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Tetrahedron
Tetrahedron 61 (2005) 5671–5677

A novel method for synthesis of arylacetic acids from aldehydes, *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)amine and trimethylsilylcyanide

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Received 27 January 2005; revised 3 March 2005; accepted 4 March 2005

Available online 19 April 2005

Abstract—A novel synthetic approach for the preparation of arylacetic acids via the reaction of aldehydes, *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)amine and trimethylsilylcyanide was developed, in which the *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)amine can be recycled conveniently and reused efficiently.

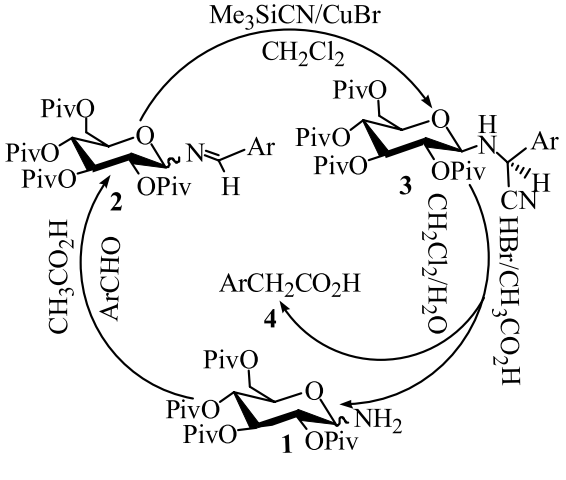
1. Introduction

In recent years, arylacetic acids and their derivatives have received much more attention because they are versatile intermediates in the synthesis of a vast range of pharmaceuticals, cosmetics, and fragrances.[1]

As a consequence of the potent biological activity associated with arylacetic acids and their derivatives, many synthetic methodologies have been developed over the past decade, including carbonylation, addition hydrolysis and electrolysis, oxidation etc.[2] However, most of them need harsh reaction conditions such as use of expensive catalysts, high pressure, high temperature etc., especially some of them suffered from long reaction time, unsatisfactory yields, tedious work-up or cumbersome product isolation procedures etc. Therefore, it is highly desirable to develop an operationally simple, effective and benign synthetic procedure for the synthesis of arylacetic acids and their derivatives from readily available materials.

Our considerable current research interest is in the asymmetric synthesis, which is enlightened by Kunz's work, etc.,[3] using *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)aldimine as chiral template. During the course of our studies on stereoselective synthesis of α-amino acids, unexpectedly, instead of the desirable formation of α-amino acids, only arylacetic acids were obtained from the reaction of aldehydes, *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)amine and trimethylsilylcyanide. To the best of our knowledge, such transformation for synthesis of arylacetic acids has not been reported previously.

Herein, we report a successful and novel synthesis of arylacetic acids by the reaction of aldehydes, *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)amine and TMSCN at ambient temperature (shown in Scheme 1).



Piv =(CH_3)$_3$CCO-

Scheme 1. (a) Ar=C_6H_5; (b) Ar=C_6H_5-4-CH_3; (c) Ar=C_6H_5-2-OH; (d) Ar=C_6H_5-4-OCH_3; (e) Ar=C_6H_5-4-Cl; (f) Ar=C_6H_5-4-F; (g) Ar=C_6H_5-2-F; (h) Ar=C_6H_5-4-NO_2; (i) Ar=C_6H_5-3-NO_2; (j) Ar=2-furyl.

Keywords: Arylacetic acids; *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopryanosyl)amine; Aldehyde; Triethylsilylcyanide.
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doi:10.1016/j.tet.2005.03.095

2. Results and discussion

2.1. Preparation of *N*-(2,3,4,6-tetra-*O*-pivaloyl-D-glucopyranosyl)aldimines

Imines are readily accessible by simple condensation of aldehydes with amines, which act as important intermediates in the synthesis of amino acids, β-lactams, heterocycles, alkaloids, aziridines, and amines etc.[4]

In order to prepare *N*-(2,3,4,6-tetra-*O*-pivaloyl-D-glucopyranosyl)aldimines, *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)amine **1** was reacted with aldehydes in the presence of acetic acid in 2-propanol. The reactions were proceeded smoothly within a short period of time at room temperature under extremely mild conditions to afford desired products **2a**–**j** in yields of 90% or higher. The results were listed in Table 1.

Based on the experiments, it was found that the rates of the condensation of the electron-poor aromatic aldehydes with **1** were much higher than those of the electron-rich aromatic aldehydes. To further, explore the structure of **2**, a single-crystal X-ray diffraction study of **2c** was performed (CCDC 264908). The molecular structure of **2c** was shown in Figure 1, and the structure was consistent with that of 2-hydroxyl-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine.[5]

Table 1. The condensation of *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)amine **1** with aldehydes at room temperature

Product **2**	Ar	Time (h)	Yield (%)	^{13}C NMR of C=N
2a	C_6H_5	0.5	90	161.1
2b	C_6H_4–CH_3	1.0	93	161.7
2c	C_6H_4-2-OH	1.5	92	165.2
2d	C_6H_4-4-OCH_3	2.5	90	162.7
2e	C_6H_4-4-Cl	1.0	92	159.9
2f	C_6H_4-4-F	0.5	93	162.7
2g	C_6H_4-2-F	0.5	91	161.9
2h	C_6H_4-4-NO_2	0.25	95	158.0
2i	C_6H_4-3-NO_2	0.25	96	157.4
2j	2-Furyl–	2.0	90	151.7

2.2. The Strecker reaction of *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)aldimines with trimethylsilylcyanide: synthesis of α-amino nitriles 3

The nucleophilic addition reaction of the imine needs to be promoted by Lewis acids,[6] especially for the Strecker reaction. So several kinds of Lewis acid were first examined for the Strecker reaction of *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)aldimines with trimethylsilylcyanide. In the case of the synthesis of **3a**, Lewis acids such as $SnCl_4$, $TiCl_4$, $AlCl_3$, CuBr, $ZnCl_2$ and ZnI_2 were studied for this transformation, the results were summarized in Table 2.

