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Note

Indium-mediated alkynylation of sugars: synthesis of *C*-glycosyl compounds bearing a protected amino alcohol moiety

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ABSTRACT

The coupling of glycals with an alkynyl iodide bearing a protected amino alcohol moiety was achieved in the presence of metallic indium under Barbier conditions. It gave functionalized *C*-glycosyl compounds, precursors of *C*-glycosyl amino acids with α configuration.

Introduction of organometallic species into the anomeric position of a glycal or a sugar derivative bearing a leaving group at C-1 is a practical approach for the synthesis of *C*-glycosyl compounds.[1–4] Among them, alkynylation with organomagnesium,[5] organoaluminum,[6] organotin[7] or organoindium[8] nucleophiles has already been reported. We have recently described an indium-mediated alkynylation reaction under Barbier conditions either on a glucal derivative following a Ferrier-type reaction[9] or by a direct substitution of an acetyl group[10] leading to various *C*-glycosyl compounds, based on our previous work concerning the alkynylation of carbonyl derivatives.[11] Since this reaction is very efficient with simple alkynyl iodides leading to the corresponding coupling compounds in a highly stereoselective manner, we were driven to apply this methodology to more functionalized derivatives. The use of alkynyl iodides bearing a protected amino alcohol moiety allowed easy access to *C*-glycosyl amino acids precursors. These latter compounds are particularly interesting targets as the C–C link between the amino acid and the sugar part provides them with a chemical and metabolic stability.

We first considered alkynyl iodide **3** obtained starting from Garner's aldehyde **1**[12] after a Seyferth–Gilbert homologation with the Ohira–Bestmann's reagent (according to Meffre's et al. procedure[13]) followed by the iodination of the terminal alkyne **2** with iodine in benzene in the presence of morpholine (Scheme 1).

The alkynyl iodide **3** was then used in the reaction with 1,5-anhydro-3,4,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hex-1-enitol (tri-*O*-acetyl-D-glucal) under the standard conditions developed in our laboratory that is in the presence of metallic indium in refluxing dichloromethane for 24 h. No coupling product was detected. Instead, we observed the formation of **4** as a pure isomer in an excellent yield. There is an uncertainty concerning the *Z* or *E* configuration of that product. Such a cyclic compound could result from the reduction of the carbamate function with indium(0) followed by cyclization at the level on the triple bond activated by indium(I). Indium(0) as a radical initiator has been largely used in cyclization approaches, but to the best of our knowledge such reduction of a carbamate has never been reported[14] (Scheme 2).

It thus appears that the use of indium is incompatible with a Boc protection of the amino group. In order to avoid this reactivity, we chose to prepare another amino alcohol synthon such as compound **10** bearing a *o*-diphenyl amido group. This particular protecting group was chosen, leading to crystalline and quite stable synthetic intermediates. Compound **5** (Scheme 3) could be prepared according to a reported procedure using iodomethane in the esterification step following the carbamoylation.[15] In order to avoid this carcinogenic compound, we have decided to esterify L-serine with methanol under acidic conditions. This modification allowed us to greatly improve the yield in **5**. Preparation of **6** was carried out according to a literature procedure.[15] The following steps (Scheme 3) include the reduction of the ester into an alcohol, oxidation into an aldehyde, Seyferth–Gilbert homologation, and iodination to afford **10** in 37% overall yield for seven steps starting from L-serine.

As described earlier,[10] the indium-mediated alkynylation at the anomeric position can only proceed in the absence of a

