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Regioselectivity of Larock Indole Synthesis Using Functionalized Alkynes

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Regioselectivity of Larock indole synthesis, a palladium-catalyzed heteroannulation between *o*-iodoaniline and internal acetylene, was estimated using acetylenes substituted with ester and/or Boc-protected amine at the homopropargylic position and with perbenzyl- and unprotected glucose. Low to moderate regioselectivities were observed in all the cases, indicating these functional groups do not exert good directing effects, in the Larock indole synthesis.

Key words: palladium; indole; acetylene; regioselectivity; Larock indole synthesis

In 1991, Larock and Yum reported palladium-catalyzed heteroannulation between internal acetylene and *o*-iodoaniline giving a 2,3-disubsituted indole in a single step.[1,2] This reaction, known as the Larock indole synthesis,[3] has been employed in the synthesis of biologically interesting natural and unnatural compounds possessing an indole nucleus.[4–6] In the course of our synthetic studies on *C*-mannosyltryptophan,[7,8] a novel *C*-glycosylamino acid found in some proteins,[9] we attempted convergent synthesis of α-*C*-glucosyltryptophan by means of the Larock indole synthesis between glucosyl ethynylalanine derivative **1** and tosyl-*o*-iodoaniline **2**. We expected that the regioselectivity of the reaction would be controlled by the steric effect of tetra-*O*-benzyl-glucose of acetylene **1** to give a tryptophan derivative **4** as the desired product (eq. 1), because Larock suggested that the larger substituent of acetylene was preferentially introduced into the 2 position of the indole product. However, the reaction between **1** and **2** under the conditions reported by Larock gave not tryptophan derivative **4** but *iso*-tryptophan derivative **3** in a high yield.[10] This unexpected result motivated us to study unknown factors determining the complete reversed regioselectivity in the Larock indole synthesis. At the outset, we hypothesized that the protected amino acid functionality of **1** would determine the regioselectivity, because Larock also suggested that a substituent containing a hydroxyl group at the propargylic position was preferentially introduced into the 2 position of indole, due to coordination of the hydroxyl group with palladium catalyst in a reaction intermediate. We disclose herein full details of our efforts to clarify the reasons for this reverse regioselectivity.[11–13]

Results and Discussions

In order to find factors determining regioselectivity in the reaction of eq. 1, we planned to investigate the regioselectivity of the Larock indole synthesis using acetylenes **7**, **10**, **13**, including Boc-protected amine, ester, and protected amino acid respectively, and tetra-*O*-benzyl-α-*C*-glucosylacetylene **18**. In addition, unprotected α-*C*-glucosylacetylene **19** was synthesized to evaluate the effect of the benzyl groups of **18** in the Larock indole synthesis.

*Synthesis of functionalized acetylenes **7**, **10**, and **13***

N-Boc-hexynylamine **7** was prepared in three steps from 3-hexyne-1-ol **5**, as shown in Scheme 1.* 3-Hexyn-1-ol **5** was condensed with phthalimide under the Mitsunobu conditions to give **6**. Removal of the phthalimide with *N*-methylhydrazine[14] in methanol, followed by Boc-protection, afforded *N*-Boc-hexynylamine **7** in a good yield. 4-Heptynoic acid methyl ester **10** was synthesized by malonate ester synthesis;[15] alkylation of diethyl malonate with 1-bromo-2-pentyne **8** gave **9**. After alkaline hydrolysis of the ester, decarboxylation, and esterification yielded **10**. Propargyl glycine derivative **13** was synthesized from Schiff base **11** of glycine methyl ester through alkylation[16] with 1-bromo-2-pentyne **8**, hydrolysis of the Schiff base, and protection with Boc group.

*Synthesis of sugar acetylene **18** and **19***

According to a synthetic method for sugar acetylenes developed in this laboratory,[17,18] we would synthesize sugar acetylene **18** by means of *C*-glycosylation of 1-*O*-acetyl-2,3,4,6-tetra-*O*-benzylgluocose **14** (Scheme 2). However, the reaction of **14** with (but-1-ynyl)tributylstannane **17** in the presence of TMSOTf gave an inseparable mixture of α- and β-*C*-glucoside **18** in moderate stereoselectivity (*ca.* 4:1). This is a contrast to the result of the reaction of **14** with (trimethylsilyl)-

* All reactions had not been optimized.

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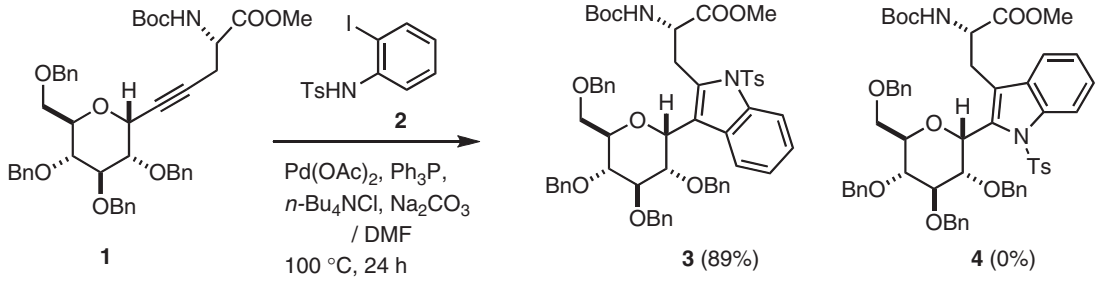
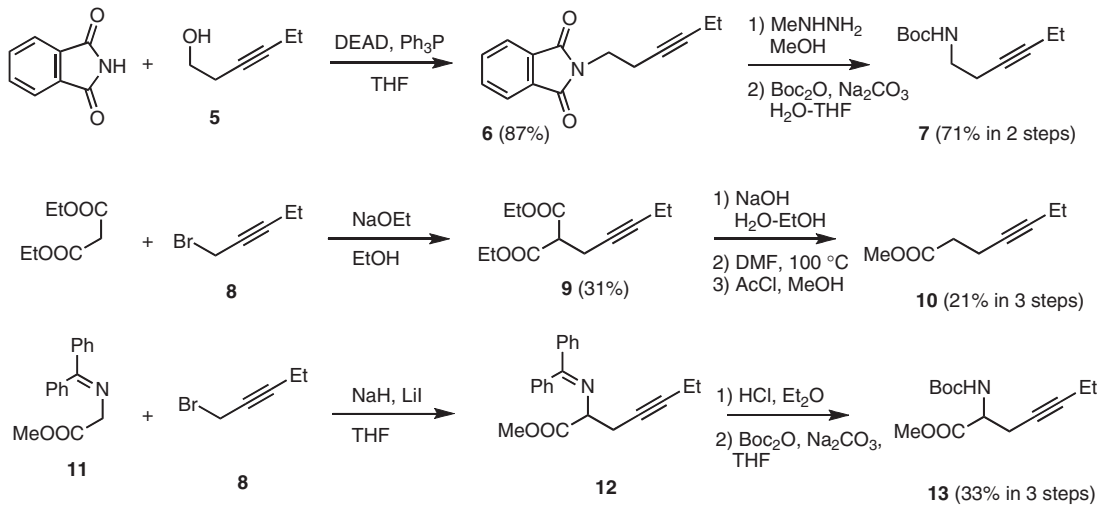
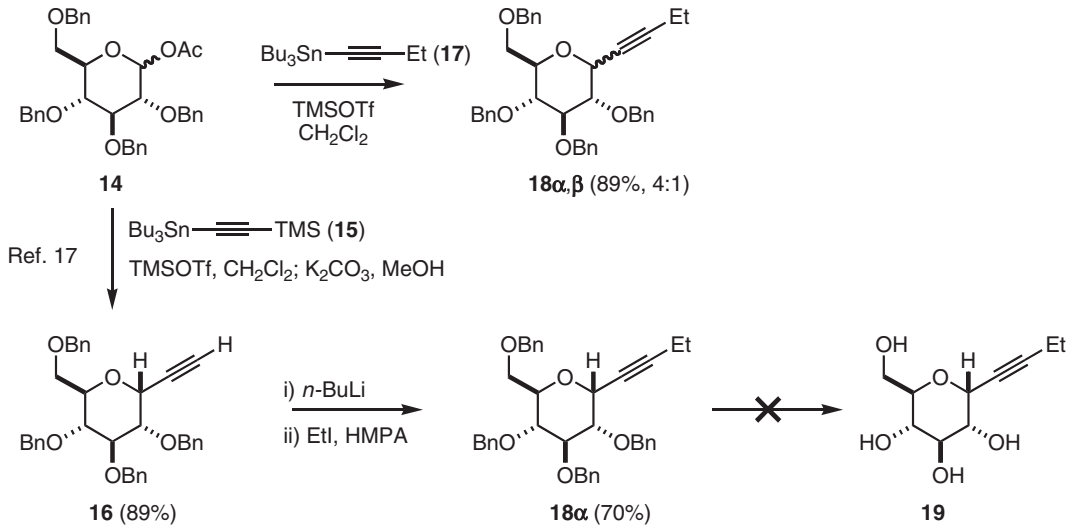


eq. 1. The Complete Reversed Regioselectivity in the Larock Indole Synthesis.