Table 2. Effects of the catalysts for the conversion from **2a** to **3a**

Entry	Lewis acid (equiv)	Reaction period (h)	Yield of **3a** (%)
1	$SnCl_4$ (1.0)	3.0	71
2	$TiCl_4$ (1.0)	3.0	60
3	$AlCl_3$ (1.0)	3.0	58
4	$ZnCl_2$ (1.0)	3.0	42
5	ZnI_2 (1.0)	3.0	45
6	CuBr (1.0)	3.0	81
7	CuBr (0.1)	4.0	40
8	CuBr (0.25)	3.5	60
9	CuBr (0.5)	3.5	72
10	CuBr (1.25)	3.0	90
11	CuBr (2.5)	3.0	89
12	CuBr (5.0)	3.0	90

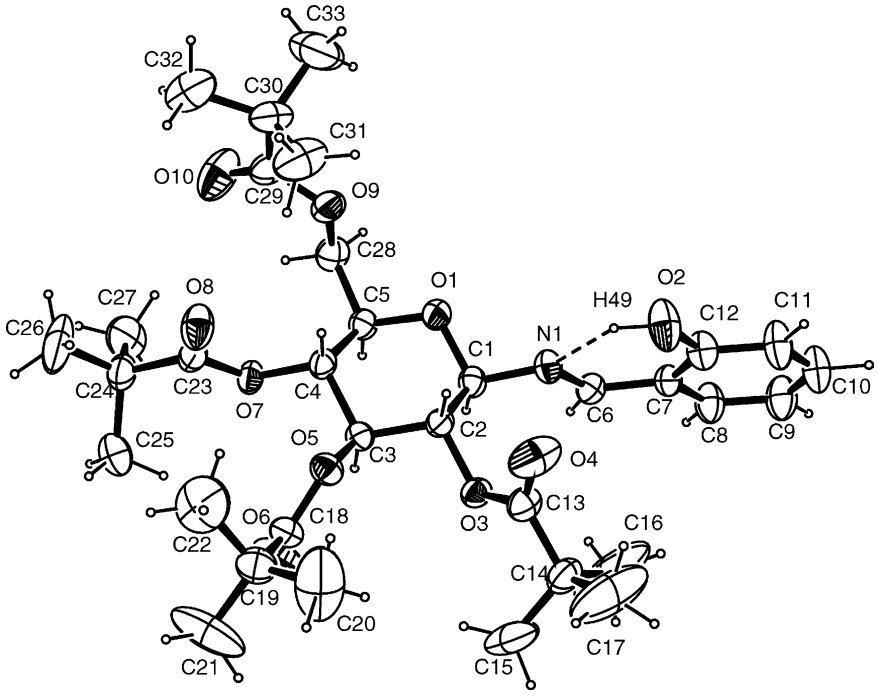


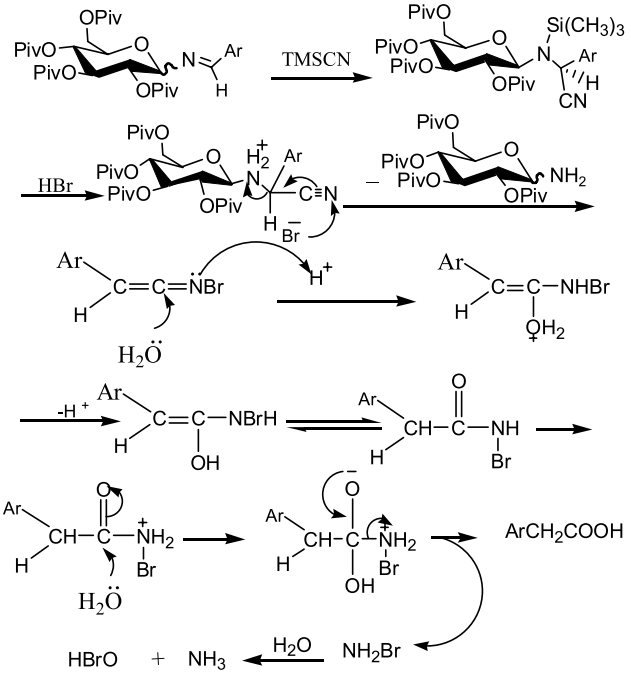
Figure 1. Crystal structure of **2c**.

It was found that the conversion of **3a** in low yields with $TiCl_4$, $AlCl_3$, $ZnCl_2$ and ZnI_2. On the other hand, $SnCl_4$ and CuBr were found to be more effective in terms of conversion and reactivity for **3a**, however, $SnCl_4$ is more sensitive to the moisture than CuBr. Therefore, CuBr was addressed as the most efficient Lewis acid in this reaction.

Under optimal condition, 1.0 mmol of **2a–j** was treated with TMSCN (1.0 mmol) in the presence of CuBr (1.25 mmol) at room temperature, using dichloromethane as the solvent.

Table 3. The Strecker reaction of *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)aldimines **2a–j** at room temperature

Product **3**	Ar	Time (h)	Yield (%)	^{13}C NMR of CN
3a	C_6H_5	3.0	90	114.3
3b	C_6H_4–CH_3	3.5	92	114.7
3c	C_6H_4-2-OH	5.0	89	113.4
3d	C_6H_4-4-OCH_3	6.0	85	114.3
3e	C_6H_4-4-Cl	4.0	86	114.7
3f	C_6H_4-4-F	2.5	88	114.3
3g	C_6H_4-2-F	3.0	90	114.5
3h	C_6H_4-4-NO_2	2.0	89	115.5
3i	C_6H_4-3-NO_2	2.0	91	116.7
3j	2-Furyl–	4.0	85	114.9



Scheme 2.

The reactions were completed in 2–8 h and gave **3a–j**, which were verified by ^{1}H NMR, ^{13}C NMR, MS and IR, in excellent yields (Table 3).

2.3. Synthesis of arylacetic acids

Acid-catalyzed hydrolysis of α-amino nitriles[5d] is the key step of the generation of arylacetic acids. Our original objective was to detach the α-amino acids from the carbohydrate moiety by the treatment of the α-amino nitriles **3** with hydrogen bromide in acetic acid at room temperature. However, during our research, we found when α-amino nitriles **3** were treated with hydrogen bromide (45%) in acetic acid/dichloromethane in the presence of water at room temperature, an unexpected process of rupture of N–C bond took place and gave arylacetic acids rather than the amino acids (Scheme 2), in which the amine **1** was regenerated.

In our process, after the hydrolysis reaction was accomplished, the arylacetic acids could be separated by a simple phase separation process and 2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosylamine **1** could be recycled conveniently from the filtrate and reused efficiently.

