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Carbohydrate-Based Pyridine-2-carboxamides for Mo-Catalyzed Asymmetric Allylic Alkylations

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Bis(pyridine-2-carboxamides) were prepared from 1,2-diamines obtained from α-D-glucose and α-D-mannose. The ligands were assessed in molybdenum-catalyzed asymmetric allylic alkylations (AAA) by using both methyl (*E*)-3-phenyl-2-propenyl and methyl *rac*-1-phenyl-2-propenyl carbonates and dimethyl malonate as nucleophile under microwave irradiation. High enantioselectivity (99 % *ee*) and high regioselectivity (49:1 in favour of the branched isomer) were observed in reactions of the linear achiral substrate in the presence of 10 mol-% of a catalyst prepared from a ligand derived from glucose. Somewhat lower enantioselectivity (up to 96 % *ee*) was observed in reactions with the branched racemic carbonate by using the same ligand.

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Introduction

Asymmetric allylic alkylations (AAA) are synthetically highly versatile reactions, which are catalyzed by a range of transition-metal complexes.[1] The stereo- and regiochemistry of the product are a function of the metal and the ligand as well as of the nucleophile and the substituents on the allyl system, and the different types of catalysts are therefore highly complimentary. Catalysts containing palladium have been most extensively employed in synthetic applications,[2] but may lead to undesired products when unsymmetrically substituted allyl derivatives are used.[3] Thus, whereas palladium complexes as a rule afford the achiral linear products from monosubstituted allylic substrates,[4] complexes based on Ir and Mo have a preference for formation of the branched chiral products. With the introduction of the (*R**,*R**)-1,2-diaminocyclohexane derivative **1**[5] as ligand by Trost,[6] highly enantioselctive Mo-catalyzed allylations became possible. Although Ir catalysts have a wider scope,[7] catalysts containing Mo have become attractive due to the lower cost of molybdenum as compared to iridium and the robustness of the in-situ formed catalytic system.[8] These factors together with our simple experimental protocol using microwave irradiation, allowing the catalytic reactions to be run in air within less than 10 min in the presence of stable, crystalline, commercially available $Mo(CO)_6$ as catalyst precursor,[9] have made Mo catalysts viable alternatives to those based on Pd and Ir for a variety of applications.

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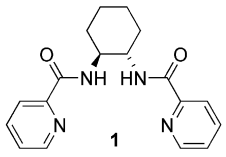

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Bis(pyridine-2-carboxamides), which still are the most efficient ligands for the Mo-catalyzed process, are easily prepared from a picolinic acid derivative and a chiral enantioenriched 1,2-diamine.[10] By comparing the results of reactions of ligands with substituted pyridines it was found that derivatives with π-donor substituents resulted in particularly high enantioselectivities and high branched/linear ratios.[11] C_2-Symmetric 1,2-diaminocyclohexanes have commonly been used as ligand precursors together with picolinic acid derivatives. In the search for more easily available diamines, Lloyd-Jones, Kočovský and co-workers used asymmetric diamines derived from naturally occurring amino acids.[12] The ligands obtained provided catalysts, some of which exhibited high enantio- and regioselectivity and high reactivity.

Carbohydrates are other examples of useful naturally occurring starting materials for ligand synthesis, and they are particularly attractive as they are available in several stereoisomeric forms.[13] α-D-Glucose[14] and α-D-mannose[15] derivatives with amino substituents in the 2- and 3-positions of the carbohydrate have been described and have successfully been used for the preparation of ligands which have been applied in metal-catalyzed enantioselective processes.[16] Inspired by the structural analogy between *trans*-cyclohexanediamine and the glucose derivative and by the possibility to obtain a chiral *cis*-substituted ligand from mannose, we decided to use the two 1,2-diamines for the

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preparation of bis(pyridine-2-carboxamides). We report here the preparation of the new ligands and their use in Mo-catalyzed allylic alkylations.

