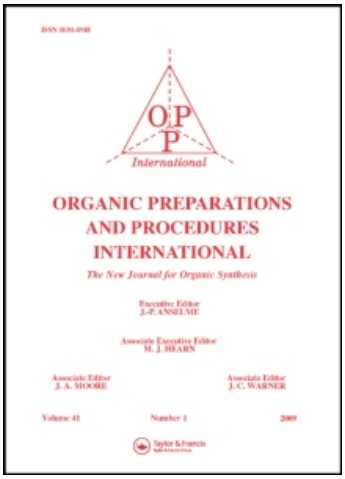

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STEREOSELECTIVE SYNTHESIS OF α-AMINO ACIDS FROM O-PIVALOYL-D-GLUCOPYRANOSYLALDIMINE

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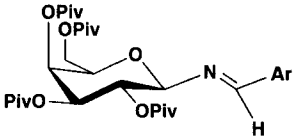
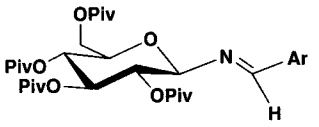
The chemistry of imines has been a topic of interest over the past 30 years due to their importance in organic synthesis. Many *N*-substituted imines have been prepared and applied to the preparation of amino acids, β-lactams, heterocycles, alkaloids, aziridines, and amines.[1-7] They are especially useful for the synthesis of optically active α-amino acids which are one of the most important types of chiral molecules for the preparation of natural products and complex biologically active compounds and the construction of selective drugs.[8]

Our current research interest has focused on the reactions of O-pivaloyl-D-glucopyranosylaldimines, and especially on their use in the stereoselective synthesis of α-amino acids. Optically active α-amino acids may be obtained by the asymmetric Strecker reaction of imines. Kunz' group have reported a series of reactions of imines by using O-pivaloyl-D-galactopyranosylaldimines as chiral templates.[9]

Since O-pivaloyl-D-glucopyranosylaldimines are more stable and less expensive and easier to prepare than O-pivaloyl-D-galactopyranosylaldimines *(Fig. 1)*, we decided to study the



O-pivaloyl-D-galactopyranosylamine

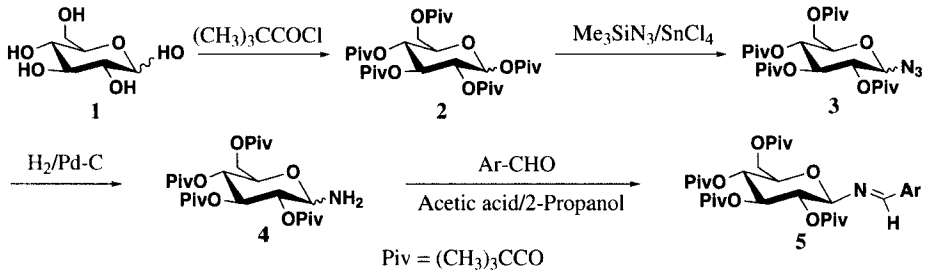


O-pivaloyl-D-glucopyranosylaldimine

Fig. 1

Strecker synthesis of α-amino acids by using these imines and now report N-(2,3,4,6-tetra-O-pivaloyl-D-glucopyranosyl)aldimines **5** as chiral templates for the stereoselective synthesis of α-amino acids (*Scheme 1*).

For the synthesis of the auxiliaries **5**, D-glucose (**1**) was converted into 2,3,4,6-tetra-O-pivaloyl-D-glucosylalmine (**4**) in three-steps. Condensation of **4** with the aldehydes in the presence of acetic acid in 2-propanol afforded the desired **5** in yields of 90% or better. In order to



Piv = $(CH_3)_3CCO$

a) Ar = 2-furyl; b) Ar = C_6H_4-4-Cl; c) Ar = C_6H_4-4-NO_2; d) Ar = C_6H_4-2-OH; e) Ar = C_6H_4-3-NO_2

Scheme 1

confirm their conformations, the X-ray crystal structure of 2-hydroxyl-N-(2,3,4,6-tetra-O-pivaloyl-D-glucopyranosyl)benzylideneamine *(Fig. 2*, with the atomic numbering scheme and 30% probability displacement ellipsoids) was determined. It is to be noted that the compound assumes a chair conformation in the solid state and is β-anomeric configuration.

