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K. Karthikeyan,[a,b] R. Senthil Kumar,[a] P. Dheenkumar[a] and Paramasivan T. Perumal[a,*]

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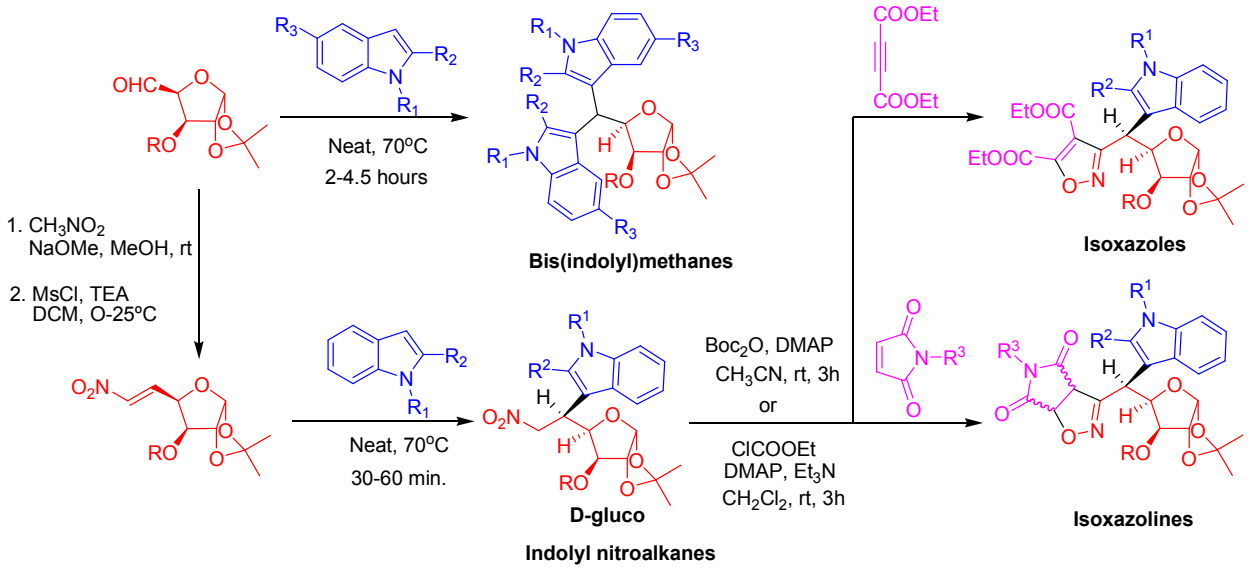

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Solvent and Catalyst free route to 3-indolyl glycoconjugates: Synthesis of sugar tethered isoxazolines and isoxazoles from 3-indolyl nitroalkanes

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An expedient, solvent and catalyst free strategy for the synthesis of sugar based bis(indolyl)methanes and indolyl nitroalkanes has been developed. The protocol works well with a wide range of substrates and tolerates various N/O protecting groups. The sugar tethered nitro alkanes were converted to the corresponding nitrile oxides and subsequently transformed to the novel isoxazolines and isoxazoles by cycloaddition with appropriate dipolarophiles.

Introduction

At the beginning of the new century, it was widely acknowledged that there is a growing need for developing environmentally benign processes in the chemical industry.[1,2] Many of the traditional organic solvents are volatile and are ecologically harmful. Hence, non conventional reaction media for chemical reactions are often highly sought after alternatives. These include, neat reaction, water, ionic liquids, eutectic melts, though the former is thus far proved to be the best.[1] Solvent-free reactions have many advantages such as reduced pollution, lower cost, operational safety etc.[3] On account of being non-toxic, non-flammable and abundant availability, water is the generally preferred alternative.[4] However, the lower solubility of reactants often makes water mediated reactions less yielding. Reaction under neat condition eliminates this issue as the reacting species are directly in contact leading to more effective collision. Thus, yields are often superior when compared with water or even conventional organic solvents as the media.

The 3-substituted indole moiety is ubiquitous in natural products and posses significant biological properties.[5-9] Various synthetic strategies, assisted by protic and Lewis acids, ionic liquids, ion exchange resin and rare earth metal have been described in the literature for bis(indolyl)methanes.[10] Michael addition is one of the most atom economic reactions in organic synthesis.[11] Among the Michael acceptors, nitro olefins are very attractive scaffolds, due to the synthetic versatility of nitro groups.[12,13] Indole is commonly used for Michael addition because many of its derivatives are found in nature and have versatile biological activity.[14] Traditionally, the Michael addition of indole to nitroalkenes is catalyzed by strong bases and Brønsted acids.[15] Recently, Lewis acids have been used to catalyze Michael addition, with high yields.[16]

Since both indoles and carbohydrates display useful biological activities, any synthesis that couples both indole and carbohydrate scaffolds will be quite interesting in anticipation of biological properties of the resultant product.

Results and discussion

In continuation of our studies in the area of heterocylic chemistry,[17] we herein report the synthesis of novel 3-indolyl glycoconjugates, sugar based isoxazolines and isoxazoles.

Synthesis of sugar tethered bis(indolyl)methanes

When Indole **1a** (2 mmol) was treated with the aldehyde **2a** (1 mmol) in solvents like acetonitrile, chloroform, the bis(indolyl)methane was not formed. With the use of Lewis or Brønsted acid catalyst, the desired product was obtained in poor yields. This may be attributed to the partial quenching of the acid catalyst by the multi oxygenated carbohydrate aldehyde. To circumvent the above problem, the reaction was attempted in the absence of catalyst and under neat condition. At room temperature stirring for 5-6 hours, the bis(indolyl)methane **3a** was obtained in 20% yield and unreacted starting materials accounted for the remaining of the mixture. However, when the temperature of the reaction is increased to 70 ^{o}C, the yield of **3a** increased to a maximum of 94%. (**Scheme 1**) To gauge the scope of this methodology, a variety of substituted indoles **1a-j** were reacted with the aldehydes **2a,b** and the corresponding bis(indolyl)methanes were obtained in good to excellent yields (**3a–l, Table 1**). The nature of substitution on the indole ring showed some effect on product yields and reactions times. Unsubstituted indole gave a maximum of 94 % yield whereas the relatively deactivated counterparts, the 5-bromo and 5-choloro derivatives gave 82 and 83% of the corresponding bis(indolyl)methanes. With N- substituted indoles such as N-Me, N-Propargyl and N-Et, the yield of bis(indolyl)methanes were around 90%.

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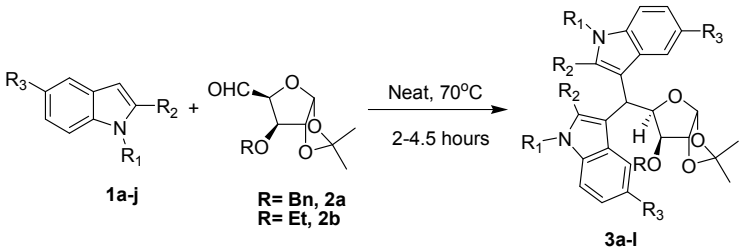


Scheme 1 Synthesis of Bis(indolyl)methanes

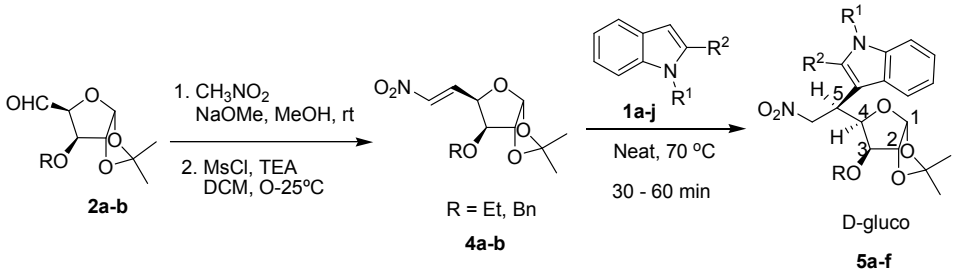
Table 1 Synthesis of Bis(indolyl)methanes

Entry	R	R_1	R_2	R_3	Product	Time (h)	Yield %
1	Bn	H	H	H	**3a**	3.0	94
2	Bn	H	H	OMe	**3b**	3.0	91
3	Bn	H	H	Br	**3c**	4.5	82
4	Bn	H	H	Cl	**3d**	4.5	83
5	Bn	Me	H	H	**3e**	2.5	90
6	Bn	Propargl	H	H	**3f**	4.5	89
7	Bn	Et	H	H	**3g**	3.0	92
8	Bn	H	Me	H	**3h**	3.5	88
9	Bn	Br-Bn	H	H	**3i**	4.5	80
10	Bn	Propargl	Me	H	**3j**	4.5	89
11	Et	H	H	H	**3k**	3.5	92
12	Et	Me	H	H	**3l**	4.0	90

[a] Isolated yield after column chromatography.