Results and Discussion

Preparation of Ligands

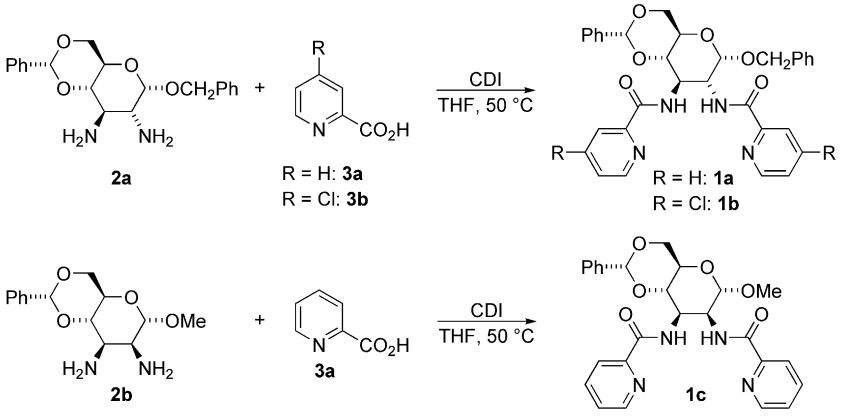
Ligands **1a**, **1b**, and **1c** were prepared from previously described diamino derivatives **2a**[14] and **2b**[15] and the appropriate picolinic acid (**3a** or **3b**) in the presence of 1,1′-carbonyldiimidazole (DCI) (Scheme 1). Ligands **1a** and **1c** were isolated after extraction (in 77 and 82% yields, respectively) and could be used without any further purification, while **1b** was obtained in pure form by chromatography (in 32% yield). The ligands were characterized by NMR spectroscopy. The ^{1}H NMR patterns typical for glucose and mannose in chair conformations were observed, and the signals of the newly formed amido protons were found in the range δ = 8.3–8.6 ppm.

Mo-Catalyzed Asymmetric Allylic Alkylations

The catalytic reactions were performed by using our previously developed experimental conditions. Thus, $Mo(CO)_6$, ligand, allylic carbonate **4**, dimethyl malonate, and *N*,*O*-bis(trimethylsilyl)acetamide (BSA) were mixed in THF and heated at 160 °C in the microwave cavity under air. After completed reaction, conversions and branched/linear ratios were determined by ^{1}H NMR spectroscopy and gas chromatography, respectively, and enantioselectivities by chiral HPLC. First, the three types of ligands were assessed by using 4 and/or 10 mol-% of Mo catalyst, a nucleophile/substrate ratio of 1.1:1, and a ligand/metal ratio of 1.3:1. The results of these initially performed reactions are shown in Table 1. In reactions with **1a** and **1b**, (+)-(*R*)-dimethyl 3-phenyl-1-butene-4,4-dicarboxylate was formed as the major product, whereas the opposite enantiomer was obtained in reactions with **1c**. Higher catalyst loadings resulted not only in higher reactivity but also in higher regioselectivity (Entries 1 and 4 vs. 2 and 5, respectively). In contrast to results obtained with ligands derived from 1,2-diaminocyclohexane,[11b] the *p*-chloro-substituted derivative (Entry 3) gave the product with lower enantioselectivity than **1a**. The enantioselection of ligands prepared from the *pseudo*-C_2-symmetric 2,3-*gluco* derivatives **1a** and **1b** turned out to be far superior to that of *pseudo*-C_s-symmetric 2,3-*manno* derivative **1c** (38–40% *ee*, Entries 3 and 4). Compound **1a** was thus the ligand of choice, exhibiting higher reactivity and providing higher enantioselectivity (99% *ee*) and higher branched/linear ratio (49:1 with 10 mol-% of catalyst) than **1b** and **1c**. Reactions using this ligand were therefore studied in more detail.

