a solution of [Cp*RuCl(cod)] (5.7 mg, 0.015 mmol) and chloroacetonitrile (34.0 mg, 0.45 mmol) in dry degassed DCE (1 mL) over 15 min at room temperature under argon atmosphere, and the solution was stirred for 0.5 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 3:1) to give **8** (97.0 mg, 83%) as a colorless solid. M.p.: 97.7–99.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.65 (s, 3H), 3.18 (s, 3H), 3.25–3.38 (m, 1H), 3.36 (s, 3H), 3.52 (dd, J = 10.8, 1.8 Hz, 1H), 3.55–3.61 (m, 1H), 3.59 (s, 3H), 3.62 (d, J = 1.5 Hz, 1H), 3.66 (dd, J = 3.0, 1.5 Hz, 1H), 3.68 (s, 3H), 3.91 (ddd, J = 9.6, 4.2, 1.8 Hz, 1H), 4.67 (s, 2H), 5.10 (d, J = 15.0 Hz, 1H), 5.15 (d, J = 15.0 Hz, 1H), 7.25 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.1, 46.5, 59.3, 60.4, 60.5, 60.8, 71.2, 72.2, 72.9, 79.6, 83.3, 84.9, 109.6, 113.0, 131.3, 151.4, 153.2, 156.3 ppm; MS (EI): m/z (%) = 388 (17) $[M]^+$, 352 (100) $[M-Cl]^+$, 342 (62) $[M-3Me]^+$; elemental analysis: calcd (%) for $C_{18}H_{26}ClNO_6$ (387.86): C 55.74, H 6.76, N 3.61; found: C 55.94, H 6.99, N 3.17.

16β: Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ = 0.09 (s, 3H), 0.09 (s, 3H), 0.92 (s, 9H), 1.30 (s, 3H), 1.59 (s, 3H), 2.69 (s, 3H), 3.73 (dd, J = 10.5, 9.3 Hz, 1H), 3.79 (dd, J = 10.5, 5.7 Hz, 1H), 4.37 (ddd, J = 9.3, 5.7, 1.5 Hz, 1H), 4.65 (d, J = 12.6 Hz, 1H), 4.67 (d, J = 5.7 Hz, 1H), 4.70 (d, J = 12.6 Hz, 1H), 4.86 (dd, J = 5.7, 1.5 Hz, 1H), 4.91 (d, J = 14.5 Hz, 1H), 5.03 (d, J = 14.5 Hz, 1H), 7.22 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ = −5.2, −5.1, 18.5, 22.7, 24.2, 26.0, 26.1, 46.6, 64.2, 70.0, 82.1, 85.8, 87.4, 112.5, 112.9, 117.7, 128.8, 151.3, 156.4, 156.7 ppm; MS (EI): m/z (%) = 454 (7) $[M-H]^+$, 412 (70) $[M-H-C(CH_3)_2]^+$, 398 (37) $[M-C(CH_3)_3]^+$, 356 (100) $[M-C(CH_3)_2-C(CH_3)_3]^+$; elemental analysis: calcd (%) for $C_{22}H_{34}ClNO_5Si$ (456.05): C 57.94, H 7.51, N 3.07; found: C 58.30, H 7.50, N 2.73.

Procedure for ruthenium-catalyzed cycloaddition of **14** with n-propylisocyanate: A solution of **14** (262.6 mg, 0.69 mmol) and n-propylisocyanate (117.4 mg, 1.38 mmol) in dry degassed DCE (8 mL) was added to a solution of [Cp*RuCl(cod)] (13.2 mg, 0.035 mmol) and n-propylisocyanate (117.4 mg, 1.38 mmol) in dry degassed DCE (2 mL) over 1 h at 90 °C under argon atmosphere, and the solution was stirred for 5 h at this temperature. The solvent was removed in vacuo, and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 1:1) to give **17β** (277.7 mg, 84%) as a colorless gummy oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.08 (s, 6H), 0.91 (s, 9H), 0.99 (t, J = 7.5 Hz, 3H), 1.32 (s, 3H), 1.54 (s, 3H), 1.60–1.78 (m, 2H), 2.50 (s, 3H), 3.70 (dd, J = 10.2, 9.0 Hz, 1H), 3.76 (dd, J = 9.9, 5.7 Hz, 1H), 3.88 (ddd, J = 13.0, 11.4, 6.0 Hz, 1H), 4.08 (ddd, J = 13.0, 10.2, 6.0 Hz, 1H), 4.28 (ddd, J = 9.2, 6.0, 1.2 Hz, 1H), 4.58 (d, J = 6.0 Hz, 1H), 4.67 (dd, J = 14.4, 1.2 Hz, 1H), 4.82 (dd, J = 6.0, 1.2 Hz, 1H), 4.85 (dd, J = 14.4, 1.2 Hz, 1H), 6.24 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = −5.5, −5.3, 11.2, 17.3, 18.2, 21.5, 23.9, 25.7, 25.8, 45.8, 64.0, 68.6, 81.9, 85.0, 86.7, 107.2, 112.5, 113.1, 116.7, 145.7, 152.4, 163.0 ppm; MS (ESI): m/z = 488 $[M+Na]^+$; elemental analysis: calcd (%) for $C_{24}H_{39}NO_6Si$ (465.66): C 61.90, H 8.44, N 3.01; found: C 61.59, H 8.79, N 2.97.

