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ACID PROMOTED METAL FREE SYNTHESIS OF TRIAZOLE-FUSED HETEROCYCLES VIA INTRAMOLECULAR [3+2] CYCLOADDITION

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Abstract – A practical and efficient protocol for the synthesis of triazole-fused heterocycles through intramolecular metal free [3+2] azide-alkyne cycloaddition reaction is described. Range of acids was selected to demonstrate the reaction conditions. Organic azides and propargyl cations generated by acids gave fused triazoles including multivariate rings and heterocycles. Various fused triazoles and bistriazoles were obtained in good yields under mild reaction conditions.

Recently, a great deal of attention has been paid to the application of 1,2,3-triazoles due to their unique properties in material, biological, and medicinal chemistry.¹ 1,2,3-Triazoles are structural motifs increasingly found in a wide array of bioactive molecules in medicinal chemistry. The triazole derivatives are found in a large number of compounds possessing antibacterial activity, anti-HIV activity, antihistamine activity and applicable in the designing of new drugs.² Because triazoles fused heterocycles become increasingly common in pharmaceutical targets and biologically active substances, such as chemotherapeutic and cardiovascular agents,³ there is considerable interest in developing synthetic methods for their facile construction. Under metal-free conditions, procedure for synthesis of substituted 1,2,3-triazoles such as enamine/dienamine–azide cycloaddition, enolate–azide cycloaddition, strained alkyne–azide cycloaddition have also been reported in the literature,⁴ but have not been explored for the synthesis of fused 1,2,3-triazoles. Moreover, metal-free reactions normally require long reaction times,⁵ high temperature,⁶ the use of microwaves or photocatalysis,⁷ the substance became unstable with the

increasing of reactivity with light.⁸ So an intramolecular reaction should provide a powerful method for the synthesis of structurally different analogues, in particular polycyclic fused triazole derivatives. According to one of our ongoing research projects, we have developed a facile intermolecular metal free [3+2] azide-alkyne cycloadditions to synthesize various triazoles^{9a} and multicomponent coupling reactions of fully substituted triazoles.^{9b} Recently, our group reported an intramolecular cycloadditions of 5-azidopentynol with the scope of substituents on alcohols.^{9c} With this method in hand, we were interested in expanding the work to include multivariate rings and heterocycles. Herein, we report an efficient and high yielding method of synthesizing unique classes of triazole-fused heterocycles.

The azide-alkyne precursors are the reacting components in a contiguous carbon chain thereby yielding two new rings. One of the rings is the connecting triazole which is fused to the second 'major' ring, depending on the azidoalkyl chain leading to a variety of annulated triazoles. Using benzyl alcohol **1a** and **3a** as model substrates, cycloaddition reaction was conducted in the presence of various acids, and the reactions were quenched with a saturated sodium bicarbonate aqueous solution in order to produce triazole fused heterocycles (Table 1).

Table 1. Optimization of reaction conditions



Entry	Substrates	Acid	equiv	Temp (°C)	Time (min)	Yield (%) ^a
1	1a	BF ₃ ·OEt ₂	1.2	0 to rt	30	86
2	1a	TMSOTf	1.2	-20 to rt	30	88
3	1a	Sc(OTf) ₃	1.5	rt	120	48
4	1a	InCl ₃	1.5	rt	120	trace
5	1a	In(OTf) ₃	1.5	0 to rt	120	23
6	1a	TsOH·H ₂ O	1.2	rt	30	90
7	1a	MsOH	1.2	rt	60	87
8	1a	TFA	1.2	rt	30	94
9	1a	TFA	1.05	rt	60	82
10	1a	TFA	1.5	rt	30	93