The following catalytic reactions using **1a** were performed by employing the same procedure as that used in the initial reactions, but equimolar amounts of nucleophile and substrate, and lower ligand/metal ratios (1.1:1) were used. These conditions allowed isolation of pure products by bulb-to-bulb distillation; in some reactions the product was isolated by chromatography, which resulted in lower yields. Again, lower amounts of catalyst resulted in lower conversion and lower regioselectivity (Table 2, Entries 1–3), although the enantioselectivity remained high (99% *ee*). With 4 mol-% of catalyst, the conversion was merely 50% after 6 min (Entry 3). Prolonged reaction times resulted in further product formation, which, however, ceased after 15 min (Entries 4 and 5), probably due to decomposition of the catalyst; this decomposition could not be prevented by higher ligand loading (Entry 6). With 1 mol-% of catalyst somewhat lower enantioselectivity (94% *ee*) and very low regioselectivity were observed (Entry 7). The best result, obtained with 10% catalyst loading, (Entry 1) allowed the product with a branched/linear ratio of 49:1 to be isolated in 90% yield (99% conversion).

Mo-catalyzed allylic alkylations are known to proceed via (η^3-allyl)molybdenum complexes, which are formed by oxidative addition of the allylic carbonate to ligated Mo^0.[17] The reactions proceed stereospecifically by *syn* displacement of the carbonate.[18] For this reason diastereomeric allyl complexes are formed from the two enantiomers of branched carbonates such as **5**. In order to



Scheme 1. Preparation of bis(pyridine-2-carboxamides).

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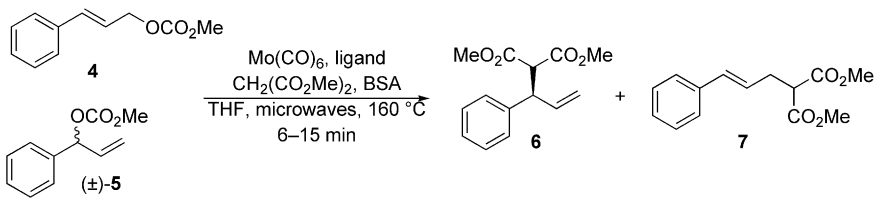
Table 1. Molybdenum-catalyzed asymmetric substitutions of **4** by using ligands **1a**–**c**.[a]



Entry	Ligand	Cat. [%]	Conversion[a] [%]	Regioselectivity[b] (**6**/**7**)	*ee*[c] [%]
1	**1a**	10	96	49:1	99 (*R*)
2	**1a**	4	50	8:1	99 (*R*)
3	**1b**	4	42	12:1	87 (*R*)
4	**1c**	10	76	14:1	38 (*S*)
5	**1c**	4	41	5:1	40 (*S*)

[a] Reactions were run at 160 °C for 6 min with ligand/metal = 1.3:1 and Nu/**4** = 1.1:1. [b] Determined by GC-MS. [c] Determined by HPLC using a Daicel OD-H (0.46 cm i.d. × 25 cm) column.

Table 2. Molybdenum-catalyzed asymmetric substitutions of **4** by using ligand **1a**.[a]

Entry	Cat. [%]	Mo/ligand	Time [min]	Conversion[b] [%]	Yield [%]	Regioselectivity[c](**6**/**7**)	*ee*[d] [%]
1	10	1:1.1	6	99	90[e]	49:1	99
2	5	1:1.1	15	78	38[f]	9:1	99
3	4	1:1.1	6	50	35[f]	8:1	99
4	4	1:1.1	15	65	33[f]	8:1	99
5	4	1:1.1	30	65	35[f]	8:1	99
6	4	1:1.5	15	50	35[f]	8:1	99
7	1	1:1.1	30	10	7[f]	1.5:1	94

[a] Reactions were run at 160 °C with ligand/metal = 1.1:1 and Nu/**4** = 1:1. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by GC-MS. [d] Determined by HPLC using a Daicel OD-H (0.46 cm i.d. × 25 cm) column. [e] Isolated by bulb-to-bulb distillation. [f] Isolated by chromatography on silica gel (eluent: petroleum ether/DCM, 1:1).