Michael addition of indoles to sugar derived nitrovinyl

Carbohydrate derived chiral Michael acceptors were used in the conjugate addition of carbon and hetero nucleophiles for the synthesis of various amino, thio and carbasugars.[18] However, additions of heteroaromatics like indole, pyrrole to such chiral Michael acceptors are not much explored. Such adducts, considering their synthetic versatility and biological activity of their individual moieties, would be anticipated to display useful biological properties and hence might serve as attractive targets for medicinal chemists in drug discovery. With the above objective in mind, we prepared a suitable Michael acceptor starting from D-glucose[19] and studied its Michael addition with various indoles. Literature report reveals a number of procedures using either Lewis or Brønsted acid as catalyst for the Michael addition of indoles to electron deficient olefins. However, use of Lewis acids such as indium trichloride, indium triflate, bismuth trichloride for model reactions did not yield the desired adduct probably because of the deactivation of Lewis acids by the multioxygenated carbohydrate moiety as mentioned earlier. On the other hand Brønsted acid catalysed reactions were attempted but the desired adducts were obtained in low yield because of the acidic pH of the medium which favours the acetal cleavage of the sugar moiety. Encouraged by the bis(indolyl) methane protocol, we next attempted the reaction under neat condition in the absence of catalyst. The reaction at room temperature did not give the product. However, when heated to 70 °C the desired Michael adducts were obtained in good to excellent yield. The reaction was highly stereoselective and only the D-gluco isomers were obtained in all the cases. (**Scheme 2, Table 2**) The stereochemistry of the products were assigned from the NMR values and correlation with our earlier work.[20]



Scheme 2 Synthesis of glycosyl nitroalkanes

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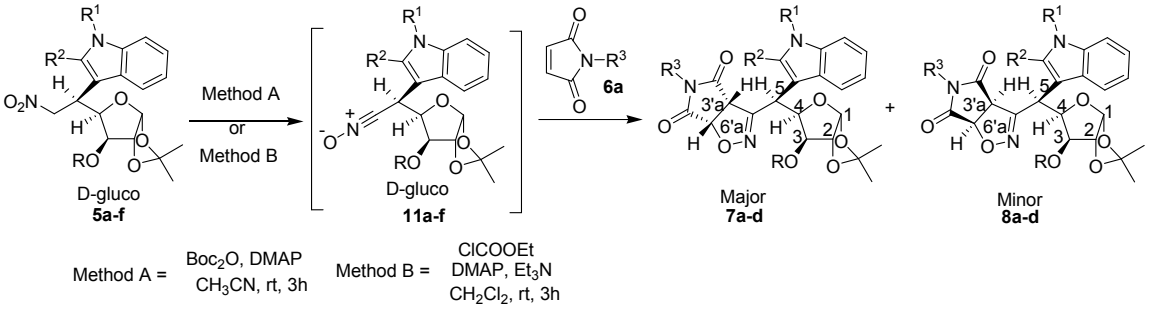
Table 2 Synthesis of glycosyl nitroalkanes

Entry	Nitrovinyl (**4**)	Indole (**1**)		Product (**5**)	Time (min)	Yield % [a]
		R^1	R^2			
1	**4a** (Bn)	Bn	H	**5a**	30	84
2	**4a**	H	Me	**5b**	40	80
3	**4a**	Me	H	**5c**	35	86
4	**4a**	4-Br-Bn	H	**5d**	60	70
5	**4a**	Et	H	**5e**	30	86
6	**4b**(Et)	H	Me	**5f**	30	75

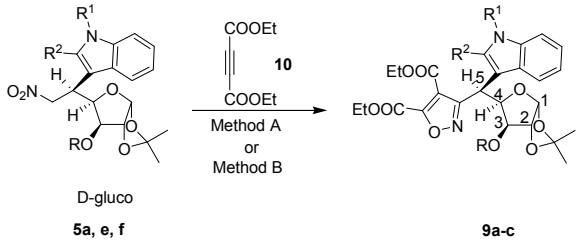
[a] Isolated yield after column chromatography.

Synthesis of sugar tethered isoxazoles and isoxazolines

The *in situ* generation of sugar tethered nitrile oxides[21] from the corresponding primary nitroalkanes and their regioselective conversion to isoxazolines and isoxazoles has been achieved. Thus, treatment of nitroalkanes **5a-f** with di-*tert*-butyl dicarbonate or ethyl chloroformate in the presence of 20 mol% equivalents of 4-dimethylaminopyridine (when using ethyl chloroformate, Et_3N (1 eqiv) was also added) and an excess of dipolarophile such as N-methyl maleimide **6a** or diethylacetylene dicarboxylate **10** at room temperature yielded the isoxazolines **7a-d, 8a-d (Scheme 3, Table 3)** or isoxazoles **9a-c (Scheme 4, Table 4).**



Scheme 3 Synthesis of glycosyl isoxazolines



Scheme 4 Synthesis of glycosyl isoxazoles

Table 3 Synthesis of glycosyl isoxazolines

Entry	Nitro alkanes **5**	R^3	Product **7, 8**	Method A			Method B		
				dr ratio[b]		Yield %[a]	dr ratio[b]		Yield %[a]
				7	**8**		**7**	**8**	
1	**5a**	Me	**7a, 8a**	65	35	74	72	28	80
2	**5b**	Me	**7b, 8b**	60	40	68	63	37	78
3	**5c**	Me	**7c, 8c**	64	36	78	74	24	81
4	**5d**	Me	**7d, 8d**	56	44	64	58	42	72

[a] Isolated yield after column chromatography.

[b] Determined by ^{1}H NMR spectrum of reaction mixture.

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Table 4 Synthesis of glycosyl isoxazoles

Entry	Nitro alkanes **5**	Product **9**	Yield %[a]	
			Method A	Method B
1	**5a**	**9a**	70	82
2	**5e**	**9b**	74	80
3	**5f**	**9c**	68	70

[a] Isolated yield after column chromatography.

Structural and stereochemical studies of diastereoisomers 7 and 8.

The systematic structure analysis of the two isomers to elucidate the exact regio and stereochemistry was performed using ^{1}H, ^{13}C and 2D NMR spectroscopic techniques.

Structural assignment of diastereoisomers (7d, 8d)

In the ^{1}H NMR spectrum of major diastereoisomer **7d,** the two doublets at δ 4.02 (J = 9.9 Hz) and 5.06 (J = 9.2 Hz) were assigned to H-3a′ and H-6a′ protons respectively. The doublet at δ 4.61 (J = 9.9 Hz) and doublet of doublet at δ 5.11 (J = 9.9, 3.1 Hz) were attributed to H-5 and H-4 protons respectively. In the ^{1}H NMR spectrum of minor diastereoisomer **8d,** the two doublet at δ 3.75 (J = 9.2 Hz) and 4.93 (J = 9.2 Hz) were assigned to H-3a′ and H-6a′ protons respectively. The doublet at δ 4.44 (J = 9.9 Hz) and doublet of doublet at δ 4.98 (J = 9.9, 3.1 Hz) were attributed to H-5 and H-4 protons respectively.

Stereochemical elucidation of the diastereoisomers (7d, 8d)

The stereochemistry of the diastereoisomers **7d**, **8d** were assigned by NOESY experiment. In the NOESY spectrum of major diastereoisomer **7d** shows, no correlation between H-3a′ and H-5 protons, but minor diastereoisomer **8d** shows H-3a′ proton make correlation with H-5 proton. From the above information, protons H-3a′ and H-5 are *trans* in the major diastereoisomer **7d** and *cis* in the minor diastereoisomer **8d**.

Structural assignment of isoxazoles 9b

In the ^{1}H NMR spectrum of **9b,** the two triplets at δ 1.09 (J = 6.9 Hz) and δ 1.36 (J = 6.9 Hz) ppm and two quartets at δ 4.07 (J = 6.9 Hz) and δ 4.39 (J = 6.9 Hz) ppm were assigned to the CH_3 and CH_2 of the two ethyl groups. The doublet at δ 5.16 (J = 10.7 Hz) ppm and doublet of doublet at δ 5.23 (J = 10.7, 3.1 Hz) ppm were assigned to H-5 and H-4 protons respectively.

Conclusions

In conclusion, we have developed an efficient synthetic protocol for sugar tethered bis-indolyl methanes. Key features of the protocol include solvent and catalyst free reaction condition, reduced reaction times, high yields and wide substrate scope. Further, stereoselective Michael addition was achieved with various indoles and sugar tethered Michael acceptors. The adducts were converted to the corresponding chiral isoxazolines and isoxazoles. The structure and stereochemistry of the products were assigned by NMR studies.

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[b]*Department of Chemistry, B.S.Abdur Rahman University, Vandalur, Chennai-600 048, India.*

† Electronic Supplementary Information (ESI) available: ^{1}H and ^{13}C NMR Spectrum of all compounds and NOESY spectrum of compounds **7d** and **8d.** See DOI: 10.1039/b000000x/

Experimental Section

IR measurements were done as KBr pellets for solids using Perkin Elmer Spectrum RXI FT-IR. The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with JEOL 500 MHz and Bruker 500 MHz high resolution NMR spectrometer. $CDCl_3$ was used as the solvent for the NMR spectral measurements and spectra were recorded in ppm with TMS as internal standard. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), multiplet (m), and broad (br). The mass were analyzed by using a Electrospray Ionisation Method with Thermo Finnigan Mass spectrometer. Melting points were determined in capillary tubes and are uncorrected. Elemental analyses were recorded using a Thermo Finnigan FLASH EA 1112 CHN analyzer. Analytical TLC was performed on precoated plastic sheets of silica gel G/UV-254 of 0.2mm thickness (Macherey-Nagel).

General procedure for the synthesis of Bis-indolyl methanes

A mixture of 3-*O*-benzyl-1,2-*O*-isopropylidene-xylopentadialdoses **2a,b** (1.00 mmol) and indoles **1a-j** (2.00 mmol) was stirred at 70 °C under neat condition for 2.5-4.5 h. The residue was dissolved in ethyl acetate (20 mL) and given a brine (1 X 20 ml) and water wash (2 X 20 mL). The ethyl acetate layer was dried over anhydrous Na_2SO_4 and removal of solvent under reduced pressure gave a crude product, which was purified by flash coloumn chromatography with ethyl acetate: petroleum ether (20:80) as a elutent to get the bis-indolyl methanes **3a-l** in 80-94% yield.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(1*H*-indol-3-yl)methyl)-1*H*-indole (3a) : Yellow solid; Mp = 132 °C; $[\alpha]^{26}_{D}$ = –91.90 (c 0.2, $CHCl_3$); IR 3402, 2929, 2324, 1078 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.57 (s, 3H), 3.71 (d, 1H, J = 2.3 Hz), 4.13 (d,1H, J = 12.2 Hz), 4.41 (d, 1H, J = 11.5 Hz), 4.58 (d, 1H, J = 3.8 Hz), 5.10 (m, 2H), 6.04 (d, 1H, J = 3.8 Hz), 6.89 (t, 1H, J = 7.6 Hz), 6.95-6.98 (m, 2H), 7.03 (t, 1H, J = 7.6 Hz), 7.11 (t, 1H, J = 7.6 Hz), 7.16 (dd, 2H, J = 6.9, 3.8 Hz), 7.22-7.23 (m, 2H), 7.25-7.28 (m, 4H), 7.46 (d, 1H, J = 8.4 Hz), 7.63 (d, 1H, J = 7.6 Hz), 7.90 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.4, 27.1, 32.9, 71.7, 81.6, 82.2, 83.1, 105.4, 110.9, 111.1, 111.5, 116.6, 117.7, 118.9, 119.3, 119.9, 120.0, 121.6, 121.9, 122.1, 122.1, 126.9, 127.5, 127.7, 129.4, 136.2, 136.6, 137.8; MS m/z = 495 M^{+}+1 ; Anal. Calcd for $C_{31}H_{30}N_2O_4$ (494.22): C, 75.28; H, 6.11;

