Glycoconjugate Journal
https://doi.org/10.1007/s10719-019-09883-1

ORIGINAL ARTICLE

Organocatalyzed preparation of 1,4,5-trisubstituted-glycosyl-1,2,3-triazole derivatives

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Received: 27 March 2019 / Revised: 31 May 2019 / Accepted: 20 June 2019

Abstract
Organocatalytic coupling of glycosyl azides with enolates of active ketones and esters through azide-enolate [3 + 2] cycloaddition in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) furnished 1,4,5-trisubstituted-glycosyl-1,2,3-triazole derivatives in excellent yield. The reaction condition is simple and can be scaled-up.

Keywords Carbohydrate; triazole · Azide · Organocatalysis · Cycloaddition

Introduction

Triazoles are interesting class of nitrogen containing heterocyclic compounds possessing significant biological activities [1–6]. In addition to their use in the medicinal chemistry and drug discovery, they have found applications in the material science [7, 8], chemical biology [9, 10], supramolecular chemistry [11, 12], catalysis [13] and biotechnology [14, 15]. Several reports have appeared in the literature on the preparation of 1,5-substituted 1,2,3-triazole derivatives using metallic and organocatalytic reaction conditions through Huisgen's azide-alkyl [3 + 2] cycloadditions [16–18]. In the recent past, glycosyl triazole derivatives have emerged as useful glycomimetics having interesting pharmaceutical potential [19, 20] against several metabolic disorders [21, 22], enzyme inhibitors [23, 24], infectious diseases [25–27] and cancer progression [28, 29]. They are stable under a broad range of chemical and biological reactions and hydrolysis. In most of the cases, 1,5-substituted glycosyl-1,2,3-triazole conjugates were prepared by Huisgen's azide-alkyl [3 + 2] cycloaddition of glycosyl azide or alkyne with an alkyne or azide counterpart respectively in the presence of a copper catalyst [30, 31], which has its own limitations in terms of toxicity, difficulties associated with its removal etc. Unlike 1,5-substituted 1,2,3-triazole derivatives, preparation of 1,4,5-trisubstituted-1,2,3-triazole derivatives through azide-enolate [3 + 2] cycloaddition are limited [32–36]. Cao *et al*. [37] reported a one-pot reaction condition for the preparation of Dimroth products (1,4,5-trisubstituted-1,2,3-triazole derivatives). Later, González-Calderón *et al*. reported [38] preparation these compounds through DBU catalyzed azide-enolate [3 + 2] cycloaddition of the *in situ* generated alkyl azide and active ketones derived enolates under one-pot organocatalytic reaction conditions. The preparation of 1,4,5-trisubstituted-glycosyl-1,2,3-triazole derivatives by coupling glycosyl azides with enolates under organocatalytic reaction conditions are not reported earlier. Earlier, Ferreira and co-workers reported the preparation of 1-benzyl-1*H*-1,2,3-triazole derivatives of carbohydrates under organocatalytic conditions [39]. In view of the biological importance of this class of compounds, it was decided to develop a synthetic methodology for the preparation of 1,4,5-trisubstituted-glycosyl-1,2,3-triazole derivatives under a organocatalytic reaction condition avoiding metallic reagents and catalysts. A straightforward approach for the synthesis of a library of 1,4,5-trisubstituted-glycosyl-1,2,3-triazole derivatives under DBU catalyzed reaction condition is reported herein (Scheme 1).

Results and discussion

In a set of initial experiments, per-*O*-acetylated β-D-glucopyranosyl azide [40] (**1**; 1.0 mmol) was treated with acetyl acetone (**10**; 1.0 mmol) in different organic solvents in the presence of a variety of amines as organo-catalysts at

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10719-019-09883-1) contains supplementary material, which is available to authorized users.

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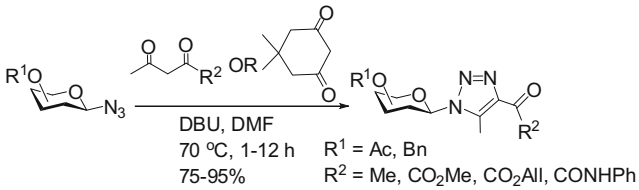
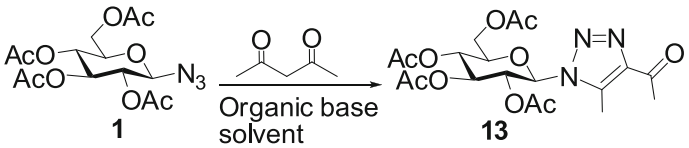
Published online: 05 July 2019



Scheme 1 DBU catalyzed organocatalytic preparation of 1,4,5-trisubstituted-glycosyl-1,2,3-triazole derivatives.

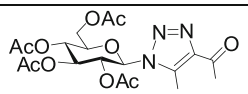
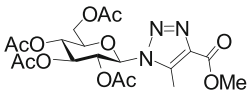
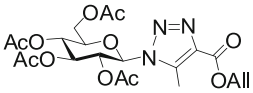
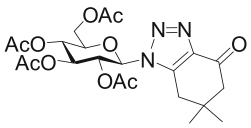
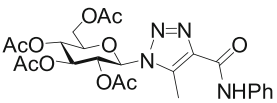
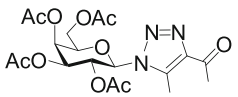
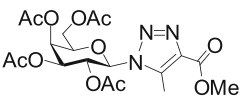
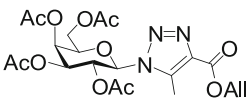
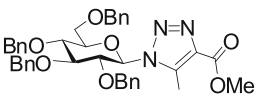
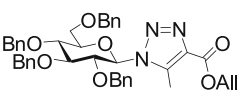
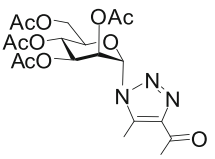
different temperatures, which is presented in Table 1. It was observed that 1-[per-*O*-acetyl-β-D-glucopyranosyl]-4-acetyl-5-methyl-1,2,3-triazole (**15**) was obtained in 90% yield in the presence of DBU (0.1 equiv.) in DMF at 70 °C in 3 h. The reaction was significantly slow at room temperature and full consumption of the starting material was not observed after 12 h. Among the variety of organic amines screened for the catalytic potential, DBU was found as the most effective catalyst to furnish clean formation of the product. Although DMF and DMSO were found superior among the commonly used organic solvents (*e.g.* CH_2Cl_2, 1,2-$(CHCl)_2$, THF, CH_3CN, Toluene, DMF, DMSO), DMF was considered as the solvent of choice because of the inherent drawbacks of DMSO (Table 1). A wide range of monosaccharide and disaccharide azides were coupled with 1,3-diketones (**10**), β-ketoesters (**11**, **12**), cyclic 1,3-diketone (dimedone) (**13**), β-ketoamide (**14**) under similar reaction condition to give corresponding 1,4,5-trisubstituted-glycosyl-1,2,3-triazole derivatives in excellent yield (Table 2). However, reaction with methyl acetopyruvate ($CH_3COCH_2COCOOMe$) did not furnish any product even after prolonged reaction condition. It is noteworthy that no trace of the formation of by products was observed and the functional groups present in the substrates were unaffected under the reaction condition. The reaction condition can be scaled up without decrease of the yield of the products. All products were unambiguously characterized using their spectral analysis.

Table 1 Optimization of glycosyl azide-enolate [3 + 2] cycloaddition in the presence of different organocatalysts



Sl. No.	Base (equiv.)	Solvent	Temp (°C)	Time (h)	Yield (%)
1	DBU (0.1)	CH_2Cl_2	rt	12	60
2	DBU (0.2)	CH_2Cl_2	40	12	70
3	DBU (0.2)	$(CHCl)_2$	60	12	70
4	DBU (0.1)	DMF	rt	12	80
5	DBU (0.1)	DMF	70	3	90
6	DBU (0.2)	DMF	70	3	90
7	DBU (0.1)	THF	70	12	30
8	DBU (0.2)	CH_3CN	70	12	30
9	DBU (0.2)	Toluene	70	12	20
10	DBU (0.2)	DMSO	70	2.5	90
11	DABCO (0.2)	DMF	70	12	50
12	DBN (0.2)	DMF	70	12	50
13	Piperidine (0.1)	DMF	rt	12	25
14	Pyrrolidine (0.1)	DMF	rt	12	30
15	DMAP (0.5)	DMF	rt	12	10

Table 2 DBU catalyzed preparation of 1,4,5-trisubstituted-glycosyl-1,2,3-triazole derivatives

