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Carbohydrate Research 343 (2008) 139–144
Carbohydrate RESEARCH

Note

A novel domino-click approach for the synthesis of sugar based unsymmetrical bis-1,2,3-triazoles

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Received 18 August 2007; received in revised form 22 October 2007; accepted 25 October 2007
Available online 30 October 2007

Abstract—Aryl or sugar azides were treated with allenylmagnesium bromide to generate 1,5-disubstituted-butynyl-*N*-aryl or *N*-glycosyl-1,2,3-bistriazoles in a domino fashion. Upon Cu(I) catalyzed 1,3-dipolar cycloaddition with sugar azides, these compounds afford novel unsymmetrical bis-1,2,3-triazoles in high yields.

Keywords: Bistriazoles; Domino addition; Click chemistry; 1,3-Dipolar cycloaddition

Copper-catalyzed click chemistry involving azides and terminal acetylenes has, in recent years, been the most widely used method for the synthesis of libraries of biologically active molecular frameworks, particularly for the regioselective synthesis of 1,2,3-triazoles.[1] The functional group tolerance of the Cu(I)-catalyzed procedure is exemplified in the synthesis of triazole-based analogues of the neuraminidase inhibitor zanamavir[2] and in the preparation of functionalized α-trifluoromethyl-substituted azahistidine analogues.[3] Similarly, by applying the click chemistry approach, *N*-glycosyl-triazoles based simple glycoside and oligosaccharide mimetics, glyco-macrocycles, glycopeptides, glyco-clusters, and carbohydrate arrays have been developed.[4] Triazole-substituted sugars have been explored as potential monovalent and multivalent galectin ligands[5a,b] and also for the investigation of substrate recognition[6] by the inhibition of glycosyltransferases.[7] Synthesis of oligomers with 1,2,3-triazole subunits is an emerging area in macromolecular chemistry and glycobiology with examples on the preparation of *N*-glycoside neoglycotrimers,[8] pseudo-oligosaccharides,[9] triazole linked disaccharides,[10] 1,2,3-triazolecarbohybrids,[11] glycoconjugates,[12] and neoglycoconjugates.[13]

Bistriazole based size-specific mRNA hairpin loop binding agents have been developed to target mRNAs coding for proteins,[14] which could be a promising approach in drug discovery. Recent studies have disclosed a series of 1,2,3-bistriazoles as potent HIV-1 protease inhibitors for the inhibition of viral replication.[15] Being inspired by the wide range of pharmacological activities and applications of *N*-glycosyl-triazoles and bistriazole systems with particular emphasis on their HIV-1 protease inhibitory potential, we envisaged the design and synthesis of a focused library of 1,5-disubstituted-1,2,3-triazoles and bis-1,2,3-triazoles with tunable hydrophilic lipophilic balance (HLB). An automated docking procedure revealed that these carbohydrate-based bistriazoles molecules can be promising non-peptide HIV protease inhibitors, based on their active site binding affinity.

A cascade reaction or tandem reaction or domino reaction is a consecutive series of intramolecular organic reactions, which often proceed via highly reactive intermediates. It allows the organic synthesis of complex multinuclear molecules from a single acyclic precursor in an ecologically and economically favorable way. We have earlier reported regiospecific domino addition of aromatic, as well as aliphatic, azides with metalated allenes, which results in the formation of 1,5-disubstituted triazoles in moderate to good yields.[16] The same strategy has been applied here for the synthesis of