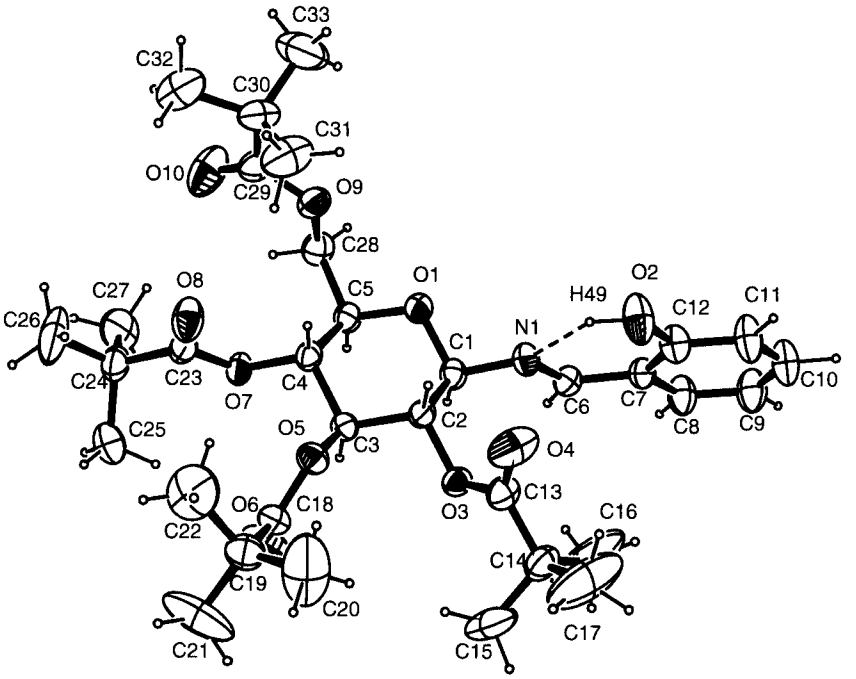
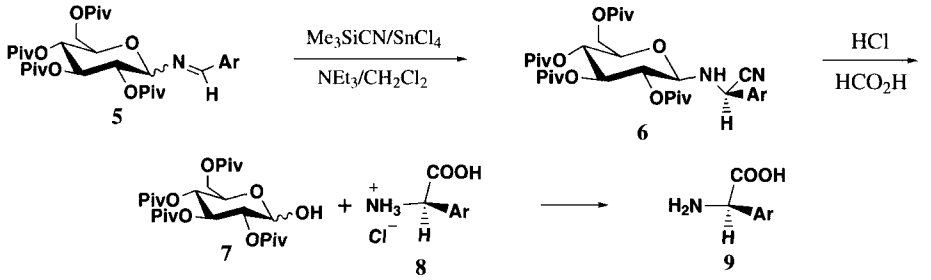


Fig. 2

The Strecker reaction of the N-(2,3,4,6-tetra-O-pivaloyl-D-glucopyranosyl)aldimines **5** with trimethylsilyl cyanide was promoted by the tin tetrachloride in dichloromethane containing a small amount of triethylamine at low temperature (*Scheme 2*), and the conversions were complete after 4~8 hours. As a result, at lower temperature the predominant α-aminonitriles **6** were obtained in nearly quantitative yields and the ratios of diastereomers ranged from 10:1 to 16:1. The pure D-α-aminonitrile diastereomers were isolated in high yields (85% or higher) by



Scheme 2

simple crystallization of the crude products **6** from heptane and were characterized by HPLC, polarimetry, ^{1}H NMR, ^{13}C NMR and MS spectrometry (*Table 1*).

Table 1. Strecker Synthesis of α-Aminonitriles **6**.

Product	Ar	Time (h)	Yield (%)	mp. (°C)	Diastereo selectivity (D:L)	$[\alpha]_D^{20}$ (c = 0.6, $CHCl_3$)	^{13}C NMR CN(C) α-C	Mass(ESI: $[M+H]^+$)	IR(cm^{-1}) (CN)
6a	2-Furyl-	5	85	129-132	11:1	+40.5	114.9, 59.3	621.7	2250
6b	4-Chlorophenyl-	6	88	210-212	13:1	+30.1	114.8, 54.8	666.2	2248
6c	4-Nitrophenyl-	5	91	223-226	16:1	+15.8	115.4, 55.6	676.7	2240
6d	2-Hydroxylphenyl-	8	86	205-208	10:1	+14.6	113.3, 59.1	647.8	2246
6e	3-Nitrophenyl-	4	90	248-251	15:1	+21.9	115.6, 52.3	676.7	2238

In order to obtain α-amino acids, the α-aminonitriles **6** were first treated with dry hydrogen chloride in formic acid at room temperature, then the α-amino acid hydrochlorides **8** were passed through an ion-exchange resin to deliver the free **9**. The pivaloylglucose derivative **7** was recovered easily by simple extraction.

The mechanism may be rationalized as shown in *Fig. 3*.[10] In the transition state, the two octahedral coordination sites of the tin(IV) chloride are occupied by the imine nitrogen and the

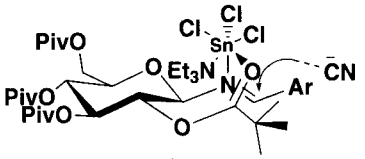


Fig. 3

carbonyl oxygen of the (C-2)pivaloyloxy group, respectively. According to this rationalization, the imine is preferably attacked by nucleophilic reagent from the less sterically hindered side. Additionally, when the triethylamine is introduced, one of the four chlorines may be replaced by triethylamine nitrogen and the steric hindrance would increase commensurately, thus favoring further the S_N2'-type attack of trimethylsilyl cyanide from *Si* side (facing the oxygen) of the imine.