Representative procedure for Sonogashira reaction with phenylacetylene: **20** from **19**: A solution of $[Pd(PPh_3)_4]$ (11.5 mg, 0.010 mmol), CuI (4.1 mg, 0.021 mmol), **19** (92.4 mg, 0.199 mmol), and phenylacetylene (61.4 mg, 0.601 mmol) in degassed iPr$_2$NH (2.2 mL) was stirred at 40 °C for 1 h. The reaction was quenched with HCl (1 N, 15 mL) and extracted with EtOAc (4 × 15 mL). The combined organic layer was then washed with brine (20 mL) and dried with $MgSO_4$. After the solvent was removed in vacuo, the residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 10:1–5:1) to give **20** (79.9 mg, 92%) as a pale-yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.47 (s, 3H), 3.14 (s, 3H), 3.32 (dd, J = 9.9, 8.1 Hz, 1H), 3.36 (s, 3H), 3.54 (dd, J = 11.4, 1.8 Hz, 1H), 3.58–3.70 (m, 3H), 3.59 (s, 3H), 3.69 (s, 3H), 3.94 (ddd, J = 10.2, 4.2, 1.8 Hz, 1H), 5.23 (d, J = 13.2 Hz, 1H), 5.29 (d, J = 13.2 Hz, 1H), 7.08 (d, J = 7.8 Hz, 1H), 7.31–7.38 (m, 3H), 7.38 (d, J = 7.8 Hz, 1H), 7.45–7.51 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 17.8, 59.3, 60.2, 60.4, 60.9, 71.5, 72.8, 73.3, 79.8, 83.8, 85.2, 86.2, 92.9, 111.0, 114.5, 123.2, 128.5, 128.6, 130.4, 131.7, 132.2, 134.1, 136.2, 143.4 ppm; MS (ESI): m/z = 461 $[M+Na]^+$; elemental analysis: calcd (%) for $C_{26}H_{30}O_6$ (438.51): C 71.21, H 6.90; found: C 71.10, H 7.01.

25: Colorless gummy oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.10 (s, 3H), 0.11 (s, 3H), 0.93 (s, 9H), 1.32 (s, 3H), 1.58 (s, 3H), 2.54 (s, 3H), 3.77 (dd, J = 10.2, 9.0 Hz, 1H), 3.82 (dd, J = 10.2, 6.0 Hz, 1H), 4.35 (ddd, J = 9.0, 6.0, 1.8 Hz, 1H), 4.71 (d, J = 5.7 Hz, 1H), 4.88 (dd, J = 5.7, 1.8 Hz, 1H), 5.02 (d, J = 13.5 Hz, 1H), 5.18 (d, J = 13.5 Hz, 1H), 7.12 (d, J = 8.1 Hz, 1H), 7.32–7.37 (m, 3H), 7.39 (d, J = 8.1 Hz, 1H), 7.46–7.51 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = −5.1, −5.0, 18.5, 19.3, 24.2, 26.0, 26.1, 64.4, 70.7, 82.3, 85.9, 86.1, 87.2, 92.7, 112.7, 113.8, 123.0, 128.3, 130.5, 131.4, 132.0, 133.3, 137.3, 142.9 ppm; MS (EI): m/z (%) = 507 (10) $[MH]^+$, 491 (34) $[M-CH_3]^+$, 450 (100) $[MH-C(CH_3)_3]^+$; elemental analysis: calcd (%) for $C_{30}H_{38}O_5Si$ (506.71): C 71.11, H 7.56; found: C 71.05, H 7.62.