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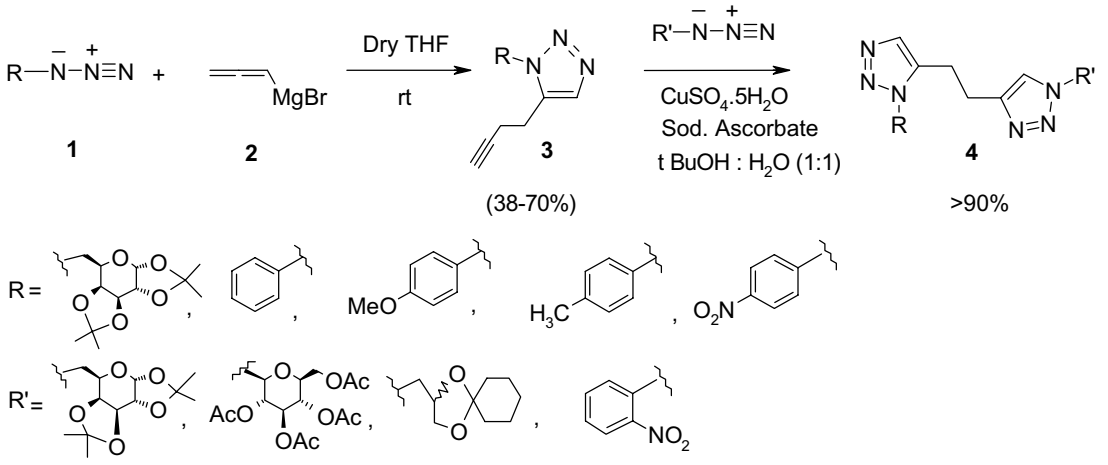
doi:10.1016/j.carres.2007.10.021

1,2,3-triazoles via addition of resonance-stabilized allenylmagnesium bromide to sugar azides, which resulted in the formation of novel 5-butynylated triazoles in good yields. These molecules, upon Cu(I) catalyzed 1,3-dipolar cycloaddition with sugar azides, generated novel unsymmetrical bis-1,2,3-triazoles (Scheme 1).

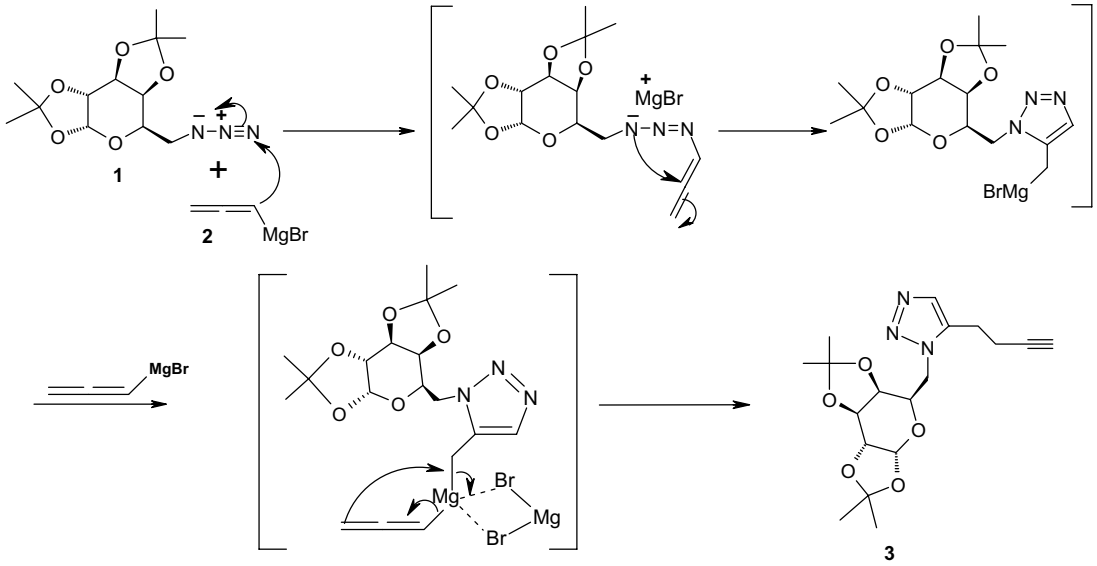
The formation of 1,5-disubstituted triazoles was unequivocally established through the characteristic chemical shift value of triazolyl proton (5-CH) at $\delta = 7.70$–7.75 ppm in non-sugar cases in contrast to the appearance of 4-CH signal at $\delta = 8.30$–8.38 in the case of 1,4-disubstituted triazoles.[17] In the case of sugar based-triazoles, the triazolyl proton (5-CH) was observed at $\delta = 7.55$ ppm.