N, 5.66. Found: C, 75.34; H, 6.15; N, 5.71.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(5-methoxy-1*H*-indol-3-yl)methyl)-5-methoxy-1*H*-indole (3b) : Pale yellow solid; Mp = 194 °C; $[\alpha]^{26}_D$ = –82.23 (c 0.2, $CHCl_3$); IR 3414, 2934, 2361, 1631, 1579, 1468 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.34 (s, 3H), 1.59 (s, 3H), 3.54 (s, 3H), 3.60 (s, 3H), 3.75 (d, 1H, *J* = 2.3 Hz), 4.04 (d, 1H, *J* = 11.5 Hz), 4.38 (d, 1H, *J* = 11.5 Hz), 4.59 (d, 1H, *J* = 3.9 Hz), 4.99 (d, 1H, *J* = 10.7 Hz), 5.11 (dd, 1H, *J* = 10.7, 2.3 Hz), 6.08 (d, 1H, *J* = 3.8 Hz), 6.69 (dd, 1H, *J* = 8.5, 2.3 Hz), 6.77 (dd, 1H, *J* = 8.4, 2.4 Hz), 6.90-6.93 (m, 2H), 7.04-7.06 (m, 2H), 7.11-7.13 (m, 4H), 7.24-7.26 (m, 3H), 7.89 (brs, 1H), 7.93 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.4, 27.1, 32.8, 55.6, 55.8, 71.9, 81.8, 82.4, 83.3, 101.1, 102.2, 105.5, 111.5, 111.5, 111.7, 111.9, 112.3, 116.4, 117.7, 122.8, 122.8, 127.5, 127.5, 127.7, 127.8, 128.4, 137.2, 131.8, 137.8, 153.4, 153.9; MS m/z = 555 M^++1 ; Anal. Calcd for $C_{33}H_{34}N_2O_6$ (554.24): C, 71.46; H, 6.18; N, 5.05. Found: C, 71.40; H, 6.14; N, 5.11.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(5-bromo-1*H*-indol-3-yl)methyl)-5-bromo-1*H*-indole (3c) : Orange solid; Mp = 140 °C; $[\alpha]^{26}_D$ = –29.71 (c 0.2, $CHCl_3$); IR: 3418, 2931, 1724, 1458 cm^{-1} ;^1H NMR (500 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.57 (s, 3H), 3.74 (d, 1H, *J* = 3.0 Hz), 4.14 (d, 1H, *J* = 10.7 Hz), 4.44 (d, 1H, *J* = 10.5 Hz), 4.62 (d, 1H, *J* = 3.8 Hz), 4.92 (d, 1H, *J* = 10.7 Hz), 5.04 (dd, 1H, *J* = 13.0, 2.3 Hz), 6.03 (d, 1H, *J* = 3.8 Hz), 6.96 (d, 1H, *J* = 8.4 Hz), 7.02 (d, 2H, *J* = 1.5, Hz), 7.07 (dd, 1H, *J* = 8.4, 1.5 Hz), 7.10-7.12 (m, 2H), 7.18 (dd, 1H, *J* = 8.4, 1.5 Hz), 7.23-7.26 (m, 3H), 7.64 (s, 1H), 7.67 (s, 1H), 8.02 (brs, 1H), 8.04 (brs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.3, 27.0, 32.8, 71.9, 81.9, 82.8, 105.3, 111.7, 112.4, 112.73, 112.77, 112.8, 115.7, 116.6, 122.1, 122.2, 123.1, 123.7, 124.5, 125.0, 127.8, 127.9, 128.4, 128.5, 128.8, 134.8, 135.2, 137.3; MS m/z = 651 M^++1, 653 M^++3, 655 M^++5; Anal. Calcd for $C_{31}H_{28}Br_2N_2O_4$ (650.04): C, 57.07; H, 4.33; N, 4.29. Found: C, 57.11; H, 4.28; N, 4.35.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(5-chloro-1*H*-indol-3-yl)methyl)-5-chloro-1*H*-indole (3d) : Yellow solid; Mp = 126 °C; $[\alpha]^{26}_D$ = –119.48 (c 0.18, $CHCl_3$); IR 3408, 2944, 1716, 1423 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): 1.33 (s, 3H), 1.59 (s, 3H), 3.76 (d, 1H, *J* = 2.3 Hz), 4.13 (d, 1H, *J* = 11.4 Hz), 4.45 (d, 1H, *J* = 11.4 Hz), 4.64 (d, 1H, *J* = 4.6 Hz), 4.94 (d, 1H, *J* = 11.4 Hz), 5.06 (dd, 1H, *J* = 10.3, 2.3 Hz), 6.04 (d, 1H, *J* = 3.8 Hz), 6.93–6.98 (m, 3H), 7.02 (d, 1H, *J* = 2.2 Hz), 7.05 (dd, 1H, *J* = 9.1, 2.3 Hz), 7.09–7.13 (m, 4H), 7.26–7.27 (m, 2H), 7.49 (d, 1H, *J* = 1.5 Hz), 7.52 (d, 1H, *J* = 2.3 Hz), 8.01 (s, 1H), 8.02 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 26.3, 27.0, 32.8, 71.9, 81.7, 81.9, 82.9, 105.3, 111.7, 112.3, 112.4, 115.7, 116.7, 118.9, 119.1, 121.9, 122.0, 123.3, 123.8, 124.7, 125.2, 127.7, 127.8, 127.9, 128.2, 128.5, 134.5, 134.9, 137.3; MS m/z = 563 M^++1; Anal. Calcd for $C_{31}H_{28}Cl_2N_2O_4$ (562.14): C, 66.08; H, 5.01; N, 4.97. Found: C, 66.13; H, 5.09; N, 5.91.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(1-methyl-1*H*-indol-3-yl)methyl)-1-methyl-1*H*-indole (3e) : Pale yellow solid; Mp = 120 °C; $[\alpha]^{26}_D$ = –86.70 (c 0.2, MeOH); IR: 2922, 2346,1465 cm-1; ^1H NMR (500 MHz, CDCl3): 1.33 (s, 3H), 1.60 (s, 3H), 3.66 (s, 3H), 3.74 (m, 4H), 4.12 (d, 1H, *J* = 12.2 Hz), 4.42 (d, 1H, *J* = 12.2 Hz), 4.59 (d, 1H, *J* = 3.85 Hz), 5.05-5.12 (m, 2H), 6.05 (d, 1H, *J* = 3.8 Hz), 6.89 (s, 1H), 6.92 (t, 1H, *J* = 8.4 Hz), 6.99 (t, 1H, *J* = 7.6 Hz), 7.10 (t, 1H, *J* = 7.6 Hz), 7.06–7.13 (m, 3H), 7.19–7.20 (m, 2H), 7.24–7.27 (m, 4H), 7.50 (d, 1H, *J* = 7.6 Hz), 7.68 (d, 1H, *J* =7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): 26.4, 27.1, 32.6, 32.8, 71.6, 81.6, 82.1, 83.3, 105.5, 108.9, 109.1, 113.4, 115.5, 116.5, 118.4, 118.8, 120.1, 120.2, 121.2, 121.4, 126.5, 126.7, 127.5, 127.6, 127.9, 128.3, 136.8, 137.3, 137.8; MS m/z = 523 M^++1; Anal. Calcd for $C_{33}H_{34}N_2O_4$ (522.25): C, 75.84; H, 6.56; N, 5.36. Found: C, 75.78; H, 6.50; N, 5.42.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(1-(prop-2-ynyl)-1*H*-indol-3-yl)methyl)-1-(prop-2-ynyl)-1*H*-indole (3f) : Colour less solid; Mp = 62-64 ºC; $[\alpha]^{26}_D$ = -6.0 (0.64, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.58 (s, 3H), 2.32 (t, 1H, *J* = 2.3 Hz), 2.35 (t, 1H, *J* = 2.3 Hz), 3.71 (s, 1H), 4.14 (d, 1H, *J* = 11.5 Hz), 4.42 (d, 1H, *J* = 11.5 Hz), 4.57 (d, 1H, *J* = 3.9 Hz), 4.75 (t, 2H, *J* = 2.3 Hz), 4.82 (d, 2H, *J* = 3.1 Hz), 5.08 (s, 2H), 6.05 (d, 1H, *J* = 3.8 Hz), 6.93 (t, 1H, *J* = 6.9 Hz), 6.99 (t, 1H, *J* = 7.6 Hz), 7.07 (s, 1H), 7.12 (t, 1H, *J* = 7.6 Hz), 7.17 – 7.21 (m, 4H), 7.25 – 7.28 (m, 4H), 7.34 (d, 1H, *J* = 8.4 Hz), 7.47 (d, 1H, *J* = 7.6 Hz), 7.62 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.4, 26.9, 32.9, 35.4, 35.8, 71.8, 73.2, 73.4, 78.0, 78.3, 81.6, 82.2, 83.0, 105.4, 109.1, 109.2, 111.4, 116.1, 117.0, 119.0, 120.3, 121.5, 121.8, 125.2, 125.3, 127.5, 127.6, 127.9, 128.5, 136.1, 136.4, 137.8; MS m/z = 571 M^++1; Anal. Calcd for $C_{37}H_{34}N_2O_4$ (570.25): C, 77.87; H, 6.01; N, 4.91. Found: C, 77.94; H, 6.11; N, 4.83.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(1-ethyl-1*H*-indol-3-yl)methyl)-1-ethyl-1*H*-indole (3g) : Colour less solid; Mp = 60-62 ºC; $[\alpha]^{27}_D$ = -11.3 (0.70, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.33 (s, 3H), 1.37 (t, 3H, *J* = 6.9 Hz), 1.43 (t, 3H, *J* = 6.9 Hz), 1.59 (s, 3H), 3.71 (s, 1H), 4.06 (q, 2H, *J* = 6.9 Hz), 4.10 – 4.14 (m, 3H), 4.42 (d, 1H, *J* = 11.5 Hz), 4.58 (d, 1H, *J* = 3.8 Hz), 5.11 (s, 2H), 6.06 (d, 1H, *J* = 3.8 Hz), 6.90 (t, 1H, *J* = 8.4 Hz), 6.97 (t, 1H, *J* = 7.6 Hz), 6.99 (s, 1H), 7.08 (t, 1H, *J* = 7.7 Hz), 7.14 – 7.17 (m, 3H), 7.21 – 7.29 (m, 6H), 7.47 (d, 1H, *J* = 7.7 Hz), 7.65 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.5, 15.6, 26.3, 27.0, 32.9, 40.8, 40.9, 71.7, 81.6, 82.3, 83.2, 105.4, 108.9, 109.1, 111.3, 115.4, 116.3, 118.2, 118.6, 120.2, 120.3, 120.9, 121.1, 124.9, 125.0, 127.4, 127.5, 127.6, 128.1, 128.3, 135.9, 136.2, 137.8; MS m/z = 551 M^++1; Anal. Calcd for $C_{35}H_{38}N_2O_4$ (550.28): C, 76.34; H, 6.96; N, 5.09. Found: C, 76.42; H, 6.88; N, 5.11.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(2-methyl-1*H*-indol-3-yl)methyl)-2-methyl-1*H*-indole (3h) : Yellow colour solid; Mp = 112-114 ºC; $[\alpha]^{27}_D$ = 175.7 (0.62, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.30 (s, 3H), 1.59 (s, 3H), 2.13 (s, 3H), 2.29 (s, 3H), 3.70 (d, 1H, *J* = 2.3 Hz), 4.11 (d, 1H, *J* = 12.3 Hz), 4.36 (d, 1H, *J* = 11.5 Hz), 4.53 (d, 1H, *J* = 4.6 Hz), 5.02 (d, 1H, *J* = 11.5 Hz), 5.48 (dd, 1H, *J* = 11.5, 3.8 Hz), 6.02 (d, 1H, *J* = 3.8 Hz), 6.91 – 6.98 (m, 3H), 7.02 (t, 1H, *J* = 7.7 Hz), 7.08 (d, 1H, *J* = 6.9 Hz), 7.14 (d, 1H, *J* = 8.4 Hz), 7.17 – 7.18 (m, 2H), 7.26 – 7.31 (m, 3H), 7.51 (s, 1H) 7.57 (s, 1H), 7.66 (dd, 2H, *J* = 7.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.5, 13.1, 26.2, 26.7, 26.9, 33.1, 71.4, 80.1, 81.7, 82.5, 105.3, 110.0, 110.1, 111.8, 111.9, 119.2,