To evaluate the scope and generality of this transformation, various substituted arylacetic acids have been synthesized successfully by the same strategy. The results were listed in Table 4.

The possible mechanism we deduced was shown in Scheme 2.

3. Conclusion

In conclusion, we have developed a method for the synthesis of arylacetic acids from the reaction of aldehydes, *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)amine and TMSCN, which has the advantages of recycling of the template amine **1** thus, high efficiency and the mild reaction conditions as well. Hence, this method could provide a convenient access to arylacetic acids, in which the imine could be transformed into methylene, a new carbon–carbon bond formed to extend the carbon chain. Further studies along this line are now in progress in our laboratory.

Table 4. Synthesis of arylacetic acids from α-amino nitriles **3**

Product **4**	Ar	Time (h)	Yield (%)	Mp (°C)	^{13}C NMR of CO_2H	^{13}C NMR of α-C
4a	Phenyl–	1.0	91	76–78	191.8	45.2
4b	C_6H_4–CH_3	1.0	89	91–92	191.9	45.8
4c	C_6H_4-2-OH	1.5	87	145–148	192.2	45.6
4d	C_6H_4-4-OCH_3	2.0	85	85–87	192.5	46.0
4e	C_6H_4-4-Cl	1.0	92	104–106	191.2	45.3
4f	C_6H_4-4-F	1.5	90	82–85	192.5	45.2
4g	C_6H_4-2-F	1.0	91	60–63	194.1	50.9
4h	C_6H_4-4-NO_2	0.5	92	153–155	193.0	46.0
4i	C_6H_4-3-NO_2	0.5	93	118–120	192.7	46.2
4j	2-Furyl–	1.5	90	90–92	181.9	44.3

4. Experimental

4.1. General

Commercially available chemicals were reagent grade and CH_2Cl_2 was distilled from CaH_2 freshly prior to use. The ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or D_2O on a Bruker AVANCE DRX-500 NMR spectrometer, using TMS as the internal standard. ESIMS were acquired on a Bruker Esquire 3000 plus spectrometer. IR spectra were determined on a Nicolet NEXUS-470 FT-IR spectrometer as KBr pellets. Melting points were determined on an X4-Data microscopic melting point apparatus. Analytical TLC was performed on a Merck precoated TLC (silica gel 60 F254) plate. Elemental analyses were performed on Carlo-Erba 1106. X-ray measurements were made on a Rigaku AFC7R diffractometer with graphite monochromated Mo Kα.

4.2. Typical procedure for the preparation of *N*-(2,3,4,6-tetra-*O*-pivaloyl-D-glucopyranosyl)aldimines 2a–j

To a solution of **1** (0.515 g, 1 mmol) and aldehyde (1.3 mmol) in 2-propanol (2.5 mL), 2–3 drops of acetic acid were added and the mixture was stirred at room temperature for 20 min to 3 h. The appearance of a precipitate from the solution indicated the formation of **2**, which was filtered and washed rapidly with ice cold 2-propanol and dried in vacuum.

4.2.1. *N*-(2,3,4,6-Tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine (2a). Mp 142–145 °C; yield 90%; *m/z* (ESI): 604.3 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 8.19 (s, 1H), 7.71 (d, $J=7.0$ Hz, 2H), 7.52 (t, $J=6.9$ Hz, 1H), 7.39 (t, $J=6.6$ Hz, 2H), 5.46 (t, $J=9.4$ Hz, 1H), 5.25 (t, $J=9.7$ Hz, 1H), 5.05 (t, $J=4.5$ Hz, 1H), 4.72 (d, $J=8.8$ Hz, 1H), 4.29 (d, $J=12.1$ Hz, 1H), 4.19 (q, $J=4.7$ Hz, 1H), 3.91 (t, $J=3.6$ Hz, 1H), 1.03–1.29 (m, 36H); ^{13}C NMR ($CDCl_3$) δ 178.3, 177.2, 177.0, 176.3, 161.1, 134.7, 131.4, 128.9, 128.5, 91.5, 72.8, 71.9, 69.2, 67.9, 61.8, 38.6, 27.0–27.1; IR (KBr, cm^{-1}) ν: 2980, 1740, 1648, 1580, 1481, 1459, 1398, 1366, 761. Anal. Calcd for $C_{33}H_{49}NO_9$: C, 65.65; H, 8.18; N, 2.32. Found: C, 65.68; H, 8.16; N, 2.33.

4.2.2. 4-Methyl-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine (2b). Mp 169–170 °C; yield 93%; *m/z* (ESI): 618.5 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 8.36 (s, 1H), 7.61 (d, $J=7.9$ Hz, 2H), 7.20 (d, $J=7.9$ Hz, 2H), 5.47 (t, $J=9.5$ Hz, 1H), 5.25 (t, $J=9.6$ Hz, 1H), 5.06 (t, $J=9.2$ Hz, 1H), 4.86 (d, $J=8.8$ Hz, 1H), 4.27 (d, $J=10.9$ Hz, 1H), 4.18 (q, $J=4.9$ Hz, 1H), 3.90–39.2 (m, 1H), 2.38 (s, 3H), 1.03–1.25 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.4, 177.5, 176.6, 176.4, 161.6, 142.2, 132.8, 129.5, 129.0, 93.8, 74.4, 73.1, 72.2, 68.2, 62.1, 38.9–39.1, 27.2–27.4, 21.8; IR (KBr, cm^{-1}): ν 2973, 1743, 1647, 1480, 1380, 1282, 1140, 1075, 763. Anal. Calcd for $C_{34}H_{51}NO_9$: C, 66.10; H, 8.32; N, 2.27. Found: C, 66.08; H, 8.29; N, 2.36.

4.2.3. 2-Hydroxyl-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine (2c). Mp 195–197 °C; yield 92%; *m/z* (ESI): 620.2 $[M+H]^+$; ^1H NMR ($CDCl_3$): 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, 36H); ^{13}C NMR ($CDCl_3$): 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}): ν 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, 7.95; N, 2.30.