A similar reaction involving azides and metalated alkynes is known to give the 1,5-disubstituted triazole regioisomers. Sharpless and co-workers reported the synthesis of 1,5-disubstituted triazoles through the addition of bromomagnesium acetylides to aryl azides[18] and proposed a mechanism beginning with the nucleophilic attack of the acetylide on the terminal nitrogen atom of the azide followed by spontaneous closure of the linear intermediate to the 4-metallotriazole species. The reaction of the bromomagnesium acetylides with azides gave, after hydrolysis, preferentially the 1,5-disubstituted triazoles; however, the yields were low. A plausible mechanism for the formation of unusual product in case of allenylmagnesium bromide can also be explained through a similar pathway involving nucleophilic attack of allenylmagnesium bromide species on the terminal nitrogen of the azide followed by concomitant ring closure through N–C heterocyclization driven by the excess of reagent. Subsequent attack by a second equivalent of allenylmagnesium species, probably through Shlenk[19] type of equilibrium, generates the final product (Scheme 2).

Sugar based bistriazoles (Table 1), were designed based on automatic docking studies, with an aim to

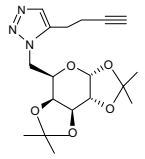
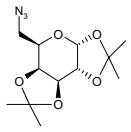
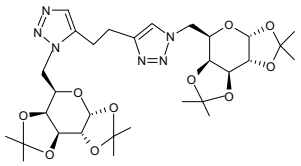
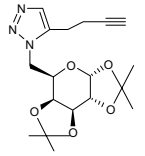
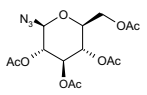
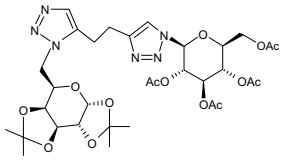
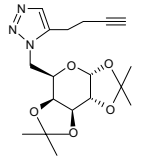
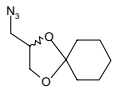
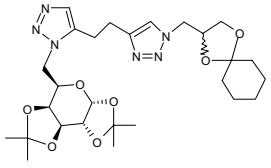
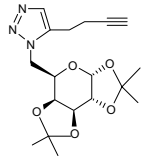
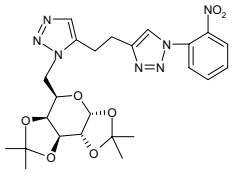
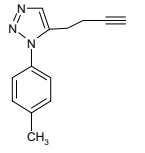
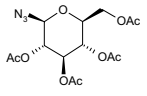
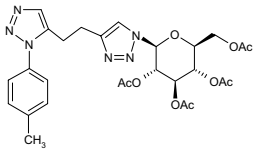
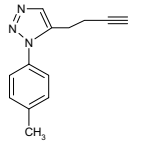
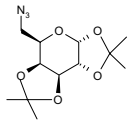
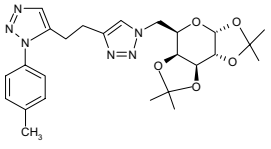
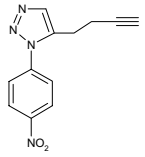
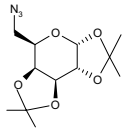
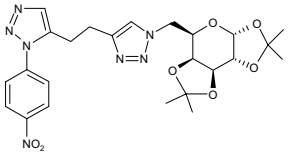
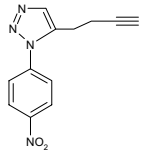
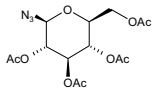
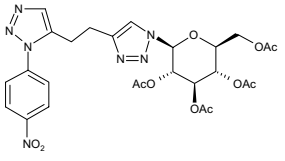
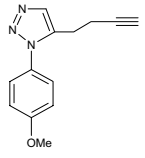
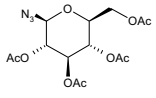
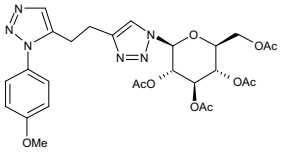
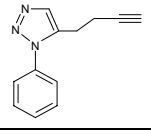
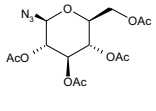
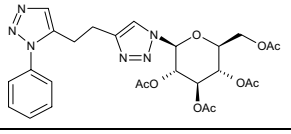


Scheme 1. Domino-click approach to novel bistriazoles.



Scheme 2. Plausible mechanism for the synthesis of 1,5-substituted triazoles.