119.5, 119.7, 120.2, 120.4, 127.5, 127.9, 128.2, 128.5, 131.5, 131.6, 135.1, 138.0; MS m/z = 523 M^++1; Anal. Calcd for $C_{33}H_{34}N_2O_4$ (522.35): C, 75.84; H, 6.56; N, 5.36. Found: C, 75.64; H, 6.60; N, 5.42.

1-(4-bromobenzyl)-3-((1-(4-bromobenzyl)-1*H*-indol-3-yl)((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)methyl)-1*H*-indole (3i): Green colour solid; Mp = 78-80 ºC; $[\alpha]^{27}_D$ = 95.4 (0.86, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.54 (s, 3H), 3.69 (s, 1H), 4.07 (d, 1H, *J* = 11.5 Hz), 4.45 (d, 1H, *J* = 11.5 Hz), 4.58 (d, 1H, *J* = 3.1 Hz), 5.12 -5.17 (m, 4H), 5.25 (s, 2H), 6.04 (d, 1H, *J* = 3.1 Hz), 6.81 (d, 2H, *J* = 8.4 Hz), 6.88 – 6.90 (m, 3H), 6.95 – 6.98 (m, 2H), 7.03 (t, 1H, *J* = 7.6 Hz), 7.07 (d, 1H, *J* = 7.6 Hz), 7.11 – 7.18 (m, 4H), 7.25 – 7.27 (m, 4H), 7.33 (d, 2H, *J* = 8.4 Hz), 7.37 (d, 2H, *J* = 7.6 Hz), 7.41 (d, 1H, *J* = 8.4 Hz), 7.59 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.3, 26.9, 33.4, 49.1, 49.3, 71.7, 81.4, 82.5, 105.4, 109.3, 109.5, 11.4, 115.9, 116.7, 118.8, 119.2, 120.2, 120.4, 121.1, 121.4, 121.5, 121.8, 126.1, 126.2, 127.3, 127.6, 128.1, 128.2, 128.3, 131.7, 131.8, 136.6, 136.7, 136.9, 137.2; MS m/z = 831 M^++1, 833 M^++3, 835 M^++5; Anal. Calcd for $C_{45}H_{40}Br_2N_2O_4$ (830.14): C, 64.91; H, 4.84; N, 3.36. Found: C, 64.95; H, 4.98; N, 3.33.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(2-methyl-1-(prop-2-ynyl)-1*H*-indol-3-yl)methyl)-2-methyl-1-(prop-2-ynyl)-1*H*-indole (3j) : Brown colour solid; Mp = 188-190 ºC; $[\alpha]^{27}_D$ = -84.3 (0.56, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.24 (s, 3H), 1.48 (s, 3H), 2.39 (s, 3H), 2.41 (s, 3H), 3.19 (s, 1H), 3.23 (s, 1H), 3.46 (s, 1H), 4.07 (d, 1H, *J* = 11.5 Hz), 4.46 (d, 1H, *J* = 11.5 Hz), 4.70 (d, 1H, *J* = 3.8 Hz), 4.84 (d, 1H, *J* = 11.5 Hz), 4.88 - 5.02 (m, 4H), 5.43 (d, 1H, *J* = 11.5 Hz), 5.88 (d, 1H, *J* = 3.8 Hz), 6.88 (t, 2H, *J* = 8.4 Hz), 6.97–7.03 (m, 2H), 7.17 (d, 2H, *J* = 6.9 Hz), 7.24 – 7.30 (m, 3H), 7.36 (d, 1H, *J* = 8.4 Hz), 7.43 (d, 1H, *J* = 7.6 Hz), 7.52 (d, 1H, *J* = 8.4 Hz), 7.62 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (125 MHz, DMSO-d_6): δ 11.2, 26.5, 26.9, 32.3, 32.5, 33.9, 71.1, 74.8, 79.6, 80.1, 80.2, 81.3, 82.1, 105.0, 109.6, 110.0, 110.8, 112.1, 112.4, 119.2, 119.3, 119.5, 120.4, 120.7, 120.8, 127.0, 127.6, 127.9, 128.0, 128.7, 133.1, 133.2, 135.9, 136.3, 138.2; MS m/z = 599 M^++1; Anal. Calcd for $C_{39}H_{38}N_2O_4$ (598.28): C, 78.24; H, 6.40; N, 4.68. Found: C, 78.35; H, 6.38; N, 4.73.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-ethoxy-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(1*H*-indol-3-yl)methyl)-1*H*-indole (3k) : Colour less solid; Mp = 100-102 ºC; $[\alpha]^{28}_D$ = -58.7 (0.72, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.09 (t, 3H, *J* = 6.9 Hz), 1.34 (s, 3H), 1.59 (s, 3H), 2.92-2.97 (m, 1H), 3.38-3.41 (m, 1H), 3.48 (s, 1H), 4.53 (d, 1H, *J* = 3.8 Hz), 5.04 (s, 2H), 6.03 (d, 1H, *J* = 3.8 Hz), 6.90 (t, 1H, *J* = 6.9 Hz), 6.99-7.07 (m, 3H), 7.12 (t, 1H, *J* = 7.7 Hz), 7.19–7.25 (m, 3H), 7.46 (d, 1H, *J* = 7.7 Hz), 7.75 (d, 1H, *J* = 7.7 Hz), 7.92 (s, 1H), 7.97 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.2, 26.4, 27.1, 32.7, 65.5, 81.8, 82.2, 83.2, 105.5, 111.0, 111.1, 111.4, 116.8, 117.9, 119.2, 119.8, 121.6, 121.8, 121.9, 122.3, 126.9, 127.5, 136.0, 136.6; MS m/z = 433 M^++1; Anal. Calcd for $C_{26}H_{28}N_2O_4$ (432.20): C, 72.20; H, 6.53; N, 6.48. Found: C, 72.32; H, 6.50; N, 6.49.

3-(((3a*R*,5*R*,6*S*,6a*R*)-6-ethoxy-tetrahydro-2,2-dimethylfuro[2,3-*d*][1,3]dioxol-5-yl)(1-methyl-1*H*-indol-3-yl)methyl)-1-methyl-1*H*-indole (3l) : Green Colour solid; Mp = 70-72 ºC; $[\alpha]^{28}_D$ = -88.3 (0.82, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.10 (t, 3H, *J* = 6.9 Hz), 1.34 (s, 3H), 1.60 (s, 3H), 2.91-2.96 (m, 1H), 3.37-3.41 (m, 1H), 3.47 (d, 1H, *J* = 3.1 Hz), 3.69 (s, 3H), 3.73 (s, 3H), 4.52 (d, 1H, *J* = 3.8 Hz), 4.98-5.06 (m, 2H), 6.02 (d, 1H, *J* = 3.8 Hz), 6.92 (t, 1H, *J* = 8.4 Hz), 6.97 (s, 1H), 7.07–7.12 (m, 2H), 7.16–7.20 (m, 3H), 7.25 (d, 1H, *J* = 6.9 Hz), 7.49 (d, 1H, *J* = 7.7 Hz), 7.80 (d, 1H, *J* = 7.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.2, 26.4, 27.1, 32.4, 32.8, 81.7, 82.3, 83.4, 105.6, 108.9, 109.0, 111.2, 115.8, 116.8, 118.4, 118.6, 119.9, 120.2, 121.2, 121.3, 126.3, 126.9, 127.5, 127.9, 136.7, 137.3; MS m/z = 461 M^++1; Anal. Calcd for $C_{28}H_{32}N_2O_4$ (460.24.): C, 73.02; H, 7.00; N, 6.08. Found: C, 72.88; H, 7.05; N, 6.01.