Representative procedure for Mizoroki–Heck reaction with styrene: **21** from **19**: A solution of $[Pd_2(dba)_3]\cdot CHCl_3$ (5.1 mg, 0.0050 mmol), S-Phos (9.1 mg, 0.022 mmol), **19** (92.6 mg, 0.199 mmol), and styrene (41.8 mg, 0.40 mmol) in degassed DMF/Et_3N (3.3 mL/0.7 mL) was stirred at 85 °C for 24 h. The reaction was quenched with HCl (1 N, 15 mL), and the mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 × 15 mL). The combined organic layer was then washed with brine (20 mL) and dried with $MgSO_4$. After the solvent was removed in vacuo, the residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 9:1) to give **21** (62.6 mg, 71%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.47 (s, 3H), 3.14 (s, 3H), 3.32 (ddd, J = 10.5, 6.0, 3.0 Hz, 1H), 3.37 (s, 3H), 3.54 (dd, J = 10.8, 1.8 Hz, 1H), 3.58–3.60 (m, 1H), 3.59 (s, 3H), 3.63–3.69 (m, 2H), 3.69 (s, 3H), 3.94 (ddd, J = 10.2, 3.9, 1.8 Hz, 1H), 5.28 (d, J = 12.5 Hz, 1H), 5.34 (d, J = 12.5 Hz, 1H), 6.92 (s, 2H), 7.10 (d, J = 7.8 Hz, 1H), 7.17–7.51 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 17.6, 59.3, 60.1, 60.3, 60.9, 71.5, 72.7, 72.8, 79.8, 83.7, 85.2, 110.5, 125.5, 126.6, 126.8, 127.9, 128.8, 129.1, 130.1, 130.7, 132.7, 136.3, 137.3, 138.7 ppm; MS (ESI): m/z = 463 $[M+Na]^+$; elemental analysis: calcd (%) for $C_{26}H_{32}O_6$ (440.53): C 70.89, H 7.32; found: C 70.57, H 7.64.

26: Colorless gummy oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.10 (s, 3H), 0.11 (s, 3H), 0.93 (s, 9H), 1.31 (s, 3H), 1.58 (s, 3H), 2.53 (s, 3H), 3.78 (dd, J = 10.2, 8.7 Hz, 1H), 3.82 (dd, J = 10.2, 6.0 Hz, 1H), 4.35 (ddd, J = 8.7, 6.0, 1.5 Hz, 1H), 4.72 (d, J = 5.7 Hz, 1H), 4.88 (dd, J = 5.7, 1.5 Hz, 1H), 5.06 (d, J = 12.6 Hz, 1H), 5.21 (d, J = 12.6 Hz, 1H), 6.88 (d, J = 16.5 Hz, 1H), 6.95 (d, J = 16.5 Hz, 1H), 7.13 (d, J = 8.1 Hz, 1H), 7.25–7.39 (m, 3H), 7.45–7.49 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = −5.1, −5.0, 18.5, 19.1, 24.2, 26.0, 26.1, 64.4, 70.2, 82.3, 85.8, 87.1, 112.7, 118.5, 125.1, 126.4, 126.7, 127.7, 128.5, 128.6, 129.7, 130.8, 133.4, 136.0, 137.1, 138.4 ppm; MS (EI): m/z (%) = 508 (16) $[M]^+$, 493 (7) $[M-CH_3]^+$, 451 (100) $[M-C(CH_3)_3]^+$, 393 (64) $[M-SiMe_2tBu]^+$; elemental analysis: calcd (%) for $C_{30}H_{40}O_5Si$ (508.72): C 70.83, H 7.93; found: C 70.66, H 8.09.