Sl. No.	Glycosyl azide	Enol source	Product	Time (h)[a]	Yield (%)
1	Per-*O*-acetylated -β-D-glucosyl azide (**1**)	Acetyl acetone (**10**)	 **15**	3	90 (88)[b]
2	**1**	Methyl acetoacetate (**11**)	 **16**	8	88
3	**1**	Allyl acetoacetate (**12**)	 **17**	8	86
4	**1**	5,5-Dimethyl-1,3-cyclohexane dione (**13**)	 **18**	10	76
5	**1**	Acetoacetanilide (**14**)	 **19**	1	80
6	**1**	Methyl acetopyruvate	--	24	--
7	Per-*O*-acetylated -β-D-galactosyl azide (**2**)	Acetyl acetone (**10**)	 **20**	3	95
8	**2**	Methyl acetoacetate (**11**)	 **21**	8	92
9	**2**	Allyl acetoacetate (**12**)	 **22**	8	88
10	Per-*O*-benzylated β-D-glucosyl azide (**3**)	Methyl acetoacetate (**11**)	 **23**	8	84
11	**3**	Allyl acetoacetate (**12**)	 **24**	8	82
12	Per-*O*-acetylated -β-D-mannosyl azide (**4**)	Acetyl acetone (**10**)	 **25**	8	78

[a]: 70 °C; [b]: 20 mmol scale

Table 2 (continued)

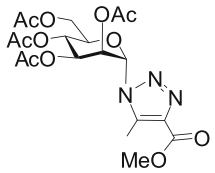
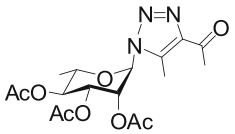
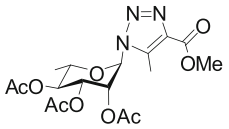
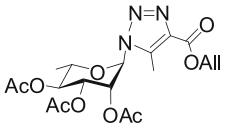
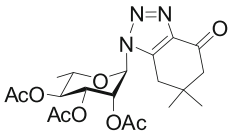
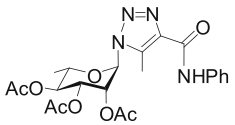
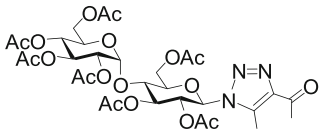
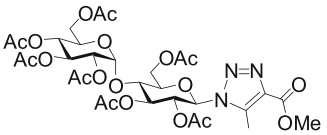
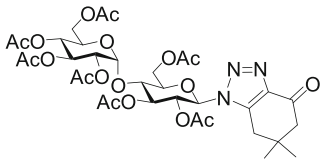
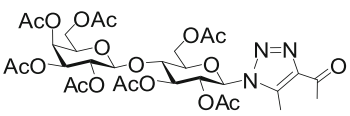
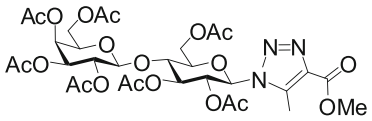
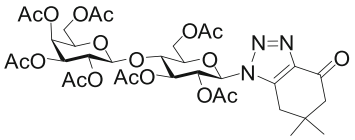
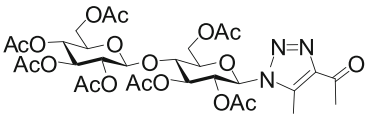
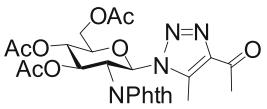
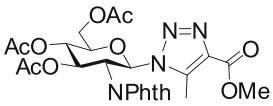
13	**4**	Methyl acetoacetate (**11**)	 **26**	8	75
14	Per-*O*-acetylated α-L-rhamnosyl azide (**5**)	Acetyl acetone (**10**)	 **27**	8	80
15	**5**	Methyl acetoacetate (**11**)	 **28**	8	76
16	**5**	Allyl acetoacetate (**12**)	 **29**	8	72
17	**5**	5,5-Dimethyl-1,3-cyclohexane dione (**13**)	 **30**	12	70
18	**5**	Acetoacetanilide (**14**)	 **31**	1	76
19	Per-*O*-acetylated maltosyl azide (**6**)	Acetyl acetone (**10**)	 **32**	3	90
20	**6**	Methyl acetoacetate (**11**)	 **33**	8	85
21	**6**	5,5-Dimethyl-1,3-cyclohexane dione (**13**)	 **34**	10	75
22	Per-*O*-acetylated lactosyl azide (**7**)	Acetyl acetone (**10**)	 **35**	3	90

Table 2 (continued)

23	**7**	Methyl acetoacetate (**11**)	 **36**	8	88
24	**7**	5,5-Dimethyl-1,3-cyclohexane dione (**13**)	 **37**	10	78
25	Per-*O*-acetylated cellobiosyl azide (**8**)	Acetyl acetone (**10**)	 **38**	1	90
26	Per-*O*-acetylated -2-deoxy-2-*N*-phthalimido-β-D-glucosyl azide (**9**)	Acetyl acetone (**10**)	 **39**	1	88
27	**9**	Methyl acetoacetate (**11**)	 **40**	1	86

Furthermore, a set of per-*O*-acetylated glycosylated triazole derivates (**15**, **25**, **26** and **27**) were also deprotected in quantitative yield under conventional de-*O*-acetylation reaction condition using sodium methoxide, indicating the compatibility of the triazole moiety under deprotection conditions (Fig. 1).

Conclusion

In summary, a straightforward organocatalyzed reaction condition has been developed for the preparation of 1,4,5-trisubstituted-glycosyl-1,2,3-triazole derivatives in excellent yield by DBU catalyzed azide-enolate cycloaddition. The reaction condition can be scaled up without loss of the yield. The reaction condition can be further extended for the preparation of glycoconjugate derivatives.

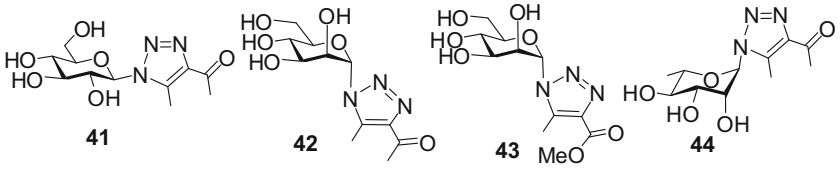
Experimental section

General methods All reactions were monitored by thin layer chromatography over silica gel coated TLC plates. The spots on TLC were visualized by warming ceric sulphate (2% $Ce(SO_4)_2$ in 2 N H_2SO_4) sprayed plates in hot plate. Silica gel 230–400 mesh was used for column chromatography. NMR spectra were recorded on Bruker Avance 500 MHz using $CDCl_3$ as solvent and TMS as internal reference unless stated otherwise. Chemical shift value is expressed in δ ppm. The complete assignment of proton and carbon spectra was carried out by using a standard set of NMR experiments. Optical rotations were recorded in a Jasco P-2000 spectrometer. Commercially available grades of organic solvents of adequate purity are used in all reactions.

Typical experimental condition: To a solution of per-*O*-acetyl-β-D-glycopyranosyl azide (**1–9**; 1 mmol) in DMF (1 mL) was added acetyl acetone (**10**; 1 mmol) or β-ketoester (**11, 12**; 1 mmol) or dimedone (**13**) or acetoacetanilide (**14**) and DBU (15 μL, 0.1 mmol) and the reaction mixture was allowed to stir at 70 °C for appropriate time (Table 2). The reaction mixture was diluted with water (10 mL) and extracted with EtOAc (5 mL). The organic layer was dried (Na_2SO_4) and concentrated. The crude product was purified over SiO_2 using hexane-EtOAc (1:1) as eluant to give pure product.

General de-O-acetylation of compounds: A solution of acetylated compound (100 mg) in 0.1 M CH_3ONa (5 mL) was allowed to stir at room temperature for 3 h. The reaction mixture was neutralized using Dowex 50 W X8 (H^+) resin, filtered and concentrated to give pure de-*O*-acetylated compound (quantitative yield).

Fig. 1 Deprotected glycosylated 1,2,3-triazole derivatives



Spectral analysis of the synthesized products

Compound 15 White solid; m.p. 180–181 °C; $[\alpha]_D$ - 40 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.84 (d, *J* = 9.5 Hz, 1 H, H-1), 5.70 (t, *J* = 9.5 Hz, 1 H, H-3), 5.41 (t, *J* = 9.5 Hz, 1 H, H-2), 5.24 (t, *J* = 9.5 Hz, 1 H, H-4), 4.26 (dd, *J* = 12.5, 5.0 Hz, 1 H, H-6_a), 4.17 (dd, *J* = 12.5, 2.5 Hz, 1 H, H-6_b), 4.00–3.96 (m, 1 H, H-5), 2.72 (s, 3 H, CH_3CO), 2.67 (s, 3 H, CH_3), 2.07 (s, 6 H, 2 COCH_3), 2.04 (s, 3 H, COCH_3), 1.87 (s, 3 H, COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.8 (*C*OCH_3), 170.1 (*C*OCH_3), 169.8 (*C*OCH_3), 169.0 (*C*OCH_3), 168.5 (*C*OCH_3), 144.1, 138.1 (Ar-C), 85.3 (C-1), 75.1 (C-3), 72.7 (C-5), 69.0 (C-4), 67.5 (C-2), 61.3 (C-6), 27.8 (CO*C*H_3), 20.5 (CO*C*H_3), 20.4 (2 C, 2CO*C*H_3), 20.1 (CO*C*H_3), 9.1 (*C*H_3); HRMS $[M + Na]^+$: Calcd. 478.1438; found: 478.1430; Anal. Calcd. for $C_{19}H_{25}N_3O_{10}$ (455.41): C, 50.11; H, 5.53; found, C, 50.00; H, 5.68.