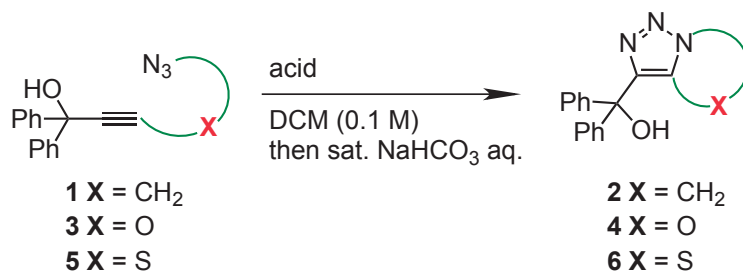
11	3a	TFA	1.2	rt	120	63
12	3a	TFA	2.0	rt	120	69
13	3a	MsOH	1.2	rt	60	51
14	3a	TsOH·H ₂ O	1.2	rt	120	59
15	3a	TMSOTf	1.2	0 to rt	30	85
16	3a	BF ₃ ·OEt ₂	1.2	rt	30	99

^a Isolation yield.

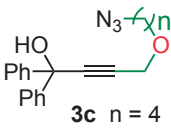
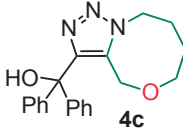
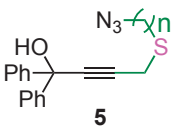
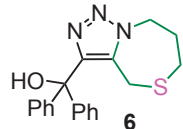
Firstly, the model reaction was performed with 1.2 equiv BF₃·OEt₂ at 0 °C, then risen to room temperature for 30 min to give desired triazole **2a** in good yield (86%, entry 1). TMSOTf showed similar activities to that of BF₃·OEt₂ (88%, entry 2). Sc(OTf)₃ worked to yield **2a** in moderate yield with longer reaction time at room temperature (48%, 120 min, entry 3). InCl₃ had a disappointing result to give the cyclized product **2a** in only a trace amount and In(OTf)₃ also resulted in a lower yield due to the competition of Meyer-Schuster rearrangement ketone (entries 4-5). Excitingly, protic acids showed much better activities than Lewis acids (entries 6-8). Specially, the optimal condition was achieved with trifluoroacetic acid (TFA), and the desired transformation was successfully demonstrated. With 1.2 equiv of TFA, benzyl alcohol **1a** could be converted to triazole **2a** in almost quantitative yield at ambient temperature (94%, entry 8). Reducing and increasing the equivalence of acid reagent could not get better results (entry 9-10). While, in the case of oxygen-heterocycle, under the same conditions, prolonged the reaction time of **3a** provided **4a** in moderate yield (63%, entry 11). Increasing loading of TFA to 2 equiv did not improve the yield (entry 12). MsOH and TsOH·H₂O were found to be as effective as TFA (entries 13-14). To our delight, we found Lewis acids can promote the reaction much more effective. When TMSOTf was used, **4a** could be produced in good yield in short reaction time (entry 15). Furthermore, when 1.2 equiv of BF₃·OEt₂ was used, the desired product **4a** was formed in almost quantitative yield at room temperature (entry 16).

Having established the optimal reaction conditions, a wide range of different substrates was explored and a series of triazole-fused heterocycles was obtained. The results were summarized in Table 2.

As mentioned above, with optimal conditions determined, our focus was directed toward studying the ‘major’ ring including multivariate rings and heterocycles which are yielded by the reacting components in a contiguous carbon chain of azide-alkyne precursors. Under the similar conditions for **2a** (entry 1), in the presence of 1.2 equiv TFA and the reaction temperature was set to rt, **1b** showed similar reactivity to give the triazole fused five-member cyclic compound **2b** in an excellent yield (entry 2). Then, the azidoalkyl chain was expanded to 7, 8 and 11 member leading to annulated triazoles to see the effect on

Table 2. Synthesis of triazole-fused heterocycles

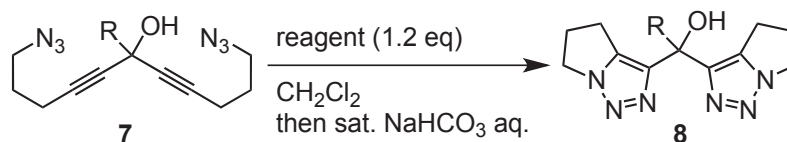
Entry	Substrates	Reagents	Conditions	Products	Yield (%) ^a
1	 1a n = 2	TFA	rt, 30 min	 2a	94
2	 1b	TFA	rt, 30 min	 2b	98
3	 1c n = 3	TFA	rt, 60 min	 2c	86
4	 1d n = 4	TFA	rt, 60 min	 2d	84
5	 1e n = 7	TFA	rt, 90 min	 2e	73
6	 1f	TFA	rt, 30 min	 2f	85
7	 3a n = 2	BF ₃ ·OEt ₂	rt, 30 min	 4a	99
8	 3b n = 3	BF ₃ ·OEt ₂	rt, 30 min	 4b	92