Table 1. Bistriazoles

Entry	Triazole[a] **3**	Azide **1**	Bistriazole[a] **4**	Bistriazole yields (%)
a				94
b				96
c				92
d				93
e				94
f				92
g				94
h				95
i				94
j				92

[a] All products were characterized by IR, ^{1}H NMR, ^{13}C NMR, DEPT spectroscopy, and mass spectrometry.

screen them both in their protected form (as lipophilic ligands) and as unprotected sugars (hydrophilic ligands) against wild HIV-1 protease to evaluate their inhibitory potential. The design of binuclear hybrid structures of this type encompassing sugar units attached to both the heterocyclic moieties, separated by a flexible two carbon methylene spacer, would possibly provide a ligand capable of effective target binding with tunable hydrophilic lipophilic balance. Thus, the combination of domino addition and click approach provides a unique method for achieving structural diversity to generate novel unsymmetrical bisheterocyclic molecular frameworks, which may find utility in pharmaceutical and material science research. Currently, efforts are underway to screen this library against wild type HIV-1 protease to establish their inhibitory potential.

In conclusion, we have developed an unprecedented, convenient strategy for the synthesis of novel, biologically important unsymmetrical bis-1,2,3-triazoles employing a domino reaction followed by the copper catalyzed click protocol.

1. Experimental

1.1. General

All commercially available reagents were used as received. Air- and moisture-sensitive reactions were performed under nitrogen atmosphere. The progress of all reactions was monitored by TLC on a 2×5 cm precoated silica gel 60 F254 plates of thickness 0.25 mm (Merck). Melting points were determined on a Büchi capillary apparatus and are uncorrected. Optical rotations were recorded using a Perkin–Elmer 241 polarimeter. IR spectra were recorded on Bruker Vector 22 instrument. NMR spectra were recorded on a Bruker DPX 200 instrument in $CDCl_3$ with $(CH_3)_4Si$ as an internal standard for ^1H NMR spectra and solvent signals as internal standard for ^{13}C NMR spectra. ^1H NMR chemical shifts and coupling constants J are given in ppm (relative to $(CH_3)_4Si$) and Hz, respectively. Mass spectra were recorded on EIMS (Shimadzu) instrument and mass-spectrometric (MS) data are reported in m/z.

1.2. Preparation of 5-but-3-ynyl-1-(2,2,7,7-tetramethyl–tetrahydro-bis[1,3]dioxolo[4,5-*b*;4′,5′-*d*]pyran-5-ylmethyl)-1*H*-[1,2,3]triazole (Table 1, entry 3a); typical procedure

To a suspension of magnesium turnings (0.631 g, 26.31 mmol) in dried THF with mercury(II) chloride (6 mg, 2% w/w of propargyl bromide) was added propargyl bromide (2.35 mL of 80 wt%, solution in toluene, 26.31 mmol) in small portions while stirring the reaction mixture at rt (*Note*: a catalytic amount of mercuric chloride is generally required to promote formation of the Grignard reagent and a small grain of iodine is added as indicator for the formation of reagent). The mixture was stirred at rt for 30 min to give a cloudy light-green solution. Then the galactose azide solution in dry THF (Table 1, entry **1a**) (0.5 g, 1.75 mmol) was added dropwise to the above generated allenylmagnesium bromide. The reaction mixture was stirred at rt for 6 h. The reaction mixture was quenched with saturated aqueous ammonium chloride solution (10 mL) and diluted with EtOAc (50 mL). The organic layer was separated and the aqueous layer extracted with EtOAc (2×20 mL). The combined organic layers were dried over anhydrous sodium sulfate and evaporated under reduced pressure to afford the crude product, which was subjected to column chromatography (basic alumina, elution; *n*-hexane–EtOAc gradient) to afford the pure triazole (Table 1, entry **3a**) as a white solid (0.19 g, 38%); mp 134–136 °C; IR (KBr, cm^{-1}): 2984.2, 2920.8, 2867.9, 2371.3, 1802.3, 1763.0, 1735.4, 1718.4, 1595.6, 1508.4, 1465.9, 1438.4, 1387.5, 1352.6, 1244.2, 1213.4, 1168.3, 1110.5, 1070.1, 999.9, 920.8, 886.3, 862.1, 753.9, 670.0, 546.6 and 526.6; ^1H NMR (200 MHz, $CDCl_3$): δ 1.27 (s, 3H), 1.35 (s, 3H), 1.51 (s, 3H), 1.65 (s, 3H), 2.02 (t, 1H, $J = 2.6$ Hz), 2.51–2.59 (m, 2H), 2.95 (t, 2H, $J = 7.4$ Hz), 4.18 (dd, 1H, $J = 6.66$, 1.2 Hz), 4.28–4.32 (m, 3H), 4.37–4.50 (m, 1H), 4.63 (dd, 1H, $J = 5.4$, 2.5 Hz), 5.45 (d, 1H, $J = 4.9$ Hz), 7.54 (s, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 19.3, 23.8, 25.8, 26.3, 27.3, 27.4, 49.1, 69.2, 71.2, 71.8, 72.2, 72.4, 83.6, 97.5, 110.5, 111.1, 133.4, 138.1; ESI-MS: 364.1 [M+1], 386.1 $[M+Na]^+$. Anal. Calcd for $C_{18}H_{25}N_3O_5$: C, 59.49; H, 6.93; N, 11.56. Found: C, 59.54; H, 6.98, N, 11.52.