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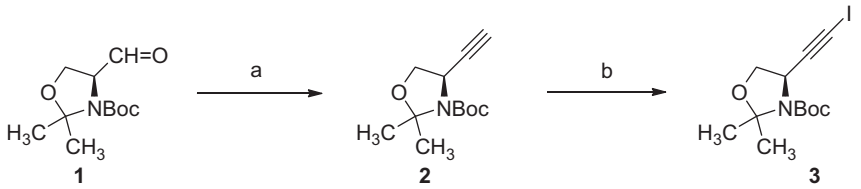
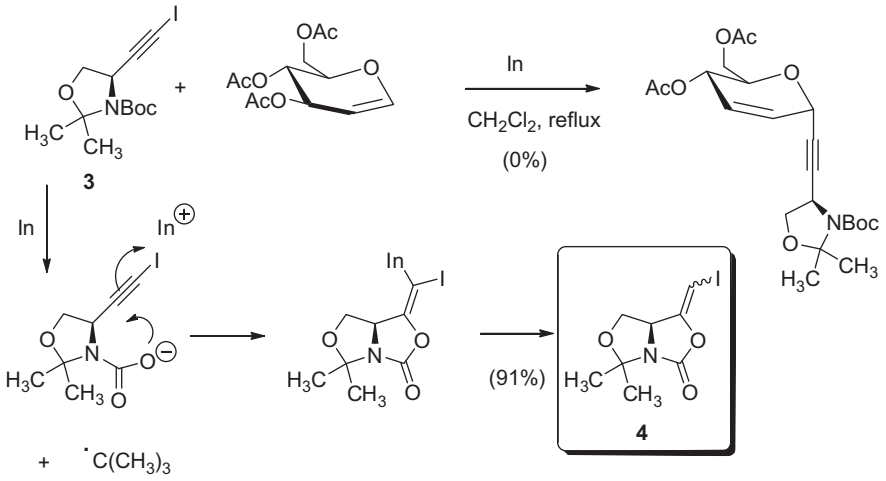
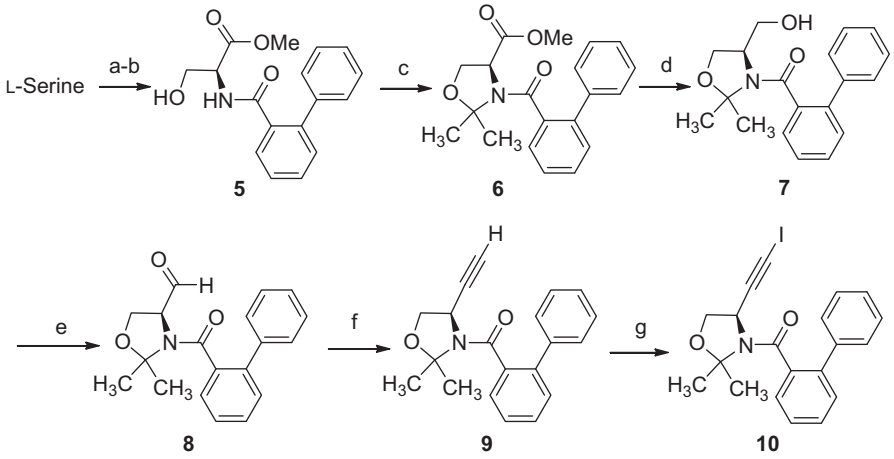


Scheme 1. Reagents and conditions: (a) $MeCOC(=N_2)P(O)(OMe)_2$, K_2CO_3, MeOH, 0 °C, 24 h, 67%; (b) I_2, morpholine, benzene, 45 °C, 24 h, 90%.



Scheme 2. Proposed mechanism for the formation of **4**.

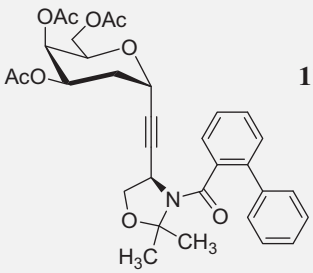
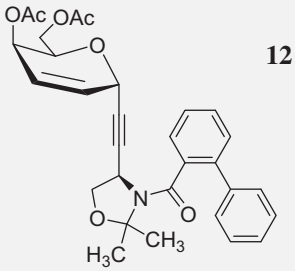
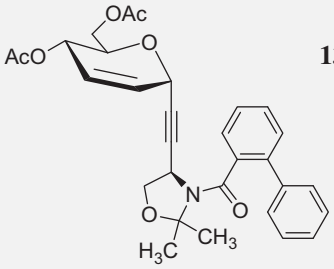