In conclusion, we have developed a novel effective, configurationally stable chiral template for the stereocontrolled synthesis of α-amino acids. This method is efficient, economical, and environmentally friendly, and provides high yield and high diastereomers ratio. Further studies along this line are now in progress.

EXPERIMENTAL SECTION

Mps were determined on an X_4-Data microscopic melting point apparatus. Microanalyses were obtained using Carlo-Erba 1106. ^{1}H NMR spectra were determined at 500 MHz (AVANCE DMX500) in $CDCl_3$ or D_2O using TMS as an intra-standard. IR specta were recorded on a Perkin Elmer 683 spectrometry at r. t. Mass spectra were acquired on HP5989B. Specific rotations were determined on a Perkin Elmer 341 polarimeter. X-ray measurements were obtained on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo-Kα radiation.

1,2,3,4,6-Penta-O-pivaloyl-D-glucopyranose (2), mp. 158-160°C; yield 96%; $[\alpha]_D^{20}$: +10.5°C (c = 2, $CHCl_3$); m/z (ESI): 601.8 $[M+H]^+$; ^{1}H NMR ($CDCl_3$): δ 5.69 (d, *J* = 8.4 Hz, 1H), 5.36 (t, *J* = 9.2 Hz, 1H), 5.21 (t, *J* = 8.4 Hz, 1H), 5.13 (q, *J* = 9.6 Hz, 1H), 4.13 (m, *J* = 2.8 Hz, 2H), 3.85 (q, *J* = 2.4 Hz, 1H), 1.11-1.29 (m, 45H); ^{13}C NMR ($DCCl_3$): δ 178.33, 177.37, 176.80, 176.75, 176.67, 92.22, 73.15, 72.72, 70.48, 68.12, 61.82, 39.06-39.20, 27.18-27.51; IR (KBr, cm^{-1}): 2950, 1745, 1455, 1250, 1150, 1050.

Anal. Calcd for $C_{31}H_{52}O_{11}$: C, 61.98; H, 8.72. Found: C, 61.96; H, 8.51

2,3,4,6-Tetra-O-pivaloyl-D-glucopyranosyl Azide (3), mp. 100-101°C; yield 92%; $[\alpha]_D^{20}$: −11.10°C (c = 2, $CHCl_3$); m/z (ESI). 542.1 $[M+H]^+$; ^{1}H NMR ($DCCl_3$): δ 5.30 (t, J = 9.5 Hz 1H), 5.13 (t, *J* = 9.7 Hz, 1H), 4.95 (t, *J* = 9.2 Hz, 1H), 4.60 (d, *J* = 8.9 Hz, 1H), 4.21 (t, *J* = 11.1 Hz, 1H), 4.07 (q, *J* = 5.0 Hz, 1H), 3.80 (m 1H), 0.95-1.32 (m, 36H); ^{13}C NMR ($DCCl_3$): δ 178.27, 177.33, 176.78, 176.53, 88.48, 74.64, 72.15, 70.71, 67.57, 61.68, 38.99-39.03, 27.25-27.35; IR (KBr, cm^{-1}): 2950, 2200, 1750, 1475, 1275, 1150, 1050, 950.

Anal. Calcd for $C_{26}H_{43}N_3O_9$: C, 57.66; H, 8.00; N. 7.76. Found: C, 57.41; H, 7.97; N, 7.72.

2,3,4,6-Tetra-O-pivaloyl-D-glucopyranosylalmine (4), mp.104-105°C; yield 96%; $[\alpha]_D^{20}$: −16.3°C (c = 2, $CHCl_3$); m/z (ESI): 516.2 $[M+H]^+$; ^{1}H NMR ($DCCl_3$): δ 5.31(m, 1H), 5.11 (q, *J* = 5.2 Hz, 1H), 4.83 (q, *J* = 9.1 Hz, 1H), 4.17 (q, *J* = 4.5 Hz, 2H), 4.07 (q, *J* = 4.6 Hz, 1H), 3.70 (q, *J* = 3.1 Hz, 1H), 1.95 (s, 2H), 1.10-1.22 (m, 36H); ^{13}C NMR ($DCCl_3$): δ 178.41, 177.83, 177.40, 176.71, 85.55, 73.395, 72.78, 72.31, 68.29, 62.26, 38.9-39.1, 27.32-27.42; IR (KBr, cm^{-1}): 3435, 2950, 1740, 1455, 1300, 1150, 1050, 950.

Anal. Calcd for $C_{26}H_{45}NO_9$: C, 60.56; H, 8.80; N, 2.72. Found: C, 60.59; H, 8.74; N, 2.83

Preparation of O-Pivaloyl-D-glucopyranosyl Aldimines (5).- To a solution of pivaloyl chloride (91.0 g, 0.75 mol) in chloroform (150 mL) were added pyridine (90 mL) and D-glucose (22.0 g, 0.12 mol). The mixture was then stirred at room temperature for 10 days to afford **2**. Additions trimethylsilyl azide (7.5 mL, 0.056 mol) and $SnCl_4$ (5 mL, 0.043 mol) to a solution of **2** (30.0 g, 0.05 mol) in dichloromethane followed by stirring for 1 h gave **3**. Dry hydrogen was

bubbled through a solution of **3** (27.1 g, 0.05 mol) in methanol (200 mL) containing Pd/C (0.06 g) yielded **4**. Finally, addition the aldehyde and fifteen drops of acetic acid to a solution **4** (5.15 g, 10 mmol) in 2-propanol (25 mL) afforded, after 0.5-4 h, **5**, which precipitated from solution. The products were collected and washed rapidly with ice-cold 2-propanol and dried.