4.2.4. 4-Methoxy-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine (2d). Mp 150–153 °C; yield 90%; *m/z* (ESI): 634.2 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 8.31 (s, 1H), 7.66 (d, $J=8.0$ Hz, 2H), 6.90 (d, $J=8.0$ Hz, 2H), 5.45 (t, $J=9.4$ Hz, 1H), 5.25 (t, $J=9.6$ Hz, 1H), 5.06 (t, $J=9.2$ Hz, 1H), 4.81 (d, $J=8.5$ Hz, 1H), 4.26 (d, $J=11.9$ Hz, 1H), 4.18 (q, $J=7.5$ Hz, 1H), 3.89 (d, $J=5.8$ Hz, 1H), 3.83 (s, 3H), 1.04–1.22 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.4, 177.6, 176.7, 176.5, 162.6, 161.5, 130.8, 128.3, 114.3, 94.5, 74.4, 73.1, 72.2, 68.2, 62.2, 55.6, 38.9–39.1, 27.2–27.4; IR (KBr, cm^{-1}): ν 2973, 1738, 1649, 1607, 1578, 1513, 1481, 1397, 1281, 1253, 1150, 762. Anal. Calcd for $C_{34}H_{51}NO_{10}$: C, 64.43; H, 8.11; N, 2.21. Found: C, 64.45; H, 8.08; N, 2.25.

4.2.5. 4-Chloro-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine (2e). Mp 178–180 °C; yield 92%; *m/z* (ESI): 638.1 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 8.36 (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, 36H); ^{13}C NMR ($CDCl_3$): 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}) ν: 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, 62.16; H, 7.57; N, 2.21.

4.2.6. 4-Fluoro-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine (2f). Mp 170–171 °C; yield. 93%; *m/z* (ESI): 622.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 8.37 (s, 1H), 7.71 (q, $J=5.6$ Hz, 2H), 7.09 (t, $J=8.5$ Hz, 2H), 5.47 (t, $J=9.5$ Hz, 1H), 5.24 (t, $J=9.6$ Hz, 1H), 5.15 (t, $J=4.7$ Hz, 1H), 4.90 (d, $J=8.9$ Hz, 1H), 4.29 (d, $J=12.1$ Hz, 1H), 4.17 (q, $J=4.9$ Hz, 1H), 3.91 (q, $J=3.5$ Hz, 1H), 1.00–1.25 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.3 177.5, 176.7, 176.5, 164.0, 162.7, 159.9, 130.9, 116.1, 93.1, 74.4, 73.0, 72.2, 68.1, 62.0, 38.9–39.1, 27.3–27.4; IR (KBr, cm^{-1}): ν 2973, 1730, 1643, 1603, 1509, 1480, 1365, 1138, 831, 763. Anal. Calcd for $C_{33}H_{48}FNO_9$: C, 63.75; H, 7.78; N, 2.25. Found: C, 63.73; H, 7.80; N, 2.26.

4.2.7. 2-Fluoro-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine (2g). Mp 140–142 °C; yield 91%; *m/z* (ESI): 622.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 8.73 (s, 1H), 7.92 (t, $J=6.8$ Hz, 1H), 7.41 (q, $J=6.0$ Hz, 1H), 7.16 (t, $J=7.5$ Hz, 1H), 7.07 (q, $J=9.0$ Hz, 1H), 5.48 (t, $J=9.5$ Hz, 1H), 5.24 (t, $J=9.6$ Hz, 1H), 5.03 (t, $J=9.3$ Hz, 1H), 4.92 (d, $J=8.9$ Hz, 1H), 4.28 (d, $J=12.1$ Hz, 1H), 4.19 (m, 1H), 3.92 (q, $J=3.5$ Hz, 1H), 0.99–1.36 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.3, 177.4, 176.7, 176.5, 163.9, 161.9, 154.7, 133.3, 128.1, 124.7, 115.9, 93.3, 74.3, 73.0, 72.1,

68.2, 62.1, 38.9–39.1, 27.2–27.4; IR (KBr, cm^{-1}): ν 2969, 1733, 1639, 1614, 1582, 1481, 1397, 1281, 1141, 941, 754. Anal. Calcd for $C_{33}H_{48}FNO_9$: C, 63.75; H, 7.78; N, 2.25. Found: C, 63.71; H, 7.76; N, 2.28.

4.2.8. 4-Nitro-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine (2h). Mp 180–185 °C; yield 95%; *m/z* (ESI): 649.2 $[M+H]^+$; ^1H NMR ($CDCl_3$): 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, 36H); ^{13}C NMR ($CDCl_3$): δ 178.4, 177.5, 176.8, 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}): ν 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.

4.2.9. 3-Nitro-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)benzylideneamine (2i). Mp 211–213.9 °C; yield 96%; *m/z* (ESI): 649.2 $[M+H]^+$; ^1H NMR ($CDCl_3$): 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, 36H); ^{13}C NMR ($CDCl_3$): 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, 77.0, 74.6, 72.9, 72.3, 68.1, 61.9, 27.33; IR (KBr, cm^{-1}): ν 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.

4.2.10. *N*-(2,3,4,6-Tetra-*O*-pivaloylated-D-glucopyranosyl)-2-furylideneamine (2j). Mp 95–98 °C; yield 90%; *m/z* (ESI): 594.2 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 8.21 (s, 1H), 7.53 (d, $J=3.3$ Hz, 1H), 6.86 (d, $J=2.5$ Hz, 1H), 6.48 (t, $J=1.8$ Hz, 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), 4.16–4.18 (m, 1H), 3.89 (d, $J=5.8$ Hz, 1H), 1.06–1.29 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.4, 177.5, 176.6, 176.6, 151.6, 149.8, 145.8, 115.6, 112.3, 93.2, 74.5, 73.1, 72.3, 68.1, 62.1, 39.0–39.1, 27.3–27.4; IR (KBr, cm^{-1}): ν 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.

4.3. General procedure for the preparation of *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)-amino nitriles 3a–j[5]

To a solution of trimethylsilylcyanide (0.186 g, 1.875 mmol) and cuprous bromide (0.488 g, 1.875 mmol) in dichloromethane (20 mL) at 0 °C, a solution of imine **2** (1.5 mmol) in dichloromethane (1 mL) was added slowly. After half an hour, the solution was allowed to slowly warm to room temperature. The reaction was monitored by TLC, after accomplished, the mixture was quenched with 2 N HCl (10 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL×3) and water (10 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was recrystallized from heptane to give *N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)-amino nitriles **3**.