achieve high enantioselectivity in reactions with branched racemic substrates, equilibration of the diastereomeric allyl complexes via η^3-η^1-η^3 isomerization therefore needs to be rapid in relation to nucleophilic attack, which also occurs by a *syn* mechanism. Under certain conditions equilibration is incomplete, resulting in modest memory effects and, as a consequence, in lower enantioselectivities than in reactions with linear substrates.[19]

The results from reactions with *rac*-**5** using the present catalytic system are shown in Table 3. The branched substrate **5** gave the product with lower enantio- and regioselectivity than the linear substrate, but the conversion remained high when the catalyst loading was decreased from 10 (Entry 1) to 5 mol-% (Entry 2). With a further decrease of the amount of catalyst, the conversion decreased, and with 1 mol-% of catalyst merely 15% conversion was observed after 30 min (Entry 4). No major difference was observed between reactions run in THF and in toluene (Entries 2 and 3).

In the η^3-allyl complex obtained after oxidative addition of the allylic carbonate, the ligand has been shown to coordinate to Mo in a tridentate manner through one pyridine nitrogen atom, one deprotonated amide nitrogen atom, and one carbonyl oxygen atom.[20] Assuming the same configuration at the metal center as that found for the complex containing **1**, two modes of coordination (**A** and **B**, Figure 1) are possible for asymmetric ligand **1a** due to the lack of twofold rotational axis, and thus two different complexes may lead to the observed major enantiomer. Although a catalyst containing (*R*)-1-(2-pyridinecarboxamido)-2-(2-pyridinecarboxy)-1-phenylethane (**1d**), an ester–amide, has been shown to exhibit some activity in Mo-catalyzed allylic

Table 3. Molybdenum-catalyzed asymmetric substitutions of *rac*-**5** by using ligand **1a**.[a]

Entry	Cat. [%]	Mo/ligand	Time [min]	Conversion[b] [%]	Yield [%]	Regioselectivity[c](**6**/**7**)	*ee*[d] [%]
1	10	1:1.1	6	99	82[f]	8:1	96
2	5	1:1.1	15	99	90[f]	8:1	95
3	5	1:1.1	15[e]	99	85[f]	8:1	96
4	1	1:1.1	30	15	12[g]	8:1	80

[a] Reactions were run at 160 °C with ligand/metal = 1.1:1 and Nu/**5** = 1:1. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by GC-MS. [d] Determined by HPLC using a Daicel OD-H (0.46 cm i.d. × 25 cm) column. [e] Reaction run in toluene. [f] Isolated by bulb-to-bulb distillation. [g] Isolated by chromatography on silica gel (eluent: petroleum ether/DCM, 1:1).

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substitutions,[12] no product formation was observed when monoamide **1e**, derived from a 2-amino-4,6-*O*-benzylidene-2-deoxyglucoside scaffold, was used as ligand. This suggests that the NH function in position 3 is essential for the reaction, and hence, diastereomer **A** should be the actual intermediate.

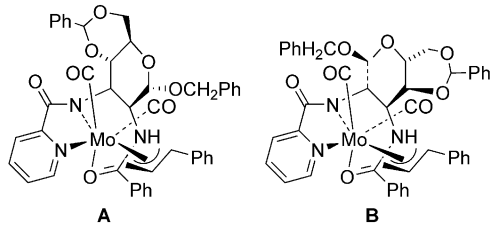
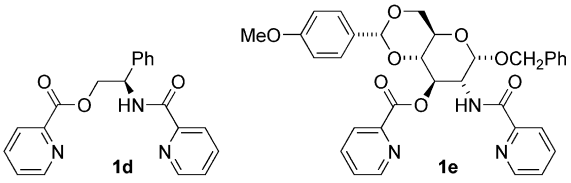


Figure 1. Diastereomeric complexes differing in the mode of coordiantion of **1a** to Mo.



Conclusions

Bis(pyridine-2-carboxamides) were conveniently prepared from 1,2-diamines obtained from α-D-glucose and α-D-mannose according to known procedures and shown to serve as efficient ligands in Mo-catalyzed microwave-mediated asymmetric allylic alkylations. The two types of structures allowed the comparison of ligands having the amide arms in *trans* and *cis* positions in the six-membered ring. The former type of ligands proved to be more successful, providing the product, (+)-(*R*)-dimethyl 3-phenyl-1-butene-4,4-dicarboxylate, with 99% enantiomeric excess and with a branched/linear ratio of 49:1 in 90% isolated yield under optimized conditions.