Scheme 3. Reagents and conditions: (a) CH_3COCl, MeOH, 99%; (b) *o*-phenylbenzoyl chloride, Na_2CO_3, THF, 85%; (c) DMP, TsOH, benzene, $CHCl_3$, 88%; (d) $NaBH_4$, $CaCl_2$, THF, EtOH, 93%; (e) Me_2SO, $(COCl)_2$, −60 °C then Et_3N, 76%; (f) $MeCOC(=N_2)P(O)(OMe)_2$, K_2CO_3, MeOH, 0 °C, 24 h, 97%; (g) I_2, morpholine, benzene, 45 °C, 24 h, 73%.

participating group at C-2. Thus, we first investigated the coupling reaction with 1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-*lyxo*-hexopyranose anomeric mixture in the presence of 2 equiv of iodide **10** and 2.4 equiv of metallic indium in refluxing dichloromethane. Only poor yield of the corresponding C-glycosylated derivative **11** showing an α configuration was obtained. However, 80% of **9** could be recovered, which is evidence that an organoindium species was formed from **10**. This species is not sufficiently reactive for the direct C-glycosylation step. Starting from this observation we decided to perform a Ferrier rearrangement with the same organoindium species. We were delighted to observe that the indium-mediated Ferrier rearrangement with **10** led to the corresponding products **12** and **13** in very good yields and with an exclusive α-selectivity when performing the reaction with either 1,5-anhydro-3,4,6-tri-*O*-acetyl-2-deoxy-D-*lyxo*-hex-1-enitol or D-*arabino*-hex-1-enitol (3,4,6-tri-*O*-acetyl-D-galactal or D-glucal, respectively) under the same experimental conditions (Table 1). Determination of the α-selectivity was based on the NMR observations of H-5 and C-5. In fact, Isobe et al.[16] and Tanaka and Isobe[17] established an empirical rule fixing the chemical shift for H-5 around 4.1 ppm for the α-anomer and 3.75 ppm for the β-anomer. Moreover, the α-anomer exhibits a chemical shift[8] for C-5 lower than 75 ppm.

We have shown that indium-mediated coupling reactions could open the way to *C*-glycosyl amino acids with an α configuration at the anomeric position. Compounds **12** and **13** are useful precursors of *C*-glycosyl amino acids. The functionalization of the carbohy-

Table 1
Indium mediated coupling reaction

Entry	Starting material	Coupling product	Yield (%)
1	1,3,4,6-Tetra-*O*-acetyl-2-deoxy-D-*lyxo*-hexopyranose	 **11**	10
2	3,4,6-Tri-*O*-acetyl-D-galactal	 **12**	69
3	3,4,6-Tri-*O*-acetyl-D-glucal	 **13**	83

drate part and the deprotection/oxidation of the amino alcohol moiety should allow access to useful building blocks for peptide synthesis.

1. Experimental

1.1. General

Infrared spectra have been recorded on a Bruker Tensor 27 spectrophotometer. ^{1}H and ^{13}C NMR spectra have been recorded on Brucker Avance 250 DPX and a JEOL ECX-400 spectrometer. Elemental analyses have been performed at the Central Service of Analysis (CNRS, Vernaison, France). High resolution mass spectra have been obtained with a JEOL GC Mate II apparatus. Rotation values have been recorded on a JASPO DIP 370 instrument. Melting points (uncorrected) have been determined on a Büchi B-545 apparatus.

The preparation of the starting material **2**[13] and the protection of compound **5** leading to compound **6**[15] have been performed according to literature procedures. L-Serine methyl ester hydrochloride[12] has been prepared in 99% yield and the crude product was involved in the following step without purification.