Representative procedure for Suzuki–Miyaura coupling with p-methoxyphenylboronic acid: A solution of $[Pd_2(dba)_3]\cdot CHCl_3$ (8.8 mg, 0.0085 mmol), S-Phos (7.7 mg, 0.019 mmol), **19** (75.9 mg, 0.164 mmol), p-methoxyphenylboronic acid (50.0 mg, 0.33 mmol), and K_3PO_4 (101.3 mg, 0.48 mmol) in degassed toluene (2.5 mL) was stirred at 110 °C for 20 h. The reaction was quenched with saturated NH_4Cl (10 mL), and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layer was then washed with brine (40 mL) and dried with $MgSO_4$. After the solvent was removed in vacuo, the residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 4:1–2:1) to give **22** (70.5 mg, 97%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.49 (s, 3H), 3.18 (s, 3H), 3.34 (ddd, J = 9.3, 7.5, 1.2 Hz, 1H), 3.37 (s, 3H), 3.54 (dd, J = 11.1, 1.8 Hz, 1H), 3.57–3.72 (m, 3H), 3.69 (s, 3H), 3.84 (s, 3H), 3.92 (ddd, J = 9.9, 4.2, 1.8 Hz, 1H), 5.16 (d, J = 12.9 Hz, 1H), 5.27 (d, J = 12.9 Hz, 1H), 6.92 (s, 2H), 6.92–6.96 (m, 2H), 7.24 (d, J = 7.8 Hz, 1H), 7.27–7.31 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 17.6, 55.3, 59.3, 60.2, 60.4, 60.9, 71.5, 72.7, 73.0, 79.9, 83.7, 85.3, 110.5, 114.2, 129.1, 129.5, 130.8, 131.9, 132.4, 133.4, 136.4, 138.5, 159.1 ppm; MS (ESI):

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$m/z=467$ $[M+Na]^+$; elemental analysis: calcd (%) for $C_{25}H_{32}O_7$ (444.52): C 67.55, H 7.26; found: C 67.36, H 7.45.

27: Yellow gummy oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta=0.08$ (s, 6H), 0.91 (s, 9H), 1.33 (s, 3H), 1.60 (s, 3H), 2.55 (s, 3H), 3.75 (dd, $J=10.2$, 9.0 Hz, 1H), 3.80 (dd, $J=10.2$, 6.0 Hz, 1H), 3.84 (s, 3H), 4.35 (ddd, $J=9.0$, 6.0, 1.8 Hz, 1H), 4.76 (d, $J=6.0$ Hz, 1H), 4.88 (dd, $J=6.0$, 1.8 Hz, 1H), 4.99 (d, $J=12.9$ Hz, 1H), 5.04 (d, $J=12.9$ Hz, 1H), 6.92–6.96 (m, 2H), 7.18 (d, $J=7.8$ Hz, 1H), 7.23–7.28 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=-5.2$, −5.0, 18.5, 18.9, 24.1, 26.1, 55.3, 64.3, 70.4, 82.4, 85.4, 87.0, 112.7, 113.9, 118.4, 128.9, 129.4, 130.8, 132.1, 132.8, 133.5, 135.0, 138.2, 158.7 ppm; MS (EI): m/z (%) = 512 (9) $[M]^+$, 497 (12) $[M-CH_3]^+$, 455 (100) $[M-C(CH_3)_3]^+$; elemental analysis: calcd (%) for $C_{29}H_{40}O_6Si$ (512.71): C 67.94, H 7.86; found: C 67.90, H 7.90.

Representative procedure for Suzuki–Miyaura coupling with **28**: **29** from **19**: A solution of $[Pd_2(dba)_3]\cdot CHCl_3$ (5.2 mg, 0.0051 mmol), SPhos (9.1 mg, 0.022 mmol), **19** (92.6 mg, 0.200 mmol), **28** (161.4 mg, 0.398 mmol), and K_3PO_4 (127.5 mg, 0.60 mmol) in degassed toluene/H_2O (3 mL/30 mL) was stirred at 110 °C for 15 h. The reaction was quenched with saturated NH_4Cl (30 mL), and the mixture was extracted with EtOAc (3×30 mL). The combined organic layer was then washed with brine (60 mL) and dried with $MgSO_4$. After the solvent was removed in vacuo, the residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 5:1–1:1) to give **29** (92.4 mg, 75 %) as a colorless gummy oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta=1.42$ (s, 9H), 2.50 (s, 3H), 3.08–3.13 (m, 2H), 3.18 (s, 3H), 3.30–3.34 (m, 1H), 3.37 (s, 3H), 3.54 (dd, $J=10.8$, 1.8 Hz, 1H), 3.59 (s, 3H), 3.63–3.70 (m, 3H), 3.69 (s, 3H), 3.72 (s, 3H), 3.92 (ddd, $J=9.9$, 3.9, 1.8 Hz, 1H), 4.58–4.64 (m, 1H), 4.98–5.02 (m, 1H), 5.15 (d, $J=12.6$ Hz, 1H), 5.26 (d, $J=12.6$ Hz, 1H), 7.14–7.31 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=17.5$, 24.7, 28.2, 38.0, 52.1, 54.3, 59.2, 60.1, 60.3, 60.8, 71.4, 72.7, 72.9, 80.0, 83.7, 85.2, 110.4, 128.0, 129.5, 129.6, 130.8, 132.4, 133.2, 135.3, 136.4, 138.6 ppm; MS (ESI): $m/z=638$ $[M+Na]^+$; elemental analysis: calcd (%) for $C_{33}H_{45}NO_{10}$ (615.71): C 64.37, H 7.37, N 2.27; found: C 64.14, H 7.75, N 2.11.