Experimental procedure for the synthesis of chiral nitroalkanes 5a-f

To a solution of 5, 6-dideoxy-5, 6-anhydro-6-nitro-3-*O*-benzyl-1,2-*O*-isopropylidene-D-glucofuranose **4 a-b** (1.00 mmol) in dichloromethane was added indole **1** (1.00mmol) and stirred for uniform mixing. The solvent was then evaporated under reduced pressure and the mixture was then heated under neat condition at 70 ^{o}C for appropriate time. After completion of the reaction, the residue was column chromatographed over silica gel using ethylacetate/petroleum ether (25/75) as eluent to get the pure product **5a-f**.

1-benzyl-3-((1*R*)-1-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)-2-nitroethyl)-1*H*-indole (5a) : Colourless solid; Mp 101-103 ˚C; IR (cm^{-1}): 3377. 2952, 2348, 1551, 1354, 756; $[\alpha]^{28}_D$ = –78.9 (c 0.52, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.30 (s, 3H, isopropylidene-CH_3), 1.47 (s, 3H, isopropylidene-CH_3), 3.80 (d, 1H, *J* = 3.1 Hz, *H*-3), 4.22 (d, 1H, *J* = 11.5 Hz, OC*H*HPh), 4.52-4.56 (m, 1H, *H*-5), 4.58-4.60 (m, 2H, OCH*H*Ph, *H*-2), 4.65 (dd, 1H, *J* = 6.9, 3.8 Hz, *H*-4), 4.89-4.90 (m, 2H, -CH_2NO$_2$), 5.15 (d, 1H, *J* = 16.1 Hz, NC*H*HPh), 5.25 (d, 1H, *J* = 16.1 Hz, NCH*H*Ph), 5.96 (d, 1H, *J* = 3.8 Hz, *H*-1), 6.80 (s, 1H, Ar-H), 7.04 (d, 2H, *J* = 7.6 Hz, Ar-H), 7.13 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.19 (t, 1H, *J* = 6.9 Hz, Ar-H), 7.24-7.36 (m, 9H, Ar-H), 7.66 (d, 1H, *J* = 7.6 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.3, 26.9, 35.4, 50.0, 71.8, 76.6, 80.2, 81.3, 82.4, 104.9, 110.0, 110.6, 111.9, 118.8, 119.9, 122.3, 126.2, 126.9, 127.5, 127.8, 128.0, 128.4, 128.8, 128.9, 136.7, 136.9, 137.4; MS m/z = 529 M^++1. Anal. Calcd for $C_{31}H_{32}N_2O_6$ (528.23): C, 70.44; H, 6.10; N, 5.30. Found: C, 70.52; H, 6.08; N, 5.12.

3-((1*R*)-1-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)-2-nitroethyl)-2-methyl-1*H*-indole (5b) : Yellow solid; Mp 207-209 ºC; IR (cm^{-1}): 3372, 2937, 2346, 1553, 1350, 751; $[\alpha]^{28}_D$ = -84.7 (0.2, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.21 (s, 3H, isopropylidene-CH_3), 1.31 (s, 3H, isopropylidene-CH_3), 2.24 (s, 3H, Indole-CH_3), 4.02 (d, 1H, *J* = 3.0 Hz, *H*-3), 4.04-4.09 (m, 1H, *H*-5), 4.59 (d, 1H, *J* = 11.4 Hz, -OC*H*HPh), 4.64-4.67 (m, 2H, *H*-4, CH*H*NO2), 4.77 (d, 1H, *J* = 11.4 Hz, OCH*H*Ph), 4.84 (d, 1H, *J* = 4.2 Hz, *H*-2), 5.01 (t, 1H, *J* = 11.4 Hz, C*H*HNO$_2$), 5.76 (d, 1H, *J* = 3.8 Hz, *H*-1), 6.89 (t, 1H, *J* = 6.9 Hz, Ar-H), 6.97 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.24 (d, 1H, *J* = 8.4 Hz, Ar-H), 7.32 (t, 1H, *J* = 6.8 Hz, Ar-H), 7.38 (t, 2H, *J* = 8.0 Hz, Ar-H), 7.45 (d, 2H, *J* = 6.9 Hz, Ar-H), 7.59 (d, 1H, *J* = 6.5 Hz, Ar-H), 10.85 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 11.9, 26.7, 27.1, 35.7, 71.0, 76.6, 78.8, 79.7,

80.8, 81.7, 104.4, 106.2, 111.2, 111.3, 118.3, 118.9, 120.5, 128.4, 128.6, 128.9, 134.2, 135.8, 138.2; MS m/z = 453 M^++1; Anal. Calcd for $C_{25}H_{28}N_2O_6$ (452.19): C, 66.36; H, 6.24; N, 6.19. Found C, 66.45; H, 6.20; N, 6.16.

3-((1*R*)-1-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)-2-nitroethyl)-1-methyl-1*H*-indole (5c) : Orange solid; Mp 189-191 ˚C; IR (cm^{-1}): 3372. 2954, 2346, 1550, 1352, 759; $[\alpha]^{28}_D$ = –176.9 (c 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.33 (s, 3H, isopropylidene-CH_3), 1.48 (s, 3H, isopropylidene-CH_3), 3.63 (s, 3H, indole-CH_3), 3.92 (d, 1H, *J* = 3.0 Hz, *H*-3), 4.45 (d, 1H, *J* = 11.5 Hz, OC*H*HPh), 4.48-4.52 (m, 1H, *H*-5), 4.63-4.67 (m, 2H, *H*-4, *H*-2), 4.75 (d, 1H, *J* = 11.5 Hz, OCH*H*Ph), 4.83 (dd, 1H, *J* = 13.0, 3.9 Hz, CH*H*NO_2), 4.90 (dd, 1H, *J* = 13.0, 9.2 Hz, C*H*HNO_2), 5.98 (d, 1H, *J* = 3.8 Hz, *H*-1), 6.71 (s, 1H, Ar-H), 7.13 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.22-7.28 (m, 2H, Ar-H), 7.40-7.47 (m, 5H, Ar-H), 7.64 (d, 1H, *J* = 8.4 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.3, 26.9, 32.9, 35.5, 71.6, 76.8, 80.3, 81.4, 81.9, 104.9, 109.6, 109.8, 111.8, 118.7, 119.5, 122.0, 126.9, 127.2, 128.4, 128.6, 128.9, 137.0; MS m/z = 453 M^++1. Anal. Calcd for $C_{25}H_{28}N_2O_6$ (452.19): C, 66.36; H, 6.24; N, 6.19. Found: C, 66.28; H, 6.18; N, 6.28.

1-(4-bromobenzyl)-3-((1*R*)-1-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)-2-nitroethyl)-1*H*-indole (5d) : Colourless solid; Mp 115-117 ˚C; IR (cm^{-1}); 3377. 2951, 2347, 1555, 1357, 759; $[\alpha]^{28}_D$ = –130.4 (c 0.90, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.31 (s, 3H, isopropylidene-CH_3), 1.48 (s, 3H, isopropylidene-CH_3), 3.80 (d, 1H, *J* = 3.1 Hz, *H*-3), 4.21 (d, 1H, *J* = 11.5 Hz, OC*H*HPh), 4.53-4.56 (m, 1H, *H*-5), 4.58-4.61 (m, 2H, *H*-2, OCH*H*Ph), 4.64 (dd, 1H, *J* = 6.9, 3.8 Hz, *H*-4), 4.93-4.95 (m, 2H, CH_2NO_2), 5.16 (d, 1H, *J* = 16.1 Hz, NC*H*HPh), 5.25 (d, 1H, *J* = 16.1 Hz, NCH*H*Ph), 5.98 (d, 1H, *J* = 3.8 Hz, *H*-1), 6.81 (s, 1H, Ar-H), 7.02 (d, 2H, *J* = 7.6 Hz, Ar-H), 7.13 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.21 (t, 1H, *J* = 6.9 Hz, Ar-H), 7.25-7.36 (m, 9H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.3, 26.9, 35.3, 50.1, 71.7, 76.6, 80.1, 81.4, 82.5, 104.8, 110.1, 110.7, 111.8, 118.9, 119.8, 122.2, 126.1, 126.8, 127.4, 127.9, 128.1, 128.4, 128.8, 128.9, 136.8, 136.9, 137.5; MS m/z = 607 M^++1. Anal. Calcd for $C_{31}H_{31}BrN_2O_6$ (606.14): C, 61.29; H, 5.14; N, 4.61. Found: C, 61.40; H, 5.16; N, 4.64.

3-((*R*)-1-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)-2-nitroethyl)-1-ethyl-1*H*-indole (5e) : Viscous Liquid; IR (cm^{-1}): 3376. 2964, 2348, 1555, 1352, 758; $[\alpha]^{28}_D$ = –16.3 (c 0.40, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.34 (s, 3H, isopropylidene-CH_3), 1.39 (t, 3H, *J* = 7.6 Hz, NCH_2CH_3), 1.50 (s, 3H, isopropylidene-CH_3), 3.91 (d, 1H, *J* = 3.1 Hz, *H*-3), 4.05 (q, 2H, *J* = 7.6 Hz, NCH_2CH_3), 4.46 (d, 1H, *J* = 11.5 Hz, OC*H*HPh), 4.53-4.57 (m, 1H, *H*-5), 4.66-4.68 (m, 2H, *H*-4, *H*-2), 4.76 (d, 1H, *J* = 11.5 Hz, OCH*H*Ph), 4.88-4.95 (m, 2H, -CH_2NO_2), 6.00 (d, 1H, *J* = 3.1 Hz, *H*-1), 6.82 (s, 1H, Ar-H), 7.14 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.24 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.33 (d, 1H, *J* = 8.4 Hz, Ar-H), 7.39-7.48 (m, 5H, Ar-H), 7.66 (d, 1H, *J* = 8.4 Hz, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.5, 26.3, 26.8, 35.5, 41.1, 71.7, 76.8, 80.3, 81.4, 82.2, 104.9, 109.7, 109.9, 111.8, 118.8, 119.5, 121.9, 125.2, 127.4, 128.2, 128.5, 128.9, 136.1, 137.1; MS m/z = 467 M^++1. Anal. Calcd for $C_{26}H_{30}N_2O_6$ (466.21): C, 66.94; H, 6.48; N, 6.00. Found: C, 66.74; H, 6.46; N, 6.12.