Compound 16 Yellow oil; $[\alpha]_D$ - 12 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.83 (d, *J* = 9.5 Hz, 1 H, H-1), 5.62 (t, *J* = 9.5 Hz, 1 H, H-3), 5.40 (t, *J* = 9.5 Hz, 1 H, H-2), 5.23 (t, *J* = 9.5 Hz, H-4), 4.27 (dd, *J* = 12.5, 5.0 Hz, 1 H, H-6_a), 4.20–4.16 (m, 1 H, H-6_b), 4.00–3.95 (m, 1 H, H-5), 3.94 (s, 3 H, OCH_3), 2.75 (s, 3 H, CH_3), 2.08 (COCH_3), 2.07 (COCH_3), 2.04 (COCH_3), 1.86 (COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1 (*C*OCH_3), 169.7 (*C*OCH_3), 169.1 (*C*OCH_3), 168.6 (*C*OCH_3), 161.5 (*C*$OOCH_3$), 139.7–137.3 (Ar-C), 85.8 (C-1), 75.2 (C-3), 72.5 (C-5), 68.9 (C-4), 67.5 (C-2), 61.3 (C-6), 51.9 (COO*C*H_3), 20.5 (CO*C*H_3), 20.4 (2 C, 2 CO*C*H_3), 20.0, (CO*C*H_3), 9.1 (*C*H_3); HRMS $[M + Na]^+$: Calcd. 494.1387; found, 494.1378; Anal. Calcd. for $C_{19}H_{25}N_3O_{11}$ (471.41): C, 48.41; H, 5.35; found: C, 48.25; H, 5.50.

Compound 17 White solid; m.p. 134–135 °C; $[\alpha]_D$ - 10 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 6.09–6.00 (m, 1 H, C*H*=CH_2), 5.86 (d, *J* = 9.5 Hz, 1 H, H-1), 5.64 (t, *J* = 9.5 Hz, 1 H, H-3), 5.44–5.41 (m, 1 H, C*H*=), 5.39 (t, *J* = 9.5 Hz, 1 H, H-2), 5.31–5.29 (m, 1 H, C*H*=), 5.22 (t, *J* = 9.5 Hz, 1 H, H-4), 4.85–4.83 (m, 2 H, OCH_2), 4.27 (dd, *J* = 12.5, 5.0 Hz, 1 H, H-6_a), 4.18 (dd, *J* = 12.5,2.5 Hz, 1 H, H-6_b), 3.99–3.95 (m, 1 H, H-5), 2.75 (s, 3 H, CH_3), 2.09 (s, 3 H, COCH_3), 2.08 (s, 3 H, COCH_3), 2.04 (s, 3 H, COCH_3), 1.86 (s, 3 H, COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1 (*C*OCH_3), 169.8 (*C*OCH_3), 169.0 (*C*OCH_3), 168.5 (*C*OCH_3), 160.8 (*C*OO), 139.8–119.1 (Ar-C, CH=CH_2), 85.9 (C-1), 75.2 (C-3), 72.6 (C-5), 68.9 (C-4), 67.6 (C-2), 65.7 (OCH_2), 61.3 (C-6), 20.6 (CO*C*H_3), 20.5 (2 C, 2 CO*C*H_3), 20.1 (CO*C*H_3), 9.1 (*C*H_3); HRMS $[M + Na]^+$: Calcd. 520.1544; found, 520.1533. Anal. Calcd. for $C_{21}H_{27}N_3O_{11}$ (497.46): C, 50.70; H, 5.47; found: C, 50.56; H, 5.60.

Compound 18 Yellow oil; $[\alpha]_D$ - 14 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.97 (d, *J* = 9.0 Hz, 1 H, H-1), 5.41 (t, *J* = 9.5 Hz, 1 H, H-2), 5.35 (t, *J* = 9.5 Hz, 1 H, H-3), 5.21 (t, *J* = 9.5 Hz, 1 H, H-4), 4.29 (dd, *J* = 12.5, 4.0 Hz, 1 H, H-6_a), 4.19 (dd, *J* = 12.5 Hz, 1 H, H-6_b), 4.11–4.03 (m, 1 H, H-5), 2.94 (d, *J* = 9.0 Hz, 2 H, CH_2), 2.48 (d, *J* = 6.0 Hz, 2 H, CH_2), 2.17 (s, 3 H, COCH_3), 2.15 (s, 3 H, COCH_3), 2.08 (s, 3 H, COCH_3), 2.04 (s, 3 H, COCH_3), 1.21 (s, 3 H, CH_3), 1.15 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.87 (*C*O), 169.8 (*C*OCH_3), 169.4 (*C*OCH_3), 169.2 (*C*OCH_3), 168.8 (*C*OCH_3), 162.3 (*C*$(CH_3)_2$), 144.2 (Ar-C), 142.2 (Ar-C), 86.2 (C-1), 75.1 (C-3), 72.3 (C-4), 69.2 (C-2), 67.6 (C-5), 61.2 (C-6), 52.5 (*C*H_2), 34.7 (*C*H_2), 28.5 (*C*H_3), 28.2 (*C*H_3), 20.6 (CO*C*H_3), 20.5 (CO*C*H_3), 20.4 (CO*C*H_3), 20.0 (CO*C*H_3); HRMS $[M + Na]^+$: Calcd. 518.1751; found, 518.1742; Anal. Calcd. for $C_{22}H_{29}N_3O_{10}$ (495.48): C, 53.33; H, 5.90; found: C, 53.16; H, 6.08.

Compound 19 Yellow oil; $[\alpha]_D$ - 16 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 8.97 (s, 1 H, N*H*), 7.67–7.09 (m, 5 H, Ar-H), 5.81 (d, *J* = 9.5 Hz, 1 H, H-1), 5.79 (t, *J* = 9.5 Hz, 1 H, H-2), 5.40 (t, *J* = 9.5 Hz, 9.0 Hz, 1 H, H-3), 5.24 (t, *J* = 9.5 Hz, 10 Hz, 1 H, H-4), 4.26 (dd, *J* = 4.5 Hz, 12.5 Hz, 1 H, H-6_a), 4.16 (d, *J* = 12.5 Hz, 1 H, H-6_b), 4.01–3.98 (m, 1 H, H-5), 2.80 (s, 3H, CH_3), 2.07 (s, 6H, COCH_3), 2.04 (s, 3H, COCH_3), 1.87 (s, 3H, COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1 (*C*OCH_3), 169.7 (*C*OCH_3), 168.9 (*C*OCH_3), 168.3 (*C*OCH_3), 158.53 (*C*ONH), 139.19–119.8 (Ar-C), 85.1 (C-1), 75.1 (C-3), 72.8 (C-4), 69.1 (C-2), 67.5 (C-5), 61.4 (C-6), 20.5 (CO*C*H_3), 20.4 (CO*C*H_3), 20.1 (CO*C*H_3), 8.8 (*C*H_3); HRMS $[M + Na]^+$: Calcd. 555.1703; found, 555.1710; Anal. Calcd. for $C_{24}H_{28}N_4O_{10}$ (532.50): C, 54.13; H, 5.30; found: C, 54.26; H, 5.48.

Compound 20 White solid; m.p. 103–104 °C; $[\alpha]_D$ - 15 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.85 (d, *J* = 9.0 Hz, 1 H, H-1), 5.76 (t, *J* = 10.0 Hz, 1 H, H-2), 5.54 (d, *J* = 3.5 Hz, 1 H, H-4), 5.21 (dd, *J* = 10.0 Hz, 3.0 Hz, 1 H, H-3), 4.20–4.10 (m, 3 H, H-5, H-6_{ab}), 2.78 (s, 3 H, COCH_3), 2.68 (s, 3 H, CH_3), 2.21 (s, 3 H, COCH_3), 2.05 (s, 3 H, COCH_3), 2.02 (s, 3 H, COCH_3), 1.89 (s, 3 H, COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.7 (*C*OCH_3), 169.9 (*C*OCH_3), 169.5 (2 C, 2 *C*OCH_3), 168.7 (*C*OCH_3), 144.3, 138.3 (Ar-C), 86.4 (C-1),

73.8 (C-3), 70.7 (C-4), 66.8 (C-2), 66.4 (C-5), 61.1 (C-6), 27.8 (CO*C*H$_3$), 20.9 (CO*C*H$_3$), 20.5 (2 C, 2 CO*C*H$_3$), 20.1 (CO*C*H$_3$), 9.1 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 478.1438; found, 478.1430; Anal. Calcd. for $C_{19}H_{25}N_3O_{10}$ (455.41): C, 50.11; H, 5.53; found: C, 50.26; H, 5.68.