1.3. Preparation of bistriazole—Typical procedure

Galactose-butynyl triazole (Table 1, entry **3a**) (0.020 g, 0.055 mmol) was stirred in tertiary butanol and water (1:1 mixture, 5 mL). Copper sulfate (0.066 mmol) and sodium ascorbate (0.28 mmol) were added to the reaction mixture. After 15 min, galactose azide (Table 1, entry **1a**) (0.0157 g, 0.055 mmol) was added to the above mixture and the reaction mixture was allowed to stir for 8 h. The mixture was diluted with water and EtOAc was added. The organic layer was separated and the aqueous layer was extracted with EtOAc (2×20 mL). The combined organic layers were dried over anhydrous sodium sulfate and evaporated under reduced pressure to afford the crude product, which was precipitated using *n*-hexane–EtOAc affording pure 1,5-disubstituted-butynyl-*N*-glycosyl-1,2,3-bistriazole (Table 1, entry **4a**) as a light brown colored viscous mass (0.019 g, 94%).

1.3.1. Bistriazole (Table 1, entry 4a). Light brown colored viscous compound; $[\alpha]_D^{28}$ −11.6 (*c* 0.0014, CH_2Cl_2); IR ($CHCl_3$, cm^{-1}): 2920.8, 2857.4, 2730.6, 2371.3,

1846.2, 1751.6, 1595.1, 1508.5, 1458.3, 1338.8, 1353.1, 1259.2, 1214.5, 1166.2, 1110.7, 1070.3, 1005.9, 919.3, 902.9, 856.0, 735.2, 647.3, 599.8 and 513.0; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.27 (s, 3H), 1.29 (s, 3H), 1.35 (s, 3H), 1.36 (s, 3H), 1.38 (s, 3H), 1.42 (s, 3H), 1.48 (s, 3H), 1.50 (s, 3H), 2.97 (s, 4H), 4.16–4.64 (m, 12H), 5.43–5.51 (m, 2H), 7.27 (s, 1H), 7.40 (s, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.6, 22.7, 24.3, 24.4, 24.9, 24.9, 25.9, 26.0, 26.1, 29.7, 31.9, 47.7, 50.4, 67.2, 67.9, 70.2, 70.4, 70.7, 70.7, 71.0, 71.1, 96.1, 96.2, 109.0, 109.1, 109.7, 109.8, 122.5, 145.5; ESI-MS: 671.4 $[M+Na]^+$. Anal. Calcd for $C_{30}H_{44}N_6O_{10}$: C, 55.55; H, 6.84; N, 12.95. Found: C, 55.58; H, 6.88; N, 12.92.

1.3.2. Bistriazole (Table 1, entry 4b). Light brown colored viscous compound; $[\alpha]_D^{28}$ −18.8 (*c* 0.037, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 3399.9, 2988.9, 2937.3, 2360.6, 2341.6, 2120.1, 1756.2, 1647.5, 1557.9, 1456.5, 1435.6, 1375.0, 1219.9, 1166.5, 1067.0, 1042.2, 1006.7, 920.4, 904.1, 857.1, 756.1, 668.8 and 600.5; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.27–1.50 (m, 12H), 1.85 (s, 3H), 2.01–2.09 (m, 9H), 3.12 (s, 4H), 4.12–4.48 (m 10H), 5.38–5.49 (m, 3H), 5.82 (d, 1H, $J = 8.76$ Hz), 7.29 (d, 1H, $J = 6.03$ Hz), 7.47 (s, 1H); ^{13}C NMR (200 MHz, $CDCl_3$): δ 20.5, 20.9, 21.1, 22.8, 24.5, 25.3, 26.4, 48.2, 61.9, 62.1, 68.1, 68.3, 68.5, 70.6, 70.8, 71.2, 71.6, 73.1, 75.4, 88.3, 96.5, 106.8, 109.6, 110.2, 120.3, 132.5, 137.4, 146.9, 169.3, 169.8, 170.3, 171.0; ESI-MS: 737.2 [M+1]. Anal. Calcd for $C_{32}H_{44}N_6O_{14}$: C, 52.17; H, 6.02; N, 11.41. Found: C, 52.22; H, 5.98; N, 11.38.