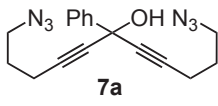
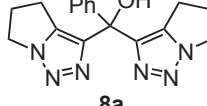
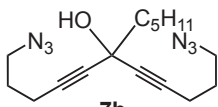
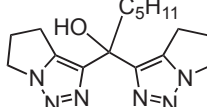
9	 3c n = 4	BF ₃ ·OEt ₂	rt, 30 min	 4c	85
10	 5	BF ₃ ·OEt ₂	rt, 60 min	 6	76
		TMSOTf	0 °C, 60 min		66
		TFA	rt, 60 min		41

^a Isolation yield.

the reactivity of cycloaddition reaction. Compared to the substrate **1a**, reaction proceeded sluggishly to give the cyclized products. **1c-d** could afford the desired 7 and 8 member triazoles **2c-d** in good yields (entry 3-4). **1e** showed lower reactivity to give the 11 member cyclized product **2e** with longer reaction time in 73% yield (entry 5). It should be noted that with diazido-propargyl compound **1f**, the corresponding cyclized product **2f** was demonstrated in good yield (entry 6). Based on this result, we designed the double [3+2] with diazido-dipropargyl to produce bistriazole products which will be discussed latter. Next, we examined the oxygen or sulphur-containing heteroatomic substrates. Under the similar conditions for **4a** (entry 7), in the presence of 1.2 equiv BF₃·OEt₂, heteroatomic substrates **3b** and **3c** also reacted smoothly to give triazole fused heterocycles **4b-c** in good yield (entry 8-9). Likewise, thiazepine triazole derivative **6** gave an essentially similar result (entry 10).

Table 3. Synthesis of bistriazoles-fused heterocycles



Entry	Substrates	Reagents	Conditions	Products	Yield (%) ^a
1	 7a	TsOH·H ₂ O	rt, 30 min	 8a	86
2	 7b	TsOH·H ₂ O	rt, 30 min	 8b	47
		BF ₃ ·OEt ₂	0 °C to rt, 30 min		65
		TMSOTf	0 °C to rt, 30 min		72

Interestingly, to develop the efficiency of our method, we conducted double [3 +2] reaction with dialkyne **7a-b** following the similar optimal conditions (Table 3). The coupled product bistriazoles **8a-b** were produced smoothly and **8a** was confirmed by X-ray crystallographic analysis (Figure 1).¹⁰