3-((1*R*)-1-((3a*R*,5*R*,6*S*,6a*R*)-6-ethoxy-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)-2-nitroethyl)-2-methyl-1*H*-indole (5f) : Yellow solid; Mp 160-162 °C; IR (cm^{-1}): 3378, 2957, 2343, 1576, 1350, 759; $[\alpha]^{30}_D$ = -129.60 (0.60, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.17-1.19 (m, 6H, isopropylidene-CH_3, OCH_2CH_3), 1.28 (s, 3H, isopropylidene-CH_3), 2.25 (s, 3H, indole-CH_3), 3.45-3.51 (m, 1H, OCH*H*CH_3), 3.70-3.75 (m, 1H, OC*H*HCH_3), 3.88 (d, 1H, *J* = 3.1 Hz, *H*-3), 3.97-4.01 (m, 1H, *H*-5), 4.60 (dd, 1H, *J* = 10.7 Hz, *J* = 3.1 Hz, *H*-4), 4.68 (d, 1H, *J* = 3.8 Hz, *H*-2), 4.79 (dd, 1H, *J* = 12.2, 4.6 Hz, -CH*H*NO_2), 5.01 (t, 1H, *J* = 11.4 Hz, -C*H*HNO_2), 5.72 (d, 1H, *J* = 3.8 Hz, *H*-1), 6.90 (t, 1H, *J* = 7.6 Hz, Ar-H), 6.97 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.23 (d, 1H, *J* = 8.4 Hz, Ar-H), 7.56 (d, 1H, *J* = 7.6 Hz, Ar-H), 10.84 (s, 1H, -NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 15.7, 26.7, 27.1, 35.9, 65.0, 76.9, 79.1, 81.4, 81.8, 104.4, 106.6, 111.1, 111.4, 118.3, 118.9, 120.5, 134.1, 135.9; MS m/z = 391 M^++1; Anal. Calcd for $C_{20}H_{26}N_2O_6$ (390.18): C, 61.53; H, 6.71; N, 7.18. Found C, 61.65; H, 6.75; N, 7.06.

Experimental procedure for glycosyl isoxazolines 7a-d, 8a-d and glycosyl isoxazoles 9a-c

Using di-*tert*-butyl dicarbonate [$(BOC)_2O$] and 4-dimethylaminopyridine (DMAP) catalyst

Di-*tert*-butyl dicarbonate (1.5 mmol) and N-methyl maleimide **6a** (1.5 mmol) or diethylacetylene dicarboxylate **10** (3 mmol) were dissolved in CH_3CN (5 mL) and DMAP (0.2 mmol) was added. The nitro compound **5a-f** (1 mmol) dissolved in CH_3CN (5 mL) was added in portions over a period of 1 h at room temperature to the dipolarophile solution and the reaction was allowed to proceed for further 3 h. After completion of the reaction, the solvent was evaporated under reduced pressure and the products were separated by column chromatography using silica gel (100-200 mesh) with ethyl acetate: petroleum ether as eluent to obtain isoxazolines **7a-d, 8a-d** or isoxazoles **9a-c**.

Using Ethyl Chloroformate and 4-Dimethylaminopyridine (DMAP) catalyst:

Et_3N (1.2 mmol), DMAP (0.2 mmol) and N-methyl maleimide **6a** (1.5 mmol) or Diethylacetylene dicarboxylate **10** (3 mmol) were dissolved in CH_2Cl_2 (5 mL). The nitro compound **5a-f** (1 mmol) and ethyl chloroformate (2 mmol) dissolved in CH_2Cl_2 (5 mL) was added in portions over a period of 1 h at room temperature to the dipolarophile solution and the reaction was allowed to proceed for further 3 h. The reaction mixture was washed with water and dil HCl. The organic layer was dried over anhydrous Na_2SO_4 and removal of solvent under reduced pressure gave a crude product, which was purified by column chromatography with ethyl acetate: petoleum ether as a elutent to obtain isoxazolines **7a-d, 8a-d** or isoxazoles **9a-c**.

(3a*R*,6a*S*)-3-((*R*)-(1-benzyl-1*H*-indol-3-yl)((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)methyl)-5-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione 7a : Colourless solid; Mp = 100-102 ºC; IR (cm^{-1}): 2981, 1727, 1660, 1495, 1382, 1196, 1044; $[\alpha]^{26}_D$ = -66.9 (1.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.26 (s, 3H, isopropylidene-CH_3), 1.43 (s, 3H, isopropylidene-CH_3), 2.46 (s, 3H, N-CH_3), 4.03 (d, 1H, *J* = 9.9 Hz, *H*-3a′), 4.36 (d, 1H, *J* = 12.2 Hz, OC*H*HPh), 4.43 (d, 1H, *J* = 3.1 Hz, *H*-3), 4.58-4.63 (m, 3H, *H*-2, *H*-5, OCH*H*Ph), 5.05 (d, 1H, *J* = 9.9 Hz, *H*-6a′), 5.13 (dd, 1H, *J* = 9.9, 3.1 Hz, *H*-4), 5.28 (s, 2H, NCH_2Ph), 5.87 (d, 1H, *J* =

3.8 Hz, *H*-1), 7.10 (t, 1H, *J* = 6.9 Hz, Ar-*H*), 7.15-7.18 (m, 3H, Ar-*H*), 7.22-7.25 (m, 3H, Ar-*H*), 7.27-7.30 (m, 5H, Ar-*H*), 7.36 (t, 2H, *J* = 6.9 Hz, Ar-*H*), 7.81 (d, 1H, *J* = 7.6 Hz, Ar-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.8, 26.4, 26.9, 35.9, 50.3, 56.3, 71.5, 78.4, 80.2, 82.2, 82.3, 104.7, 108.9, 110.2, 111.6, 119.4, 119.9, 122.1, 126.5, 126.9, 127.1, 127.5, 127.6, 127.7, 128.5, 128.6, 128.8, 137.1, 137.2, 154.3, 170.4, 172.5; MS m/z = 622 M^++1; Anal. Calcd for $C_{36}H_{35}N_3O_7$ (621.25): C, 69.55; H, 5.67; N, 6.76. Found: C, 69.41; H, 5.69; N, 6.85.

(3a*S*,6a*R*)-3-((*R*)-(1-benzyl-1*H*-indol-3-yl)((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)methyl)-5-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione 8a: Colourless solid; Mp = 66-68 ºC; IR (cm^{-1}): 2987, 1725, 1665, 1497, 1381, 1197, 1048; $[\alpha]^{26}_D$ = +30.9 (0.54, $CHCl_3$); H NMR (500 MHz, $CDCl_3$): δ 1.29 (s, 3H, isopropylidene-CH_3), 1.42 (s, 3H, isopropylidene-CH_3), 2.20 (s, 3H, N-CH_3), 3.75 (d, 1H, *J* = 9.2 Hz, *H*-3a′), 4.24 (d, 1H, *J* = 3.1 Hz, *H*-3), 4.38 (d, 1H, *J* = 11.5 Hz, OC*H*HPh), 4.45 (d, 1H, *J* = 9.9 Hz, *H*-5), 4.71 (d, 1H, *J* = 3.8 Hz, *H*-2), 4.76 (d, 1H, *J* = 11.5 Hz, OCH*H*Ph), 4.91 (d, 1H, *J* = 9.2 Hz, *H*-6a′), 5.00 (dd, 1H, *J* = 9.9, 3.8 Hz, *H*-4), 5.23 (s, 2H, NCH_2Ph), 5.94 (d, 1H, *J* = 3.8 Hz, *H*-1), 7.01 (t, 1H, *J* = 6.9 Hz, Ar-*H*), 7.05-7.08 (m, 2H, Ar-*H*), 7.15 (d, 3H, *J* = 7.7 Hz, Ar-*H*), 7.23-7.29 (m, 3H, Ar-*H*), 7.32-7.39 (m, 5H, Ar-*H*), 7.64 (d, 1H, *J* = 7.6 Hz, Ar-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.4, 26.4, 26.9, 36.5, 50.2, 57.5, 72.2, 78.9, 81.4, 82.0, 82.6, 104.9, 108.6, 109.9, 111.7, 119.4, 119.7, 121.7, 126.9, 127.1, 127.6, 128.2, 128.3, 128.6, 128.7, 128.8, 136.8, 137.3, 137.5, 153.8, 170.1, 172.5; MS m/z = 622 M^++1; Anal. Calcd for $C_{36}H_{35}N_3O_7$ (621.25): C, 69.55; H, 5.67; N, 6.76. Found: C, 69.70; H, 5.71; N, 6.52.