N-(2, 3, 4, 6-tetra-O-pivaloyl-D-glucopyranosyl)-2-furylideneamine (5a), mp. 95-98°C; yield 90%; $[\alpha]_D^{20}$: –34.6°C(c = 0.6, $CHCl_3$); m/z (ESI) 594.2$[M+H]^+$; ^1H NMR ($DCCl_3$): δ 8.21 (s, 1H), 7.53 (s, 1H), 6.86 (d, *J* = 2.5 Hz 1H), 6.48 (s, 1H), 5.45 (t, *J* = 9.4 Hz, 1H), 5.23 (t, *J* = 9.6 Hz, 1H), 5.00 (t, *J* = 9.62 Hz, 1H), 4.88 (d, *J* = 8.6 Hz, 1H), 4.26 (d, *J* = 12 Hz 1H), 4.17 (m, 1H), 3.89 (d, *J* = 5.8 Hz, 1H), 1.06-1.29 (m, 36H); ^{13}C NMR ($DCCl_3$): δ 178.4, 177.5, 176.6, 176.6, 151.6, 149.8, 145.8, 115.6, 112.26, 93.2, 74.5, 73.1, 72.3, 68.1, 62.1, 39.0-39.1, 27.3-27.4; IR (KBr, cm^{-1}): 2974, 1741, 1648, 1480, 1397, 1368, 1283, 1140, 1070, 896, 761.

Anal. Calcd. for $C_{31}H_{47}NO_{10}$: C, 62.71; H, 7.98; N, 2.36. Found: C, 62.76; H, 7.88; N, 2.38

4-Chloro-N-(2,3,4,6-tetra-O-pivaloyl-D-glucopyranosyl)benzylideneamine (5b), mp. 78-180°C; yield. 93%; $[\alpha]_D^{20}$: –39.6°C (c = 0.6, $CHCl_3$); m/z (ESI): 638.1$[M+H]^+$; ^1H NMR ($DCCl_3$): 8.14 (s, 1H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 5.47 (t, *J* = 9.5 Hz, 1H), 5.23 (t, *J* = 9.6 Hz, 1H), 5.00 (t, *J* = 9.2 Hz, 1H), 4.91 (d, *J* = 8.9 Hz, 1H), 4.30 (d, *J* = 1.3 Hz, 1H), 4.17 (q, *J* = 4.9 Hz, 1H), 3.90 (q, *J* = 3.5 Hz, 1H), 1.02-1.25 (m, 36 H); ^{13}C NMR ($DCCl_3$): δ 178.4, 177.4, 176.7, 176.6, 159.8, 137.8, 134.1, 130.1, 129.2, 92.9, 74.5, 73.0, 72.2, 68.2, 62.1, 39.0-39.1, 27.3-27.4; IR (KBr, cm^{-1}): 2945, 1742, 1646, 1616, 1577, 1505, 1450, 822.

Anal. Calcd. for $C_{33}H_{48}ClNO_9$: C, 62.11; H, 7.58; N, 2.19. Found: C, 62.37; H, 7.57; N, 2.05

4-Nitro-N-(2,3,4,6-Tetra-O-pivaloyl-D-glucopyranosyl)benzylideneamine (5c), mp. 180-185°C; yield 96%; $[\alpha]_D^{20}$: –13.9°C (c = 0.6, $CHCl_3$); m/z (ESI): 649.2$[M+H]^+$. ^1H NMR ($DCCl_3$): δ 8.50 (s, 1H), 8.26 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 8.4 Hz, 2H), 5.50 (t, *J* = 9.5 Hz, 1H), 5.23 (t, *J* = 9.7 Hz, 1H), 5.00 (t, *J* = 9.2 Hz, 1H), 4.96 (t, *J* = 9.2 Hz, 1H), 4.31 (d, *J* = 12 Hz, 1H), 4.18 (q, *J* = 4.9 Hz, 1H), 3.92 (t, *J* = 5.9 Hz, 1H), 1.02-1.23 (m, 36 H); ^{13}C NMR ($DCCl_3$): δ 178.4, 177.5, 176.7, 176.7, 157.9, 150.0, 141.1, 129.5, 124.2, 91.6, 74.5, 72.9, 72.2, 68.0, 61.9, 39.0-39.1, 27.3-27.4; IR (KBr, cm^{-1}): 2940, 1735, 1600, 1578, 1528 1480, 1457, 1342, 832.