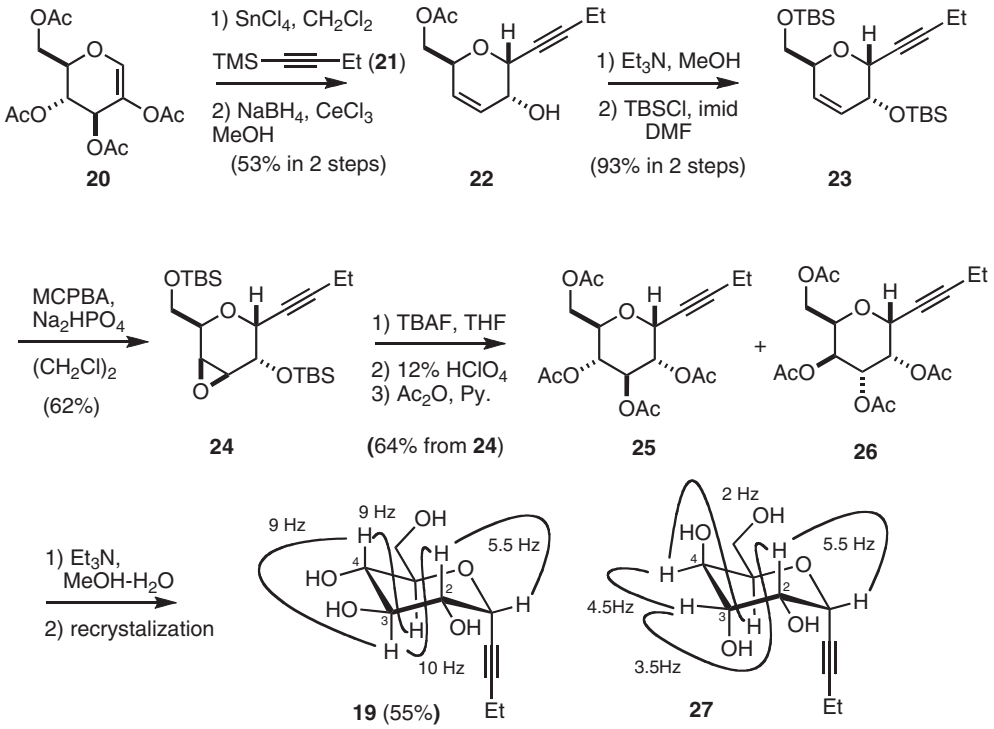
Scheme 1. Preparation of Functionalyzed Acetylenes **7**, **10**, and **13**.



Scheme 2. Synthesis of Sugar Acetylene Protected by Benzyl Groups.

ethynyltributylstannane **15** under the same conditions, giving α-*C*-glucosylacetylene **16** as a single product. Hence, sugar acetylene **18**α was prepared as a pure form from **16** by alkylation with ethyl bromide by a conventional method. On the other hand, preparation of unprotected glucosylacetylene **19** from **18**α by debenzylation proved difficult.[19] Since all attempted deprotection of **18**α were unsuccessful, we explored an alternative route for unprotected sugar acetylene **19**.

After extensive studies, we finally found a new route for the synthesis of **19**, as shown in Scheme 3, on the basis of *C*-glycosylation developed in this laboratory.[20–22] Reaction of 2-acetoxyl-D-glucal **20** with TMS-butyne **21** in the presence of $SnCl_4$ gave an unstable enol



Scheme 3. Synthesis of Unprotected Sugar Acetylene **19**.

acetate, which was treated with a large amount of $NaBH_4$ in the presence of $CeCl_3$ to afford allylic alcohol **22** in 53% overall yield from **20**. In the next epoxidation with MCPBA, we found that bis-TBS ether **23** derived from **22** was the best substrate to obtain high yield of β-epoxide **24**. After removal of the silyl groups of **24**, the epoxide was hydrolyzed with 12% $HClO_4$.[23] The products were purified as a mixture of the corresponding acetates **25** and **26** in a 7:1 ratio (by ^{1}H NMR). Deacetylation followed by re-precipitation gave α-*C*-glucosylacetylene **19** as a pure form in 55% isolated yield. The stereochemistry was determined by three large coupling constants ($J_{2-3} = 10$ Hz, $J_{3-4} = 9$ Hz, and $J_{4-5} = 9$ Hz) of the ^{1}H NMR spectra, as shown in Scheme 3. The structure of isomer **27** was also confirmed by NMR analysis.

Regioselectivity in the Larock indole synthesis

The Larock indole synthesis using acetylenes **7**, **10**, **13**, **18**, and **19** with *N*-tosyl-*o*-iodoaniline **2** were conducted under the conditions reported by Larock. The regioselectivities were summarized in Table 1. The regiochemistries of the products were determined by NOESY spectra, depicted in eq. 2. Unexpectedly, all the reactions gave low selectivities (entries 1 to 5). The slight preferences observed may be attributed to the steric effect of the substituents. These results indicate that ester, carbamate, and protected amino acid at the homopropargylic position have little effect on regioselectivity (entries 1 to 3). More surprisingly, the reaction with the tetra-*O*-benzyl-glucosylacetylene **18** and the corresponding unprotected glucosylacetylene **19** exhibited low selectivities, to give **31** and **32**** (entries 4 and 5), indicating the tetra-*O*-benzylglucose moiety was not recognized as a sterically hindered substituent in this reaction and none of the four hydroxyl groups of **19** was involved in the reaction.

Conclusion

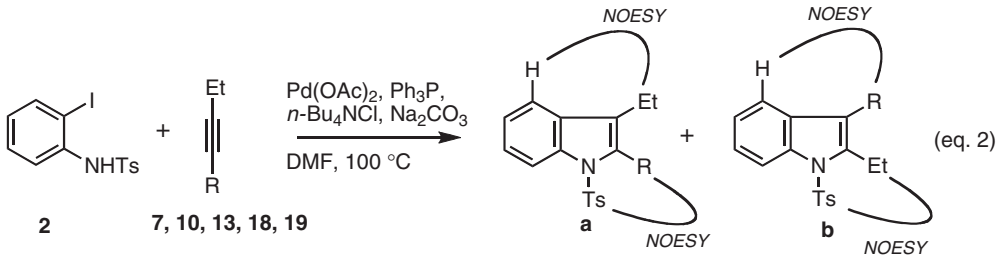
Despite our systematic studies, we have not yet identified the factors determining the regioselectivity of eq. 1. However, these studies have revealed that the ester and carbamate group at the homopropargylic position and glucose moiety did not afford high regioselectivity, although these functional groups were seemingly the controlling factors, through coordination to a palladium catalyst or the steric hindrance. These results should provide an important guideline as to when the Larock indole synthesis would be employed in the syntheses of complex compounds. Further examination to control the regioselectivity of the Larock indole synthesis with functionalized acetylene is in progress in our laboratory.

Experimental

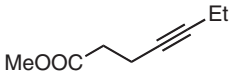
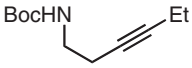
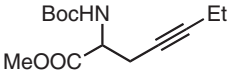
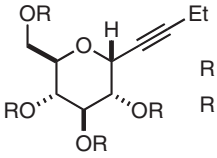
General procedure. Melting points (Mp) were recorded on a Yanaco MP-S3 melting point apparatus. Optical rotations ($[\alpha]_D$) were measured on a JASCO

** The structure of **32a** was confirmed by NMR analysis of the corresponding acetate **33a**, because ^{1}H NMR signals of **32a** were heavily overlapped. For the details, see the experimental.