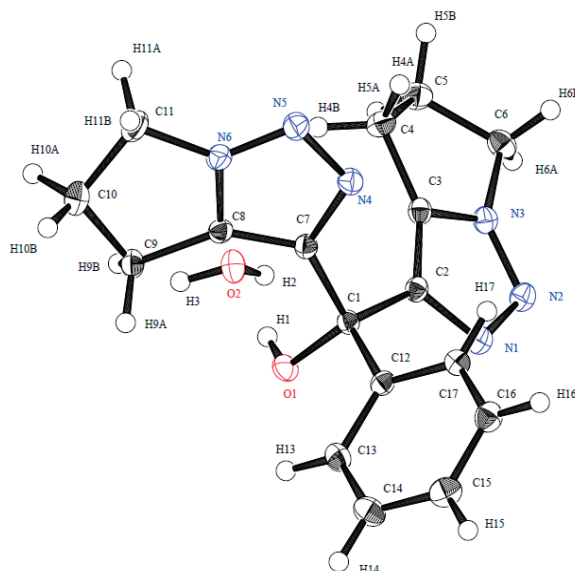
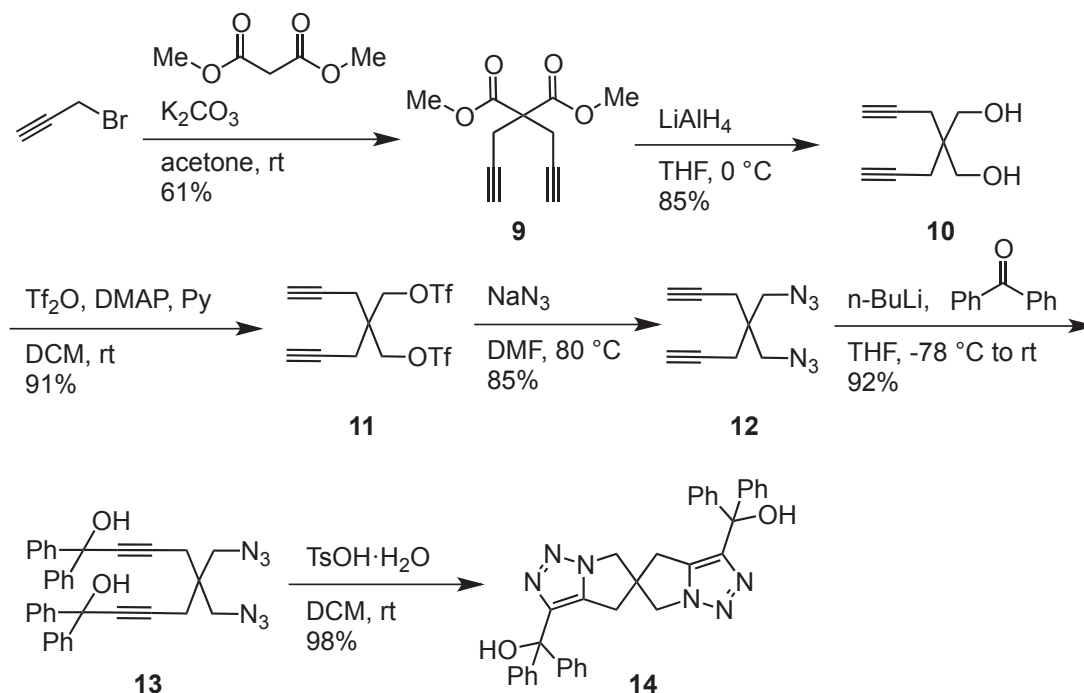


Figure 1. X-Ray structure of **8a**

Moreover, we also designed and synthesized the spiro bistriazole **14**. Beginning with common available 3-bromopropyne and dimethyl malonate, the known diol **10** was obtained after treatment with LiAlH_4 . Then converted into its corresponding ditriflate compound **11**, followed by azidation with NaN_3 , diazide



Scheme 1. Synthesis of the spiro bistriazole **14**

12 was generated smoothly. Reacted with benzophenone to give azido-propargyl alcohol **13** which underwent an intramolecular double cycloaddition, the spiro bistriazole **14** was demonstrated in the present of TsOH·H₂O with good to excellent yield.

In conclusion, we have developed an efficient intramolecular [3+2] cycloaddition of azido-propargyl alcohols to produce fused triazoles under metal-free conditions. Via propargyl cations derived from the corresponding alcohols, the desired triazoles was demonstrated in good yields under mild reaction conditions. Both carbon and hetero chain alkynes were acceptable, and the bistriazoles could also be afforded smoothly. This reaction provides a convenient and general method for the preparation of triazole-fused cyclic compounds. Our method can provide an extension of the preparation of triazoles and their uses in synthetic organic chemistry.

EXPERIMENTAL

Unless otherwise stated, all chemicals and solvents were of analytical grade and used without further purification. The ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AV-400 spectrometer and a JEOL JNM-ECP500 spectrometer with tetramethylsilane (TMS) as the internal standard. The chemical shifts were recorded in ppm and the following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet. Mass spectra were measured by an HP-1100 LC-MS spectrometer. X-Ray crystallography was performed on Rigaku R-AXIS RAPID/S imaging plate diffractometer. Flush column chromatography was performed by MERCK Silica gel 60. The progress of reactions was monitored by silica gel thin layer chromatography plates (MERCKTLC Silicagel 60 F₂₅₄).