Anal. Calcd. for $C_{33}H_{48}N_2O_{11}$: C, 61.10; H, 7.46; N, 4.32. Found: C, 61.08; H, 7.49; N, 4.30

2-Hydroxy-N-(2,3,4,6-Tetra-O-pivaloyl-D-glucopyranosyl)benzylideneamine (5d), mp. 195-197°C; yield 92%; $[\alpha]_D^{20}$: –7.3°C (c = 0.6, $CHCl_3$); m/z (ESI): 620.2 $[M+]^+$; ^1H NMR ($DCCl_3$): δ 8.54 (s, 1H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.89 (t, *J* = 7.0 Hz, 1H), 5.49 (t, *J* = 9.3 Hz, 1H), 5.24 (t, *J* = 9.6 Hz, 1H), 5.06 (t, *J* = 9.2 Hz, 1H), 4.97 (d, *J* = 8.8 Hz, 1H), 4.31 (d, *J* = 12.3 Hz, 1H), 4.18 (q, *J* = 4.7 Hz,1H), 3.92 (t, *J* = 4.4 Hz, 1H), 1.07-1.29 (m, 36 H); ^{13}C NMR ($DCCl_3$): δ 178.3, 177.5, 176.7, 176.6, 165.2, 161.0, 133.6, 132.7, 119.2, 118.4, 117.5, 90.3, 74.6, 73.0, 72.4, 68.0, 61.8, 39.0-39.2, 27.3-27.4; IR (KBr, cm^{-1}): 3480, 2990, 1750, 1625, 1614, 1495, 1530, 1300, 1250, 750.

Anal. Calcd. for $C_{33}H_{49}NO_{10}$: C, 63.95; H, 7.97; N, 2.26. Found: C, 63.93; H, 7.90; N, 2.31

3-Nitro-N-(2,3,4,6-Tetra-O-pivaloyl-D-glucopyranosyl)benzylideneamine (5e), mp. 211-213.9°C; yield 95%; $[\alpha]_D^{20}$: +13.8°C (c = 0.6, $CHCl_3$); m/z (ESI): 649.2 $[M+H]^+$; ^1H NMR ($DCCl_3$): δ 8.73 (s, 1H), 8.50 (s, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 7.6 Hz ,1H) , 7.60 (t, *J* = 7.8 Hz, 1H), 5.52 (t, *J* = 9.6 Hz, 1H), 5.22 (t, *J* = 9.6 Hz, 1H), 5.07 (d, *J* = 9.1 Hz,1H), 4.95 (t, *J* = 9.3 Hz, 1H), 4.33 (d, *J* = 12 Hz, 1H) , 4.19 (q, 1H) , 3.93 (q, 1H), 1.04-1.26 (m, 36 H); ^{13}C NMR ($DCCl_3$): δ 178.3, 177.5, 176.9, 176.7, 157.3, 148.8, 137.5, 134.5, 129.9, 125.8, 123.2, 91.3, 77.5, 77.30, 77.05, 74.6, 72.9, 72.3, 68.1, 61.9, 27.33; IR (KBr, cm^{-1}): 2945, 1746, 1644, 1614, 1580, 1530, 1490, 1462, 1356, 794.

Anal. Calcd. for $C_{33}H_{48}N_2O_{11}$: C, 61.10; H, 7.46; N, 4.32. Found: C, 61.11; H, 7.43; N, 4.28

Preparation of α-Aminonitriles (6).- To a solution of trimethylsilyl cyanide (0.198 g, 2 mmol) and tin tetrachloride (0.521 g, 2 mmol) in dichloromethane (20 mL) was added small amount of triethylamine (0.05 g, 0.5 mmol) at –40°C. Then a solution of imine **5** (1.5 mmol) in dichloromethane (1 mL) was added slowly, after half an hour, the solution was allowed to slowly warm to –18°C. The reaction was monitored by TLC, when completed, the mixture was extracted with 1N HCl, washed with saturated aqueous $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated *in vacuo* at room temp. The residue was recrystallized from heptane to give the diastereomers the N-(2,3,4,6-tetra-O-pivaloyl-D-glucopyranosyl)-α-aminonitriles

N-(2,3,4,6-Tetra-O-pivaloyl-D-glucopyranosyl)-2-furylglycinonitrile (6a), mp. 129-132°C; Yield 85%; $[\alpha]_D^{20}$: +40.5°C (c = 0.6, $CHCl_3$); % ee = 83%; m/z (ESI): 621.7 $[M+H]^+$; ^1H NMR ($DCCl_3$): δ 7.43 (s, 1H), 6.75 (d, *J* = 2.5 Hz, 1H), 6.39 (s, 1H), 5.32 (t, *J* = 9.4 Hz, 1H), 5.28 (t, *J* = 9.6 Hz, 1H), 5.14 (s, 1H), 4.98 (t, *J* = 9.62 Hz, 1H), 4.80 (d, *J* = 8.6 Hz, 1H), 4.55 (d, *J* = 12 Hz, 1H), 4.17 (m, 2H), 1.06-1.24 (m, 36H); ^{13}C NMR ($DCCl_3$): δ 177.4, 176.3, 175.8, 175.2, 152.6, 148.6, 115.0, 111.0, 106.2, 75.3, 71.5, 70.3, 69.2, 654.5, 59.3, 45.1, 38.7-39.0, 25.1.3-27.3; IR (KBr cm^{-1}): 2979, 2250, 1740, 1650, 1482, 1380, 1283, 1177, 893.