Experimental Section

General: THF and toluene were dried by using a Glass-contour solvent dispensing system. Dichloromethane was distilled from CaH_2. Microwave heating was performed by using a Smith Creator™ single-mode cavity from Biotage. ^{1}H NMR spectra were recorded at 400 or 300 MHz, and ^{13}C NMR spectra at 100 or 75.3 MHz. The ^{1}H and ^{13}C chemical shifts are reported relative to $CHCl_3$.

Synthesis of Ligands 1a and 1c: A suspension of picolinic acid (138 mg, 1.12 mmol) and 1,1′-carbonyldiimidazole (182 mg, 1.12 mmol) in dry tetrahydrofuran (2 mL) was heated in a flame-dried flask at 50 °C under nitrogen for 1 h. Then the appropriate diamine (0.56 mmol) was added, and the mixture was stirred at the same temperature for 2 h. The solvent was removed under vacuum and the residue extracted with dichloromethane. The organic phase was extracted with water (3 × 5 mL) and the aqueous phases were combined and extracted with dichloromethane (2 × 5 mL). The collected organic phases were dried with sodium sulfate, and the solvent was evaporated to afford ligands **1a** (245 mg, 77%) and **1c** (225 mg, 82%). Use of the ligands in the catalytic reactions did not require any further purification. Recrystallization of **1a** from methanol afforded 136 mg (43%) of the product. **Ligand 1a:** $[\alpha]_D^{20}$ = +107 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.53 (d, *J* = 4.4 Hz, 1 H, H6-py), 8.52 (d, *J* = 10.4 Hz, 1 H, NH), 8.38 (d, *J* = 4.7 Hz, 1 H, H6-py), 8.10 (d, *J* = 10.4 Hz, 1 H, NH), 7.97 (d, *J* = 7.8 Hz, 1 H, H3-py), 7.90 (d, *J* = 7.8 Hz, 1 H, H3-py), 7.66–7.62 (m, 2 H, H4-py), 7.36–7.30 (m, 4 H, H5-py and Ph H), 7.28–7.16 (m, 8 H, Ph), 5.50 (s, 1 H, OCHO), 4.97 (d, *J* = 3.6 Hz, 1 H, H1), 4.81 (q, *J* = 10.4 Hz, 1 H, H3), 4.77 (d, *J* = 12.2 Hz, 1 H, C*H*HPh), 4.58 (dt, *J* = 10.4, 3.6 Hz, 1 H, H2), 4.54 (d, *J* = 12.2 Hz, 1 H, CH*H*Ph), 4.22 (dd, *J* = 10.2, 4.9 Hz, 1 H, $H6_{eq}$), 4.06 (dt, *J* = 9.9, 4.9 Hz, 1 H, H5), 3.86 (dd, *J* = 10.2, 9.9 Hz, 1 H, $H6_{ax}$), 3.76 (t, *J* = 10.3 Hz, 1 H, H4) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.5, 165.1, 149.9, 149.8, 148.7, 148.3, 137.6 (2 C, overlapped), 137.4 (2 C, overlapped), 129.3, 128.8, 128.6, 128.4, 128.3, 126.7, 126.5, 126.4, 122.7, 122.6, 102.2, 97.5, 80.3, 70.2, 69.5, 64.6, 53.4, 50.7 ppm. $C_{32}H_{30}N_4O_6$ (566.6): calcd. C 67.83, H 5.34, N 9.89; found C 67.01, H 5.31, N 9.77. **Ligand 1c:** $[\alpha]_D^{20}$ = –121 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57 (d, *J* = 4.8 Hz, 1 H, H6-py), 8.45 (d, *J* = 10 Hz, 1 H, NH), 8.29 (d, *J* = 4.7 Hz, 1 H, H6-py), 8.11 (d, *J* = 7.9 Hz, 1 H, H3-py), 8.09 (d, *J* = 10 Hz, 1 H, NH), 8.03 (d, *J* = 7.9 Hz, 1 H, H3-py), 7.76 (t, *J* = 7.9 Hz, 1 H, H4-py), 7.71 (t, *J* = 7.9 Hz, 1 H, H4-py), 7.40 (dd, *J* = 7.9, 4.7 Hz, 1 H, H5-py), 7.41–7.36 (m, 2 H, Ph), 7.26–7.22 (m, 4 H, H5-py and Ph H), 5.58 (s, 1 H, OCHO), 4.93–4.86 (m, 2 H, H2, H3), 4.69 (s, 1 H, H1), 4.27 (dd, *J* = 10.3, 4.8 Hz, 1 H, $H6_{eq}$), 4.07 (dt, *J* = 9.9, 4.8 Hz, 1 H, H5), 3.90–3.85 (m, 2 H, H4, $H6_{ax}$), 3.40 (s, 3 H, OCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.4 (2 C, overlapped), 149.4, 149.1, 148.0, 147.6, 137.3, 137.0 (2 C overlapped), 128.9, 128.0, 126.4, 126.1, 125.9, 122.3 (2 C, overlapped), 102.1, 100.8, 77.1, 68.8, 64.1, 55.0, 51.7, 48.1 ppm.