Starting Materials. General experimental procedure of azido-propargyl alcohols were prepared using previously reported procedures,⁹ see ESI. All other chemicals in this study were commercially available.

Typical Procedure for the Preparation of Triazole-Fused Heterocycle

Diphenyl(4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-*a*]pyridin-3-yl)methanol (2a). To the mixture of azido-propargyl alcohol **1a** (47.0 mg, 0.154 mmol) in CH₂Cl₂ (2 mL) under nitrogen atmosphere, TFA (38.5 μL, 0.173 mmol, 1.2 equiv) was added at ambient temperature. After 30 min, the reaction was quenched with saturated sodium hydrogencarbonate aqueous solution, and was washed with brine. Drying the organic layer over magnesium sulfate followed by concentration in vacuo and silica gel column chromatography afforded triazole (EtOAc/petroleum ether = 1/4 to 1/1) afforded **2a** (44.1 mg, 94%). Colorless oil; R_f value 0.22 (EtOAc/petroleum ether = 1/2); ¹H NMR (500 MHz, CDCl₃) δ 7.32–7.28 (m, 10H), 4.34 (t, 2H, *J* = 6.0 Hz), 4.28 (br, 1H, OH), 2.00 (t, 2H, *J* = 7.0 Hz), 1.93 (m, 2H), 1.67 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 147.7, 145.2, 131.0, 127.9, 127.7, 127.5, 77.4, 46.6, 22.2, 20.6, 19.9; HRMS (ESI) calcd for C₁₉H₁₉N₃ONa [M+Na]⁺ 328.1426, found 328.1426.

(5,6-Dihydro-4*H*-pyrrolo[1,2-*c*][1,2,3]triazol-3-yl)diphenylmethanol (2b). White crystal; R_f value 0.10 (EtOAc/petroleum ether = 1/2); ^1H NMR (500 MHz, CDCl_3) δ 7.34–7.25 (m, 10H), 4.24 (t, 2H, $J = 7.5$ Hz), 4.19 (br-s, 1H, OH), 2.56 (tt, 2H, $J = 7.5, 7.5$ Hz), 2.07 (t, 2H, $J = 7.5$ Hz); ^{13}C NMR (126 MHz, CDCl_3) δ 145.5, 145.1, 140.2, 127.8, 127.34, 127.29, 76.6, 46.2, 27.9, 20.8; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 314.1269, found 314.1267.

Diphenyl(5,6,7,8-tetrahydro-4*H*-[1,2,3]triazolo[1,5-*a*]azepin-3-yl)methanol (2c). White solid; R_f value 0.37 (EtOAc/petroleum ether = 1/10); ^1H NMR (400 MHz, CDCl_3) δ 7.41–7.29 (m, 8H), 7.21–7.19 (m, 2H), 6.58 (s, 1H), 3.20 (t, 2H, $J = 6.8$ Hz), 2.24 (t, 2H, $J = 6.8$ Hz), 1.53–1.45 (m, 4H), 1.23–1.18 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 141.0, 139.0, 129.5, 128.4, 128.3, 126.6, 77.2, 51.2, 42.8, 28.6, 26.2, 23.7; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{21}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 342.1582, found 342.1582.

(4,5,6,7,8,9-Hexahydro-[1,2,3]triazolo[1,5-*a*]azocin-3-yl)diphenylmethanol (2d). White solid; R_f value 0.4 (EtOAc/petroleum ether = 1/10); ^1H NMR (400 MHz, CDCl_3) δ 7.41–7.29 (m, 8H), 7.21–7.19 (m, 2H), 6.58 (s, 1H), 3.22 (t, 2H, $J = 6.8$ Hz), 2.23 (t, 2H, $J = 6.8$ Hz), 1.57–1.46 (m, 4H), 1.30–1.23 (m, 2H), 1.21–1.13 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 141.0, 139.0, 129.5, 128.4, 128.3, 126.6, 77.2, 51.3, 42.9, 28.59, 28.57, 26.4, 24.0; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{23}\text{N}_3\text{ONa}$ $[\text{M}+\text{Na}]^+$ 356.1739, found 356.1747.

