Synthesis and density functional theory study of [1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine derivatives: A novel heterocyclic system

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Several 3*H*-[1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine derivatives of a novel ring system have been synthesised. The initial substitution of the 4-Cl function of 2,4-dichloro-6-methylpyrimidin-5-amine with benzylamine followed by treatment with sodium nitrite generated 3-benzyl-5-chloro-7-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine. Nucleophilic substitution of the 5-Cl moiety of the latter compound with hydrazine hydrate and subsequent treatment with carbon disulfide in boiling pyridine gave, quantitatively, the corresponding [1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine derivatives. Density functional theory (DFT) studies were also performed to reveal regioselectivity of the ring closure *via* Gauge-Independent Atomic Orbital (GIAO) ^{1}H NMR calculations. The WP04 method was used as the DFT code to yield accurate chemical shift values. Theoretical results correlated well with the expected regioisomer and aided assignment of the final structure.

Keywords: [1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine, heterocyclisation, DFT, NMR spectroscopy

Nitrogen-containing heterocycles are important targets for synthetic endeavours because of their exciting biological properties and their roles as pharmacophores of many biologically active compounds.[1] Among them, triazolopyrimidines with a bridgehead nitrogen are interesting purine analogues as they possess significant therapeutic properties for pharmacological applications.[2] They have been reported to be versatile ligands in which their coordination compounds can be considered as model systems for the metal–ligand interactions observed in biological systems.[3–6] More specifically, as 1,2,4- and 1,2,3-triazolopyrimidines are interesting purine analogues, they possess significant therapeutic and pharmacological applications in their basic structures[2,7–10] including anticancer,[11] antitumor,[12] anti-inflammatory,[13] antibacterial,[14] antifungal[15] and antimalarial[16] properties.

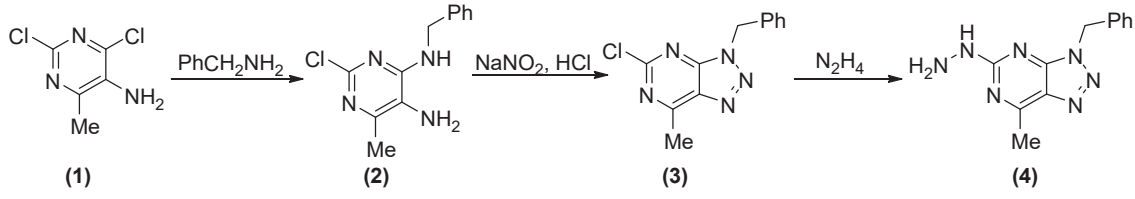
Additionally, these compounds have been used as important and useful starting materials for the synthesis of other fused heterocyclic systems.[17–19] Some recently published protocols for assembling this bicyclic system have been accomplished through a one-pot multicomponent reaction using substituted aromatic aldehydes, malononitrile and 3-amino-1,2,4-triazole catalysed by boric acid in aqueous micellar conditions,[20] oxidative cyclisation of 4-amino-6-arylidene(heteroarylmethylidene) hydrazinyl-1,3,5-triazin-2-ones with $Pb(OAc)_4$ *via* a Dimroth-type rearrangement,[21] treatment of chloro-5,6-diaminopyrimidines with $NaNO_2$/HCl[22] and cyclisation of diethyl 2,4,6-trifluorophenylmalonate with 3-amino-1,2,4-triazole.[11]

Regarding these points, and due to our interest in the synthesis of various fused heterocyclic derivatives with a pyrimidine core,[23–28] herein we wish to report a convenient method for the synthesis of 7-substituted-3-benzyl-9-methyl-3*H*-[1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine derivatives **6a**–**f** as members of a new heterocyclic system and theoretical evaluation of their ring closure orientation.

Results and discussion

The starting material, 2,4-dichloro-6-methylpyrimidin-5-amine **1**, can be easily obtained from the reduction of 2,4-dichloro-6-methyl-5-nitropyrimidine with iron powder in boiling acetic acid according to our previously published method.[29] Treatment of compound **1** with benzylamine in boiling *i*-PrOH and subsequent diazotisation in the presence of $NaNO_2$/HCl afforded 3-benzyl-5-chloro-7-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine **3** in quantitative yield (Scheme 1). The selective nucleophilic displacement of the C-4 chlorine atom in compound **1** by NH_2-containing nucleophiles proceeded according to our similar, previously reported, procedure.[30,31] This phenomenon can be explained *via* the repulsive interaction between the lone pairs on the pyrimidine ring nitrogen atoms and the NH_2 nucleophile, with the result that substitution of the Cl-2 function requires a higher temperature than the Cl-4 substituent. The 2-hydrazino-substituted derivative **4** was synthesised by treating compound **3** with hydrazine hydrate in boiling EtOH. The spectral and microanalytical data of the entire range of synthesised compounds **2**–**4** have been summarised in the experimental section.