4.3.1. *N*-(2,3,4,6-Tetra-*O*-pivaloylated-D-glucopyranosyl)phenylglycinonitrile (3a). Mp 152–155 °C; yield 90%; *m/z* (ESI): 631.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 7.70 (d, $J=7.2$ Hz, 2H), 7.41 (t, $J=6.8$ Hz, 2H), 7.31 (t, $J=6.5$ Hz, 1H), 5.45 (t, $J=9.4$ Hz, 1H), 5.26 (t, $J=9.6$ Hz, 1H), 5.14 (t, $J=9.2$ Hz, 1H), 4.75 (d, $J=8.8$ Hz, 1H), 4.58 (s, 1H) 4.29–4.32 (m, 2H), 3.92 (d, $J=1.6$ Hz, 1H), 1.07–1.33 (m, 36H); ^{13}C NMR ($CDCl_3$) δ 178.5, 177.9, 176.8, 176.5, 130.1, 129.5, 128.8, 127.9, 114.2, 73.5, 72.3, 71.6, 68.2, 67.8.3, 66.8, 48.7, 39.0–39.2, 27.3–27.4; IR (KBr, cm^{-1}): ν 2979, 2245, 1744, 1633, 1481, 1398, 1279, 1139, 1033, 941, 893. Anal. Calcd for $C_{34}H_{50}N_2O_9$: C, 64.74; H, 7.99; N, 4.44. Found: C, 64.73; H, 7.96; N, 4.47.

4.3.2. 4-Methyl-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)phenylglycinonitrile (3b). Mp 195–197 °C; yield 92%; *m/z* (ESI): 645.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 7.63 (d, $J=7.9$ Hz, 2H), 7.23 (d, $J=7.9$ Hz, 2H), 5.73 (t, $J=9.5$ Hz, 1H), 5.56 (t, $J=9.6$ Hz, 1H), 5.08 (t, $J=9.2$ Hz, 1H), 4.86 (d, $J=8.8$ Hz, 1H), 4.79 (s, 1H), 4.27 (d, $J=10.9$ Hz, 1H), 4.18 (q, $J=4.9$ Hz, 1H), 3.80–3.82 (m, 1H), 2.39 (s, 3H), 1.03–1.25 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.4, 177.5, 176.7, 176.4, 142.2, 132.1, 129.7, 129.2, 114.7, 70.5, 68.9, 68.6, 60.7, 59.2, 58.2, 48.5, 39.6–39.4, 27.2–27.4, 21.8; IR (KBr, cm^{-1}): ν 2976, 2254, 1747, 1609, 1575, 147–81, 1398, 1368, 1138, 762. Anal. Calcd for $C_{35}H_{52}N_2O_9$: C, 65.20; H, 8.13; N, 4.34. Found: C, 65.23; H, 8.10; N, 4.13.

4.3.3. 2-Hydroxyl-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)phenylglycinonitrile (3c). Mp 205–208 °C; yield 89%; *m/z* (ESI): 647.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 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), 5.61 (d, $J=9.6$ Hz, 1H), 5.50 (t, $J=3.5$ Hz, 1H), 5.34 (d, $J=9.9$ Hz, 1H), 4.89 (s, 1H), 4.60 (d, $J=9.9$ Hz, 1H), 4.13 (t, $J=4.4$ Hz, 1H), 3.87 (d, $J=3.0$ Hz, 1H), 3.75 (q, $J=1.5$ Hz, 1H), 1.07–1.29 (m, 36H); ^{13}C NMR ($CDCl_3$): 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, 49.1, 39.0–39.2, 27.3–27.4. IR (KBr, cm^{-1}): ν 3490, 2950, 2246, 1720, 1600, 1498, 1250, 1125, 750. Anal. Calcd for $C_{34}H_{50}N_2O_{10}$: C, 63.14; H, 7.79; N, 4.33. Found: C, 63.18; H, 7.75; N, 4.31.

4.3.4. 4-Methoxy-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)phenylglycinonitrile (3d). Mp 182–185 °C; yield 85%; *m/z* (ESI): 661.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 7.76 (d, $J=8.4$ Hz, 2H), 6.96 (d, $J=8.4$ Hz, 2H), 5.74 (t, $J=9.6$ Hz, 1H), 5.28 (t, $J=9.6$ Hz, 1H), 5.06 (t, $J=9.2$ Hz, 1H), 4.81 (s, 1H), 4.26 (d, $J=5.3$ Hz, 1H), 4.13–4.16 (m, 2H), 3.89 (s, 3H), 3.85 (d, $J=5.8$ Hz, 1H), 1.04–1.22 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.4, 177.6, 177.3, 176.8, 162.8, 130.9, 128.0, 114.9, 114.3, 75.1, 74.4, 73.1, 72.2, 68.2, 62.2, 55.6, 49.5, 38.9–39.1, 27.2–27.4; IR (KBr, cm^{-1}): ν 2976, 2246, 1739, 1607, 1580, 1520, 1481, 1396, 1284, 1254, 1150, 763. Anal. Calcd for $C_{35}H_{52}N_2O_{10}$: C, 63.62; H, 7.93; N, 4.24. Found: C, 63.58; H, 7.96; N, 4.21.

4.3.5. 4-Chloro-*N*-(2,3,4,6-tetra-*O*-pivaloyl-D-glucopyranosyl)phenylglycinonitrile (3e). Mp 210–212 °C; yield

86%; *m/z* (ESI): 665.2 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 7.76 (d, $J=8.3$ Hz, 2H), 7.42 (d, $J=8.3$ Hz, 2H), 5.44 (t, $J=7.3$ Hz, 1H), 5.21 (d, $J=10$ Hz, 1H), 4.93 (d, $J=1.9$ Hz, 1H), 4.80 (s, 1H), 4.12 (d, $J=7.0$ Hz, 1H), 3.56–3.58 (m, 2H), 3.10–3.13 (m, 1H), 1.05–1.30 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 179.0, 177.4, 177.2, 176.6, 138.6, 133.3, 130.3, 129.3, 114.7, 69.6, 68.8, 67.5, 65.8, 59.5, 57.8, 45.17, 39.1–39.5, 27.1–27.5; IR (KBr, cm^{-1}): ν 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, 61.36; H, 7.46; N, 4.19.