(3a*R*,6a*S*)-3-((*R*)-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)(2-methyl-1*H*-indol-3-yl)methyl)-5-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione 7b : Colourless solid; Mp = 210-212 ºC; IR (cm^{-1}): 2979, 1728, 1661, 1499, 1384, 1197, 1044; $[\alpha]^{27}_D$ = -13.4 (0.68, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.23 (s, 3H, isopropylidene-CH_3), 1.37 (s, 3H, isopropylidene-CH_3), 2.49 (s, 6H, N-CH_3, indole-CH_3), 3.81 (d, 1H, *J* = 9.2 Hz, *H*-3a′), 4.36 (d, 1H, *J* = 11.5 Hz, OC*H*HPh), 4.41-4.46 (m, 2H, *H*-3, *H*-5), 4.59-4.61 (m, 2H, *H*-2, OCH*H*Ph), 4.87 (d, 1H, *J* = 9.9 Hz, *H*-6a′), 5.12 (dd, 1H, *J* = 9.9, 3.1 Hz, *H*-4), 5.82 (d, 1H, *J* = 3.8 Hz, *H*-1), 7.00-7.58 (m, 3H, Ar-*H*), 7.21 (d, 2H, *J* = 7.7 Hz, Ar-*H*), 7.25-7.28 (m, 1H, Ar-*H*), 7.34 (t, 2H, *J* = 6.9 Hz, Ar-*H*), 7.50 (s, 1H, Ar-*H*), 7.91 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 11.8, 24.8, 26.4, 26.9, 29.7, 35.3, 56.4, 71.6, 78.3, 79.9, 82.3, 82.4, 104.5, 110.8, 111.7, 117.5, 119.5, 121.1, 126.6, 127.7, 128.5, 135.0, 135.5, 137.6, 154.2, 170.6, 172.6; MS m/z = 546 M^++1; Anal. Calcd for $C_{30}H_{31}N_3O_7$ (545.22): C, 66.04; H, 5.73; N, 7.70. Found: C, 66.21; H, 5.74; N, 7.79.

(3a*S*,6a*R*)-3-((*R*)-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)(2-methyl-1*H*-indol-3-yl)methyl)-5-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione 8b : Viscous liquid; IR (cm^{-1}): 2997, 1721, 1669, 1497, 1384, 1195, 1047; $[\alpha]^{27}_D$ = +108.4 (0.28, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.27 (s, 3H, isopropylidene-CH_3), 1.36 (s, 3H, isopropylidene-CH_3), 1.92 (s, 3H, indole-CH_3), 2.43 (s, 3H, NCH_3), 3.66 (d, 1H, *J* = 8.4 Hz, *H*-3a′), 4.23 (d, 1H, *J* = 9.9 Hz, *H*-5), 4.37-4.39 (m, 2H, *H*-3, OC*H*HPh), 4.71 (d, 1H, *J* = 3.8 Hz, *H*-2), 4.77 (d, 1H, *J* = 11.5 Hz, OCH*H*Ph), 4.95 (d, 1H, *J* = 8.4 Hz, *H*-6a′), 5.04 (dd, 1H, *J* = 9.9, 3.1 Hz, *H*-4), 5.90 (d, 1H, *J* = 3.8 Hz, *H*-1), 6.90 (t, 1H, *J* = 6.9 Hz, Ar-*H*), 6.97 (t, 1H, *J* = 7.6 Hz, Ar-*H*), 7.03 (d, 1H, *J* = 7.6 Hz, Ar-*H*), 7.18 (d, 1H, *J* = 7.7 Hz, Ar-*H*), 7.32-7.39 (m, 4H, Ar-*H*), 7.43 (d, 1H, *J* = 7.6 Hz, Ar-*H*), 8.12 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.2, 26.4, 26.8, 29.7, 31.9, 36.3, 57.7, 72.4, 79.1, 80.8, 82.4, 82.6, 104.8, 110.5, 111.7, 117.7, 119.6, 120.6, 128.2, 128.3, 128.7, 135.2, 136.7, 137.6, 153.1, 169.9, 172.5; MS m/z = 546 M^++1; Anal. Calcd for $C_{30}H_{31}N_3O_7$ (545.22): C, 66.04; H, 5.73; N, 7.70. Found: C, 65.95; H, 5.73; N, 7.84.

(3a*R*,6a*S*)-3-((*R*)-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)(1-methyl-1*H*-indol-3-yl)methyl)-5-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione 7c : Colourless solid; Mp = 86-88 ºC; IR (cm^{-1}): 2997, 1729, 1665, 1497, 1384, 1197, 1044; $[\alpha]^{27}_D$ = -108.3 (1.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.25 (s, 3H, isopropylidene-CH_3), 1.42 (s, 3H, isopropylidene-CH_3), 2.46 (s, 3H, NCH_3), 3.74 (s, 3H, indole-CH_3), 4.01 (d, 1H, *J* = 9.2 Hz, *H*-3a′), 4.35 (d, 1H, *J* = 12.2 Hz, OC*H*HPh), 4.42 (d, 1H, *J* = 3.8 Hz, *H*-3), 4.56 (d, 1H, *J* = 9.9 Hz, *H*-5), 4.59-4.62 (m, 2H, *H*-2, OCH*H*Ph), 5.00 (d, 1H, *J* = 9.2 Hz, *H*-6a′), 5.10 (dd, 1H, *J* = 9.9, 3.1 Hz, *H*-4), 5.86 (d, 1H, *J* = 3.8 Hz, *H*-1), 7.10 (t, 1H, *J* = 6.9 Hz, Ar-*H*), 7.18 (s, 1H, Ar-*H*), 7.21-7.24 (m, 3H, Ar-*H*), 7.29 (d, 2H, *J* = 7.7 Hz, Ar-*H*), 7.36 (t, 2H, *J* = 6.9 Hz, Ar-*H*), 7.78 (d, 1H, *J* = 8.4 Hz, Ar-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.7, 26.4, 26.9, 32.9, 35.8, 56.3, 71.5, 78.3, 80.3, 82.2, 82.3, 104.6, 108.2, 109.7, 111.6, 119.2, 119.6, 121.9, 126.5, 126.8, 127.6, 128.2, 128.9, 137.5, 137.6, 154.4, 170.5, 172.6; MS m/z = 546 M^++1; Anal. Calcd for $C_{30}H_{31}N_3O_7$ (545.22): C, 66.04; H, 5.73; N, 7.70. Found: C, 66.14; H, 5.77; N, 7.64.

(3a*S*,6a*R*)-3-((*R*)-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)(1-methyl-1*H*-indol-3-yl)methyl)-5-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione 8c : Colourless solid; Mp = 90-92 ºC; IR (cm^{-1}): 2996, 1727, 1661, 1490, 1384, 1196, 1048; $[\alpha]^{28}_D$ = -68.9 (1.32, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.29 (s, 3H, isopropylidene-CH_3), 1.43 (s, 3H, isopropylidene-CH_3), 2.33 (s, 3H, NCH_3), 3.70 (s, 3H, indole-CH_3), 3.79 (d, 1H, *J* = 9.2 Hz, *H*-3a′), 4.18 (d, 1H, *J* = 3.8 Hz, *H*-3), 4.40 (d, 1H, *J* = 11.5 Hz, OC*H*HPh), 4.49 (d, 1H, *J* = 9.9 Hz, *H*-5), 4.70 (d, 1H, *J* = 3.8 Hz, *H*-2), 4.75 (d, 1H, *J* = 11.5 Hz, OCH*H*Ph), 4.91 (d, 1H, *J* = 9.2 Hz, *H*-6a′), 4.99 (dd, 1H, *J* = 9.9, 3.1 Hz, *H*-4), 5.93 (d, 1H, *J* = 3.8 Hz, *H*-1), 6.98 (s, 1H, Ar-*H*), 7.03 (t, 1H, *J* = 7.6 Hz, Ar-*H*), 7.15 (t, 1H, *J* = 7.6 Hz, Ar-*H*), 7.21-7.24 (m, 1H, Ar-*H*), 7.32-7.37 (m, 5H, Ar-*H*), 7.62 (d, 1H, *J* = 8.4 Hz, Ar-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.6, 26.4, 26.9, 32.8, 36.2, 57.3, 72.1, 79.1, 81.2, 81.9, 82.3, 104.9, 108.2, 109.3, 111.7, 119.2, 119.4, 121.6, 126.8, 128.2, 128.4, 128.7, 129.0, 137.3, 137.4, 153.9, 170.3, 172.5; MS m/z = 546 M^++1; Anal. Calcd for $C_{30}H_{31}N_3O_7$ (545.22): C, 66.04; H, 5.73; N, 7.70. Found: C, 66.01; H, 5.74; N, 7.78.

(3a*R*,6a*S*)-3-((*R*)-(1-(4-bromobenzyl)-1*H*-indol-3-yl)((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)methyl)-5-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione 7d : Colourless solid; Mp = 70-72 ºC; IR (cm^{-1}): 2993, 1727, 1664, 1496, 1381, 1197, 1048; $[\alpha]^{28}_D$ = -69.9 (1.22, $CHCl_3$); ^{1}H NMR (500 MHz,

$CDCl_3$): δ 1.26 (s, 3H, isopropylidene-CH_3), 1.41 (s, 3H, isopropylidene-CH_3), 2.47 (s, 3H, NCH_3), 4.02 (d, 1H, *J* = 9.9 Hz, *H*-3a′), 4.35 (d, 1H, *J* = 12.3 Hz, OC*H*HPh), 4.42 (d, 1H, *J* = 3.8 Hz, *H*-3), 4.57-4.59 (m, 2H, *H*-2, OCH*H*Ph), 4.61 (d, 1H, *J* = 9.9 Hz, *H*-5), 5.06 (d, 1H, *J* = 9.2 Hz, *H*-6a′), 5.11 (dd, 1H, *J* = 9.9, 3.1 Hz, *H*-4), 5.21 (s, 2H, NCH_2Ph), 5.86 (d, 1H, *J* = 3.8 Hz, *H*-1), 7.01 (d, 2H, *J* = 8.4 Hz, Ar-*H*), 7.11 (t, 1H, *J* = 7.6 Hz, Ar-*H*), 7.16 (t, 1H, *J* = 8.4 Hz, Ar-*H*), 7.19-7.23 (m, 3H, Ar-*H*), 7.26-7.29 (m, 2H, Ar-*H*), 7.35 (t, 2H, *J* = 7.6 Hz, Ar-*H*), 7.41 (d, 2H, *J* = 8.4 Hz, Ar-*H*), 7.79 (d, 1H, *J* = 7.6 Hz, Ar-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.8, 26.3, 26.9, 35.9, 49.7, 56.3, 71.5, 78.4, 80.1, 82.2, 82.3, 104.6, 109.3, 110.1, 111.6, 119.5, 120.1, 121.6, 122.3, 126.5, 127.1, 127.6, 128.5, 128.6, 128.7, 131.9, 136.2, 136.9, 137.5, 154.2, 170.4, 172.5; MS m/z = 700 M^++1, 702 M^++3; Anal. Calcd for $C_{36}H_{34}BrN_3O_7$ (699.16): C, 61.72; H, 4.89; N, 6.00. Found: C, 61.85; H, 4.91; N, 6.05.