Synthesis of Ligand 1b: 4-Chloropyridine-2-carboxylic acid hydrochloride (285 mg, 1.14 mmol), 1,1′-carbonyldiimidazole (185 mg, 1.14 mmol) and potassium carbonate (158 mg, 1.14 mmol) were mixed at 50 °C in dry tetrahydrofuran (2 mL) under nitrogen, and the suspension obtained was stirred for 1 h. Then the glucosediamine (200 mg, 0.56 mmol) was added, and the mixture was stirred at the same temperature for an additional 1 h. The crude product was concentrated under rotatory evaporation and purified by column chromatography on silica gel (eluent: hexane/AcOEt, from 1:1 to 3:7) to yield 113 mg (32%) of the pure product. Additional ligand was eluted together with an unidentified product. $[\alpha]_D^{20}$ = +12 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.43 (d, *J* = 5.2 Hz, 1 H, H6-py), 8.40 (d, *J* = 9.8 Hz, 1 H, NH), 8.26 (d, *J* = 5.6 Hz, 1 H, H6-py), 8.01 (d, *J* = 9.3 Hz, 1 H, NH), 7.96 (s, 1 H, H3), 7.91 (s, 1 H, H3), 7.36–7.28 (m, 4 H, H5 and Ph H), 7.27–7.12 (m, 8 H, Ph), 5.49 (s, 1 H, OCHO), 4.94 (d, *J* = 3.5 Hz, 1 H, H1), 4.76 (q, *J* = 9.8 Hz, 1 H, H3), 4.75 (d, *J* = 12.2 Hz, 1 H, C*H*HPh), 4.52 (d, *J* = 12.2 Hz, 1 H, CH*H*Ph), 4.53 (dt, *J* = 9.3, 3.5 Hz, 1 H, H2), 4.22 (dd, *J* = 10.3, 4.8 Hz, 1 H, $H6_{eq}$), 4.09–4.02 (m, 1 H, H5), 3.78 (t, *J* = 9.8 Hz, 1 H, $H6_{ax}$), 3.73 (t, *J* = 10.3 Hz, 1 H, H4) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.4, 164.0, 151.2, 151.1, 149.7, 149.2, 146.0 (2 C overlapped), 137.5, 137.2, 129.4, 128.9, 128.6 (2 C overlapped), 128.5, 128.4, 126.8, 126.7, 123.3 (2 C overlapped), 102.2, 97.3, 80.1, 70.3, 69.4, 64.6, 53.4, 50.9 ppm.