4.3.6. 4-Fluoro-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)phenylglycinonitrile (3f). Mp 192–195 °C; yield 88%; *m/z* (ESI): 649.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 7.76 (t, $J=5.5$ Hz, 2H), 7.11 (t, $J=8.5$ Hz, 2H), 5.76 (t, $J=9.5$ Hz, 1H), 5.57 (t, $J=9.6$ Hz, 1H), 5.13 (d, $J=4.7$ Hz, 1H), 4.88 (s, 1H), 4.05 (d, $J=8.9$ Hz, 1H), 3.80–3.82 (m, 2H), 3.54–3.57 (m, 1H), 0.930–1.38 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.2, 177.3, 176.8, 176.4, 166.2, 131.3, 130.3, 116.1, 114.3, 70.3, 68.9, 64.5, 60.4, 59.0, 58.1, 48.1 39.0–39.5, 26.9–27.4; IR (KBr, cm^{-1}) ν: 2976, 1746, 1603, 1510, 1481, 1398, 1368, 1276, 1139, 763. Anal. Calcd for $C_{34}H_{49}FN_2O_9$: C, 62.95; H, 7.61; N, 4.32. Found: C, 62. 91; H, 7.65; N, 4.28.

4.3.7. 2-Fluoro-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)phenylglycinonitrile (3g). Mp 166–168 °C; yield. 90%; *m/z* (ESI): 649.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 7.9 (t, $J=6.8$ Hz, 1H), 7.46 (q, $J=6.0$ Hz, 1H), 7.17 (t, $J=7.5$ Hz, 1H), 7.09 (q, $J=9.0$ Hz, 1H), 5.73 (t, $J=9.5$ Hz, 1H), 5.56 (t, $J=9.6$ Hz, 1H), 5.14 (d, $J=9.3$ Hz, 1H), 4.86 (s, 1H), 4.25 (d, $J=8.9$ Hz, 1H), 3.82–3.84 (m, 2H), 3.54 (t, $J=12.6$ Hz, 1H), 0.85–1.34 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.4, 177.5, 176.7, 176.3, 161.8, 158.7, 134.3, 129.1, 124.7, 116.3, 114.5, 74.3, 70.4, 69.8, 68.9, 61.4, 60.7, 49.3, 39.1–39.6, 27.2–27.4; IR (KBr, cm^{-1}): ν 2914, 1731, 1614, 1583, 1486, 1396, 1281, 1128, 762. Anal. Calcd for $C_{34}H_{49}FN_2O_9$: C, 62.95; H, 7.61; N, 4.32. Found: C, 62.93; H, 7.63; N, 4.30.

4.3.8. 4-Nitro-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)phenylglycinonitrile (3h). Mp 223–226 °C; yield 89%; *m/z* (ESI): 676.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 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), 3.89–3.91 (m, 2H), 1.0–1.22 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 178.4, 177.6, 176.7, 176.5, 147.7, 136.2, 129.9, 122.8, 115.4, 74.4, 73.1, 72.2, 68.3, 62.2, 55.6, 46.04, 39.1–38.9, 27.3–27.4; IR (KBr, cm^{-1}): ν 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, 60.39; H, 7.28; N, 6.26.

4.3.9. 3-Nitro-*N*-(2,3,4,6-tetra-*O*-pivaloylated-D-glucopyranosyl)phenylglycinonitrile (3i). Mp 248–251 °C; yield 91%; *m/z* (ESI): 676.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 8.41 (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 (s, 1H), 4.07 (t, $J=9.3$ Hz, 2H), 3.58–3.60 (m, 1H), 1.08–1.30 (m, 36H); ^{13}C NMR ($CDCl_3$): 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, 46.17, 39.4, 27.3–27.4. IR (KBr, cm^{-1}): ν 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, 60.47; H, 7.28; N, 6.24.

4.3.10. *N*-(2,3,4,6-Tetra-*O*-pivaloylated-D-glucopyranosyl)-2-furylglycinonitrile (3j). Mp 129–132 °C; yield 85%; *m/z* (ESI): 621.4 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ 7.43 (d, $J=3.3$ Hz, 1H), 6.75 (d, $J=2.5$ Hz, 1H), 6.39 (t, $J=1.8$ Hz, 1H), 5.32 (t, $J=9.4$ Hz, 1H), 5.28 (t, $J=9.6$ Hz, 1H), 5.14 (d, $J=8.6$ Hz, 1H), 4.98 (t, $J=9.62$ Hz, 1H), 4.80 (s, 1H), 4.55 (d, $J=12$ Hz, 1H), 4.16–4.18 (m, 2H), 3.88 (d, $J=12$ Hz, 1H), 1.06–1.24 (m, 36H); ^{13}C NMR ($CDCl_3$): δ 177.4, 176.3, 175.8, 175.2, 152.6, 114.9, 148.6, 111.0, 106.2, 75.3, 71.5, 70.3, 69.2, 654.5, 59.3, 45.1, 38.7–39.0, 25.1–27.3; IR (KBr cm^{-1}): ν 2979, 2250, 1740, 1650, 1482, 1380, 1283, 1177, 893. Anal. Calcd for $C_{32}H_{48}N_2O_{10}$: C, 61.92; H, 7.79; N, 4.51. Found: C, 61.86; H, 7.80; N, 4.49.

4.4. General procedure for preparation of aromatic acetic acids 4a–j

To a solution of **3** (2.0 mmol) in dichloromethane (20 mL) was added 0.5 mL of 45% HBr in acetic acid in presence of H_2O (0.1 mL) at room temperature, forming deposits in the solution, which were filtered and washed with ethyl acetate, to give the product **4** in excellent yields. The filtrate was concentrated by rotary evaporation. Recrystallization of the residue from petroleum ether furnished **1** which was restored as the starting material.

4.4.1. Phenylacetic acid (4a). Mp 76–78 °C (lit.[7a] 75–78 °C); yield 91%; *m/z* (ESI): 137.1 $[M+H]^+$; ^1H NMR (D_2O): δ 7.89 (d, $J=7.6$ Hz, 2H), 7.64 (t, $J=7.0$ Hz, 1H), 7.49 (t, $J=7.6$ Hz, 2H), 4.60 (s, 2H); ^{13}C NMR (D_2O): δ 191.76, 135.21, 131.43, 129.08, 128.17, 45.17; IR (KBr, cm^{-1}): ν 3300–2200, 1698, 1500, 1460, 1402, 1299, 1225, 1180, 925, 756.