1.3.3. Bistriazole (Table 1, entry 4c). Light yellow colored viscous compound; $[\alpha]_D^{28}$ −4.8 (*c* 0.0028, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 2920.7, 2339.6, 2107.1, 1720.7, 1630.9, 1590.0, 1509.4, 1382.6, 1350.9, 1282.3, 1097.3, 1039.2, 743.4 and 601.9; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.26–1.59 (m, 22H), 3.13 (s, 2H), 3.50 (s, 2H), 3.74 (d, 2H, $J = 5.62$ Hz), 4.08 (s, 1H), 4.22–4.64 (m, 8H), 5.45 (d, 1H, $J = 4.8$ Hz), 7.37 (d, 2H, $J = 3.46$ Hz); ^{13}C NMR (200 MHz, $CDCl_3$): δ 21.7, 22.7, 22.9, 23.5, 24.1, 24.4, 24.7, 24.8, 25.4, 26.4, 30.1, 35.1, 36.9, 48.2, 52.8, 65.6, 67.2, 69.7, 70.2, 73.5, 88.4, 94.2, 106.1, 122.9, 132.3; ESI-MS: 561.3 [M+1], 583.3 $[M+Na]^+$. Anal. Calcd for $C_{27}H_{40}N_6O_7$: C, 57.84; H, 7.19; N, 14.99. Found: C, 57.86; H, 7.24; N, 14.96.

1.3.4. Bistriazole (Table 1, entry 4d). Light brown colored viscous compound; $[\alpha]_D^{28}$ −20.74 (*c* 0.0054, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 3385.7, 3142.8, 2987.7, 2926.2, 2854.3, 2630.3, 2341.2, 1588.3, 1538.1, 1455.9, 1383.8, 1357.9, 1305.8, 1255.4, 1212.7, 1165.9, 1110.8, 1068.4, 1044.5, 1006.1, 919.5, 902.7, 883.9, 853.2, 749.6 and 668.9; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.20 (s, 3H), 1.25 (s, 3H), 1.35 (s, 3H), 1.51 (s, 3H), 3.23 (s, 4H), 4.23–4.66 (m, 6H), 5.42 (d, 1H, $J = 4.83$ Hz), 7.49–7.77 (m, 5H), 8.06 (d, 1H, $J = 7.9$ Hz); ^{13}C NMR (500 MHz, $CDCl_3$): δ 22.4, 24.0, 24.3, 24.8, 25.9, 26.0, 29.6, 48.0, 68.1, 70.3, 70.6, 71.2, 95.9, 109.1, 109.8, 123.0, 125.4, 127.8, 130.5, 130.6, 133.7; ESI-MS: 528.1 [M+1]. Anal. Calcd for $C_{24}H_{29}N_7O_7$: C, 54.64; H, 5.54; N, 18.59. Found: C, 54.68; H, 5.58; N, 18.63.