Table 1. Regioselectivity of the Larock Indole Synthesis with *o*-Iodoaniline **2** and Functionalized Acetylenes



2 **7, 10, 13, 18, 19**

entry	acetylene		time (h)	products	yield (%)	ratio (**a**:**b**)[a]
1		**7**	2	**28**	75	60:40
2		**10**	24	**29**	90	56:44
3		**13**	40	**30**	50	56:44
4		R = Bn **18**	1	**31**	60	65:35
5		R = H **19**	48	**32**	16	69:31

[a]Ratios were determined by ^{1}H-NMR spectra

DIP-370 digital polarimeter. Infrared spectra (IR) were recorded on a JASCO FT/IR-8300 spectrophotometer, and are reported in wave number (cm^{-1}). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a BRUKER ARX-400 (400 MHz), a BRUKER AVANCE-400 (400 MHz), or a Varian Gemini-2000 (300 MHz) spectrometers. NMR samples were dissolved in $CDCl_3$ or CD_3OD. Measured in $CDCl_3$, chemical sifts are reported in ppm from tetramethylsilane ($\delta = 0.00$ ppm), or in ppm relative to the residual undeuterated $CHCl_3$ ($\delta = 7.26$ ppm) for compounds containing the Si group. Measured in CD_3OD, chemical sifts are reported in ppm relative to residual undeuterated CD_2HOD ($\delta = 3.30$ ppm). The data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broadening, m = multiplet), coupling constant, and assignment. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a BRUKER ARX-400 (100 MHz), a BRUKER AVANCE-400 (100 MHz), or a Varian Gemini-2000 (75 MHz) spectrometers. NMR samples were dissolved in $CDCl_3$ or CD_3OD, and chemical sifts are reported in ppm relative to the solvent ($CDCl_3$ as $\delta = 77.0$, CD_3OD as $\delta = 49.3$ ppm). 2D NMR (COSY, NOESY, HMBC, HMQC) were measured on a BRUKER AVANCE-400 (400 MHz) spectrometer. All NMR were measured at 300 K. High resolution mass spectra (HRMS) were recorded on a JEOL JMS-LCmate spectrometer, and are reported in m/z. Elemental analyses were performed by the Analytical Laboratory at the Graduate School of Bioagricultural Sciences of Nagoya University. The reactions were monitored by thin-layer chromatography (TLC) on 0.25 mm silica gel-coated glass plates 60 F_{254} (Merck, #1.05715). Visualization was achieved using UV light and an appropriate reagent (7% ethanolic phosphomolybdic acid or *p*-anisaldehyde solution), followed by heating. Silica gel (spherical, particle size 0.063–0.2 mm, Merck, # 1.07734.9929) and silica gel (N) (spherical, neutral, particle size 0.063–0.210 mm, Kanto, # 37565-84) were used for open-column chromatography. Silica gel (spherical, particle size 40–50 μm, Kanto, # 37562-84) and silica gel (N) (spherical, neutral, particle size 40–50 μm, Kanto, # 37563-79) were used for flash-column chromatography. Preparative thin-layer chromatographic separations were carried out on 0.5 mm silica gel plates 60 F_{254} (Merck, #1.05774). Non-aqueous reactions were carried out in oven-dried (120 °C) or flame-dried glassware under nitrogen or argon atmosphere. Anhydrous THF and CH_2Cl_2 were purchased from Kanto Chemical Co., Inc. Anhydrous DMF was purchased from Wako Pure Chemical Industries, Ltd. Et_3N was distilled from CaH_2. All other commercially available reagents were used as received.

*2-(Hex-3-ynyl)isoindoline-1,3-dione (**6**).* To a solution of phthalimide (4.19 g, 20.0 mmol), Ph_3P (5.34 g, 20.0 mmol), and 3-hexyne-1-ol (**5**) (2.2 ml, 20 mmol)

in anhydrous THF (162 ml) was added DEAD (9.3 ml, 20 mmol) dropwise under N_2 atmosphere. The mixture was stirred at room temperature for 1.5 h, and then concentrated. The Ph_3PO in the residue was recrystallized from Et_2O-hexane and removed by filtration. The mother liquor was evaporated, and the residue was purified by open-column chromatography (silica gel 190 g, AcOEt:hexane = 1:5) to afford **6** (3.93 g, 87%) as yellow crystals. Mp: 75–77 °C. IR (KBr) ν_{max} 3460, 2974, 1771, 1705, 1401, 1112 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.02 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.08 (2H, qt, $J = 7.5$, 2.5 Hz, CH_2CH_3), 2.54 (2H, tt, $J = 7$, 2.5 Hz, NCH_2CH_2), 3.83 (2H, t, $J = 7$ Hz, NCH_2CH_2), 7.68–7.75 (2H, m, aromatic), 7.81–7.88 (2H, m, aromatic). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.1, 13.8, 18.5, 37.0, 75.2, 83.7, 123.2, 132.1, 134.0, 168.1. Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.85; H, 5.52; N, 6.11.

*tert-Butyl hex-3-ynylcarbamate (**7**).* A solution of **6** (2.27 g, 10.0 mmol) and $MeNHNH_2$ (5.2 ml, 0.10 mol) in MeOH (42.0 ml)-THF (42.0 ml) was stirred at 70 °C for 3 h under N_2 atmosphere. The solution was diluted with H_2O and extracted with AcOEt (x3). The combined organic layers were concentrated, and the residue was dissolved in THF (21.0 ml) and H_2O (21.0 ml). To the solution were added Na_2CO_3 (4.24 g, 40.0 mmol) and Boc_2O (8.72 g, 40.0 mmol). After stirring at room temperature for 1 h, the reaction mixture was extracted with AcOEt (x3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by open-column chromatography (silica gel 80 g, AcOEt:hexane = 1:10 → 1:7) to afford Boc hexynylamine **7** (1.41 g, 71%) as a yellow oil. IR (KBr) ν_{max} 3419, 3312, 2978, 1699, 1522, 1367, 1252, 1173, 965, 870 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.10 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 1.43 (9H, s, CH_3 of Boc), 2.14 (2H, qt, $J = 7.5$, 2.5 Hz, CH_2CH_3), 2.31 (2H, tt, $J = 6.5$, 2.5 Hz, NCH_2CH_2), 3.21 (2H, br s, $NHCH_2CH_2$), 4.81 (1H, br s, NH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.3, 14.1, 20.2, 28.4, 39.7, 76.3, 79.2, 83.3, 155.7. Anal. Calcd. for $C_{11}H_{19}NO_2$: C, 66.97; H, 9.71; N, 7.10. Found: C, 66.88; H, 9.92; N, 7.23.

*Diethyl pent-2-ylmalonate (**9**).* To a solution of EtONa (33 mmol, prepared from 0.75 g of Na in 25 ml EtOH) was added diethyl malonate (4.6 ml, 30 mmol). After stirring at room temperature for 10 min, a solution of 1-bromopent-2-yne (**8**) (3.0 ml, 30 mmol) in EtOH (25 ml) was added dropwise. The mixture was stirred at room temperature for 2 h and then evaporated. To the residue was added H_2O and the mixture was extracted with CH_2Cl_2 (x3). The combined organic layers were washed with brine (x1), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash-column chromatography (silica gel (N) 150 g, AcOEt:hexane 1:10) to afford **9** (2.10 g, 31%) as a pale yellow oil. IR (KBr) ν_{max} 3652, 3462, 2981, 2239, 1736, 1465, 1371, 1155, 1036 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.08 (3H, t, $J = 7.5$ Hz, CCH_2CH_3), 1.28 (6H, t, $J = 7$ Hz, $COOCH_2CH_3$), 2.13 (2H, qt, $J = 7.5$, 2.5 Hz, CCH_2CH_3), 2.73 (2H, dt, $J = 8$, 2.5 Hz, $CHCH_2$), 3.51 (1H, t, $J = 8$ Hz, $CHCH_2$), 4.22 (2H, q, $J = 7$ Hz, $COOCH_2CH_3$). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.2, 13.9(x2), 18.7, 51.8, 61.5, 74.9, 83.8, 168.3. Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.49; H, 7.84.