Compound 21 White solid; m.p. 140–141 °C; [α]$_D$ - 30 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.89 (d, *J* = 9.5 Hz, 1 H, H-1), 5.71 (t, *J* = 9.5 Hz, 1 H, H-2), 5.54 (d, *J* = 3.0 Hz, 1 H, H-4), 5.21 (dd, *J* = 10.0, 3.0 Hz, 1 H, H-3), 4.23–4.18 (m, 3 H, H-5, H-6$_{ab}$), 3.95 (s, 3 H, OC*H*$_3$), 2.79 (s, 3 H, C*H*$_3$), 2.21 (s, 3 H, COC*H*$_3$), 2.05 (s, 3 H, COC*H*$_3$), 2.02 (s, 3H, COC*H*$_3$), 1.88 (s, 3H, COC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.0 (*C*OCH$_3$), 169.5 (2 C, 2 *C*OCH$_3$), 168.9 (*C*OCH$_3$), 161.6 (*C*OOCH$_3$), 139.9, 137.4 (Ar-C), 86.7 (C-1), 73.9 (C-3), 70.7 (C-4), 66.9 (C-2), 66.4 (C-5), 61.1 (C-6), 51.9 (COO*C*H$_3$), 20.5 (2 C, 2 CO*C*H$_3$), 20.4 (CO*C*H$_3$), 20.1 (CO*C*H$_3$), 9.0 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 494.1387; found, 494.1380; Anal. Calcd. for $C_{19}H_{25}N_3O_{11}$ (471.41): C, 48.41; H, 5.35; found: C, 48.30; H, 5.50.

Compound 22 White solid; m.p. 52–53 °C; [α]$_D$ - 2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.10–6.01 (m, 1 H, C*H*=CH$_2$), 5.88 (d, *J* = 9.5 Hz, 1 H, H-1), 5.72 (t, *J* = 9.5 Hz, 1 H, H-2), 5.54 (d, *J* = 3.5 Hz, 1 H, H-4), 5.45–5.29 (m, 2 H, CH=C*H*$_2$), 5.22 (dd, *J* = 10.0, 3.0 Hz, 1 H, H-3), 4.87–4.84 (m, 2 H, OC*H*$_2$), 4.21–4.09 (m, 3 H, H-5, H-6$_{ab}$), 2.79 (s, 3 H, C*H*$_3$), 2.21 (s, 3 H, COC*H*$_3$), 2.05 (s, 3 H, COC*H*$_3$), 2.02 (s, 3 H, COC*H*$_3$), 1.88 (s, 3 H, COC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9 (*C*OCH$_3$), 169.5 (2 C, 2 *C*OCH$_3$), 168.9 (*C*OCH$_3$), 160.9 (*C*OOAll), 139.9, 137.4, 131.8, 119.0 (Ar-C, *C*H=*C*H$_2$-), 86.7 (C-1), 73.9 (C-3), 70.7 (C-4), 66.9 (C-5), 66.4 (C-2), 65.6 (O*C*H$_2$), 61.1 (C-6), 20.9 (2 C, 2 CO*C*H$_3$), 20.4 (CO*C*H$_3$), 20.1 (CO*C*H$_3$), 9.0 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 520.1544; found, 520.1536; Anal. Calcd. for $C_{21}H_{27}N_3O_{11}$ (497.45): C, 50.70; H, 5.47; found: C, 50.56; H, 5.58.

Compound 23 Yellow oil; [α]$_D$ - 6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–6.92 (m, 20 H, Ar-H), 5.41 (d, *J* = 9.5 Hz, 1 H, H-1), 4.92 (br s, 2 H, PhC*H*$_2$), 4.84 (d, *J* = 11.0 Hz, 1 H, PhC*H*$_2$), 4.63 (d, *J* = 11.0 Hz, 1 H, PhC*H*$_2$), 4.60 (d, *J* = 11.0 Hz, 1 H, PhC*H*$_2$), 4.50 (d, *J* = 11.5 Hz, 1 H, PhC*H*$_2$), 4.46 (d, *J* = 11.5 Hz, 1 H, PhC*H*$_2$), 4.36 (t, *J* = 9.5 Hz, 1 H, H-3), 4.33 (d, *J* = 11.5 Hz, 1 H, PhC*H*$_2$), 3.96 (s, 3 H, OC*H*$_3$), 3.83 (t, *J* = 9.5 Hz, 1 H, H-4), 3.80 (t, *J* = 9.5 Hz, 1 H, H-2), 3.70–3.63 (m, 3 H, H-5, H-6$_{ab}$), 2.50 (s, 3 H, C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.9 (*C*OOCH$_3$), 139.7–127.6 (Ar-C), 86.0 (C-1), 85.9 (C-5), 78.8 (C-3), 78.1 (C-4), 77.1 (C-2), 75.8 (Ph*C*H$_2$), 75.2 (Ph*C*H$_2$), 74.9 (Ph*C*H$_2$), 73.5 (Ph*C*H$_2$), 68.3 (C-6), 51.8 (COO*C*H$_3$), 8.8 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 686.2843; found, 686.2836; Anal. Calcd. for $C_{39}H_{41}N_3O_7$ (663.75): C, 70.57; H, 6.23; found: C, 70.40; H, 6.38.

Compound 24 Yellow oil; [α]$_D$ - 5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32–6.90 (m, 20 H, Ar-H), 6.12–6.01 (m, 1 H, C*H*=CH$_2$), 5.44–5.41 (m, 1 H, CH=C*H*$_2$), 5.40 (d, *J* = 9.5 Hz, 1 H, H-1), 5.32–5.30 (m, 1 H, CH=C*H*$_2$), 4.92 (br s, 2 H, PhC*H*$_2$), 4.88–4.86 (m, 2 H, OC*H*$_2$), 4.85 (d, *J* = 11.0 Hz, 1 H, PhC*H*$_2$), 4.61 (dd, *J* = 11.0 Hz, 2 H, 2 PhC*H*$_2$), 4.52 (d, *J* = 11.5 Hz, 1 H, PhC*H*$_2$), 4.46 (d, *J* = 11.5 Hz, 1H, PhC*H*$_2$), 4.34 (t, *J* = 9.5 Hz, 1 H, H-3), 4.32 (d, *J* = 11.0 Hz, 1 H, PhC*H*$_2$), 3.80 (t, *J* = 9.5 Hz, 1 H, H-2), 3.77 (t, *J* = 9.5 Hz, 1 H, H-4), 3.69–3.63 (m, 3 H, H-5, H-6$_{ab}$), 2.49 (s, 3 H, C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.1 (*C*OOAll), 139.8–118.9 (Ar-C, *C*H=*C*H$_2$), 86.0 (C-1), 85.9 (C-5), 78.7 (C-3), 78.1 (C-4), 77.1 (C-2), 75.8 (Ph*C*H$_2$), 75.2 (Ph*C*H$_2$), 74.8 (Ph*C*H$_2$), 73.5 (Ph*C*H$_2$), 68.3 (O*C*H$_2$-), 65.5 (C-6), 8.9 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 712.2999; found, 712.2990; Anal. Calcd. for $C_{41}H_{43}N_3O_7$ (689.79): C, 71.39; H, 6.28; found: C, 71.20; H, 6.40.

Compound 25 White solid; m.p. 84–85 °C; [α]$_D$ + 50 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.07 (dd, *J* = 9.5 Hz, 3.0 Hz, 1 H, H-3), 5.95 (br s, 1 H, H-1), 5.91 (br s, 1 H, H-2), 5.35 (t, *J* = 9.5 Hz, 1 H, H-4), 4.35–4.28 (m, 1 H, H-6$_a$), 4.06–3.96 (m, 1 H, H-6$_b$), 3.75–3.72 (m, 1 H, H-5), 2.67 (s, 3 H, COC*H*$_3$), 2.64 (s, 3 H, C*H*$_3$), 2.21 (s, 3 H, COC*H*$_3$), 2.06 (s, 6 H, 2 COC*H*$_3$), 2.02 (s, 3 H, COC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.7 (*C*OCH$_3$), 169.9 (*C*OCH$_3$), 169.4 (*C*OCH$_3$), 169.3 (*C*OCH$_3$), 168.9 (*C*OCH$_3$), 143.6, 138.1 (Ar-C), 81.9 (C-1), 71.4 (C-4), 68.8 (C-2), 68.3 (C-3), 65.8 (C-5), 61.5 (C-6), 27.7 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.5 (2 C, 2 CO*C*H$_3$), 20.4 (CO*C*H$_3$), 8.7 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 478.1438; found, 478.1430; Anal. Calcd. for $C_{19}H_{25}N_3O_{10}$ (455.41): C, 50.11; H, 5.53; found: C, 50.00; H, 5.68.