1.3.5. Bistriazole (Table 1, entry 4e). Light brown colored viscous compound; $[\alpha]_D^{28}$ −17.57 (*c* 0.0057, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 3419.3, 2925.2, 2854.0, 2360.8, 2340.9, 1753.4, 1652.5, 1558.5, 1518.6, 1431.2, 1369.9, 1324.6, 1225.8, 1094.9, 1040.4, 924.8, 823.9, 756.7 and 669.1; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.25 (s, 3H), 2.03–2.08 (m, 9H), 2.45 (s, 3H), 3.02–3.09 (m, 4H), 3.97–4.32 (m, 3H), 5.22–5.42 (m, 3H), 5.82 (d, 1H, $J = 8.08$ Hz), 7.27–7.32 (m, 4H), 7.46 (s, 1H), 7.56 (s, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 18.5, 18.9, 19.1, 19.6, 21.5, 22.6, 59.9, 66.0, 66.6, 68.4, 71.0, 73.5, 74.1, 84.0, 117.9, 123.5, 124.2, 128.6, 129.2, 132.5, 138.3, 144.6, 167.4, 167.8, 168.3, 168.9; ESI-MS: 585.2 [M+1], 607.2 $[M+Na]^+$. Anal. Calcd for $C_{27}H_{32}N_6O_9$: C, 55.47; H, 5.52; N, 14.37. Found: C, 55.45; H, 5.57; N, 14.34.

1.3.6. Bistriazole (Table 1, entry 4f). Light brown colored viscous compound; $[\alpha]_D^{28}$ −20.00 (*c* 0.0085, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 3422.9, 2924.1, 2853.4, 2361.4, 2340.2, 1752.6, 1654.8, 1612.1, 1598.7, 1526.6, 1501.3, 1458.9, 1383.6, 1345.1, 1253.9, 1214.0, 1067.9, 1048.0, 1019.5, 920.3, 903.5, 856.2, 753.6, 691.6 and 669.7; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.27 (s, 3H), 1.34 (s, 6H), 1.46 (s, 3H), 2.42 (s, 3H), 2.99–3.08 (m, 4H), 4.14–4.63 (m, 6H), 5.48 (d, 1H, $J = 4.85$ Hz), 7.26–7.42 (m, 6H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.7, 21.2, 22.2, 23.1, 23.9, 24.4, 24.9, 25.4, 25.5, 26.0, 31.1, 50.1, 66.7, 69.7, 69.8, 70.2, 70.7, 95.7, 108.6, 109.4, 124.6, 124.7, 129.7, 139.4; ESI-MS: 519.2 $[M+Na]^+$. Anal. Calcd for $C_{25}H_{32}N_6O_5$: C, 60.47; H, 6.50; N, 16.92. Found: C, 60.52; H, 6.48; N, 16.95.

1.3.7. Bistriazole (Table 1, entry 4g). Light yellow colored viscous compound; $[\alpha]_D^{28}$ −22.86 (*c* 0.0028, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 3378.4, 2986.6, 2925.8, 2955.2, 2360.1, 1733.8, 1653.1, 1518.3, 1456.4, 1383.2, 1307.3, 1255.1, 1212.5, 1166.0, 1111.1, 1068.8, 1005.9, 978.1, 919.5, 902.8, 858.0, 822.3, 755.7 and 667.6; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.24 (s, 3H), 1.29 (s, 3H), 1.36 (s, 3H), 1.48 (s, 3H), 3.03–3.24 (m, 4H), 4.12–4.20 (m, 2H), 4.31–4.42 (m, 2H), 4.54–4.66 (m, 2H), 5.49 (d, 1H, $J = 4.9$ Hz), 7.44 (s, 1H), 7.63–7.71 (m, 3H), 8.42 (d, 2H, $J = 8.9$ Hz); ^{13}C NMR (500 MHz, $CDCl_3$): δ 23.6, 24.4, 24.9, 25.9, 26.0, 29.7, 50.6, 67.2, 70.2, 70.7, 71.2, 96.2, 109.1, 109.9, 122.6, 125.1, 125.7, 133.3, 137.3, 141.2, 144.6, 147.9; ESI-MS: 528.2 [M+1]. Anal. Calcd for $C_{24}H_{29}N_7O_7$: C, 54.64; H, 5.54; N, 18.59. Found: C, 54.67; H, 5.58; N, 18.58.