*Methyl hept-4-ynoate (**10**).* To a solution of **9** (2.10 g, 9.28 mmol) in EtOH (26 ml) was added 2 N NaOH aq. (26.0 ml, 46.4 mmol), and stirring was continued at room temperature for 1 h. After removal of ethanol by evaporation, the solution was acidified to pH 2 with 1 N HCl, and extracted with AcOEt (x3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The resulting white crystals (dicarboxylic acid, 1.52 g) were dissolved in DMF (30 ml), and the solution was heated at 100 °C for 1 h. After dilution with AcOEt, the mixture was washed with 1 N HCl solution, dried over anhydrous Na_2SO_4, and concentrated to give hept-4-ynoic acid (1.13 g) as yellow crystals. A solution of the crude carboxylic acid (1.13 g) in MeOH (45 ml) was treated with AcCl (64 µl, 0.90 mmol) and stirred at room temperature for 10.5 h. The solution was diluted with Et_2O, quenched with sat. $NaHCO_3$ solution, and extracted with Et_2O (x3). The combined organic layers were washed with H_2O (x2) and brine (x1), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure (>20 mmHg). The residue was distilled (96–97 °C under 50 mmHg) to afford methyl hept-4-ynoate **10** (242 mg, 21% in 3 steps) as a colorless oil. IR (KBr) ν_{max} 2977, 1742, 1438, 1367, 1169 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.10 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.14 (2H, qt, $J = 7.5$, 2 Hz, CH_2CH_3), 2.43–2.55 (4H, m, CH_2CH_2), 3.70 (3H, s, $COOCH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.3, 14.1, 14.8, 33.9, 51.8, 82.3 (x2), 172.6. Anal. Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.43; H, 8.55.

*t-Butyl-1-(methoxycarbonyl)hex-3-ynylcarbamate (**13**).* A solution of ketimine **11** (1.27 g, 5.00 mmol) in anhydrous THF (23 ml) was added to a flask charged with NaH (0.2 g, 5 mmol, 60% dispersion in oil, washed with hexane) and LiI (67 mg, 0.50 mmol). The suspension was stirred at room temperature for 20 min, and then 1-bromo-2-pentyne **8** (0.6 ml, 6 mmol) was added dropwise *via* a cannular tubing. The mixture was stirred vigorously at room temperature for 85 h and evaporated. The residue was dissolved in sat. NH_4Cl solution at 0 °C, and the solution was extracted with Et_2O (x2). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated to give propargyl ketimine **12** as a yellow oil. The crude product was dissolved in Et_2O (10.0 ml), and 1 N HCl (3.0 ml, 3.0 mmol) was added. The mixture was stirred at room temperature for 22.5 h and then partitioned. The aqueous layer was diluted with

THF (12.5 ml), and then Boc_2O (1.4 ml, 6.0 mmol) and Na_2CO_3 (636 mg, 6.00 mmol) were added. The mixture was stirred at room temperature for 12 h, and then extracted with Et_2O (x3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by open-column chromatography (silica gel 30 g, AcOEt:hexane = 1:20 → 1:7) to afford **13** (422 mg, 33% in 3 steps) as low-melting white crystals. Mp: 31–32 °C. IR (KBr) ν_{max} 3553, 3482, 2979, 1749, 1717, 1508, 1367, 1168 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.08 (3H, t, J = 7.5 Hz, CH_2CH_3), 1.44 (9H, s, CH_3 of Boc), 2.12 (2H, qt, J = 7.5, 2.5 Hz, CH_2CH_3), 2.60 (1H, ddt, J = 17, 5, 2.5 Hz, $CHCH_aH_b$), 2.69 (1H, br d, J = 17 Hz, $CHCH_aH_b$), 3.74 (3H, s, $COOCH_3$), 4.41 (1H, m, $CHCH_aH_b$), 5.26 (1H, br s, NHBoc). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.3, 14.0, 23.1, 28.3, 52.3, 52.4, 73.2, 80.0, 85.3, 155.2, 171.5. Anal. Calcd. for $C_{13}H_{21}NO_4$: C, 61.16; H, 8.29; N, 5.49. Found: C, 61.38; H, 8.34; N, 5.54.

*(2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl)but-1-yne (**18**α,β).* Glucosylacetate **14** (1.46 g, 2.50 mmol, azeotropically dried with toluene) was placed in a flask connected to a vacuum/N_2 line. The flask was evacuated and filled with N_2. After this evacuated/filling cycle was repeated three times, anhydrous CH_2Cl_2 (45 ml) and stannylacetylene **17** (1.6 ml, 5.0 mmol) were added. To the solution cooled to 0 °C was added TMSOTf (0.5 ml, 2.5 mmol). After stirring at 4 °C for 12 h, additional TMSOTf (0.3 ml, 2.5 mmol) was added. The mixture was stirred for 23 h, and then quenched with sat. Na_2CO_3 solution. After extraction with CH_2Cl_2 (x3), the combined organic layers were washed with H_2O (x2) and brine (x1), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash-chromatography (silica gel 70 g, AcOEt:hexane = 0:1 → 1:5) to afford glucosylacetylene **18**α,β (1.46 g, 89%, α:β = 4:1 by ^1H NMR spectra) as a yellow oil.

*(2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl)but-1-yne (**18**α).* Glucosylacetylene **16** (165 mg, 0.300 mmol, azeotropically dried with toluene) and a trace of Ph_3CH (as an indicator) were placed in a flask that was connected to a vacuum/N_2 line. The flask was evacuated and filled with N_2. After this evacuation/filling cycle was repeated 3 times, anhydrous THF (4.9 ml) was added, and the flask was cooled to −78 °C. *n*-BuLi (0.5 ml, 0.8 mmol) was added dropwise until the color of the solution turned to orange. After stirring for 1 h, EtI (0.11 ml, 1.2 mmol) and HMPA (0.12 ml, 0.80 mmol) were added. The reaction mixture was allowed to warm to room temperature, and stirring was continued for an additional 8 h. The reaction was quenched with sat. $NaHCO_3$ solution, and the mixture was extracted with AcOEt (x3). The combined organic layers were washed with H_2O (x2) and brine (x1), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash-chomatography (silica gel 15 g, AcOEt:hexane = 1:10 → 1:5) to afford glucosylacetylene **18**α (121 mg, 70%) as a pale yellow oil. $[\alpha]_D^{28}$ 65.5° (*c* 1.70, $CHCl_3$). IR (KBr) ν_{max} 2869, 2230, 1497, 1455, 1364, 1092 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.18 (3H, t, J = 7.5 Hz, CH_2CH_3), 2.29 (2H, qd, J = 7.5, 2 Hz, CH_2CH_3), 3.62 (1H, dd, J = 9.5, 5.5 Hz, H-2), 3.62 (1H, dd, J = 10, 9.5 Hz, H-4), 3.67 (1H, dd, J = 11, 2 Hz, H-6), 3.75 (1H, dd, J = 11, 3.5 Hz, H-6′), 3.94 (1H, t, J = 9.5 Hz, H-3), 4.00 (1H, ddd, J = 10, 3.5, 2 Hz, H-5), 4.49 (1H, d, J = 12 Hz, OCH_aH_bPh), 4.49 (1H, d, J = 10.5 Hz, OCH_cH_dPh), 4.61 (1H, d, J = 12 Hz, OCH_aH_bPh), 4.70 (2H, s, OCH_2Ph), 4.80 (1H, dt, J = 5.5, 2 Hz, H-1), 4.82 (1H, d, J = 11 Hz, OCH_eH_fPh), 4.83 (1H, d, J = 10.5 Hz, OCH_cH_dPh), 4.99 (1H, d, J = 11 Hz, OCH_eH_fPh), 7.13–7.17 (2H, m, aromatic), 7.25–7.40 (18H, m, aromatic). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.6, 13.7, 66.7, 68.6, 72.6, 73.1, 73.4, 73.8, 75.2, 75.5, 77.5, 79.1, 83.0, 91.6, 127.6, 127.7, 127.8 (x2), 127.9, 128.0 (x2), 128.1, 128.4 (x2), 138.0, 138.1, 138.2, 138.9. Anal. Calcd. for $C_{38}H_{40}O_5$: C, 79.14; H, 6.99. Found: C, 79.01; H, 6.78.