Compound 26 White solid; m.p. 145–147 °C; [α]$_D$ + 34 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.02 (dd, *J* = 9.5, 3.0 Hz, 1 H, H-3), 5.96 (br s, 1 H, H-1), 5.91 (br s, 1 H, H-2), 5.34 (t, *J* = 9.5 Hz, 1 H, H-4), 4.31–4.27 (m, 1 H, H-6$_a$), 3.99–3.95 (m, 1 H, H-6$_b$), 3.94 (s, 3 H, COOC*H*$_3$), 3.76–3.74 (m, 1 H, H-5), 2.65 (s, 3 H, C*H*$_3$), 2.19 (s, 3 H, COC*H*$_3$), 2.07 (s, 6 H, 2COC*H*$_3$), 2.02 (s, 3 H, COC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9 (*C*OCH$_3$), 169.4 (2 C, 2*C*OCH$_3$), 168.9 (*C*OCH$_3$), 161.5 (*C*OOCH$_3$), 139.8, 136.8 (Ar-C), 82.1 (C-1), 71.5 (C-4), 68.8 (C-2), 68.4 (C-3), 65.8 (C-5), 61.5 (C-6), 51.9 (COO*C*H$_3$), 20.9 (CO*C*H$_3$), 20.6 (2C, 2 CO*C*H$_3$), 20.4 (CO*C*H$_3$), 8.6 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 494.1387; found, 494.1380; Anal. Calcd. for $C_{19}H_{25}N_3O_{11}$ (471.41): C, 48.41; H, 5.35; found: C, 48.30; H, 5.50.

Compound 27 White solid; m.p. 111–112 °C; [α]$_D$ - 72 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.07 (dd, *J* = 9.5, 3.5 Hz, 1 H, H-3), 5.90 (br s, 1 H, H-2), 5.84 (br s, 1 H, H-1), 5.18 (t, *J* = 9.5 Hz, 1 H, H-4), 3.65–3.60 (m, 1 H,

H-5), 2.69 (s, 3 H, COCH_3), 2.64 (s, 3 H, CH_3), 2.21 (s, 3 H, COCH_3), 2.06 (s, 3 H, COCH_3), 2.03 (s, 3 H, COCH_3), 1.19 (d, J = 6.5 Hz, 3 H, CCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.9 (*C*OCH$_3$), 169.7 (*C*OCH$_3$), 169.6 (*C*OCH$_3$), 169.1 (*C*OCH$_3$), 143.6, 138.0 (Ar-C), 82.0 (C-1), 70.7 (C-2), 69.4 (C-3), 68.8 (C-4), 68.5 (C-5), 27.8 (COCH$_3$), 20.9 (COCH$_3$), 20.7 (COCH$_3$), 20.4 (COCH$_3$), 17.2 (CCH$_3$), 8.8 (CH$_3$); HRMS $[M + Na]^+$: Calcd. 420.1383; found, 420.1376; Anal. Calcd. for $C_{17}H_{23}N_3O_8$ (397.38): C, 51.38; H, 5.83; found: C, 51.20; H, 6.08.

Compound 28 White solid; m.p. 113–115 °C; $[\alpha]_D$ - 55 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.04 (dd, J = 9.5, 3.5 Hz, 1 H,H-3), 5.90 (br s, 1 H, H-2), 5.84 (br s, 1 H, H-1), 5.15 (t, J = 9.5 Hz, 1 H, H-4), 3.96 (s, 3 H, COOCH$_3$), 3.65–3.60 (m, 1 H, H-5), 2.65 (s, 3 H, CH$_3$), 2.20 (s, 3 H, COCH$_3$), 2.06 (s, 3 H, COCH$_3$), 2.03 (s, 3 H, COCH$_3$), 1.18 (d, J = 6.5 Hz, 3 H, CCH$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7 (*C*OCH$_3$), 169.6 (*C*OCH$_3$), 169.1 (*C*OCH$_3$), 161.7 (*C*OOCH$_3$), 139.6, 136.8 (Ar-C), 82.1 (C-1), 70.8 (C-2), 69.5 (C-3), 68.9 (C-4), 68.8 (C-5), 51.9 (COO*C*H$_3$), 20.7 (2 C, 2 CO*C*H$_3$), 20.5 (CO*C*H$_3$), 17.2 (*C*CH$_3$), 8.7 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 436.1332; found, 436.1325; Anal. Calcd. for $C_{17}H_{23}N_3O_9$ (413.37): C, 49.39; H, 5.61; found: C, 49.20; H, 5.80.

Compound 29 Yellow oil; $[\alpha]_D$ - 35 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.10–6.02 (m, 2 H, H-3, C*H*=CH$_2$), 5.91–5.89 (m, 1 H, H-2), 5.83 (d, J = 2.0 Hz, 1 H, H-1), 5.46–5.30 (m, 2 H, CH=C*H*$_2$), 5.15 (t, J = 9.5 Hz, 1 H, H-4), 4.90–4.82 (m, 2 H, OC*H*$_2$-), 3.65–3.60 (m, 1 H, H-5), 2.65 (s, 3 H, C*H*$_3$), 2.20 (s, 3 H, COC*H*$_3$), 2.06 (s, 3 H, COC*H*$_3$), 2.03 (s, 3 H, COC*H*$_3$), 1.18 (d, J = 6.5 Hz, 3 H, CC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7 (*C*OCH$_3$), 169.6 (*C*OCH$_3$), 169.0 (*C*OCH$_3$), 160.9 (*C*OOCH$_3$), 139.6–118.9 (Ar-C, *C*H=*C*H$_2$), 82.1 (C-1), 70.8 (C-2), 69.4 (C-3), 68.9 (C-4), 68.8 (C-5), 65.6 (O*C*H$_2$), 20.7 (COCH$_3$), 20.6 (COCH$_3$), 20.5 (COCH$_3$), 17.2 (*C*CH$_3$), 8.8 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 462.1489; found, 462.1480; Anal. Calcd. for $C_{19}H_{25}N_3O_9$ (439.41): C, 51.93; H, 5.73; found: C, 51.80; H, 5.88.

Compound 30 Yellow oil; $[\alpha]_D$ - 40 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.89 (dd, J = 9.0, 3.0 Hz, 1 H, H-3), 5.87 (br s, 2 H, H-1, H-2), 5.12 (t, J = 9.0 Hz, 1 H, H-2), 3.70–3.67 (m, 1 H, H-5), 2.83 (s, 2 H, C*H*$_2$), 2.49 (s, 2 H, C*H*$_2$), 2.19 (s, 3 H, COC*H*$_3$), 2.08 (s, 3 H COC*H*$_3$), 2.04 (s, 3 H, COC*H*$_3$), 1.16 (s, 3 H, C*H*$_3$), 1.15 (s, 3 H, C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.67 (*C*O), 169.6 (*C*OCH$_3$), 169.5 (*C*OCH$_3$), 169.0 (*C*OCH$_3$), 163.8 (*C*(CH$_3$)$_2$), 144.6 (Ar-C), 141.5 (Ar-C), 82.4 (C-1), 70.6 (C-2), 69.9 (C-4), 68.8 (C-3), 68.5 (C-5), 52.4 (*C*H$_2$), 33.9 (*C*H$_2$), 28.4 (*C*H$_3$), 28.3 (*C*H$_3$), 20.7 (2 C, 2 CO*C*H$_3$), 20.5 (CO*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 460.1686; found, 460.1678; Anal. Calcd. for $C_{20}H_{27}N_3O_8$ (437.44): C, 54.91; H, 6.22; found: C, 54.80; H, 6.08.

Compound 31 Yellow oil; $[\alpha]_D$ - 30 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz $CDCl_3$): δ 9.01 (s, 1 H, N*H*), 7.67–7.01 (m, 5 H, Ar-H), 6.04 (dd, J = 9.5, 3.5 Hz, 1 H, H-3), 5.93 (br s, 1 H, H-2), 5.86 (br s, 1 H, H-1), 5.16 (t, J = 7.5 Hz, 1 H, H-4), 3.62–3.57 (m, 1 H, H-5), 2.71 (s, 3 H, C*H*$_3$), 2.22 (s, 3 H, COC*H*$_3$), 2.06 (s, 3 H COC*H*$_3$), 2.04 (s, 3 H, COC*H*$_3$), 1.20 (d, J = 6.0 Hz, 3 H, C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.6 (*C*OCH$_3$), 169.5 (*C*OCH$_3$), 169.1 (*C*OCH$_3$), 158.6 (*C*ONH), 138.9–119.8 (Ar-C), 82.3 (C-1), 70.7 (C-2), 69.4 (C-4), 69.0 (C-3), 68.7 (C-5), 20.7 (CO*C*H$_3$), 20.5 (CO*C*H$_3$), 20.3 (CO*C*H$_3$), 8.6 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 497.1649; found, 497.1640; Anal. Calcd. for $C_{22}H_{26}N_4O_8$ (474.46): C, 55.69; H, 5.52; found: C, 55.50; H, 5.65.