1.2. *tert*-Butyl (*R*)-4-iodoethynyl-2,2-dimethyloxazolidine-3-carboxylate (3)

In a mixture obtained by stirring iodine (1.64 g, 6.46 mmol) and morpholine (1.53 mL, 17.57 mmol) for 30 min in benzene (7 mL) was added a soln of the alkyne **2** (1.318 g, 5.85 mmol) in benzene (10 mL). The reaction mixture was stirred for 24 h at 45 °C, then filtered and washed with diethyl ether (30 mL). The combined organic phases were washed successively with satd aq NH_4Cl (15 mL), a satd aq $NaHCO_3$ (15 mL), with water (15 mL), and then dried over $MgSO_4$. The obtained product was purified by flash chromatography on silica gel (9:1 petroleum ether–EtOAc), yielding **3** (1.85 g, 90%), R_f 0.6 (9:1 cyclohexane–EtOAc); mp 61 °C. $[\alpha]_D$ −104 (*c* 3.4, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ 4.62 (m, 1H, CH), 4.01 (m, 2H, CH_2), 1.62 (s, 3H, CH_3), 1.49 (s, 12H, $4 \times CH_3$). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 151.4 (C=O), 94.3 (C^{quat} isopropyl), 92.9 (C^{quat} C≡C), 80.4 (C^{quat} Boc), 68.5 (CH_2), 50.0 (CH), 28.3, 26.8, 25.7, 24.9, 24.4 ($5 \times CH_3$), −1.3 (≡C–I). IR: ν 1677, 2980 cm^{-1}. Anal. Calcd for $C_{12}H_{18}INO_3$: C, 41.04; H, 5.17; N, 3.99. Found: C, 41.10; H, 5.27; N, 3.84.

1.3. 1-(Iodomethylene)-5,5-dimethyldihydro-1*H*-oxazolo[3,4-*c*]oxazol-3(5*H*)-one (4)

Indium (0.2 g, 1.75 mmol) was stirred for 30 min under diminished pressure/argon in a sealed tube. Then, a soln of *tert*-butyl (*R*)-4-iodoethynyl-2,2-dimethyloxazolidine-3-carboxylate **3** (0.51 g, 1.46 mmol) and tri-*O*-acetyl-D-glucal (0.2 g, 0.73 mmol) in anhyd CH_2Cl_2 (15 mL) was added to the reaction mixture which was then heated to reflux for 1 d. The mixture was filtered over Celite and the crude mixture was purified by flash chromatography on silica gel (7:3 cyclohexane–EtOAc), yielding **4** as the sole isomer (0.39 g, 91%). $[\alpha]_D$ −1 (*c* 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.24 (d, 1H, *J* 0.6 Hz, C=CH), 4.76 (td, 1H, *J* 2.8, 0.6 Hz, CH), 4.12 (dd, 1H, *J* 3.3, 2.8 Hz, CH_2), 3.63 (t, 1H, *J* 3.3 Hz, CH_2), 1.66 (s, 1H, CH_3), 1.40 (s, 1H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.1 (C=O), 151.3 (C=C), 95.7 (C^{quat} isopropyl), 67.6 (CH_2), 61.8 (CH), 47 (C–I), 27.5 (CH_3), 23.0 (CH_3). IR: ν 1742, 2361, 2921 cm^{-1}. HRMS: Calcd for $C_8H_{10}NO_3I$: 294.9706. Found: 294.9698.

1.4. (*S*)-2-(*o*-Phenylbenzoyl)amino-3-hydroxypropionic acid methyl ester (5)

To a L-serine methyl ester hydrochloride (511 mg, 3.28 mmol) soln in a saturated aq soln of sodium carbonate (13 mL) was added THF (15 mL). The soln was cooled to 0 °C and *o*-phenylbenzoyl chloride (1.07 g, 4.93 mmol) was added dropwise. The soln was maintained at pH 8–9 by further addition of carbonate. After stirring at room temperature for 12 h, THF was evaporated under diminished pressure. The soln was then extracted with EtOAc (3×35 mL) and the combined organic layers were washed with saturated $NaHCO_3$ (3×10 mL), saturated $KHSO_4$ (3×10 mL), and saturated NaCl (3×10 mL). The organic layer was dried over $MgSO_4$, filtered, and evaporated. Purification by flash chromatography on silica gel (1:1 cyclohexane–EtOAc) yielded (*S*)-2-(*o*-phenylbenzoyl)amino-3-hydroxypropionic acid methyl ester (839 mg, 85%). Spectroscopic data (^{1}H NMR, ^{13}C NMR, and HRMS) were similar to literature data.[15]