While investigating the treatment of compound **4** with CS_2 in dry pyridine, as depicted in Scheme 2, to obtain either the corresponding 3-benzyl-9-methyl-3*H*-[1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine-7(6*H*)-thione **5** or the isomeric 1-benzyl-4-methyl-1*H*-[1,2,3]triazolo[4,5-*e*][1,2,4]



Scheme 1

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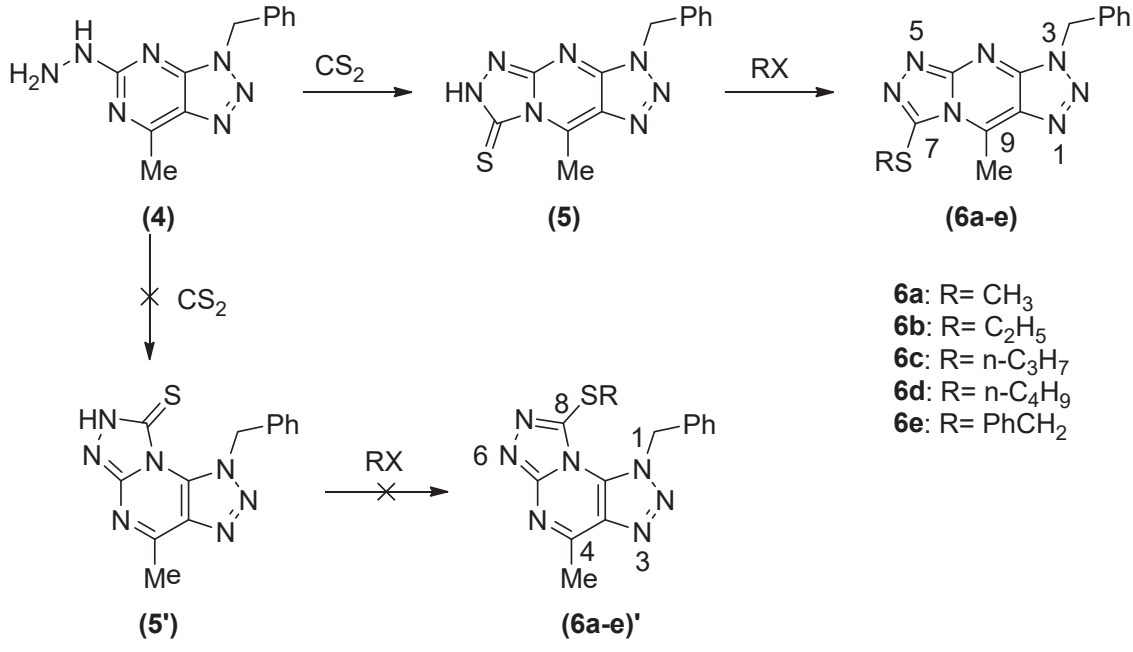

Scheme 2

triazolo[4,3-*a*]pyrimidine-8(7*H*)-thione **5**' and its subsequent alkylation with various alkyl halides in the presence of Et_3N in boiling CH_3CN, the regioselectivity of the cyclisation was found to be ambiguous in these reactions. Therefore, the evidence that confirmed which nitrogen atom available on the pyrimidine core was cyclised by CS_2 and the outcome from subsequent alkylation by the appropriate alkyl halide was deduced *via* computational results and by comparing them with the experimental data.

All the newly synthesised compounds **6a**–**e** and (**6a**–**e**)' have been characterised *via* their physical, chemical and spectral data. The IR spectrum of compound **5** or **5**' displayed the stretching vibration band of the NH group at 3100 cm^{-1} which was removed after alkylation. On the other hand, the ^1H NMR spectrum of either product **6b** or **6b**', as an example, showed a triplet signal at 1.53 ppm with a coupling constant of 7.2 Hz due to the methyl group of the ethyl moiety, a singlet peak at 3.29 ppm corresponding to the methyl group on the pyrimidine ring, a quartet signal at 3.36 ppm for the methylene protons of the ethyl group with a coupling constant of 7.2 Hz and two multiplet signals at around 7.26–7.36 and 7.51–7.54 ppm due to the phenyl group in the product. The ^{13}C NMR spectrum of **6b** or **6b**' also showed 12 signals at 13.9, 15.2, 25.8, 50.6, 128.7, 128.9, 129.2, 134.4, 142.9, 146.9, 155.8 and 172.5 ppm. The mass spectrum displayed the molecular ion peak at *m/z* = 234 (M^+) related to the molecular formula of $C_{15}H_{15}N_7S$.

Further structural confirmations were made using two-dimensional nuclear Overhauser effect spectroscopy (NOESY) for compound **6b**. The hydrogens of the methylene moiety of SEt as a quartet at 3.37 ppm show interactions with the hydrogens of the C-9 Me group as a singlet at 3.29 ppm, whilst the N-3 benzyl protons are unaffected. These results indicate that the correct structures of products **6a**–**e** are those shown in Scheme 1.

Computational evaluations

We decided to conduct a theoretical evaluation of the ^1H NMR spectra *via* the Gauge-Independent Atomic Orbital (GIAO) method.[32] Therefore, quantum calculations of NMR were performed to indicate the direction of ring closure. Accordingly, two main structures were presumed, anthracene-like structures for **6a**–**e** and phenanthrene-like structures for (**6a**–**e**)'. In addition, the corresponding Gibbs free energy data were extracted for the gas phase at 298 K and 1 atm. to evaluate the thermodynamic stability of the regioisomers.