30: Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta=0.08$ (s, 6H), 0.91 (s, 9H), 1.33 (s, 3H), 1.41 (s, 9H), 1.60 (s, 3H), 2.55 (s, 3H), 3.05 (dd, $J=13.5$, 5.7 Hz, 1H), 3.15 (dd, $J=13.5$, 6.0 Hz, 1H), 3.73 (s, 3H), 3.75 (dd, $J=9.9$, 9.0 Hz, 1H), 3.80 (dd, $J=10.2$, 5.7 Hz, 1H), 4.35 (ddd, $J=9.0$, 6.0, 1.5 Hz, 1H), 4.56–4.66 (m, 1H), 4.76 (d, $J=5.7$ Hz, 1H), 4.88 (dd, $J=6.0$, 1.5 Hz, 1H), 4.98 (d, $J=12.6$ Hz, 1H), 5.04 (d, $J=12.6$ Hz, 1H), 7.18 (t, $J=7.8$ Hz, 3H), 7.26 ppm (d, $J=7.8$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=-5.4$, −5.3, 18.3, 18.7, 24.0, 25.2, 25.9, 26.0, 28.2, 38.1, 52.2, 54.3, 64.3, 70.3, 80.0, 82.4, 85.5, 87.1, 112.9, 118.6, 128.1, 129.7, 131.1, 132.9, 133.9, 135.3, 135.8, 138.5, 138.6, 155.2, 172.5 ppm; MS (ESI): $m/z=706$ $[M+Na]^+$; elemental analysis: calcd (%) for $C_{37}H_{53}NO_9Si$ (683.90): C 64.98, H 7.81, N 2.05; found: C 64.87, H 8.08, N 1.89.

Representative procedure for copper-catalyzed coupling of iodophthalans with **32a**: **33a** from **31**: A solution of CuI (9.51 mg, 0.050 mmol), *N,N'*-dimethylethylenediamine (17.6 mg, 0.20 mmol), **31** (259.4 mg, 0.997 mmol), **32a** (140.6 mg, 1.20 mmol), and K_3PO_4 (446.4 mg, 2.10 mmol) in degassed toluene (1 mL) was stirred at 110 °C for 20 h. The reaction mixture was diluted with EtOAc (10 mL) and filtered through a pad of celite. The residue was washed with EtOAc (10 mL), and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 30:1) to give **33a** (236.1 mg, 95 %) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta=2.33$ (s, 3H), 5.02–5.03 (m, 2H), 5.18 (s, 2H), 6.67 (d, $J=3.3$ Hz, 1H), 7.13–7.27 (m, 6H), 7.68 ppm (dd, $J=6.3$, 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=18.4$, 72.9, 73.4, 103.3, 110.3, 120.2, 121.0, 122.2, 125.2, 127.6, 128.6, 129.6, 130.5, 131.2, 134.8, 136.1, 140.3 ppm; MS (ESI): $m/z=250$ $[M+H]^+$; elemental analysis: calcd (%) for $C_{17}H_{15}NO$ (249.31): C 81.90, H 6.06, N 5.62; found: C 82.00, H 6.02, N 5.52.

34: Colorless solid. M.p.: 55.1–56.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta=0.08$ (s, 6H), 0.91 (s, 9H), 1.36 (s, 3H), 1.62 (s, 3H), 2.61 (s, 3H), 3.73 (dd, $J=10.2$, 9.0 Hz, 1H), 3.79 (dd, $J=10.5$, 6.0 Hz, 1H), 4.38 (ddd, $J=9.0$, 6.0, 1.5 Hz, 1H), 4.78 (d, $J=6.0$ Hz, 1H), 4.82 (s, 2H), 4.89 (dd, $J=6.0$, 1.8 Hz, 1H), 6.65 (d, $J=3.0$ Hz, 1H), 7.13 (d, $J=3.0$ Hz, 1H), 7.13–7.34 (m, 5H), 7.66–7.69 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=-5.3$, −5.2, 18.4, 18.8, 24.1, 25.9, 26.0, 64.2, 69.1, 82.3, 85.7, 87.2, 103.4, 110.4, 112.9, 118.6, 120.3, 121.0, 122.3, 127.3, 127.7, 128.6, 130.9, 131.8, 135.4, 136.3, 136.4, 137.2 ppm; MS (ESI): $m/z=544$ $[M+Na]^+$; elemental analysis: calcd (%) for $C_{30}H_{39}NO_5Si$ (521.72): C 69.06, H 7.53, N 2.68; found: C 69.29, H 7.77, N 2.62.