1.5. (*R*)-3-(*o*-Phenylbenzoyl)-2,2-dimethyloxazolidine-4-methanol (7)

In a suspension of calcium chloride (3.44 g, 31 mmol) in THF (18 mL) was added a soln of (*S*)-3-(*o*-phenylbenzoyl)-2,2-dimethyloxazolidine-4-carboxylic acid methyl ester (**6**) (1.38 g, 4.1 mmol) in freshly distilled EtOH (30 mL). The mixture was cooled down to −20 °C and sodium borohydride (2 g, 53 mmol) was added in small portions. After overnight stirring at room temperature, the reaction mixture was diluted with diethyl ether (60 mL) and treated with satd aq Na_2SO_4 (50 mL). The white suspension was separated from the liquid phase by decantation and the supernatant was reduced to 10 mL by evaporation under diminished pressure. Diethyl ether (50 mL) was added and the soln was washed with brine (2×10 mL) and then dried over $MgSO_4$. The crude mixture was purified by flash chromatography on silica gel (2:3 cyclohexane–EtOAc), yielding (*R*)-3-(*o*-phenylbenzoyl)-2,2-dimethyloxazolidine-4-methanol (**7**) (1.27 g, 93%), R_f 0.1 (2:3 cyclohexane–EtOAc). $[\alpha]_D$ −185 (*c* 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (m, 9H, aromatics), 3.69 (d, 1H, *J* 8.7 Hz, CH_2), 3.29 (dd, 1H, *J* 8.7, 8.2 Hz, CH_2OH), 3.21 (m, 1H, CH), 3.16 (m, 1H, CH_2OH), 3.01 (dd, 1H, *J* 8.7, 5.0 Hz, CH_2), 1.66 (s, 3H), 1.49 (br s, 1H, OH), 1.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1 (C=O), 139.5, 137.8, 136.6, 129.7, 129.1, 128.8, 128.1, 127.9, 127.7 (aromatics), 95.5 (C^{quat} isopropyl), 65.0 (CH_2), 62.1 (CH_2OH), 58.9 (CH), 27.0, 21.9 ($2 \times CH_3$). IR: ν 1610, 2982, 3409 cm^{-1}. HRMS: Calcd for $C_{19}H_{21}NO_3$: 311.1521. Found: 311.1534.

1.6. (*S*)-3-(*o*-Phenylbenzoyl)-2,2-dimethyloxazolidine-4-formaldehyde (8)

To a soln of oxalyl chloride (0.5 mL, 6.1 mmol) in CH_2Cl_2 (12 mL) cooled down to −78 °C was added dropwise a soln of Me_2O (0.9 mL, 12 mmol) in CH_2Cl_2 (2 mL). After 10 min, a soln of the above (*R*)-3-(*o*-phenylbenzoyl)-2,2-dimethyloxazolidine-4-methanol in CH_2Cl_2 (6 mL) was added dropwise and the reaction mixture was maintained at −60 °C for 30 min. Then a soln of Et_3N (2.8 mL, 20.4 mmol) in CH_2Cl_2 (2 mL) was added dropwise; the reaction mixture was warmed up to room temperature and water (6 mL) was added. After the separation of the layers, the aq one was extracted with CH_2Cl_2 (3×3 mL). The combined organic layers were washed with water (3×20 mL) and brine (20 mL). After drying over $MgSO_4$, the crude aldehyde **8** was obtained in quantitative yield and could be used in the next step without any purification. However, it was purified by flash chromatography on silica gel (7:3 cyclohexane–EtOAc) (0.96 g, 76%), R_f 0.1 (7:3 cyclohexane–EtOAc). $[\alpha]_D$ −84 (*c* 10.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.23 (s, 1H, CH=O), 7.44 (m, 9H, aromatics), 3.88 (dd, 1H, *J* 7.5, 1.8 Hz, CH_2), 3.65 (dl, 1H, *J* 6.8 Hz, CH), 3.28 (dd, 1H, *J* 7.5, 6.8 Hz, CH_2), 1.71 (s, 3H), 1.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9 (CH=O), 168.2 (C=O), 139.3, 137.6, 136.2, 130.1, 129.6, 129.0, 128.3, 128.0 (aromatics), 96.8 (C^{quat} isopropyl), 65.8 (CH), 63.9 (CH_2), 25.8, 22.4 ($2 \times CH_3$). IR: ν 1641, 1735, 2984, 3061 cm^{-1}. HRMS: Calcd for $C_{19}H_{19}NO_3$: 309.1379. Found: 309.1365.