Compound 32 White solid; m.p. 151–152 °C; $[\alpha]_D$ + 53 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.80 (d, J = 9.5 Hz, 1 H, H-1$_A$), 5.68 (t, J = 9.5 Hz, 1 H, H-2$_A$), 5.47 (t, J = 9.5 Hz, 1 H, H-3$_B$), 5.46 (br s, 1 H, H-1$_B$), 5.34 (t, J = 10.0 Hz, 1 H, H-4$_B$), 5.04 (t, J = 9.5 Hz, 1 H, H-3$_A$), 4.85 (dd, J = 9.5, 3.0 Hz, 1 H, H-2$_B$), 4.51 (dd, J = 12.5, 2.0 Hz, 1 H, H-6$_{aB}$), 4.24–4.20 (m, 2 H, H-6$_{abA}$), 4.18 (t, J = 9.5 Hz, 1 H, H-4$_A$), 4.05 (dd, J = 12.5, 2.5 Hz, 1 H, H-6$_{bB}$), 4.02–3.92 (m, 2 H, H-5$_A$, H-5$_B$), 2.67 (br s, 6 H, CH$_3$CO, CH$_3$), 2.11 (s, 3 H, COC*H*$_3$), 2.10 (s, 3 H, COC*H*$_3$), 2.05 (s, 3 H, COOC*H*$_3$), 2.04 (s, 3 H, COC*H*$_3$), 2.03 (s, 3 H, COC*H*$_3$), 2.01 (s, 3 H, COC*H*$_3$), 1.84 (s, 3 H, COC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.8 (*C*OCH$_3$), 170.3 (*C*OCH$_3$), 170.2 (*C*OCH$_3$), 170.0 (*C*OCH$_3$), 169.9 (*C*OCH$_3$), 169.7 (*C*OCH$_3$), 169.1 (*C*OCH$_3$), 168.7 (*C*OCH$_3$), 143.9, 138.0 (Ar-C), 95.7 (C-1$_B$), 83.9 (C-1$_A$), 75.4, 75.3, 72.0, 69.9, 69.7, 69.1, 68.7, 67.9, 62.3 (C-6$_A$), 61.3 (C-6$_B$), 27.8 (*C*H$_3$CO), 20.9 (COC*H*$_3$), 20.8 (2 C, 2 COC*H*$_3$), 20.6 (2 C, 2 OC*H*$_3$), 20.4 (COC*H*$_3$), 20.2 (COC*H*$_3$), 8.9 (C*H*$_3$); HRMS $[M + Na]^+$: Calcd. 766.2283; found, 766.2275; Anal. Calcd. for $C_{31}H_{41}N_3O_{18}$ (743.66): C, 50.07; H, 5.56; found: C, 49.89; H, 5.70.

Compound 33 Yellow oil; $[\alpha]_D$ + 39 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.83 (d, J = 9.5 Hz, 1 H, H-1$_A$), 5.60 (t, J = 9.5 Hz, 1 H, H-2$_A$), 5.47 (t, J = 9.5 Hz, 1 H, H-3$_A$), 5.45 (br s, 1 H, H-1$_B$), 5.34 (t, J = 9.5 Hz, 1 H, H-3$_B$), 5.05 (t, J = 9.5 Hz, 1 H, H-4$_B$), 4.85 (dd, J = 9.5, 3.0 Hz, 1 H, H-2$_B$), 4.50 (dd, J = 12.0, 2.5 Hz, 1 H, H-6$_{aB}$), 4.27–4.21 (m, 2 H, H-6$_{abA}$), 4.17 (t, J = 9.5 Hz, 1 H, H-4$_A$), 4.05 (dd, J = 12.0, 2.0 Hz, 1 H, H-6$_{bB}$), 3.99–3.94 (m, 2 H, H-5$_A$, H-5$_B$), 3.92 (s, 3 H, COOC*H*$_3$), 2.68 (s, 3 H, C*H*$_3$), 2.12 (s, 3 H, COC*H*$_3$), 2.10 (s, 3 H, COC*H*$_3$), 2.05 (s, 3 H, COC*H*$_3$), 2.03 (s, 6 H, 2 COC*H*$_3$), 2.01 (s, 3 H, COC*H*$_3$), 1.83 (s, 3 H, COC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3 (*C*OCH$_3$), 170.2 (*C*OCH$_3$),

169.9 (*C*OCH$_3$), 169.7 (2 C, 2 *C*OCH$_3$), 169.1 (*C*OCH$_3$), 168.8 (*C*OCH$_3$), 161.6 (*C*OOCH$_3$), 139.6, 137.1 (Ar-C), 95.8 (C-1$_B$), 84.5 (C-1$_A$), 75.4, 75.3, 72.0, 70.0, 69.8, 69.2, 68.8, 67.9, 62.2 (C-6$_A$), 61.3 (C-6$_B$), 51.9 (COO*C*H$_3$), 20.9 (CO*C*H$_3$), 20.8 (CO*C*H$_3$), 20.6 (2 C, 2 CO*C*H$_3$), 20.5 (2 C, 2 CO*C*H$_3$), 20.1 (CO*C*H$_3$), 8.8 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 782.2232; found, 782.2225; Anal. Calcd. for $C_{31}H_{41}N_3O_{19}$ (759.66): C, 49.01; H, 5.44; found: C, 48.82; H, 5.60.

Compound 34 Yellow oil; [α]$_D$ + 46 (*c* 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.93 (d, *J* = 9.5 Hz, 1 H, H-1$_A$), 5.51–4.72 (m, 2 H, H-3$_A$, H-1$_B$), 5.32 (t, *J* = 10.0 Hz, 1 H, H-2$_A$), 5.23 (t, *J* = 9.5 Hz, 1 H, H-3$_B$), 5.03 (t, *J* = 10.0 Hz, 1 H, H-4$_B$), 4.84 (dd, *J* = 11.0, 4.0 Hz, 1 H, H-6$_{aA}$), 4.58 (d, *J* = 10.0 Hz, 1 H, H-6$_{bA}$), 4.30–4.28 (m, 2 H, H-5$_A$, H-5$_B$), 4.23–4.19 (m, 3 H, H-4$_A$, H-6$_{abB}$), 2.88 (s, 2 H, C*H*$_2$), 2.86 (s, 2 H, C*H*$_2$), 2.47 (s, 3 H, COC*H*$_3$), 2.41 (s, 3 H, COC*H*$_3$), 2.38 (s, 6 H, 2 COC*H*$_3$), 2.33 (s, 3 H, COC*H*$_3$), 2.03 (s, 6 H, 2 COC*H*$_3$), 1.18 (s, 3 H, C*H*$_3$), 1.12 (s, 3 H, C*H*$_3$); ^{13}C NMR (125 MHz, CDCl$_3$): δ 188.6 (*C*O), 170.3 (*C*OCH$_3$), 170.1 (*C*OCH$_3$), 169.8 (*C*OCH$_3$), 169.7 (*C*OCH$_3$), 169.6 (*C*OCH$_3$), 169.5 (*C*OCH$_3$), 169.1 (*C*OCH$_3$), 162.3 (*C*(CH$_3$)$_2$), 143.9 (Ar-C), 142.1 (Ar-C), 95.5 (C-1$_B$), 85.6 (C-1$_A$), 77.4 (C-2$_A$), 77.3 (C-2$_B$), 75.7 (C-4$_A$), 75.1 (C-4$_B$), 74.6 (C-3$_A$), 71.74 (C-3$_B$), 70.0 (C-5$_A$), 69.3 (C-5$_B$), 61.9 (C-6$_A$), 60.2 (C-6$_B$), 52.4 (*C*H$_2$), 34.6 (*C*H$_2$), 28.6 (*C*H$_3$), 28.1 (*C*H$_3$), 21.2 (CO*C*H$_3$), 20.9 (CO*C*H$_3$), 20.8 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.5 (CO*C*H$_3$), 20.4 (CO*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 806.2596; found, 806.2588; Anal. Calcd. for $C_{34}H_{45}N_3O_{18}$ (783.73): C, 52.11; H, 5.79; found: C, 52.00; H, 6.00.