Synthesis of Ligand 1e: A solution of picolinic acid (520 mg, 4.2 mmol), 4-(dimethylamino)pyridine (48 mg, 0.43 mmol) and 1,3-dicyclohexylcarbodiimide (890 mg, 4.3 mmol) in dry dichloromethane (7 mL) was added to a solution of benzyl 2-amino-2-deoxy-4,6-*O*-(4-methoxybenzylidene)-α-D-glucopyranoside,[21] (2.0 mmol)

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in the same solvent (7 mL). The resulting mixture was stirred at room temperature under an inert gas for 12 h to afford a yellow suspension. The precipitate was removed by filtration. The resulting yellow solution was concentrated under vacuum, and the residue was chromatographed on silica gel (ethyl acetate/hexane, 1:5) to afford the pure product as a white solid (yield: 777 mg, 65%). $[\alpha]_D^{20}$ = +107.5 (c = 0.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 298 K): δ = 8.60 (d, J = 4.8 Hz, 1 H, H6-py), 8.55 (d, J = 5.1 Hz, 1 H, H6-py), 8.48 (d, J = 9.9 Hz, 1 H, NH), 8.05 (d, J = 7.5 Hz, 1 H, H3-py), 7.95 (d, J = 7.8 Hz, 1 H, H3-py), 7.71 (t, J = 7.8 Hz, 2 H, H4-py), 7.40–7.10 (m, 9 H, H5-py and Ph H), 6.80 (d, J = 8.4 Hz, 2 H, Ph), 5.85 (t, J = 9.9 Hz, 1 H, H3), 5.50 (s, 1 H, OCHO), 5.01 (d, J = 3.6 Hz, 1 H, H1), 4.73 (m, 2 H, H2, C*H*HPh), 4.58 (d, J = 12 Hz, 1 H, CH*H*Ph), 4.25 (dd, J = 10.2, 4.5 Hz, 1 H, $H6_{eq}$), 4.11 (dt, J = 10.2, 4.5 Hz, 1 H, H5), 3.96 (t, J = 9.6 Hz, 1 H, $H6_{ax}$), 3.82 (t, J = 10.2 Hz, 1 H, H4), 3.70 (s, 3 H, OCH_3) ppm. ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 164.7, 164.6, 160.3, 150.1, 149.4, 148.5, 147.8, 137.3, 137.0, 136.8, 129.7, 128.6, 128.4, 128.3, 127.7, 127.0, 126.5, 125.7, 122.3, 113.8, 101.7, 97.6, 79.6, 71.9, 70.2, 69.1, 63.5, 55.4, 52.6 ppm. $C_{33}H_{31}N_3O_8$ (597.6): calcd. C 66.32, H 5.23, N 7.03; found C 66.40, H 5.29, N 7.10.

Microwave-Assisted Allylic Alkylations. General Procedure: Two different stock solutions were prepared: solution N, containing the nucleophile, was prepared by adding dimethyl malonate (880 μL, 7.7 mmol) to a suspension of 60% NaH in mineral oil in tetrahydrofuran (10 mL), and solution S, containing the substrate, was prepared by dissolving the allylic carbonate (4 or 5) (7.1 mmol) in THF (10 mL). Then the appropriate ligand (0.034 mmol) and $Mo(CO)_6$ (6.9 mg, 0.026 mmol) were transferred to a flame-dried SmithProcessVial™. Solution N (1 mL), solution S, and BSA (208 μL) were added in this order, and the suspension was heated in the microwave cavity at 160 °C for the desired time. The brown solution obtained was diluted with Et_2O to a total volume of 10 mL, resulting in a dark precipitate. A sample of the solution was filtered through silica gel and analysed by ^1H NMR spectroscopy and GC-MS to determine the conversion and the regioselectivity. The crude product was then purified either by bulb-to-bulb distillation or by chromatography on silia gel (eluent: petroleum ether/DCM, 1:1). The *ee* was determined by HPLC using a Daicel OD-H (0.46 cm i.d. × 25 cm) column. The structures of the products were confirmed by comparison with published spectroscopic data[21] and GC-MS analyses.

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