Anal. Calcd. for $C_{32}H_{48}N_2O_{10}$: C, 61.82; H, 7.72; N, 4.51. Found: C, 61.53; H, 7.80; N, 4.48

4-Chloro-N-(2,3,4,6-Tetra-O-pivaloyl-D-glucopyranosyl)phenylglycinonitrile (6b), mp. 210-212°C; yield: 88%; $[\alpha]_D^{20}$: +30.1°C (c = 0.6, $CHCl_3$); % ee = 85.7%; m/z (ESI): 665.2 $[M+H]^+$. ^1H NMR ($DCCl_3$): δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 2H), 5.44 (t, *J* = 7.3 Hz, 2H), 5.21 (d, *J* = 10 Hz, 1H), 4.93 (d, *J* = 1.9 Hz, 1H), 4.80 (q, *J* = 6.5 Hz, 1H), 4.12 (d, *J* = 7 Hz, 1H), 3.58 (t, *J* = 3.8 Hz, 1H), 3.10 (m, 1H), 1.05-1.30 (m, 36 H); ^{13}C NMR ($DCCl_3$): δ 179.0, 177.4, 177.2, 176.6, 138.6, 133.3, 130.3, 129.3, 114.8, 69.6, 68.8, 67.5, 65.8, 59.5, 57.8, 54.8, 39.1-39.5, 27.1-27.5; IR (KBr, cm^{-1}): δ 2980, 2248, 1760, 1550, 1450, 1300, 150, 870.

Anal. Calcd. for $C_{34}H_{49}ClN_2O_9$: C, 61.39; H, 7.42; N, 4.21. Found: C, 61.02; H, 7.46; N, 4.09

4-Nitro-N-(2,3,4,6-Tetra-O-pivaloyl-D-glucopyranosyl)phenylglycinonitrile (6c), mp. 223-226°C; yield: 91%; $[\alpha]_D^{20}$: +15.8°C (c = 0.6, $CHCl_3$); %ee = 88%; m/z(ESI): 676.4$[M+H]^+$; ^1H NMR ($DCCl_3$): δ 8.31(s, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 8.15 (d, *J* = 8.4 Hz, 2H), 5.45 (t, *J* = 9.4 Hz, 1H), 5.25 (t, *J* = 9.5 Hz, 1H), 5.06 (t, *J* = 9.1 Hz, 1H), 4.90 (s, 1H), 4.81 (d, *J* = 8.5 Hz, 1H), 4.26 (d, *J* = 11.9 Hz, 1H), 3.90 (q, *J* = 4.7 Hz, 1H), 1.0-1.22 (m, 36H); ^{13}C NMR ($DCCl_3$): δ

178.4, 177.6, 176.7, 176.5, 147.7, 136.2, 129.9, 122.8, 114.9, 74.4, 73.1, 72.2, 68.3, 62.2, 55.6, 44.0, 39.1-38.9, 27.3-27.4; IR (KBr, cm^{-1}): 2976, 2240, 1739, 1605, 1529, 1481, 1462, 1398, 1279, 1136, 856.

Anal. Calcd. for $C_{34}H_{49}N_3O_{11}$: C, 60.43; H, 7.31; N, 6.22. Found: C, 60.33; H, 7.28; N, 6.27

2-Hydroxy-N-(2,3,4,6-Tetra-O-pivaloyl-D-glucopyranosyl)phenylglycinonitrile (6d), mp. 205-208°C; yield: 86%; $[\alpha]_D^{20}$: +14.6°C (c = 0.6, $CHCl_3$); % ee = 81.8%; m/z (ESI): 647.4 $[M+H]^+$; ^1H NMR ($DCCl_3$): δ 8.56 (d, *J* = 1.5 Hz, 1H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.89 (t, *J* = 7.0 Hz, 1H), 5.74 (d, *J* = 2.0 Hz, 1H), 5.50 (t, *J* = 10.0 Hz, 1H), 5.36 (s, 1H), 5.30 (q, *J* = 3.0 Hz, 1H), 4.32 (d, *J* = 1.5 Hz, 1H), 4.27 (d, *J* = 4.0 Hz, 1H), 1.07-1.29(m, 36H); ^{13}C NMR ($DCCl_3$): δ 179.1, 178.9, 177.6, 176.3, 160.7, 134.4, 132.9, 119.7, 117.8, 113.3, 69.8, 68.3, 68.6, 67.2, 64.3, 60.3, 59.1, 39.0-39.2, 27.3-27.4; IR (KBr, cm^{-1}): 3490. 2950, 2246, 1720, 1600, 14980, 1250, 1125, 750.