*6-O-Acetyl-1-(but-1-ynyl)-3,4-dideoxy-α-D-(2S,5S)-hex-3-enopyranose (**22**).* To a solution of 2-acetoxy-D-glucal **20** (5.0 g, 15 mmol) and TMS-butyne **21** (4.8 ml, 30 mmol) in anhydrous CH_2Cl_2 (100 ml) was added $SnCl_4$ (3.5 ml, 30 mmol) at −10 °C. After stirring at −10 °C for 5 min, the reaction was quenched with sat. Na_2CO_3 solution and sat. potassium sodium (+)-tartrate solution. After filtration through a pad of Super-Cel, the filtrate was extracted with CH_2Cl_2 (x3). The combined organic layers were washed with brine (x1), dried over anhydrous Na_2SO_4, and concentrated. The residue (enol acetate) was dissolved in MeOH (100 ml), and $CeCl_3 \cdot 7H_2O$ (11.2 g, 30.0 mmol) and $NaBH_4$ (0.28 g, 7.5 mmol) were added at 0 °C. After stirring at 0 °C for 30 min, additional $NaBH_4$ (5.10 g, 135 mmol) was added portionwise over 5 h, until the enol acetate was consumed [judged by TLC (Et_2O:hexane = 4:1)]. The reaction was quenched with sat. Na_2CO_3 solution and extracted with AcOEt (x3). The combined organic layers were washed with brine (x1), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography (silica gel 100 g, AcOEt:hexane = 1:5 → 1:4 → 1:3) to afford allylic alcohol **22** (1.79 g, 53%) as white crystals. Mp: 67.0 °C–67.1 °C. $[\alpha]_D^{25}$ −116.0° (*c* 0.15, $CHCl_3$). IR (KBr) ν_{max} 3524, 2978, 2242, 1743, 1456, 1369, 1239, 1039 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17 (3H, t, J = 7.5 Hz, CH_2CH_3), 1.96 (1H, d, J = 11 Hz, OH), 2.10 (3H, s, CH_3 of Ac), 2.27 (2H, qd, J = 7.5, 2 Hz, CH_2CH_3), 4.15 (2H, d, J = 5 Hz, H-6), 4.26 (1H, m, H-2), 4.56 (1H, m, H-5), 4.89 (1H, dt, J = 5.5, 2 Hz, H-1), 5.73 (1H, dt, J = 10.5, 2 Hz, H-3), 5.87 (1H, dtd, J = 10.5, 2.5, 0.5 Hz, H-4). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.3, 13.6, 20.8, 63.5, 65.1, 67.4, 69.0, 73.1, 91.1, 127.1, 129.8, 171.0. Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.28; H, 7.28.

*2,6-O-bis-(t-Butyldimethylsilyl)-1-but-1-ynyl-3,4-dideoxy-α-D-(2S,5S)-hex-3-enopyranose (**23**).* A solution of allylic alcohol **22** (1.79 g, 7.99 mmol) in MeOH (25 ml), Et_3N (5 ml), and H_2O (5 ml) was stirred at room temperature for 16 h and evaporated. The residue was dissolved in DMF (45 ml), and imidazole (3.26 g, 48.0 mmol) and TBSCl (3.61 g, 24.0 mmol) were added. After stiring at room temperature for 4 h, the reaction was quenched with ice-cold H_2O and extracted with AcOEt (x3). The combined extract was washed with H_2O (x2) and brine (x1), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography (silica gel 150 g, AcOEt:hexane = 1:20) to afford bis-TBS ether **23** (3.06 g, 93%) as a colorless oil. $[\alpha]_D^{28}$ −62.8° (*c* 0.60, $CHCl_3$). IR (KBr) ν_{max} 2930, 1473, 1256, 1117 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.06 (6H, s, $SiCH_3$), 0.10 (6H, s, $SiCH_3$), 0.89 (9H, s, CH_3 of *t*-Bu), 0.91 (9H, s, CH_3 of *t*-Bu), 1.13 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.23 (2H, qd, $J = 7.5$, 2 Hz, CH_2CH_3), 3.57 (1H, dd, $J = 10$, 6 Hz, H-6), 3.62 (1H, dd, $J = 10$, 5 Hz, H-6′), 4.31–4.41 (2H, m, H-2 and 5), 4.74 (1H, br d, $J = 5$ Hz, H-1), 5.70 (1H, br d, $J = 11$ Hz, olefinic), 5.82 (1H, br d, $J = 11$ Hz, olefinic).^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.4, −4.8, 12.5, 13.7, 18.1, 18.3, 25.7, 25.8, 65.1, 65.4, 67.7, 70.9, 74.7, 88.5, 127.9, 129.0. Anal. Calcd. for $C_{22}H_{42}O_3Si_2$: C, 64.33; H, 10.31. Found: C, 64.20; H, 10.56.

*2,6-O-bis-(t-Butyldimethylsilyl)-1-(but-1-ynyl)-3,4-anhydro-α-D-galactose (**24**).* To a solution of bis-TBS ether **23** (1.97 g, 4.80 mmol) in $(CH_2Cl)_2$ (48 ml) were successively added Na_2HPO_4 (1.36 g, 9.60 mmol) and MCPBA (0.83 g, 4.80 mmol). After stirring at room temperature for 36 h, the reaction mixture was filtered through a cotton plug, and additional NaH_2PO_4 (2.72 g, 19.2 mmol) and MCPBA (1.66 g, 9.60 mmol) were added. After stirring for 24 h, the mixture was treated with sat. $NaHCO_3$ solution and sat. $NaHSO_3$ solution, and then filtered through a pad of Super-Cel. The filtrate was extracted with AcOEt (x2). The combined organic layers were washed with brine (x1), dried over anhydrous Na_2SO_4, and concentrated. The residue was suspended in hexane and then filtered through a Kiriyama-funnel to remove the *m*-chlorobenzoic acid. The filtrate was concentrated and then purified by flash-chromatography (silica gel 60 g, AcOEt:hexane = 0:1 → 1:100) to afford epoxide **24** (1.44 g, 70%) as a colorless oil. $[\alpha]_D^{26}$ −16.9° (*c* 0.70, $CHCl_3$). IR (KBr) ν_{max} 2931, 2859, 1473, 1362, 1258, 1118 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.08 (6H, s, $SiCH_3$), 0.10 (3H, s, $SiCH_3$), 0.13 (3H, s, $SiCH_3$), 0.90 (9H, s, CH_3 of *t*-Bu), 0.92 (9H, s, CH_3 of *t*-Bu), 1.14 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.24 (2H, qd, $J = 7.5$, 2 Hz, CH_2CH_3), 3.24 (1H, d, $J = 4$ Hz, H-3), 3.32 (1H, dd, $J = 4$, 1.5 Hz, H-4), 3.74 (2H, d, $J = 7$ Hz, H-6), 3.87 (1H, d, $J = 5.5$ Hz, H-2), 4.28 (1H, td, $J = 7$, 1.5 Hz, H-5), 4.45 (1H, dt, $J = 5.5$, 2 Hz, H-1). ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.6, −5.5, −5.0, −4.9, 12.4, 13.7, 18.0, 18.3, 25.6, 25.8, 50.8, 55.4, 62.4, 65.7, 65.8, 68.9, 73.9, 90.1. Anal. Calcd. for $C_{22}H_{42}O_4Si_2$: C, 61.92; H, 9.92. Found: C, 61.92; H, 10.12.

*(2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosyl)but-1-yne (**25**) and (2,3,4,6-tetra-O-acetyl-α-D-gulopyranosyl)but-1-yne (**26**).* To a solution of epoxide **24** (0.28 g, 0.64 mmol) in THF (5.5 ml) was added TBAF (1.0 m in THF, 2.6 ml, 2.6 mmol). After stirring at room temperature for 1.5 h, the solution was concentrated. The residue was dissolved in a 12% $HClO_4$ solution (13 ml), and stirring was continued at room temperature for 12 h. After the reaction mixture was filtered through a cotton plug, an additional 12% $HClO_4$ solution (6 ml) was added, and stirring was continued for 34 h. The reaction was quenched with $NaHCO_3$ solid and concentrated azeotropically with EtOH. The residue (18.8 g) was dissolved in Ac_2O (6 ml) and pyridine (6 ml), and the solution was stirred at room temperature for 21 h. The reaction was quenched with ice-H_2O, and the mixture was extracted with AcOEt (x3). The combined organic layers were washed with sat. NH_4Cl solution (x1), sat. $NaHCO_3$ solution (x1), and brine (x1), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash-chromatography (AcOEt:hexane = 1:3 → 1:2 → 1:1) to afford a mixture of **25** and **26** (157 mg, 64%, 25:26 = 7:1).