4.4.2. 4-Methyl-phenylacetic acid (4b). Mp 91–92 °C (lit.[7b] 90–93 °C); yield 89%; *m/z* (ESI): 151.1 $[M+H]^+$; ^1H NMR (D_2O): δ 7.76 (d, $J=8.0$ Hz, 2H), 7.28 (d, $J=8.0$ Hz, 2H); 4.54 (s, 2H), 2.28 (s, 3H); ^{13}C NMR (D_2O): δ 191.9, 142.3, 132.9, 129.7, 129.3, 45.8, 21.9; IR (KBr, cm^{-1}): ν 3300–2500, 1699, 1525, 1410, 1330, 1250, 760.

4.4.3. 2-Hydroxyl-phenylacetic acid (4c). Mp 145–148 °C (lit.[7c] 143–147 °C); yield 87%; *m/z* (ESI): 153.1 $[M+H]^+$ ^1H NMR (D_2O): δ 7.36 (t, $J=8.0$ Hz, 1H), 7.29 (d, $J=7.8$ Hz, 1H), 6.95 (d, $J=7.7$ Hz, 1H), 6.89 (t, $J=7.0$ Hz, 1H), 4.60 (s, 2H); ^{13}C NMR (D_2O): δ 191.2, 161.0, 133.6, 132.7, 119.2, 118.4, 117.5, 45.6; IR (KBr, cm^{-1}): ν 3400, 3300–2500, 1720, 1610, 1500, 1470, 1380, 1310, 1100, 760.

4.4.4. 4-Methoxy-phenylacetic acid (4d). Mp 85–87 °C (lit.[7d] 85–88 °C); yield 85%; *m/z* (ESI): 167.1 $[M+H]^+$; ^1H NMR (D_2O): δ 7.78 (d, $J=8.4$ Hz, 2H), 6.97 (d, $J=8.4$ Hz, 2H), 4.62 (s, 2H), 3.83 (s, 3H); ^{13}C NMR (D_2O): δ 192.5, 162.8, 130.9, 128.0, 114.3, 55.6, 46.0; IR (KBr, cm^{-1}): ν 3400–2500, 1710, 1610, 1520, 1240, 1180, 1020, 820.

4.4.5. 4-Chloro-phenylacetic acid (4e). Mp 104–106 °C

(lit.[7e] 103–107 °C); yield 92%; *m/z* (ESI): 171.0 $[M+H]^+$; ^1H NMR (D_2O): δ 8.10 (d, $J=8.5$ Hz, 2H), 7.64 (d, $J=8.5$ Hz, 2H), 4.69 (s, 2H); ^{13}C NMR (D_2O): δ 191.2, 140.9, 132.5, 129.9, 129.3, 45.3; IR (KBr, cm^{-1}): ν 3400–2300, 1700, 1600, 1495, 1445, 1350, 1249, 1099, 930, 820.

4.4.6. 4-Fluoro-phenylacetic acid (4f). Mp 82–85 °C (lit.[7f] 82–86 °C); yield 90%; *m/z* (ESI): 155.1 $[M+H]^+$; ^1H NMR (D_2O): δ 7.91 (q, $J=5.4$ Hz, 2H), 7.14 (t, $J=8.5$ Hz, 2H), 4.52 (s, 2H); ^{13}C NMR (D_2O): δ 192.5, 165.7, 131.4, 129.7, 116.3, 45.1; IR (KBr, cm^{-1}): ν 3300–2500, 1700, 1490, 1420, 1338, 1255, 1080, 1020, 805.

4.4.7. 2-Fluoro-phenylacetic acid (4g). Mp 60–63 °C (lit.[7g] 60–645 °C; yield 91%; *m/z* (ESI): 155.1 $[M+H]^+$; ^1H NMR (D_2O): δ 7.85 (q, $J=7.5$ Hz, 1H), 7.59–7.62 (m, 1H), 7.24 (t, $J=7.7$ Hz, 1H), 7.18 (q, $J=8.7$ Hz, 1H), 4.48 (s, 2H); ^{13}C NMR (D_2O): δ 194.1, 166.1 140.2, 132.9, 127.8, 124.0, 119.6, 50.9; IR (KBr, cm^{-1}): ν 3400– 2500, 1710, 1600, 1500, 1470, 1415, 1295, 1240, 1100, 760.

4.4.8. 4-Nitro-phenylacetic acid (4h). Mp 153–155 (lit.[7h] 153–156 °C); yield 92%; *m/z* (ESI): 182.0 $[M+H]^+$; ^1H NMR (D_2O): δ 8.28 (br, 2H), 8.13 (br, 2H), 4.75 (s, 2H); ^{13}C NMR (D_2O): δ 193.0, 151.1, 138.0, 129.8, 124.5, 46.0; IR (KBr, cm^{-1}): ν 3400–2450, 1720, 1600, 1520, 1430, 1350, 1310, 1260, 1200, 1110, 950, 830.

4.4.9. 3-Nitro-phenylacetic acid (4i). Mp 118–120 °C (lit.[7i] 116–120 °C); yield 93%; *m/z* (ESI): 182.0 $[M+H]^+$; ^1H NMR (D_2O): δ 8.69 (s, 1H), 8.43 (d, $J=8.1$ Hz, 1H), 8.30 (d, $J=7.8$ Hz, 1H), 7.75 (t, $J=8.0$ Hz, 1H), 4.72 (s, 2H); ^{13}C NMR (D_2O): δ 192.7, 148.7, 134.8, 131.2, 129.7, 123.7, 46.2; IR (KBr, cm^{-1}): ν 3440–2460, 1746, 1620, 1543, 1455, 1353, 1300, 1270, 1125, 980, 828.

4.4.10. 2-Furyl-acetic acid (4j). Mp 90–92 °C; yield 90%; *m/z* (ESI): 127.0 $[M+H]^+$; ^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), 4.57 (s, 2H); ^{13}C NMR (D_2O): δ 181.9, 149.9, 149.3, 121.9, 113.5, 44.3; IR (KBr, cm^{-1}): ν 3460–2400, 1748, 1680, 1618, 1469, 1400, 129, 1168, 972, 910, 796.

Acknowledgements

The authors thank the National Natural Science Foundation of China (No 20376016) and the Natural Science Foundation of Zhejiang Province. (No 202075).