(5,6,7,8,9,10,11,12-Octahydro-4*H*-[1,2,3]triazolo[1,5-*a*][1]azacycloundecin-3-yl)diphenylmethanol (2e). White solid; R_f value 0.45 (EtOAc/petroleum ether = 1/10); ^1H NMR (400 MHz, CDCl_3) δ 7.40–7.28 (m, 8H), 7.20–7.19 (m, 2H), 6.58 (s, 1H), 3.25 (t, 2H, $J = 6.8$ Hz), 2.23 (t, 2H, $J = 6.8$ Hz), 1.61–1.54 (m, 2H), 1.52–1.45 (m, 2H), 1.35–1.31 (m, 10H); ^{13}C NMR (100 MHz, CDCl_3) δ 141.0, 139.0, 129.5, 128.4, 128.2, 126.6, 77.2, 51.4, 43.2, 29.22, 29.18, 29.1, 29.0, 28.8, 26.6, 24.3; HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{30}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 376.2389, found 376.2388.

(5-(Azidomethyl)-5,6-dihydro-4*H*-pyrrolo[1,2-*c*][1,2,3]triazol-3-yl)diphenylmethanol (2f). White solid; R_f value 0.38 (EtOAc/petroleum ether = 1/1); ^1H NMR (400 MHz, CDCl_3) δ 7.32 (s, 10H), 4.44 (dd, 1H, $J = 8.4, 12.0$ Hz), 4.12 (dd, 1H, $J = 8.4, 12.0$ Hz), 3.49–3.38 (m, 2H), 3.24–3.17 (m, 1H), 2.20 (dd, 1H, $J = 8.4, 12.0$ Hz), 1.92 (dd, 1H, $J = 8.4, 12.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 145.6, 145.2, 138.9, 128.0, 127.6, 127.3, 76.6, 53.5, 49.5, 42.3, 25.0; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{19}\text{N}_6\text{O}$ $[\text{M}+\text{H}]^+$ 347.1620, found 347.1627.

(6,7-Dihydro-4*H*-[1,2,3]triazolo[5,1-*c*][1,4]oxazin-3-yl)diphenylmethanol (4a). White solid; R_f value 0.25 (EtOAc/petroleum ether = 1/2); ^1H NMR (400 MHz, CDCl_3) δ 7.31 (s, 10H), 4.35 (t, 2H, $J = 4.2$ Hz), 4.12 (s, 2H), 3.99 (s, 1H), 3.93 (t, 2H, $J = 4.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 146.9, 145.1, 134.5, 128.1, 127.8, 127.4, 77.2, 63.0, 62.5, 45.7; HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{18}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ 308.1399, found 308.1402.

Diphenyl(4,6,7,8-tetrahydro-[1,2,3]triazolo[5,1-*c*][1,4]oxazepin-3-yl)methanol (4b). White solid; R_f value 0.18 (EtOAc/petroleum ether = 1/2); ^1H NMR (400 MHz, CDCl_3) δ 7.34–7.29 (m, 10H), 4.65 (t, 2H,

$J = 4.2$ Hz), 4.08 (s, 2H), 4.03 (s, 1H), 3.95 (t, 2H, $J = 4.2$ Hz), 2.03 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.1, 145.0, 134.2, 128.1, 127.8, 127.6, 77.6, 73.6, 62.1, 50.3, 29.0; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{20}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ 322.1556, found 322.1562.

Diphenyl(6,7,8,9-tetrahydro-4H-[1,2,3]triazolo[5,1-c][1,4]oxazocin-3-yl)methanol (4c). White solid; R_f value 0.25 (EtOAc/petroleum ether = 1/2); ^1H NMR (400 MHz, CDCl_3) δ 7.34–7.28 (m, 10H), 4.81 (t, 2H, $J = 4.2$ Hz), 4.10 (s, 2H), 3.65 (t, 2H, $J = 4.2$ Hz), 1.98 (tt, 2H, $J = 4.2, 4.2$ Hz), 1.52 (tt, 2H, $J = 4.2, 4.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 148.0, 144.9, 134.8, 128.2, 127.9, 127.7, 71.7, 63.4, 49.7, 29.7, 27.5, 24.5; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{22}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ 336.1712, found 336.1712.