Anal. Calcd. for $C_{34}H_{59}N_2O_{10}$: C, 63.14; H, 7.79; N, 4.33. Found: C, 63.18; H, 7.70; N, 4.31

3-Nitro-N-(2,3,4,6-Tetra-o-pivaloyl-D-glucopyranosyl)phenylglycinonitrile (6e), mp. 248-251°C; yield 90%; $[\alpha]_D^{20}$: +21.9°C (c = 0.6, $CHCl_3$); % ee = 87.5%; m/z (ESI): 676.4 $[M+H]^+$; ^1H NMR ($DCCl_3$): δ 8.47 (s, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 5.99 (t, *J* = 1.8 Hz, 1H), 5.76 (t, *J* = 9.6 Hz, 1H), 5.40 (t, *J* = 9.6 Hz, 1H), 5.21 (d, *J* = 9.1 Hz, 1H), 4.95 (t, *J* = 9.3 Hz, 1H), 4.07 (d, *J* = 1.2 Hz, 2H), 3.59 (d, 1H), 1.08-1.30 (m, 36H); ^{13}C NMR($DCCl_3$): δ 179.3, 178.1, 177.9, 176.6, 149.2, 135.5, 134.2, 130.5, 125.2, 123.3, 116.6, 71.2, 70.3, 69.8, 60.2, 59.3, 52.3, 49.5, 39.4, 27.3-27.4. IR (KBr, cm^{-1}): 2975, 2238, 1736, 1536, 1481, 1399, 1352, 1279, 1139,1036, 940, 809.

Anal. Calcd. for $C_{34}H_{49}N_3O_{11}$: C, 60.43; H, 7.31; N, 6.22. Found: C, 60.33; H, 7.28; N, 6.27

Preparation of α-Amino Acids(9)[9a].- Dry hydrogen chloride was bubbled through a solution of **6** (1 mmol) in formic acid (20 mL) for 6-10 hours at room temperature, followed by concentration *in vacuo* and filtration through sillca gel (20 g) and washed with light petroleum ether/ethyl acetate (1:1) to recover compound **7**. The silica gel was then dried, extracted four times with 2N HCl (100 mL); the combined acidic extracts were concentrated to dryness *in vacuo*, diluted with conc. HCl (10 mL) and heated to 80°C for 1-2 hours. Concentration to dryness, gave **8** as a solid; it was converted to **9** by washing with water through D354 ion-exchange resin for 3-4 hours.

2-Furylglycine (9a), mp. 210-212°C (*lit.*[11a] 212-213°C); yield 86%; $[\alpha]_D^{20}$: –332°C (c = 0.6, H_2O); % ee = 84.5%; m/z (ESI): 142.1$[M+H]^+$; ^1H NMR (D_2O): δ 7.94 (s, 1H), 7.62 (d, *J* = 3.3 Hz 1H), 6.80 (t, *J* = 1.8 Hz, 1H), 4.90 (s, 1H); ^{13}C NMR (D_2O): δ 181.8, 149.9, 149.3, 121.8, 113.5, 61.2. IR (KBr, cm^{-1}): 3500-2500, 1680, 1618, 1469, 1400, 129, 1168, 972, 910, 796.

4-Chlorophenylglycine (9b), mp. 272-274°C (*lit.*[11b] 270-272°C); Yield 88%; $[\alpha]_D^{20}$: –157.3°C (c = 0.6, H_2O); % ee = 86.6%; m/z (ESI): 186.1$[M+H]^+$; ^1H NMR (D_2O): δ 8.10 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.3 Hz, 2H), 4.92 (s, 1H); ^{13}C NMR (D_2O): δ 191.2, 140.8, 132.5, 129.9, 129.3 61.3. IR (KBr, cm^{-1}): 3500-2500, 1685, 1620, 1590, 1465, 1403, 1249, 969, 827.

4-Nitrophenylglycine (9c), mp. 153-156°C (*lit.*[11c] 156-158°C); Yield 89%; $[\alpha]_D^{20}$: –175°C (c =

0.6, H_2O); % ee = 88.8%; m/z (ESI): 197.1 $[M+H]^+$; ^1H NMR (D_2O): δ 8.28 (d, J = 8.4 Hz, 2H), 8.13 (d, J = 8.4 Hz, 2H), 4.88 (s, 1H); ^{13}C NMR (D_2O): δ 192.9, 151.1, 137.9, 129.7, 124.5, 62.3; IR (KBr, cm^{-1}): 3500-2500, 1687, 1603, 1530, 1476, 1402, 1344, 1241, 858.

2-Hydroxyphenylglycine (9d), mp.193-195°C (*lit.*[11d] 194-195°C); Yield 86%; m/z (ESI): 168.2 $[M+H]^+$; $[\alpha]_D^{20}$: −128.5°C (c = 0.6, H_2O); % ee = 83.3%; ^1H NMR (D_2O): δ 7.39 (t, J = 7.5 Hz, 1H), 7.33 (d, J = 1.3 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.92 (t, J = 7.4 Hz 1H), 5.51 (s 1H); ^{13}C NMR (D_2O): δ 191.2, 161.2, 133.4, 132.6, 119.1, 117.8, 117.5, 62.1; IR (KBr, cm^{-1}): δ 3500-2500, 3080, 1700, 1625, 1614, 1530, 1495, 1300, 1250, 750.