*(α-D-Glucopyranosyl)but-1-yne (**19**) and (α-D-gulopyranosyl)but-1-yne (**27**).* A solution of a mixture of **25** and **26** (157 mg) in MeOH (2.5 ml), Et_3N (0.5 ml), and H_2O (0.5 ml) was stirred at room temperature for 12 h, and then concentrated azeotropically with toluene. Recrystallization from AcOEt and MeOH afforded glucosyl acetylene **19** (48 mg, 55%) as a white solid. Isomer **27** was obtained by flash-chromatography (MeOH:AcOEt = 1:20) of the mother liquor for spectroscopic analysis. **19**: $[\alpha]_D^{30}$ 116.1° (*c* 2.65, CH_3OH). IR (KBr) ν_{max} 3463, 2928, 2654, 2520, 2228, 1733, 1564, 1460, 1319, 1243, 1062 cm^{-1}. ^1H NMR (CD_3OD, 300 MHz) δ 1.15 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.26 (2H, qd, $J = 7.5$, 2 Hz, CH_2CH_3), 3.26 (1H, dd, $J = 10$, 9 Hz, H-3), 3.45 (1H, dd, $J = 10$, 5.5 Hz, H-2), 3.63 (1H, t, $J = 9$ Hz, H-4), 3.66 (1H, dd, $J = 12$, 5 Hz, H-6), 3.76 (1H, ddd, $J = 9$, 5, 2 Hz, H-5), 3.79 (1H, dd, $J = 12$, 2 Hz, H-6′), 4.63 (1H, dt, $J = 5.5$, 2 Hz, H-1). ^{13}C NMR (CD_3OD, 75 MHz) δ 14.0, 15.0, 63.7, 70.8, 72.6, 73.3, 76.2, 77.0, 77.3, 93.2. Anal. Calcd. For $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.59; H, 7.45. **27**: $[\alpha]_D^{30}$ 63.1° (*c* 2.00, CH_3OH). IR (KBr) ν_{max} 3334, 2940, 2239, 1508, 1457, 1245, 1074 cm^{-1}. ^1H NMR (CD_3OD, 300 MHz) δ 1.14 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.24 (2H, qd, $J = 7.5$, 2 Hz, CH_2CH_3), 3.68 (1H, dd, $J = 6$ Hz, H-6), 3.69 (1H, dd, $J = 6.5$ Hz, H-6′), 3.79 (1H, dd, $J = 4$, 2 Hz, H-4), 3.85 (1H, dd, $J = 4.5$, 3.5 Hz, H-3), 3.93 (1H, dd, $J = 5.5$, 3.5 Hz, H-2), 4.20 (1H, ddd, $J = 6.5$, 6, 2 Hz, H-5), 4.61 (1H, dt, $J = 5.5$, 2 Hz, H-1). ^{13}C NMR (CD_3OD, 75 MHz) δ 14.1, 14.9,

63.1, 67.5, 68.7, 71.7, 72.1, 73.6, 77.8, 91.6. Anal. Calcd. For $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.55; H, 7.49.

General procedure for the Larock indole synthesis as in Table 1. *N*-Tosyl-*o*-iodoanilide (**2**) (37 mg, 0.10 mmol), acetylene (0.20 mmol), $Pd(OAc)_2$ (6.7 mg, 30 μmol), Ph_3P (7.9 mg, 30 μmol), Na_2CO_3 (53 mg, 0.50 mmol), and *n*-Bu_4NCl (27 mg, 0.10 mmol) were placed in a flask, which was evacuated and filled with N_2. After this evacuation/filling cycle was repeated 3 times, anhydrous DMF (10 ml) was added. The reaction mixture was stirred at 100 °C, and then cooled to 0 °C. After the addition of sat. NH_4Cl solution, the mixture was extracted with AcOEt (x3). The combined organic layers were washed with H_2O (x2) and brine (x1), dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash-chromatography to afford a mixture of regioisomer.

*3-Ethyl-2-(methoxycarbonyl)ethyl-1-Ts-indole (**28a**) and 2-ethyl-3-(methoxycarbonyl)ethyl-1-Ts-indole (**28b**).* Purification by flash-chromatography (Et_2O:hexane = 1:2) afforded a mixture of regioisomer of indole (29 mg, 75%, **28a**:**28b** = 60:40 by ^1H NMR spectra), which was separated by preparative TLC for spectroscopic analysis. **28a**: IR (KBr) ν_{max} 3068, 2970, 2931, 2875, 1739, 1598, 1455, 1437, 1365, 1188, 1172, 1122, 1090, 1008, 988 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.13 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.31 (3H, s, CH_3 of Ts), 2.64 (2H, q, $J = 7.5$ Hz, CH_2CH_3), 2.78 (2H, m, CH_2CH_2CO), 3.28 (2H, m, CH_2CH_2CO), 3.70 (3H, s, $COOCH_3$), 7.15 (2H, d, $J = 8$ Hz, aromatic of Ts), 7.23 (1H, td, $J = 7.5$, 1 Hz, H-5 or 6), 7.28 (1H, td, $J = 7.5$, 1 Hz, H-5 or 6), 7.41 (1H, br d, $J = 7.5$ Hz, H-4 or 7), 7.56 (2H, d, $J = 8$ Hz, aromatic of Ts), 8.17 (1H, br d, $J = 7.5$ Hz, H-4 or 7). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.7, 19.7, 19.8, 21.6, 34.3, 51.6, 115.3, 118.2, 118.8, 123.4, 124.1, 126.2, 129.7, 130.2, 136.2, 136.8, 139.9, 144.5, 173.1. Anal. Calcd. for $C_{21}H_{23}NO_4$ S: C, 65.43; H, 6.01; N, 3.63. Found: C, 65.38; H, 5.75; N, 3.76. HRMS (FAB) (M^+): Calcd for $C_{21}H_{23}NO_4S$: 385.1348. Found: 385.1353. **28b**: IR (film) ν_{max} 2967, 1737, 1598, 1455, 1365, 1172 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.29 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 2.31 (3H, s, CH_3 of Ts), 2.53 (2H, m, CH_2CH_2CO), 2.94 (2H, m, CH_2CH_2CO), 3.02 (2H, q, $J = 7.5$ Hz, CH_2CH_3), 3.62 (3H, s, $COOCH_3$), 7.15 (2H, d, $J = 8$ Hz, aromatic of Ts), 7.22 (1H, td, $J = 7$, 1.5 Hz, H-5 or 6), 7.26 (1H, td, $J = 7.5$, 1.5 Hz, H-5 or 6), 7.39 (1H, br d, $J = 7$ Hz, H-4 or 7), 7.55 (2H, d, $J = 8$ Hz, aromatic of Ts), 8.17 (1H, br d, $J = 7.5$ Hz, H-4 or 7). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.8, 19.7, 19.8, 21.5, 34.3, 51.7, 115.3, 118.2, 118.8, 123.5, 124.2, 126.2, 129.7, 130.2, 136.1, 136.7, 139.8, 144.4, 173.2. Anal. Calcd. for $C_{21}H_{23}NO_4$ S: C, 65.43; H, 6.01; N, 3.63. Found: C, 65.56; H, 5.80; N, 3.69. HRMS (FAB) (M^+): Calcd for $C_{21}H_{23}NO_4S$: 385.1348. Found: 385.1325.

*2-(tert-Buthoxycarbamoyl)ethyl-3-ethyl-1-tosyl-indole (**29a**) and 3-(tert-buthoxycarbamoyl)ethyl-2-ethyl-1-tosyl-indole (**29b**).* Purification by flash-chromatography (AcOEt:hexane = 1:2) afforded a mixture of regioisomer of indole (41 mg, 75%, **29a**:**29b** = 56:44 by ^1H NMR spectra [Anal. Calcd. for $C_{24}H_{30}N_2O_4$ S: C, 65.13; H, 6.83; N 6.33. Found: C, 65.22; H, 7.04; N, 6.27.]), which was further separated by preparative TLC for spectroscopic analysis. **29a**: IR (film) ν_{max} 3422, 2975, 1699, 1455, 1367, 1251, 1173 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.16 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 1.43 (9H, s, CH_3 of Boc), 2.31 (3H, s, CH_3 of Ts), 2.64 (2H, q, $J = 7.5$ Hz, CH_2CH_3), 3.19 (2H, br t, $J = 6.5$ Hz, CH_2CH_2NH), 3.44 (2H, br q, $J = 6.5$ Hz, CH_2CH_2NH), 4.75 (1H, br t, $J = 6$ Hz, N*H*Boc), 7.14 (2H, d, $J = 8.5$ Hz, aromatic of Ts), 7.24 (1H, td, $J = 7$, 1 Hz, H-5 or 6), 7.28 (1H, td, $J = 7$, 1.5 Hz, H-5 or 6), 7.43 (1H, br d, $J = 7$ Hz, H-4 or 7), 7.53 (2H, d, $J = 8.5$ Hz, aromatic of Ts), 8.17 (1H, br d, $J = 7$ Hz, H-4 or 7). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.7, 17.4, 21.4, 27.0, 28.3, 40.9, 79.1, 115.4, 118.8, 123.5, 124.4, 125.5, 126.2, 129.8, 130.5, 133.3, 135.8, 137.1, 144.6, 156.0. HRMS (FAB) (M^+): Calcd for $C_{24}H_{30}N_2O_4S$: 442.1926. Found: 442.1918. **29b**: IR (KBr) ν_{max} 3429, 3339, 2977, 1706, 1599, 1508, 1366, 1174 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.30 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 1.43 (9H, s, CH_3 of Boc), 2.31 (3H, s, CH_3 of Ts), 2.81 (2H, t, $J = 7$ Hz, CH_2CH_2NH), 3.00 (2H, q, $J = 7.5$ Hz, CH_2CH_3), 3.27 (2H, br q, $J = 6.5$ Hz, CH_2CH_2NH), 4.42 (1H, br s, $J = 6$ Hz, N*H*Boc), 7.15 (2H, d, $J = 8$ Hz, aromatic of Ts), 7.22 (1H, td, $J = 7$, 1.5 Hz, H-5 or 6), 7.27 (1H, td, $J = 7$, 1.5 Hz, H-5 or 6), 7.40 (1H, br d, $J = 7$ Hz, H-4 or 7), 7.55 (2H, d, $J = 8$ Hz, aromatic of Ts), 8.17 (1H, br d, $J = 8$ Hz, H-4 or 7). HRMS (FAB) (M^+): Calcd for $C_{24}H_{30}N_2O_4S$: 442.1926. Found: 442.1905.