Diphenyl(4,6,7,8-tetrahydro-[1,2,3]triazolo[5,1-c][1,4]thiazepin-3-yl)methanol (6). White crystal; R_f value 0.28 (EtOAc/petroleum ether = 1/1); ^1H NMR (400 MHz, CDCl_3) δ 7.31–7.28 (m, 10H), 4.56 (t, 2H, $J = 4.8$ Hz), 3.12 (s, 2H), 2.92–2.89 (m, 2H), 2.17–2.12 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.5, 144.8, 136.0, 128.1, 127.8, 127.7, 77.5, 50.5, 34.3, 28.8, 23.9; HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{20}\text{N}_3\text{OS}$ $[\text{M}+\text{H}]^+$ 338.1327, found 338.1320.

Bis(5,6-dihydro-4H-pyrrolo[1,2-c][1,2,3]triazol-3-yl)(phenyl)methanol (8a). White crystal; R_f value 0.14 ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 10/1$); ^1H NMR (500 MHz, CDCl_3) δ 7.57–7.55 (m, 2H), 7.31–7.28 (m, 2H), 7.25–7.22 (m, 1H), 5.72 (s, 1H, OH), 4.30–4.19 (m, 4H), 2.64–2.43 (m, 8H); ^{13}C NMR (126 MHz, CDCl_3) δ 144.8, 143.9, 140.2, 127.9, 127.4, 126.3, 71.9, 46.3, 27.9, 21.3; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{18}\text{N}_6\text{ONa}$ $[\text{M}+\text{Na}]^+$ 345.1440, found 345.1430.

1,1-Bis(5,6-dihydro-4H-pyrrolo[1,2-c][1,2,3]triazol-3-yl)hexan-1-ol (8b). White crystal; R_f value 0.1 ($\text{MeOH}/\text{CH}_2\text{Cl}_2 = 1/20$); ^1H NMR (500 MHz, CDCl_3) δ 4.31 (s, 1H, OH), 4.24 (t, 4H, $J = 7.5$ Hz), 2.98–2.87 (m, 4H), 2.71 (tt, 4H, $J = 7.5, 7.5$ Hz), 2.21–2.17 (m, 2H), 1.30–1.23 (m, 6H), 0.81–0.79 (m, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 144.7, 138.9, 71.3, 46.3, 41.4, 31.8, 28.1, 22.9, 22.5, 21.6, 14.0; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{24}\text{N}_6\text{ONa}$ $[\text{M}+\text{Na}]^+$ 339.1909, found 339.1903.

(4,4',6,6'-Tetrahydro-5,5'-spirobi[pyrrolo[1,2-c][1,2,3]triazole]-3,3'-diyl)bis(diphenylmethanol) (14). White solid; R_f value 0.36 ($\text{MeOH}/\text{CH}_2\text{Cl}_2 = 1/20$); ^1H NMR (400 MHz, CDCl_3) δ 7.32–7.27 (m, 20H), 4.34 (d, 2H, $J = 12.0$ Hz), 4.20 (d, 2H, $J = 12.0$ Hz), 2.29 (d, 2H, $J = 16.4$ Hz), 2.07 (d, 2H, $J = 16.4$ Hz); ^{13}C NMR (100 MHz, DMSO) δ 146.9, 146.3, 138.3, 127.6, 127.0, 126.7, 75.7, 60.1, 55.8, 34.7; HRMS (ESI) calcd for $\text{C}_{35}\text{H}_{30}\text{N}_6\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 589.2328, found 589.2326.

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SUPPORTING INFORMATION

Supplementary data (experimental procedures, compound characterization data and copies of NMR spectra for all products) associated with this article can be found, in the online version.

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10. Crystallographic data of **8a** has been deposited with Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-1549993. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/data_request/cif.