1.7. (*R*)-3-(*o*-Phenylbenzoyl)-4-ethynyl-2,2-dimethyloxazolidine (9)

Into a vigorously stirred soln of aldehyde **8** (5.26 g, 17 mmol) in MeOH (360 mL) were added at 0 °C potassium carbonate (4.4 g, 31.8 mmol) and a soln of dimethyl 1-diazo-2-oxopropylphosphonate (5.53 g, 28.8 mmol) in MeOH (5 mL). After 16 h of stirring at room temperature, the reaction mixture was diluted with diethyl ether (400 mL), washed with a 5% solution of $NaHCO_3$ (50 mL), and dried over $MgSO_4$. The crude mixture was purified by flash chromatography on silica gel (9:1 cyclohexane–EtOAc) yielding compound **9** (5.05 g, 97%), R_f 0.9 (9:1 cyclohexane–EtOAc). $[\alpha]_D$ −6 (*c* 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (m, 9H, aromatics), 3.81 (sl, 1H, CH), 3.70 (d, 1H, *J* 7.8 Hz, CH_2), 3.16 (sl, 1H, CH_2), 2.10 (d, 1H, *J* 1.8 Hz, C≡CH), 1.74 (s, 3H), 1.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7 (C=O), 139.5, 136.5, 129.7, 129.3, 128.9, 128.7, 128.1, 128.0, 127.7 (aromatics), 96.1 (C^{quat} isopropyl), 81.4 (C^{quat} C≡C), 71.7 (C≡CH), 68.9 (CH_2), 49.6 (CH), 26.2, 22.7 ($2 \times CH_3$). IR: ν 1613, 1739, 2176, 2983, 3058, 3287 cm^{-1}. HRMS: Calcd for $C_{20}H_{19}NO_2$: 305.1416. Found: 305.1414.

1.8. (*R*)-3-(*o*-Phenylbenzoyl)-4-iodoethynyl-2,2-dimethyloxazolidine (10)

In a mixture obtained after stirring for 45 min iodine (6.28 g, 24.7 mmol) and morpholine (4.4 mL, 0.5 mmol) in benzene (60 mL) was added a soln of **9** in benzene (15 mL). The mixture was stirred for 48 h at 45 °C, then filtered and washed with diethyl ether (100 mL). After filtration and concentration up to 30 mL, washing successively with satd aq NH_4Cl (2×20 mL), satd aq $NaHCO_3$ (20 mL), water (20 mL), and then drying over $MgSO_4$, the resulting product was purified by flash chromatography on silica gel (9:1 cyclohexane–EtOAc) yielding compound **10** (5.2 g, 73%), R_f 0.9 (9:1 cyclohexane–EtOAc). $[\alpha]_D$ −5 (*c* 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (m, 9H, aromatics), 3.87 (sl, 1H, CH), 3.70 (d, 1H, *J* 6.9 Hz, CH_2), 3.23 (sl, 1H, CH_2), 1.73 (s, 3H), 1.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9 (C=O), 139.6, 137.6, 136.6, 129.8, 129.4, 128.9, 128.7, 128.3, 128.1, 127.7 (aromatics), 96.2 (C^{quat} isopropyl), 91.7 (C^{quat} C≡C), 68.8 (CH_2), 51.2 (CH), 26.1, 22.9 ($2 \times CH_3$), 1.3 (≡C–I). IR: ν 1613, 2177, 2982 cm^{-1}. HRMS: Calcd for $C_{20}H_{18}INO_2$: 431.0383; Found: 431.0379.