Compound 35 White solid; m.p. 175–176 °C; [α]$_D$ - 21 (*c* 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.73 (d, *J* = 9.5 Hz, 1 H, H-1$_A$), 5.72 (t, *J* = 9.5 Hz, 1 H, H-2$_A$), 5.39 (t, *J* = 9.5 Hz, 1 H, H-3$_A$), 5.34 (d, *J* = 3.5 Hz, 1 H, H-4$_B$), 5.15 (dd, *J* = 9.5 Hz, 1 H, H-2$_B$), 4.96 (dd, *J* = 9.5, 3.0 Hz, 1 H, H-3$_B$), 4.55 (d, *J* = 7.5 Hz, 1 H, H-1$_B$), 4.51 (dd, *J* = 12.0, 2.0 Hz, 1 H, H-6$_{aB}$), 4.15–4.09 (m, 3 H, H-5$_B$, H-6$_{aA}$, H-6$_{bB}$), 3.95 (t, *J* = 9.5 Hz, 1 H, H-4$_A$), 3.92–3.87 (m, 2 H, H-5$_A$, H-6$_{bA}$), 2.67 (br s, 6 H, C*H*$_3$, COC*H*$_3$), 2.17 (s, 3 H, COC*H*$_3$), 2.09 (s, 3 H, COC*H*$_3$), 2.08 (s, 6 H, 2 COC*H*$_3$), 2.06 (s, 3 H, COC*H*$_3$), 1.97 (s, 3 H, COC*H*$_3$), 1.87 (s, 3 H, COC*H*$_3$); ^{13}C NMR (125 MHz, CDCl$_3$): δ 170.1 (*C*OCH$_3$), 169.9 (*C*OCH$_3$), 169.8 (*C*OCH$_3$), 169.7 (*C*OCH$_3$), 169.4 (*C*OCH$_3$), 168.8 (*C*OCH$_3$), 168.6 (*C*OCH$_3$), 143.9, 138.1 (Ar-C), 101.1 (C-1$_B$), 84.4 (C-1$_A$), 75.9, 75.5, 72.1, 70.8 (2 C), 69.3, 69.0, 66.5, 61.5 (C-6$_A$), 60.6 (C-6$_B$), 27.8 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 20.6 (2 C, 2 CO*C*H$_3$), 20.5 (CO*C*H$_3$), 20.4 (2 C, 2 CO*C*H$_3$), 20.2 (CO*C*H$_3$), 8.9 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 766.2283; found, 766.2276; Anal. Calcd. for $C_{31}H_{41}N_3O_{18}$ (743.66): C, 50.07; H, 5.56; found: C, 49.90; H, 5.70.

Compound 36 White solid; m.p. 168–170 °C; [α]$_D$ - 19 (*c* 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.78 (d, *J* = 9.5 Hz, 1 H, H-1$_A$), 5.67 (t, *J* = 9.5 Hz, 1 H, H-2$_A$), 5.39 (t, *J* = 9.5 Hz, 1 H, H-3$_A$), 5.35 (d, *J* = 3.5 Hz, 1 H, H-4$_B$), 5.11 (dd, *J* = 9.5, 9.5 Hz, 1 H, H-2$_B$), 4.97 (dd, *J* = 9.5, 3.0 Hz, 1 H, H-3$_B$), 4.55 (d, *J* = 7.5 Hz, 1 H, H-1$_B$), 4.52 (dd, *J* = 12.0, 2.0 Hz, 1 H, H-6$_{aA}$), 4.19–4.08 (m, 3 H, H-5$_B$, H-6$_{bA}$, H-6$_{aB}$), 3.98 (t, *J* = 9.5 Hz, 1 H, H-4$_A$), 3.95 (s, 3 H, COOC*H*$_3$), 3.92–3.87 (m, 2 H, H-5$_A$, H-6$_{bB}$), 2.69 (s, 3 H, C*H*$_3$), 2.17 (s, 3 H, COC*H*$_3$), 2.09 (s, 3 H, COC*H*$_3$), 2.07 (s, 6 H, 2 COC*H*$_3$), 2.06 (s, 3 H, COC*H*$_3$), 1.97 (s, 3 H, COC*H*$_3$), 1.85 (s, 3 H, COC*H*$_3$); ^{13}C NMR (125 MHz, CDCl$_3$): δ 170.1 (*C*OCH$_3$), 169.9 (*C*OCH$_3$), 169.8 (*C*OCH$_3$), 169.7 (*C*OCH$_3$), 169.4 (*C*OCH$_3$), 168.8 (*C*OCH$_3$), 168.7 (*C*OCH$_3$), 161.6 (*C*OCH$_3$), 139.6, 137.1 (Ar-C), 101.1 (C-1$_B$), 84.9 (C-1$_A$), 75.9, 75.5, 72.7, 70.8, 69.3, 69.1, 66.5, 61.5, (Ar-C), 60.6 (C-6$_B$), 51.9 (COO*C*H$_3$), 20.7 (CO*C*H$_3$), 20.6 (2C, 2CO*C*H$_3$), 20.5 (2 C, 2 CO*C*H$_3$), 20.4 (2 C, 2 CO*C*H$_3$), 20.1 (CO*C*H$_3$), 8.8 (*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 782.2232; found, 782.2225; Anal. Calcd. for $C_{31}H_{41}N_3O_{19}$ (759.66): C, 49.01; H, 5.44; found: C, 48.85; H, 48.98.

Compound 37 Yellow oil; [α]$_D$ - 25 (*c* 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.88 (d, *J* = 9.0 Hz, 1 H, H-1$_A$), 5.36 (t, *J* = 9.0 Hz, 1 H, H-3$_A$), 5.34 (br s, 1 H, H-4$_B$), 5.32 (t, *J* = 9.5 Hz, H-2$_A$), 5.10–4.97 (m, 2 H, 6$_{abA}$), 4.58 (d, *J* = 7.5 Hz, 1 H, H-1$_B$), 4.50 (dd, *J* = 12.0, 1.5 Hz, 1 H, H-6$_{aB}$), 4.21–4.17 (m, 2 H, H-5$_A$, H-5$_B$), 4.08 (t, *J* = 9.0 Hz, 1 H, H-2$_B$), 4.05 (t, *J* = 9.0 Hz, 1 H, H-3$_B$), 3.98–3.92 (m, 2 H, H-4$_A$, H-6$_{bB}$), 2.80 (s, 2 H, C*H*$_2$), 2.48 (s, 2 H, C*H*$_2$), 2.17 (s, 3 H, COC*H*$_3$), 2.16 (s, 3 H, COC*H*$_3$), 2.11 (s, 6 H, 2 COC*H*$_3$), 2.07 (s, 3 H, COC*H*$_3$), 2.06 (s, 3 H, COC*H*$_3$), 2.03 (s, 3 H, COC*H*$_3$), 1.19 (s, 3 H, C*H*$_3$), 1.13 (s, 3 H, C*H*$_3$); ^{13}C NMR (125 MHz, CDCl$_3$): δ 188.7 (*C*O), 169.9 (*C*OCH$_3$), 169.8 (*C*OCH$_3$), 169.7 (*C*OCH$_3$), 169.6 (*C*OCH$_3$), 169.5 (*C*OCH$_3$), 169.0 (*C*OCH$_3$), 168.7 (*C*OCH$_3$), 162.2 (*C*(CH$_3$)$_2$), 144.0 (Ar-C), 142.1 (Ar-C), 101.2 (C-1$_B$), 85.7 (C-1$_A$), 76.2 (C-3$_A$), 75.5 (C-3$_B$), 72.1 (C-4$_A$), 70.8 (C-4$_B$), 70.7 (C-2$_A$), 69.6 (C-2$_B$), 69.1 (C-5$_A$), 66.4 (C-5$_B$), 61.3 (C-6$_B$), 60.5 (C-6$_A$), 52.5 (*C*H$_2$), 34.6 (*C*H$_2$), 28.6 (*C*H$_3$), 28.2 (*C*H$_3$), 22.7 (CO*C*H$_3$), 20.9 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.5 (CO*C*H$_3$), 20.4 (CO*C*H$_3$), 20.1 (CO*C*H$_3$); HRMS [M + Na]$^+$: Calcd. 806.2596; found, 806.2588; Anal. Calcd. for $C_{34}H_{45}N_3O_{18}$ (783.73): C, 52.11; H, 5.79; found: C, 51.93; H, 6.05.

Compound 38 White solid; m.p. 229–230 °C; [α]$_D$ - 20 (*c* 1.0, CHCl$_3$); ^{1}H NMR (500 MHz, CDCl$_3$): δ 5.80–5.70 (m, 2 H, H-1$_A$, H-3$_B$), 5.40 (t, *J* = 9.5 Hz, 1 H, H-2$_A$), 5.15 (t, *J* = 9.5 Hz, 1 H, H-2$_B$), 5.05 (t, *J* = 9.5 Hz, 1 H, H-3$_A$), 4.95 (t, *J* = 9.5 Hz, 1 H, H-4$_B$), 4.60 (d, *J* = 9.5 Hz, 1 H, H-1$_B$), 4.55 (dd, *J* = 12.0, 1.5 Hz, 1 H, H-6$_{aB}$), 4.40 (dd, *J* = 12.0, 1.5 Hz, 1 H, H-6$_{aA}$), 4.15–4.05 (m, 2 H, H-6$_{bA}$, H-6$_{bB}$), 4.02–4.10 (m, 2 H, H-4$_A$, H-5$_B$), 3.75–3.65 (m, 1 H, H-5$_A$), 2.65 (s, 6 H, C*H*$_3$,

COCH_3), 2.10 (s, 3 H, COCH_3), 2.09 (s, 3 H, COCH_3), 2.05 (s, 3 H, COCH_3), 2.04 (s, 3 H, COCH_3), 2.01 (s, 3 H, COCH_3), 1.99 (s, 3 H, COCH_3), 1.86 (s, 3 H, COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.8 (*C*OCH$_3$), 170.1 (*C*OCH$_3$), 169.9 (*C*OCH$_3$), 169.7 (*C*OCH$_3$), 169.5 (*C*OCH$_3$), 169.0 (*C*OCH$_3$), 168.8 (*C*OCH$_3$), 168.6 (*C*OCH$_3$), 143.9, 138.1 (Ar-C), 96.1 (C-1$_B$), 84.3 (C-1$_A$), 75.9, 75.8, 72.8, 72.6, 72.1, 71.6, 69.2, 67.6, 61.4 (C-6$_B$), 61.3 (C-6$_A$), 27.8 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.5 (CO*C*H$_3$), 20.4 (3 C, 3 CO*C*H$_3$), 20.3 (CO*C*H$_3$), 20.2 (CO*C*H$_3$), 8.9 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 766.2283; found, 766.2275; Anal. Calcd. for $C_{31}H_{41}N_3O_{18}$ (743.66): C, 50.07; H, 5.56; found: C, 49.90; H, 5.70.