3-Nitrophenylglycine (9e), mp. 170-172°C (*lit.*[11e] 171-173°C); yield 90%; $[\alpha]_D^{20}$: −173.5°C (c = 0.6, H_2O); % ee = 88%; m/z(ESI): 197.1$[M+H]^+$. ^1H NMR (D_2O): δ 8.69 (s, 1H), 8.42 (d, J = 8.1 Hz 1H), 8.30 (d, J = 7.7 Hz 1H), 7.75 (t, J = 8.0 Hz, 1H), 4.86 (s, 1H); ^{13}C NMR (D_2O): δ 192.4, 148.3, 134.5, 130.9, 129.3, 123.3, 62.2; IR (KBr, cm^{-1}): δ 3500-2500, 1685, 1625, 1563, 1475, 1343, 1125, 1050, 718.

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REFERENCES

1. (a) J. P. Adams, *Contemp. Org. Synth.* **4,** 517 (1997). (b) R. Bloch, *Chem. Rev.*, **98**, 1407 (1998). (c) D. Enders and U. Reinhold, *Tetrahedron: Asymmetry,* **8**, 1895 (1997). (d) S. Kobayashi and H. Ishitani, *Chem. Rev.*, **99**, 1069 (1999).

2. S. M. Weinreb, *Top. Curr. Chem.*, **190**, 131 (1997)

3. F. A. Davis, and B. C. Chen, *Chem. Soc. Rev.*, **27**, 13 (1998).

4. M. Panunzio and P. Zarantonello, *Org. Process Res. Dev.*, **2**, 49 (1998).

5. G. Cainelli, M. Panunzio, P. Andreoli, G. Martelli, G. Spunta, D. Giacomini and E. Bandini, *Pure Appl. Chem.* **62**, 605 (1990).

6. W. Chunmei and J. L. Chao, *J. Am. Chem. Soc.,* **124**, 5638 (2002).

7. H. Tamio and I. Mitsuo, *J. Am. Chem. Soc.,* **122**, 976- (2000).

8. (a) R. M. Williams, J. E. Baldwin and P. D. Magnus, *Synthesis of Optically Active alpha Amino Acids, Eds Pergamon Press: Oxford.* (**1989**). (b) R. O. Duthaler, *Tetrahedron,* **50**, 1539 (1995). (c) T. Lescrinier, R. Busson, J. Rozenski, G. Janssen, A.V.Aerschot and P. Herdewijin, *Tetrahedron,* **52**, 6965 (1996). (d) D. A. Dougherty, *Curr. Opin. Chem. Biol.*, **4**, 645 (2000). (e) L. Wang and P.G. Schultz, *J. Chem. Soc. Chem. Commun.*,111 (**2000**). (f) J. C. Horng and P. D. Raleeigh, *J. Am. Chem. Soc.,* **125**, 9286 (2003). (g) B. Cohen, T. McAnaney, E. S. Park Y. N, Jan, S. G. Boxer and L. Y. Jan, *Science*, **296**, 1700 (2002).

9. (a) H. Kunz, W. Sager, D. Schanzenbach and M. Decker, *Ann.*, 649 (**1991**). (b) S. Dziadek and H. Kunz, The Chemical Record **3**, 308 (2004). (c) T. Opatz, C. Kallus, T. Wunberg, W. Schmidt, and H. Kunz, Eur. *J. Org. Chem.* **68**, 1527 (2003). (d) T. Opatz, C. Kallus, T. Wunberg, W. Schmidt and H. Kunz, *Carbohydr. Res.* **337**, 2089 (2002). (e) M. Follmann, A. Rösch. E. Klegraf and H. Kunz, *Synlett.* 1569, (**2001**). (f) S. Deloisy, H. Tietgen, H. Kunz, *Chem. Commun.* **65**, 816 (2000). (g) P. Allef and H. Kunz, *Tetrahedron Asymmetry* **11**, 375 (2000). (h) H. Tietgen, M. Schultz-Kukula and H. Kunz, *Modern Amination Methods (A. Ricci, Hrsg.) Wiley-VCH Weinheim,* 103 (**2000**).

10. F. K. Matsmoto, M. Suzuki and M. Miyoshi, *J. Org. Chem.*, **34.** 2324 (1976).

11. (a) J. M. Janusz, P. A. Young, R. B. Blum and C. M. Riley, *J. Med. Chem.* **33**, 167 (1990). (b) E. L. Compere andcrystalliz D. A. Weinstein, *Synthesis*, 852 (**1977**). (c) K. Heyns, H. Schultze, *Justus Liebigs' Ann. Chim.*, **611**, 55 (1958). (d) E. K. Harvill and R. M. Herbst, *J. Org. Chem.*, **2,** 21 (1944). (e) G. Smith and T. Sivakua, *J. Org. Chem.*, **48**, 627 (1983).

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