1.9. 2-[(*R*)-3-(*o*-Phenylbenzoyl)-2,2-dimethyloxazolidin-4-yl]ethyne 3,4,6-tri-*O*-acetyl-2-deoxy-D-*lyxo*-hexopyranosyl (11)

Indium (0.40 g, 3.41 mmol) was stirred for 30 min under diminished pressure/argon in a sealed tube. Then, a soln of (*R*)-3-(*o*-phenylbenzoyl)-4-iodoethynyl-2,2-dimethyloxazolidine **10** (0.61 g, 1.41 mmol) and tri-*O*-acetyl-D-galactal (0.24 g, 0.70 mmol) in anhyd CH_2Cl_2 (25 mL) was introduced into the reaction mixture which was refluxed for 3 d. The reaction mixture was filtered over Celite and the crude product was purified by flash chromatography on silica gel (2:1 cyclohexane–EtOAc), leading to the precursor compound **9** (0.34 g, 80%), R_f 0.9 (9:1 cyclohexane–EtOAc), and to the coupling compound **11** (0.04 g, 10%), R_f 0.3 (2:1 cyclohexane–EtOAc). $[\alpha]_D$ −35 (*c* 7, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (m, 9H, aromatics), 5.25 (m, 1H, H-4), 4.99 (m, 1H, H-3), 4.67 (sl, 1H, H-1), 4.28 (m, 1H, H-5), 4.14 (m, 2H, H-6,6′), 3.85 (sl, 1H, CH_2), 3.68 (sl, 1H, CH_2), 3.18 (s, 1H, CH), 2.45 (m, 1H, H-2), 2.10 (s, 3H, Ac), 2.06

(s, 3H, Ac), 2.04 (s, 3H, Ac), 1.93 (m, 1H, H-2), 1.73 (s, 3H isopropyl), 1.27 (s, 3H isopropyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6 (C=O), 170.5 (C=O, Ac), 170.0 (C=O, Ac), 167.6 (C=O), 128.8–128.0 (aromatics), 95.9 (C^{quat} isopropyl), 83.3 (C≡C), 81.3 (C≡C), 74.7, 73.8, 70.2, 68.7 (C-1, C-3, C-4, C-5), 67.8 (CH_2), 62.7 (C-6), 49.7 (CHN), 38.5 (C-2), 26.9, 22.7 ($2 \times CH_3$, isopropyl), 20.9, 20.8, 20.7 ($3 \times CH_3$, Ac). IR: ν 1643, 1745, 2160, 2919 cm^{-1}. HRMS: Calcd for $C_{32}H_{35}NO_9$: 577.2311. Found: 577.2339.

1.10. 2-[(*R*)-3-(*o*-Phenylbenzoyl)-2,2-dimethyloxazolidin-4-yl]ethyne 4,6-di-*O*-acetyl-2,3-dideoxy-D-*threo*-hex-2-enopyranosyl (12)