(3a*S*,6a*R*)-3-((*R*)-(1-(4-bromobenzyl)-1*H*-indol-3-yl)((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)methyl)-5-methyl-3a*H*-pyrrolo[3,4-*d*]isoxazole-4,6(5*H*,6a*H*)-dione 8d : Colourless solid; Mp = 78-80 ºC; IR (cm^{-1}): 2997, 1721, 1669, 1495, 1385, 1198, 1047; $[\alpha]^{28}_D$ = -1.2 (1.02, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.29 (s, 3H, isopropylidene-CH_3), 1.41 (s, 3H, isopropylidene-CH_3), 2.19 (s, 3H, NCH_3), 3.75 (d, 1H, *J* = 9.2 Hz, *H*-3a′), 4.26 (d, 1H, *J* = 3.8 Hz, *H*-3), 4.38 (d, 1H, *J* = 11.5 Hz, OC*H*HPh), 4.44 (d, 1H, *J* = 9.9 Hz, *H*-5), 4.71 (d, 1H, *J* = 3.8 Hz, *H*-2), 4.76 (d, 1H, *J* = 11.5 Hz, OCH*H*Ph), 4.93 (d, 1H, *J* = 9.2 Hz, *H*-6a′), 4.98 (dd, 1H, *J* = 9.9, 3.1 Hz, *H*-4), 5.16 (s, 2H, NCH_2Ph), 5.94 (d, 1H, *J* = 3.8 Hz, *H*-1), 7.00-7.03 (m, 3H, Ar-*H*) 7.06-7.08 (m, 3H, Ar-*H*), 7.32-7.40 (m, 7H, Ar-*H*), 7.62 (d, 1H, *J* = 7.6 Hz, Ar-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.4, 26.4, 26.9, 36.5, 49.6, 57.5, 72.8, 79.0, 81.2, 82.0, 82.5, 104.9, 108.8, 109.8, 111.7, 119.3, 119.8, 121.4, 121.9, 127.0, 128.2, 128.3, 128.5, 128.6, 128.7, 131.8, 136.4, 136.6, 137.5, 153.6, 170.2, 172.5; MS m/z = 700 M^++1, 702 M^++3; Anal. Calcd for $C_{36}H_{34}BrN_3O_7$ (699.16): C, 61.72; H, 4.89; N, 6.00. Found: C, 61.88; H, 4.90; N, 6.25.

Diethyl 3-((*R*)-(1-benzyl-1*H*-indol-3-yl)((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)methyl)isoxazole-4,5-dicarboxylate 9a : Viscous liquid; IR (cm^{-1}): 2989, 1727, 1667, 1496, 1382, 1198, 1041; $[\alpha]^{26}_D$ = +249.9 (0.58, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.05 (t, 3H, *J* = 7.6 Hz, $COOCH_2CH_3$), 1.29 (s, 3H, isopropylidene-CH_3), 1.37 (t, 3H, *J* = 7.6 Hz, $COOCH_2CH_3$), 1.46 (s, 3H, isopropylidene-CH_3), 3.89-4.00 (m, 2H, $COOCH_2CH_3$), 4.22-4.24 (m, 2H, *H*-3, OC*H*HPh), 4.39 (q, 2H, *J* = 7.6 Hz, $COOCH_2CH_3$), 4.58 (d, 1H, *J* = 11.5 Hz, OCH*H*Ph), 4.67 (d, 1H, *J* = 3.8 Hz, *H*-2), 5.12-5.27 (m, 4H, *H*-5, *H*-4, NCH_2Ph), 5.94 (d, 1H, *J* = 3.8 Hz, *H*-1), 7.00-7.02 (m, 2H, Ar-*H*), 7.05 (d, 2H, *J* = 6.9 Hz, Ar-*H*), 7.08 (t, 1H, *J* = 7.6 Hz, Ar-*H*), 7.15-7.17 (m, 3H, Ar-*H*), 7.20-7.27 (m, 6H, Ar-*H*), 7.72 (d, 1H, *J* = 7.6 Hz, Ar-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.8, 14.1, 26.5, 27.0, 34.7, 50.1, 61.6, 62.9, 71.9, 81.3, 81.8, 82.3, 105.1, 109.8, 111.4, 111.7, 114.8, 119.5, 119.9, 121.8, 126.9, 127.3, 127.6, 127.8, 127.9, 128.1, 128.4, 128.8, 136.9, 137.2, 137.5, 156.7, 160.1, 160.2, 162.8; MS m/z = 681 M^++1; Anal. Calcd for $C_{39}H_{40}N_2O_9$ (680.27): C, 68.81; H, 5.92; N, 4.12. Found: C, 68.92; H, 5.93; N, 4.31.

Diethyl 3-((*R*)-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)(1-ethyl-1*H*-indol-3-yl)methyl)isoxazole-4,5-dicarboxylate 9b : Viscous liquid; IR (cm^{-1}): 2999, 1727, 1664, 1491, 1388, 1198, 1046; $[\alpha]^{27}_D$ = +162.4 (0.88, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.09 (t, 3H, *J* = 6.9 Hz, $COOCH_2CH_3$), 1.29 (s, 3H, isopropylidene-CH_3), 1.36 (t, 3H, *J* = 7.6 Hz, $COOCH_2CH_3$), 1.43 (t, 3H, *J* = 6.9 Hz, NCH_2CH_3), 1.47 (s, 3H, isopropylidene-CH_3), 3.97-4.03 (m, 2H, NCH_2CH_3), 4.07 (q, 2H, *J* = 6.9 Hz, $COOCH_2CH_3$), 4.22-4.25 (m, 2H, *H*-3, OC*H*HPh), 4.39 (q, 2H, *J* = 6.9 Hz, $COOCH_2CH_3$), 4.59 (d, 1H, *J* = 11.5 Hz, OCH*H*Ph), 4.68 (d, 1H, *J* = 3.8 Hz, *H*-2), 5.16 (d, 1H, *J* = 10.7 Hz, *H*-5), 5.23 (dd, 1H, *J* = 10.7, 3.1 Hz, *H*-4), 5.95 (d, 1H, *J* = 3.8 Hz, *H*-1), 6.99 (s, 1H, Ar-*H*), 7.03 (t, 1H, *J* = 7.6 Hz, Ar-*H*), 7.13 (t, 1H, *J* = 7.6 Hz, Ar-*H*), 7.18-7.27 (m, 6H, Ar-*H*), 7.73 (d, 1H, *J* = 7.6 Hz, Ar-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.9, 14.1, 15.4, 26.5, 27.0, 34.5, 40.9, 61.6, 62.9, 71.9, 81.6, 81.9, 82.2, 105.1, 109.4, 110.8, 111.7, 114.7, 119.1, 119.9, 121.5, 126.5, 127.3, 127.9, 128.1, 128.4, 136.4, 137.2, 156.8, 160.1, 163.0; MS m/z = 619 M^++1; Anal. Calcd for $C_{34}H_{38}N_2O_9$ (618.26): C, 66.01; H, 6.19; N, 4.53. Found: C, 66.22; H, 6.11; N, 4.41.

Diethyl 3-((*R*)-((3a*R*,5*R*,6*S*,6a*R*)-6-ethoxy-tetrahydro-2,2-dimethylfuro[3,2-*d*][1,3]dioxol-5-yl)(2-methyl-1*H*-indol-3-yl)methyl)isoxazole-4,5-dicarboxylate 9c : Viscous Liquid; IR (KBr): 3476, 2931, 2345, 1727, 1556, 1349, 751 cm^{-1}; $[\alpha]^{30}_D$ = +139.34 (0.54, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.01 (t, 3H, *J* = 6.9 Hz, $COOCH_2CH_3$), 1.12 (t, 3H, *J* = 7.6 Hz, $COOCH_2CH_3$), 1.27 (s, 3H, isopropylidene-CH_3), 1.33 (t, 3H, *J* = 7.6 Hz, OCH_2CH_3), 1.41 (s, 3H, isopropylidene-CH_3), 2.42 (s, 3H, indole-CH_3), 3.16-3.19 (m, 1H, OCH*H*CH_3), 3.57-3.61 (m, 1H, OC*H*HCH_3), 4.05-4.08 (m, 2H, $COOCH_2CH_3$), 4.20 (d, 1H, *J* = 3.1 Hz, *H*-3), 4.36 (q, 2H, *J* = 7.6 Hz, $COOCH_2CH_3$), 4.59 (d, 1H, *J* = 3.8 Hz, *H*-2), 4.98 (d, 1H, *J* = 9.9 Hz, *H*-5), 5.26 (dd, 1H, *J* = 9.9, 3.1 Hz, *H*-4), 5.88 (d, 1H, *J* = 3.8 Hz, *H*-1), 6.95 (t, 1H, *J* = 6.9 Hz, Ar-*H*), 7.00 (t, 1H, *J* = 8.4 Hz, Ar-*H*), 7.16 (d, 1H, *J* = 6.9 Hz, Ar-*H*), 7.62 (d, 1H, *J* = 8.4 Hz, Ar-*H*), 7.83 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): 13.9, 14.0, 14.9, 26.5, 27.1, 29.8, 34.2, 61.7, 62.8, 65.9, 80.8, 82.3, 82.9, 104.9, 110.3, 111.6, 118.7, 119.4, 120.8, 123.5, 127.6, 133.4, 135.4, 155.6, 156.7, 160.5, 162.9; MS m/z = 543 M^++1; Anal. Calcd for $C_{28}H_{34}N_2O_9$ (542.33): C, 61.98; H, 6.32; N, 5.16. Found C, 61.90; H, 6.35; N, 5.31.

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