*3-Ethyl-2-[2-(methoxycarbonyl)-(tert-buthoxycarbamoyl)ethyl]-1-tosyl-indole (**30a**) and 2-ethyl-3-[2-(methoxycarbonyl)-(tert-buthoxycarbamoyl)ethyl]-1-tosyl-indole (**30b**).* Purification by flash-chromatography (AcOEt:hexane = 1:5) afforded a mixture of regioisomer of indole (25 mg, 50%, **30a**:**30b** = 56:44 by ^1H NMR spectra [Anal. Calcd. for $C_{26}H_{32}N_2O_6$ S: C, 62.38; H, 6.44; N, 5.60. Found: C, 62.28; H, 6.40; N, 5.49.]), which was separated by flash-chromatography for spectroscopic analysis. **30a**: IR (film) ν_{max} 3398, 2977, 1717, 1508, 1456, 1367, 1172 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.16 (3H, t, $J = 7.5$ Hz, CH_2CH_3), 1.26 (3H, br s, CH_3 of Boc), 1.33 (6H, br s, CH_3 of Boc), 2.31 (3H, s, CH_3 of Ts), 2.66 (2H, br q, $J = 7.5$ Hz, CH_2CH_3), 3.45–3.57 (2H, m, CH_2CH), 3.76 (3H, s, $COOCH_3$), 4.62 (1H, br s, C*H*NH), 5.36 (1H, br d, $J = 8$ Hz, N*H*Boc), 7.13 (2H, d, $J = 8$ Hz, aromatic of Ts), 7.23 (1H, td, $J = 7.5$, 1 Hz, H-5 or 6), 7.28 (1H, br t, $J = 7.5$ Hz, H-5 or 6), 7.43 (1H, br d, $J = 8$ Hz, H-4 or 7), 7.52 (2H, d, $J = 8$ Hz, aromatic of Ts), 8.15 (1H, br d, $J = 8$ Hz, H-4 or 7). HRMS (FAB) (M^+): Calcd for

$C_{26}H_{32}N_2O_6S$: 500.1981. Found: 500.2003. **30b**: IR (film) ν_{max} 3412, 2977, 1716, 1507, 1367, 1172 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.30 (3H, br t, J = 7.5 Hz, CH_2CH_3), 1.55 (9H, br s, CH_3 of Boc), 2.32 (3H, s, CH_3 of Ts), 2.91–3.05 (2H, m, CH_2CH_3), 3.10 (2H, br d, J = 6.5 Hz, CH_2CH), 3.43 (3H, s, $COOCH_3$), 4.50 (1H, m, CHNH), 4.93 (1H, br d, J = 7.5 Hz, NHBoc), 7.16 (2H, d, J = 8 Hz, aromatic of Ts), 7.18–7.26 (2H, m, H-5, 6), 7.35 (1H, br d, J = 7 Hz, H-4 or 7), 7.51 (2H, d, J = 8 Hz, aromatic of Ts), 8.14 (1H, d, J = 8 Hz, H-4 or 7). HRMS (FAB) (M^+): Calcd for $C_{26}H_{32}N_2O_6S$: 500.1981. Found: 500.1991.

*2-(2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl)-3-ethyl-1-tosyl-indole (**31a**) and 3-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-2-ethyl-1-tosyl-indole (**31b**).* Purification by flash-chromatography (AcOEt:hexane = 1:7) afforded a mixture of regioisomer of indole and glucosyl acetylene **18** (117 mg, 64%, **31a**:**31b** = 67:33 by ^{1}H NMR spectra [Anal. Calcd. for $C_{51}H_{51}NO_7$ S: C, 74.52; H, 6.25; N, 1.70. Found: C, 74.50; H, 6.31; N, 1.80.]), which was separated by flash-chromatography for spectroscopic analysis. **31a**: $[\alpha]_D^{28}$ 107.3° (*c* 0.45, $CHCl_3$). IR (film) ν_{max} 3032, 2868, 1455, 1367, 1218, 1172, 1090 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.12 (3H, t, J = 7.5 Hz, $CH_AH_BCH_3$), 2.22 (3H, s, CH_3 of Ts), 2.79 (1H, dq, J = 14, 7.5 Hz, $CH_AH_BCH_3$), 3.03 (1H, dq, J = 14, 7.5 Hz, $CH_AH_BCH_3$), 3.69 (1H, dd, J = 11, 3 Hz, H-6), 3.75 (1H, dd, J = 11, 4.5 Hz, H-6′), 3.91 (1H, dd, J = 5, 2.5 Hz, H-3), 3.93 (1H, dd, J = 8.5, 5 Hz, H-4), 4.17 (1H, d, J = 12 Hz, OCH_aH_bPh), 4.26 (1H, d, J = 12 Hz, OCH_aH_bPh), 4.26 (1H, ddd, J = 8.5, 4.5, 3 Hz, H-5), 4.30 (1H, t, J = 2.5 Hz, H-2), 4.41 (1H, d, J = 11.5 Hz, OCH_cH_dPh), 4.47 (1H, d, J = 12 Hz, OCH_eH_fPh), 4.54 (1H, d, J = 12 Hz, OCH_eH_fPh), 4.56 (1H, d, J = 11.5 Hz, OCH_gH_hPh), 4.71 (1H, d, J = 11.5 Hz, OCH_gH_hPh), 4.72 (1H, d, J = 11.5 Hz, OCH_cH_dPh), 5.98 (1H, d, J = 2.5 Hz, H-1), 6.98 (4H, m, aromatic), 7.05–7.18 (4H, d, aromatic), 7.23–7.40 (16H, aromatic), 7.46 (1H, br d, J = 7 Hz, H-4′ or 7′), 7.54 (2H, d, J = 8.5 Hz, aromatic of Ts), 8.20 (1H, br d, J = 8 Hz, H-4′ or 7′). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.9, 18.4, 21.4, 69.6, 70.3, 71.7, 72.8(x2), 73.2, 73.7, 76.9, 77.7, 80.7, 115.6, 118.8, 123.4, 124.4, 126.3, 127.4(x2), 127.5(x2), 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5, 128.8, 129.6, 131.6, 132.0, 135.6, 137.0, 137.7, 138.1, 138.5(x2), 144.4. MS (FAB) *m*/*z* 821 (M^+). **31b**: $[\alpha]_D^{28}$ 40.7° (*c* 0.15, $CHCl_3$). IR (film) ν_{max} 2870, 1598, 1454, 1364, 1175, 1091 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (3H, t, J = 7.5 Hz, $CH_AH_BCH_3$), 2.16 (3H, s, CH_3 of Ts), 2.93 (1H, dq, J = 14, 7.5 Hz, $CH_AH_BCH_3$), 2.99 (1H, dq, J = 14, 7.5 Hz, $CH_AH_BCH_3$), 3.59 (1H, t, J = 3 Hz, H-2), 3.72 (2H, d, J = 3 Hz, H-6), 3.82 (1H, d, J = 12 Hz, OCH_aH_bPh), 3.91 (1H, dd, J = 6.5, 3 Hz, H-3), 4.00 (1H, d, J = 12 Hz, OCH_aH_bPh), 4.02 (1H, dd, J = 9, 6.5 Hz, H-4), 4.16 (1H, dt, J = 9, 3 Hz, H-5), 4.41 (1H, d, J = 12 Hz, OCH_cH_dPh), 4.50 (1H, d, J = 12 Hz, OCH_eH_fPh), 4.52 (1H, d, J = 12 Hz, OCH_cH_dPh), 4.55 (1H, d, J = 11.5 Hz, OCH_eH_fPh), 4.59 (1H, d, J = 11 Hz, OCH_gH_hPh), 4.75 (1H, d, J = 11 Hz, OCH_gH_hPh), 5.28 (1H, d, J = 3 Hz, H-1), 6.58 (2H, d, J = 8 Hz, aromatic), 7.00–7.09 (4H, m, aromatic), 7.12–7.18 (2H, m, aromatic), 7.22–7.37 (16 H, m, aromatic), 7.57 (2H, d, J = 8 Hz, aromatic of Ts), 7.78 (1H, d, J = 8 Hz, H-4′), 8.19 (1H, d, J = 8 Hz, H-7′). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 20.2, 21.3, 69.7, 69.9, 72.5, 72.9, 73.4(x2), 73.9, 76.7, 81.2, 82.3, 114.6, 118.8, 122.5, 123.4, 123.9, 126.2, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.5, 129.6, 130.1, 136.2, 136.6, 137.3, 138.0, 138.3, 138.4, 139.6, 144.5. HRMS (FAB) $(M+H)^+$: Calcd for $C_{51}H_{52}NO_7S$: 822.3644. Found: 822.3474.