Indium (0.5 g, 4.4 mmol) was stirred for 30 min under diminished pressure/argon in a sealed tube. Then, a soln of (*R*)-3-(*o*-phenylbenzoyl)-4-iodoethynyl-2,2-dimethyloxazolidine **10** (1.58 g, 3.67 mmol) and tri-*O*-acetyl-D-galactal (0.5 g, 1.84 mmol) in anhyd CH_2Cl_2 (30 mL) was introduced into the reaction mixture which was refluxed for 3 d. The reaction mixture was filtered over Celite and the crude product was purified by flash chromatography on silica gel (2:1 cyclohexane–EtOAc), yielding **12** (0.66 g, 69%), R_f 0.8 (3:1 cyclohexane–EtOAc). $[\alpha]_D$ −4 (*c* 5.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (m, 9H, aromatics), 5.96 (dd, 1H, *J* 8.5, 4.1 Hz, H-3), 5.85 (d, 1H, *J* 8.5 Hz, H-2), 5.01 (m, 1H, H-4), 4.84 (sl, 1H, H-1), 4.20 (m, 2H, H-6,6′), 4.11 (m, 1H, H-5), 3.82 (sl, 1H, CH), 3.66 (d, 1H, *J* 7.8 Hz, CH_2), 3.19 (m, 1H, CH_2), 2.07 (s, 3H, Ac), 2.05 (s, 3H, Ac), 1.71 (s, 3H isopropyl), 1.26 (s, 3H isopropyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7 (C=O, Ac), 170.4 (C=O, Ac), 167.7 (C=O), 139.5, 137.7, 136.6, 131.5, 129.8, 129.7, 129.5, 128.9, 128.7, 128.1, 127.5 (aromatics), 122.6 (C-3), 96.1 (C^{quat} isopropyl), 84.9 (C≡C), 78.6 (C≡C), 69.8 (C-5), 68.9 (CH_2), 63.6 (C-1), 63.1 (C-4), 62.9 (C-6), 49.8 (CHN), 26.4, 22.7 ($2 \times CH_3$, isopropyl), 20.9 ($2 \times CH_3$, Ac). IR: ν 1641, 1740, 2986, 3058 cm^{-1}. HRMS: Calcd for $C_{30}H_{31}NO_7$: 517.2100. Found: 517.2106.

1.11. 2-[(*R*)-3-(*o*-Phenylbenzoyl)-2,2-dimethyloxazolidin-4-yl]ethyne 4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranosyl (13)

Indium (0.08 g, 0.66 mmol) was stirred for 30 min under diminished pressure/argon in a sealed tube. Then, a soln of (*R*)-3-(*o*-phenylbenzoyl)-4-iodoethynyl-2,2-dimethyloxazolidine **10** (0.23 g, 0.55 mmol) and tri-*O*-acetyl-D-glucal (0.08 g, 0.27 mmol) in anhyd CH_2Cl_2 (5 mL) was introduced into the reaction mixture which was refluxed for 24 h. The reaction mixture was filtered over Celite and the crude product was purified by flash chromatography on silica gel (2:1 cyclohexane–EtOAc), yielding **13** (0.12 g, 83%), R_f 0.8 (3:1 cyclohexane–EtOAc). $[\alpha]_D$ −3 (*c* 2.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (m, 9H, aromatics), 5.74 (d,1 H, *J* 10.5 Hz, H-3), 5.66 (d, 1H, *J* 10.5 Hz, H-2), 5.24 (m, 1H, H-4), 4.77 (sl, 1H, H-1), 4.14 (m, 2H, H-6,6′), 3.89 (m, 1H, H-5), 3.83 (sl, 1H, CH), 3.67 (d, 1H, *J* 7.8 Hz, CH_2), 3.16 (m, 1H, CH_2), 2.10 (s, 3H, Ac), 2.07 (s, 3H, Ac), 1.72 (s, 3H isopropyl), 1.26 (s, 3H isopropyl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9 (C=O, Ac), 170.3 (C=O, Ac), 167.7 (C=O), 139.4, 137.7, 136.6, 129.7, 129.5, 128.9, 128.7, 128.1, 127.5 (aromatics), 125.6 (C-3), 96.0 (C^{quat} isopropyl), 84.8 (C≡C), 79.0 (C≡C), 70.0 (C-5), 68.8 (CH_2), 64.6 (C-4), 63.7 (C-1), 63.1 (C-6), 49.8 (CHN), 26.4, 22.6 ($2 \times CH_3$, isopropyl), 21.1, 20.9 ($2 \times CH_3$, Ac). IR: ν 1640, 1741, 2939, 3019 cm^{-1}. HRMS: Calcd for $C_{30}H_{31}NO_7$: 517.2100. Found: 517.2106.

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