1.3.8. Bistriazole (Table 1, entry 4h). Light brown colored viscous compound; $[\alpha]_D^{28}$ −13.33 (*c* 0.0037, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 3417.2, 2922.5, 2852.1, 2360.1, 2341.1, 2117.7, 1752.7, 1612.6, 1598.7, 1526.5, 1501.9, 1429.9, 1367.1, 1345.6, 1224.8, 1063.9, 1040.8, 978.7, 924.9, 856.1, 753.4, 691.9, 669.5 and 601.6; ^1H NMR (200 MHz, $CDCl_3$): δ 1.85 (s, 3H), 2.03–2.08 (m, 9H), 3.05–3.25 (m, 4H), 3.96–4.03 (m, 1H), 4.10–4.17 (m, 1H), 4.27–4.33 (m, 1H), 5.21–5.42 (m, 3H), 5.8 (d, 1H, $J = 8.9$ Hz), 7.51 (s, 1H), 7.63 (s, 1H), 7.71 (d, 2H, $J = 8.9$ Hz), 8.44 (d, 2H, $J = 8.9$ Hz); ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.2, 20.5, 20.6, 20.7, 23.3, 24.2, 61.5, 67.6, 70.1, 72.5, 75.2, 85.7, 119.6, 125.2, 125.5, 125.8, 133.3, 136.5, 141.6, 145.7, 147.6, 169.2, 169.7, 170.2; ESI-MS: 638.1 $[M+Na]^+$. Anal. Calcd for $C_{26}H_{29}N_7O_{11}$: C, 50.73; H, 4.75; N, 15.93. Found: C, 50.76; H, 4.77; N, 15.95.

1.3.9. Bistriazole (Table 1, entry 4i). Light brown colored viscous compound; $[\alpha]_D^{28}$ −12.07 (*c* 0.0027, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 3381.9, 2926.6, 2854.5, 2361.8, 2119.7, 1752.6, 1650.7, 1612.2, 1517.3, 1436.2, 1372.0, 1227.6, 1093.7, 1040.7, 922.1, 838.5, 757.4 and 667.1; ^1H NMR (200 MHz, $CDCl_3$): δ 1.85 (s, 3H), 2.01–2.11 (m, 9H), 3.04 (d, 4H, $J = 8.08$ Hz), 3.88 (s, 3H), 3.95–4.33 (m, 3H), 5.10–5.42 (m, 3H), 5.8 (d, 1H, $J = 8.9$ Hz), 7.04 (d, 2H, $J = 8.8$ Hz), 7.34 (d, 2H, $J = 8.9$ Hz), 7.47 (s, 2H); ^{13}C NMR (200 MHz, $CDCl_3$): δ 20.5, 20.9, 21.1, 23.5, 24.7, 30.1, 52.8, 56.0, 61.9, 68.1, 70.5, 71.1, 73.0, 75.6, 86.1, 115.2, 119.9, 127.2, 136.9, 146.6, 159.0, 160.9, 167.8, 169.8, 170.9; ESI-MS: 601.2 [M+1]. Anal. Calcd for $C_{27}H_{32}N_6O_{10}$: C, 54.00; H, 5.37; N, 13.99. Found: C, 54.03; H, 5.42; N, 13.97.

1.3.10. Bistriazole (Table 1, entry 4j). Light yellow colored solid; mp 109–111 °C; $[\alpha]_D^{28}$ −16.8 (*c* 0.0034, CH_2Cl_2); IR (KBr, cm^{-1}): 2920.8, 2846.8, 2360.8, 1752.5, 1630.9, 1596.7, 1498.9, 1456.6, 1377.4, 1229.4, 1102.6, 1039.2, 970.6, 917.7, 764.5, 690.6, 606.0 and 537.4; ^1H NMR (200 MHz, $CDCl_3$): δ 1.85 (s, 3H), 2.02–2.08 (m, 6H), 2.17 (s, 3H), 3.08–3.15 (m, 4H), 4.00 (m, 1H), 4.16 (m, 1H), 4.27 (m, 1H), 5.22 (m, 1H), 5.37–5.42 (m, 2H), 5.82 (d, 1H, $J = 9.24$ Hz), 7.42–7.57 (m, 7H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.1, 20.4, 20.5, 20.6, 22.7, 24.3, 29.3, 29.7, 61.5, 67.7, 69.5, 72.6, 75.2, 85.7, 119.4, 125.3, 129.6, 129.7, 132.6, 136.3, 136.6, 146.2, 168.9, 169.3, 169.8, 170.4; ESI-MS: 571.2 [M+1], 593.2 $[M+Na]^+$. Anal. Calcd for $C_{26}H_{30}N_6O_9$: C, 54.73; H, 5.29; N, 14.73. Found: C, 54.78; H, 5.31; N, 14.69.

Acknowledgments

The authors thank CSIR and UGC, New Delhi, for the award of fellowships to graduate students.

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