Representative procedure for copper-catalyzed coupling of iodophthalans with **32b**: **33b** from **31**: A solution of CuI (9.50 mg, 0.050 mmol), *N,N'*-dimethylethylenediamine (17.6 mg, 0.20 mmol), **31** (259.4 mg, 0.997 mmol), **32b** (136.2 mg, 2.00 mmol), and Cs_2CO_3 (683.4 mg, 2.10 mmol) in degassed DMF (1 mL) was stirred at 110 °C for 25 h. The reaction mixture was diluted with EtOAc (10 mL) and filtered through a pad of celite. The residue was washed with EtOAc (10 mL), and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 1:1–0:1) to give **33b** (186.2 mg, 93 %) as a colorless solid. M.p.: 81.9–82.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta=2.30$ (s, 3H), 5.15 (s, 2H), 5.16 (s, 2H), 7.11–7.20 (m, 4H), 7.66 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=18.4$, 72.8, 73.4, 118.8, 122.6, 129.6, 129.9, 130.1, 131.2, 132.3, 136.3, 140.7 ppm; MS (EI): m/z (%) = 200 (100) $[M]^+$, 172 (77) $[M-CO]^+$, 156 (21) $[M-O(CH_2)_2]^+$, 145 (45) $[M-CO-HCN]^+$, 130 (58) $[M-O(CH_2)_2-CN]^+$; elemental analysis: calcd (%) for $C_{12}H_{12}N_2O$ (200.24): C 71.98, H 6.04, N 13.99; found: C 72.24, H 5.89, N 13.88.

35: Colorless solid. M.p.: 62.5–63.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta=1.31$ (s, 3H), 1.58 (s, 3H), 2.55 (s, 3H), 3.66 (br s, 1H), 3.72–3.84 (m, 2H), 4.54 (s, 1H), 4.78 (d, $J=6.0$ Hz, 1H), 4.98 (s, 2H), 5.03 (dd, $J=6.0$, 1.8 Hz, 1H), 7.05 (s, 1H), 7.17–7.28 (m, 3H), 7.60 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=18.5$, 23.8, 25.7, 63.5, 68.7, 80.8, 86.2, 88.4, 113.0, 118.3, 118.9, 124.8, 129.1, 130.0, 131.9, 134.2, 134.9, 136.3, 137.0 ppm; MS (ESI): $m/z=381$ $[M+Na]^+$; elemental analysis: calcd (%) for $C_{19}H_{22}N_2O_5$ (358.39): C 63.67, H 6.19, N 7.82; found: C 63.83, H 6.23, N 7.61.

Crystallographic Structural Determination

8: Single crystals suitable for X-ray analysis were obtained by recrystallization from EtOAc/hexane. A crystal was mounted on a glass fiber, and X-ray diffraction data were collected at 293 K on a Brucker SMART APEX CCD diffractometer with graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda=0.71073$ Å). Absorption correction was made with SADABS. The structure was solved by direct methods and refined by full-matrix least squares on F^2 by using SHELXTL.[41] All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in calculated positions.

35: Single crystals suitable for X-ray analysis were obtained by recrystallization from $CHCl_3$. A crystal was mounted on a glass fiber, and X-ray diffraction data were collected at 93 K on a Rigaku Saturn CCD area detector with graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda=0.71070$ Å). An empirical absorption correction was applied, which resulted in transmission factors of 0.844–0.952. The data were corrected for Lorentz and polarization effects. The structure was solved by direct methods and refined by full-matrix least squares on F^2 by using the CrystalStructure program package.[42] All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in calculated positions.

CCDC-633441 (**8**) and -656904 (**35**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk) or at www.ccdc.cam.ac.uk/conts/retrieving.html.

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