*2-(α-D-Glucopyranosyl)-3-ethyl-1-tosyl-indole (**32a**) and 3-(α-D-glucopyranosyl)-2-ethyl-1-tosyl-indole (**32b**).* Purification by flash-chromatography (AcOEt:hexane = 1:7) afforded recovered iodoaniline **2** (17 mg, 57%) and a mixture of regioisomer of indole (6 mg, 16%, **32a**:**32b** = 69:31 by ^{1}H NMR spectra [Anal. Calcd. for $C_{23}H_{27}NO_7$ S: C, 59.85; H, 5.90; N, 3.03. Found: C, 59.97; H, 5.76; N, 3.03.]), which was separated by flash-chromatography for spectroscopic analysis. **32a**: $[\alpha]_D^{30}$ 82.7° (*c* 0.55, $CHCl_3$). IR (KBR) ν_{max} 3688, 3318, 3318, 3070, 2406, 1906, 1727, 1595, 1455, 1367, 1171 cm^{-1}. ^{1}H NMR (CD_3OD, 400 MHz) δ 1.14 (3H, t, J = 7.5 Hz, $CH_AH_BCH_3$), 2.31 (3H, s, CH_3 of Ts), 2.89 (1H, dq, J = 13.5, 7.5 Hz, $CH_AH_BCH_3$), 3.09 (1H, dq, J = 13.5, 7.5 Hz, $CH_AH_BCH_3$), 3.76 (1H, ddd, J = 4.5, 3, 1 Hz, H-5), 3.81 (1H, dd, J = 14.5, 7.5 Hz, H-6), 3.78 (1H, dd, J = 4.5, 3.5 Hz, H-3), 3.94–4.08 (4H, m, H-2, 3, 4, 6′), 6.09 (1H, d, J = 1.5 Hz, H-1), 7.17–7.27 (4H, m, aromatic of Ts, H-5′, 6′), 7.43 (1H, br d, J = 7 Hz, H-4′), 7.60 (2H, d, J = 8.5 Hz, aromatic of Ts), 8.10 (1H, br d, J = 7.5 Hz, H-7′). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.2, 21.2, 21.4, 61.3, 68.3, 70.1, 72.0, 75.2, 81.1, 115.5, 120.5, 123.5, 124.1, 124.7, 127.4, 130.9, 131.7, 137.5, 137.9, 141.3, 146.3. HRMS (FAB) (M^+): Calcd for $C_{23}H_{27}NO_7S$: 461.1508. Found: 461.1518. **32b**: $[\alpha]_D^{27}$ 68.0° (*c* 0.10, $CHCl_3$). IR (KBr) ν_{max} 3568, 3335, 2933, 1451, 1364 cm^{-1}. ^{1}H NMR (CD_3OD, 400 MHz) δ 1.31 (3H, t, J = 7.5 Hz, $CH_AH_BCH_3$), 2.32 (3H, s, CH_3 of Ts), 3.09 (1H, dq, J = 14.5, 7.5 Hz, $CH_AH_BCH_3$), 3.19 (1H, dq, J = 14.5, 7.5 Hz, $CH_AH_BCH_3$), 3.59 (1H, m, H-2), 3.70 (1H, dd, J = 12, 3.5 Hz, H-6), 3.78 (1H, dd, J = 4.5, 3.5, 1 Hz, H-3), 3.93 (1H, br t, J = 4 Hz, H-4), 4.02 (1H, dt, J = 7.5, 3.5 Hz, H-5), 4.09 (1H, dd, J = 12, 7.5 Hz, H-6′), 5.34 (1H, d, J = 2 Hz, H-1), 7.13 (1H, td, J = 7.5, 1 Hz, H-5′), 7.18 (1H, td, J = 7.5, 1.5 Hz, H-6′), 7.24 (2H, d, J = 8.5 Hz, aromatic of Ts), 7.59 (2H, d, J = 8.5 Hz, aromatic of Ts), 7.84 (1H, br d, J = 8 Hz, H-4′), 8.07 (1H, br d, J = 8 Hz, H-7′). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.3, 19.7, 21.4, 61.8, 69.6, 70.0, 72.3, 73.8, 81.4, 116.7, 120.0, 124.7, 125.3, 127.6, 130.2, 130.7, 133.2, 133.8, 136.6, 138.6, 146.3. HRMS (FAB) (M^+): Calcd for $C_{23}H_{27}NO_7S$: 461.1508. Found: 461.1508.

*2-(2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosyl)-3-ethyl-1-tosyl-indole (**33a**).* A solution of 2-glucopyranosyl-3-ethyl-1-tosyl-indole **32a** (4 mg) in Ac_2O (0.5 ml) and pyridine (0.5 ml was stirred at room temperature for 5 h and concentrated azeotropically with toluene. The residue was purified by column chromatography (AcOEt:hexane = 1:2 → 2:1) to afford the **33a** (3 mg, 55%) as a yellow oil. $[\alpha]_D^{27}$ 111.3° (*c* 0.15, $CHCl_3$). IR (KBr) ν_{max} 2963, 1748, 1371, 1228, 1047 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.17 (3H, t, $J = 7.5$ Hz, $CH_AH_BCH_3$), 1.90 (3H, s, CH_3 of Ac), 2.05 (3H, s, CH_3 of Ac), 2.12 (3H, s, CH_3 of Ac), 2.21 (3H, s, CH_3 of Ac), 2.32 (3H, s, CH_3 of Ts), 2.71 (1H, dq, $J = 13$, 7.5 Hz, $CH_AH_BCH_3$), 3.15 (1H, dq, $J = 13$, 7.5 Hz, $CH_AH_BCH_3$), 4.29–4.36 (2H, m, H-5 & H-6), 4.50 (1H, m, H-6′), 5.03 (1H, td, $J = 4$, 0.5 Hz, H-4), 5.22 (1H, ddd, $J = 4$, 3, 0.5 Hz, H-3), 5.41 (1H, ddd, $J = 3$, 2, 0.5 Hz, H-2), 6.15 (1H, d, $J = 2$ Hz, H-1), 7.17 (2H, d, $J = 8$ Hz, aromatic of Ts), 7.21 (1H, td, $J = 7.5$, 1 Hz, H-5′ or 6′), 7.26 (1H, td, $J = 7.5$, 1.5 Hz, H-5′ or 6′), 7.43 (1H, br d, $J = 7.5$ Hz, H-4′ or 7′), 7.57 (2H, d, $J = 8$ Hz, aromatic of Ts), 8.04 (1H, br d, $J = 7.5$ Hz, H-4′ or 7′). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1, 18.4, 20.6, 20.7, 20.9, 21.5, 61.4, 66.6, 67.4, 68.7, 69.4, 73.4, 115.5, 118.9, 123.5, 125.0, 126.4, 128.5, 129.7(2), 130.8, 135.5, 136.8, 144.7, 168.7, 169.0, 169.6, 170.5. HRMS (FAB) (M^+): Calcd for $C_{31}H_{35}NO_{11}S$: 629.1931. Found: 629.1930.

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