Compound 39 White solid; m.p. 161–162 °C; $[\alpha]_D$ + 6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85–7.65 (m, 4 H, Ar-H), 6.75 (d, *J* = 9.5 Hz, 1 H, H-1), 5.95 (t, *J* = 9.5 Hz, 1 H, H-3), 5.42, 5.30 (2 t, *J* = 9.5 Hz each, 2 H, H-2, H-4), 4.35–4.25 (m, 1 H, H-6$_a$), 4.25–4.05 (m, 2 H, H-5, H-6$_b$), 2.69 (s, 3 H, COCH_3), 2.60 (s, 3 H, CH_3), 2.09 (s, 3 H, COCH_3), 2.07 (s, 3 H, COCH_3), 1.90 (s, 3 H, COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.8 (*C*OCH$_3$), 169.9 (2 C, 2 *C*OCH$_3$), 168.9 (*C*OCH$_3$), 143.8–123.8 (Ar-C), 81.2 (C-1), 75.2 (C-3), 70.8 (C-4), 68.1 (C-5), 61.5 (C-6), 52.2 (C-2), 27.8 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.5 (CO*C*H$_3$), 20.3 (CO*C*H$_3$), 8.8 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 565.1547; found, 565.1540; Anal. Calcd. for $C_{25}H_{26}N_4O_{10}$ (542.49): C, 55.35; H, 4.83; found: C, 55.20; H, 5.00.

Compound 40 White solid; m.p. 188–190 °C; $[\alpha]_D$ + 5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76–7.68 (m, 4 H, Ar-H), 6.75 (d, *J* = 9.5 Hz, 1 H, H-1), 5.90 (t, *J* = 10.0 Hz, 1 H, H-3), 5.33 (t, *J* = 10.0 Hz, 1 H, H-4), 5.27 (t, *J* = 10.0 Hz, 1 H, H-2), 4.33 (dd, *J* = 12.0, 5.0 Hz, 1 H, H-6$_a$), 4.20 (dd, *J* = 12.0, 2.5 Hz, 1 H, H-6$_b$), 4.17–4.10 (m, 1 H, H-5), 3.87 (s, 3 H, COO*C*H$_3$), 2.71 (s, 3 H, CH_3), 2.10 (s, 3 H, COCH_3), 2.08 (s, 3 H, COCH_3), 1.89 (s, 3 H, COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1 (*C*OCH$_3$), 169.8 (*C*OCH$_3$), 169.0 (*C*OCH$_3$), 161.5 (*C*OOCH$_3$), 139.7–128.8 (Ar-C), 81.7 (C-1), 75.2 (C-3), 70.8 (C-4), 68.0 (C-5), 61.5 (C-6), 52.3 (C-2), 51.8 (COO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.5 (CO*C*H$_3$), 20.3 (CO*C*H$_3$), 8.7 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 581.1496; found, 581.1488; Anal. Calcd. for $C_{25}H_{26}N_4O_{11}$ (558.49): C, 53.76; H, 4.69; found: C, 53.60; H, 4.90.

Compound 41 Powder; $[\alpha]_D$ - 55 (*c* 1.0, H_2O); ^{1}H NMR (500 MHz, D_2O): δ 5.69 (d, *J* = 9.5 Hz, 1 H, H-1), 4.23 (t, *J* = 9.5 Hz, 1 H, H-4), 3.93 (d, *J* = 12.5 Hz, 1 H, H-6$_a$), 3.82–3.78 (m, 2 H, H-5, H-6$_b$), 3.74 (t, *J* = 9.5 Hz, 1 H, H-3), 3.64 (t, *J* = 9.0 Hz, 1 H, H-2), 2.68 (s, 3 H, CH_3), 2.65 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, D_2O): δ 196.8 (*C*O), 142.9 (Ar-C), 140.4 (Ar-C), 84.8 (C-1), 78.9 (C-3), 75.9 (C-4), 71.5 (C-2), 68.9 (C-5), 60.4 (C-6), 27.4 (*C*H$_3$), 8.4 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 310.1015; found, 310.1002; Anal. Calcd. for $C_{11}H_{17}N_3O_6$ (287.26): C, 45.99; H, 5.96; found: C, 45.75; H, 6.18.

Compound 42 Powder; $[\alpha]_D$ + 59 (*c* 1.0, H_2O); ^{1}H NMR (500 MHz, D_2O): δ 6.03 (br s, 1 H, H-1), 4.76 (br s, 1 H, H-2), 4.40 (dd, *J* = 9.0, 3.5 Hz, 1 H, H-3), 3.76–3.65 (m, 3 H, H-4, H-6$_{ab}$), 3.14–3.10 (m, 1 H, H-5), 2.58 (s, 3 H, CH_3), 2.56 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, D_2O): δ 196.9 (*C*O), 143.0 (Ar-C), 140.4 (Ar-C), 85.1 (C-1), 75.5 (C-5), 70.8 (C-3), 68.4 (C-2), 66.8 (C-4), 60.3 (C-6), 27.4 (*C*H$_3$), 8.7 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 310.1015; found, 310.1002; Anal. Calcd. for $C_{11}H_{17}N_3O_6$ (287.26): C, 45.99; H, 5.96; found: C, 45.77; H, 6.20.

Compound 43 Powder; $[\alpha]_D$ + 43 (*c* 1.0, H_2O); ^{1}H NMR (500 MHz, D_2O): δ 6.09 (br s, 1 H, H-1), 4.78 (br s, 1 H, H-2), 4.45 (dd, *J* = 9.0, 3.0 Hz, 1 H, H-3), 3.93 (s, 3 H, OCH_3), 3.84–3.74 (m, 3 H, H-4, H-6$_{ab}$), 3.21–3.19 (m, 1 H, H-5), 2.62 (s, 3 H, CH_3); ^{13}C NMR (125 MHz, D_2O): δ 169.7 (*C*OOCH$_3$), 141.4 (Ar-C), 136.1 (Ar-C), 85.2 (C-1), 75.4 (C-5), 70.8 (C-3), 68.4 (C-2), 66.7 (C-4), 60.3 (C-6), 52.4 (O*C*H$_3$), 8.5 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 326.0964; found, 326.0956; Anal. Calcd. for $C_{11}H_{17}N_3O_7$ (303.26): C, 43.56; H, 5.65; found: C, 43.35; H, 5.90.

Compound 44 Powder; $[\alpha]_D$ - 80 (*c* 1.0, H_2O); ^{1}H NMR (500 MHz, D_2O): δ 5.95 (br s, 1 H, H-1), 4.77 (br s, 1 H, H-2), 4.35 (dd, *J* = 3.5, 9.5 Hz, 1 H, H-3), 3.5 (t, *J* = 9.5 Hz, 1 H, H-4), 3.18–3.15 (m, 1 H, H-5), 2.54 (s, 3 H, CH_3), 2.52 (s, 3 H, CH_3), 1.15 (d, *J* = 6.5 Hz, 3 H, CH_3); ^{13}C NMR (125 MHz, D_2O): δ 196.8 (*C*O), 142.9 (Ar-C), 140.3 (Ar-C), 85.0 (C-1), 71.9 (C-3), 71.5 (C-2), 70.6 (C-4), 68.6 (C-5), 27.4 (*C*H$_3$), 16.5 (*C*H$_3$), 8.7 (*C*H$_3$); HRMS $[M + Na]^+$: Calcd. 294.1066; found, 294.1057; Anal. Calcd. for $C_{11}H_{17}N_3O_5$ (271.26): C, 48.70; H, 6.32; found: C, 48.48; H, 6.56.

Acknowledgements M.K. and I.B. thank CSIR, New Delhi for providing senior research fellowships. This work was supported by SERB, New Delhi (Project No. EMR/2015/000282) (AKM).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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