References and notes

1. (a) Robert, W.; Shack, H. S.; Myers, C.; et al *Biochem. Pharmacol.* **1995**, *50*, 1273–1278. (b) Harrison, L. E.; Wojciechowicz, D. C.; Brennan, M. F.; Patuy, P. B. *Surgery* **1998**, *124*, 541–543. (c) White, S.; Berry, D. R.; Mcneil, B. *Biotechnology* **1999**, *75*, 173–185. (d) Duan, J. R.; Jiang, J.; Gong, J. F.; Fan, Q. H.; Jiang, D. Z. *Jiangxi Sci.* **2000**, *159*, 89–96. (e) Dinoiu, V.; Fukuhara, T.; Miura, K.; Yoneda, N. J. *Fluorine Chem.* **2003**, *121*, 227–231. (f) Santini, C.; Berger, G. D.; Han, W.; et al *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1277–1280. (g) Jonson, S. D.; Welch, J. *Nucl. Med. Biol.* **2002**, *29*, 211–215. (h) Sobotkova, L.; Grafkova, J.; Kyslik, P. *Enzyme Microb. Technol.* **2002**, *31*, 992–999. (i) Pan, W. B.; Chang, F. R.; Wei, L. M. *Tetrahedron Lett.* **2003**, *44*, 331–334.
2. (a) Shrinivansan, B. *J. Indian Chem.* **1970**, *5*, 113–115. (b) Satyanra, Y. N.; Periasamy, M. *Tetrahedron Lett.* **1987**, *28*, 2633–2636. (c) Hu, Y. L.; Wang, J. X.; Cui, W. F. *Synth. Commun.* **1994**, 1763–1768. (d) Zhong, Y.; Godfrey, V. M.; Lim, P. *Chem. Eng. Sci.* **1996**, *51*, 757–767. (e) Lapidus, A. L.; Petrovdkii, K. B.; Beletskaya, I. P. *J. Org. Chem.* **1997**, *33*, 1083–1086. (f) Kohlpaintner, C. W.; Beller, M. *J. Mol. Catal.* **1997**, *116*, 259–267. (g) Gong, J. F. *Hua Xue Xue Bao* **1999**, *1*, 20–23. (h) Giroux, A.; Nadeau, C.; Han, Y. G. *Tetrahedron Lett.* **2000**, *41*, 7601–7604. (i) Liu, F. F.; Shi, X. B.; Zheng, D. M. *Jiangxi Sci.* **2001**, *19*, 98–102. (j) Gandolfi, R.; Cavenago, K.; Gualandris, R.; Molinari, F. *Process Biochem.* **2004**, *39*, 747–751.
3. (a) Wang, W.; Zhong, Y. W.; Lin, G. Q. *Tetrahedron Lett.* **2003**, *44*, 4613–4616. (b) Deloisy, S.; Tietgen, H.; Kunz, H.; Czechoslov, C. *Chem. Commun.* **2000**, *65*, 816–826. (c) Follmann, M.; Rosch, A.; Klegraf, E.; Kunz, H. *Synlett* **2001**, 1569–1570. (d) Weymann, M.; Schultz-Kukula, M.; Knauer, S.; Kunz, H. *Monatsh. Chem.* **2002**, *133*, 571–587. (e) Zech, G.; Kunz, H. *Angew. Chem.* **2003**, *115*, 811–814. *Angew. Chem., Int. Ed.* **2003**, *42*, 787–790. (f) Pleub, N.; Kunz, H. *Angew. Chem., Int. Ed.* **2003**, *42*, 3174–3176. (g) Pleub, N. Kunz. *Angew. Chem., Int. Ed.* **2003**, *42*, 3174–3176. (h) Dziadek, S.; Kunz, H. *Synlett* **2003**, 1623–1626. (i) Obwald, M.; Lang, U.; Friedrich-Bochnitschek, S.; Pfrengle, W.; Kunz, H. Z. *Naturforsch B.* **2003**, *58b*, 764–774. (j) Hünger, U.; Ohnsmann, J.; Kunz, H. *Angew. Chem., Int. Ed.* **2004**, *116*, 1125–1128. (k) Hünger, U.; Ohnsmann, J.; Kunz, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 1104–1107.
4. (a) Enders, D.; Reinhold, U. *Tetrahedron: Asymmetry* **1997**, *8*, 1895–1946. (b) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407–1428. (c) Chunmei, W.; Chao, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 5638–5639. (d) Tamio, H.; Mitsuo, I. *J. Am. Chem. Soc.* **2000**, *122*, 976–977.
5. Zhou, G. B.; Zhang, P. F.; Pan, Y. J. *Acta Crystallogr. E* **2004**, *E60*, o1959–o1960.
6. (a) Maurizio, B.; Diego, N.; Gianmaria, D. A. *Tetrahedron Lett.* **2004**, *45*, 8705–8708. (b) Makoto, S.; Toshiki, O.; Takafumi, N. *Tetrahedron Lett.* **2001**, *42*, 5463–5466. (c) Batia, B. A.; Bar, N.; Moshe, P. *Tetrahedron Lett.* **2000**, *41*, 6143–6147. (d) Kunz, H.; Schanzenbach, D. W.; Decker, M. *Liebigs Ann. Chem.* **1991**, 649–654. (e) Ojima, I.; Inaba, S. *Chem. Lett.* **1975**, 737. (f) Yu, N. F.; Deprez, B.; Gesqulere, J. C. *Tetrahedron Lett.* **1998**, *39*, 829–832. (g) Shimizu, M.; Morita, A.; Kaga, T. *Tetrahedron Lett.* **1999**, *40*, 8401–8405. (h) Hayashi, T.; Ishigedani, M. *J. Am. Chem. Soc.* **2000**, *122*, 976–977. (i) Kelin, A. V.; Sromek, A. W.; Gevorgyan, V. *J. Am. Chem. Soc.* **2001**, *123*, 2075. (j) Wei, C. M.; Li, C. J. *J. Am. Chem. Soc.* **2002**, *124*, 5639–5642. (k) Sammis, G. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2003**, *125*, 4443. (l) Masumoto, S. J.; Usuda, H.; Suzuki, M.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 5634–5635.
7. (a) Merk 13. 7352. (b) Beil. 9. 530. (c) Beil. 10. 187. (d) Beil. 10. 190. (e) Beil. 9. IV. 1675. (f) Beil. 9. 2261. (g) Beil. 9. 2260. (h) Beil. 9. IV. 1687. (i) Merk 13. 6655.