Relative ^1H chemical shifts for the model structures were calculated as follows:

$$\delta_I = \sigma_{TMS} - \sigma_i \quad (1)$$

where σ_i and σ_{TMS} were the calculated isotropic magnetic shielding tensors for the desired proton of the model and TMS, respectively. It should be mentioned that σ_{TMS} = 32.01 ppm was obtained at the polarized continuum model (PCM) (chloroform)/WP04/*aug*-cc-pVDZ//B3LYP/6-311+g(2d,p) level of calculations.

The chemical shifts of the two benzylic hydrogens on the carbon attached to nitrogen N-3 in (**6a**–**e**)' or on nitrogen N-1 in (**6a**–**e**)' are summarised in Table 1. It can be seen from the data that if compounds (**6a**–**e**)' actually existed they would exhibit a characteristic signal with a lower field (> 6 ppm) shift. The hypothetical larger chemical shifts of the benzylic hydrogens in models (**6a**–**e**)' belong to the protons that are located near to the sulfur atom. The comparison of theoretical with experimental chemical shifts indicated that the reaction goes forward to yield compounds **6a**–**e** as the final structures.

Among the benzylic protons, H #2 of compounds **6a**–**e** has the best match with experimental values. The observed increasing differences in calculated chemical shifts with experimental values of H #1 in models **6a**–**e** belong to the proton located adjacent to nitrogen N-4.

From an energy viewpoint, all derivatives were checked against each other to determine which structure was more favourable thermodynamically. For this purpose, the calculated sum of electronic energy and corrected Gibbs free energy of models **6a**–**e** were compared with their peer derivatives (**6a**–**e**)'. The results showed that **6a**, **6b**, **6c**, **6d** and **6e** are 2.50, 2.25, 1.68, 1.85 and 1.33 kcal mol^{-1}, respectively, more thermodynamically stable than their corresponding isomers (**6a**', **6b**', **6c**', **6d**' and **6e**'). These data were obtained from frequency calculations in the gas phase, 298 K and 1 atm., for models at the B3LYP/6-311+g(2d,p) level of theory.

Table 1 Experimental and unscaled GIAO ^{1}H NMR chemical shifts in ppm relative to TMS for benzylic protons (on carbon attached to nitrogen N-3 of (**6a–e**)' or nitrogen N-4 of (**6a–e**') in PCM(chloroform)/WP04/aug-cc-pvdz//B3LYP/6-311+g(2d,p)

Compound	Benzylic		Experimental		$\Delta\delta_H$ (ppm)	
	H #1[a]	H #2[b]	Benzylic	Integration	H #1[a]	H #2[b]
6a	5.86	5.84	5.83	2	0.03	0.01
6a'	6.15	6.39			0.32	0.56
6b	5.85	5.83	5.83	2	0.02	0.00
6b'	6.14	6.50			0.31	0.67
6c	5.85	5.83	5.83	2	0.02	0.00
6c'	6.27	6.71			0.44	0.88
6d	5.88	5.84	5.83	2.02	0.05	0.01
6d'	6.27	6.70			0.44	0.87
6e	5.66	5.60	5.84	2	0.18	0.24
6e'	6.34	6.44			0.50	0.60

[a]Adjacent proton to nitrogen N-4 of **6a–e** (see Scheme 2).
[b]Adjacent proton to sulfur atom in (**6a–e**)'.

Conclusions

The chemical procedures outlined in this paper provided very simple and straightforward routes to obtain various derivatives of [1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine. The compounds designed and synthesised were studied for their true regiochemistry *via* theoretical calculations, and the results showed that the cyclisation reaction proceeds in such a way as to give the anthracene-like heterocycle. DFT calculations at the PCM/WP04/*aug*-cc-pVDZ//B3LYP-6-311+g(2d,p) level of theory were used to calculate the proton chemical shifts, and compounds **6a**–**e** correlated well with the experimental data in comparison with models (**6a**–**e**)'. Moreover, the relative Gibbs free energy revealed that compounds **6a**–**e** are more favourable thermodynamically than (**6a**–**e**)'. Further studies are in progress to improve our knowledge of their biological activities.

Experimental

Melting points were recorded on an Electrothermal Type 9100 melting point apparatus. The IR spectra were obtained on an Avatar 370 FTIR Thermo-Nicolet spectrophotometer for KBr disks and only noteworthy absorptions are listed. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker Avance DRX-400 Fourier Transform spectrometer. Chemical shifts are reported in ppm downfield from tetramethylsilane (TMS) as internal standard. The mass spectra were scanned on a Varian Mat CH-7 instrument at 70 eV. Elemental analyses were performed on a Thermo Finnigan Flash EA Microanalyzer.

N⁴-Benzyl-2-chloro-6-methylpyrimidine-4,5-diamine (**2**)

To a stirred solution of 2,6-dichloro-4-methylpyrimidine-3-amine **1** (10 mmol, 1.78 g) in *i*-PrOH (15 mL), benzylamine (10 mmol, 1.1 g) was added and the resulting mixture was heated under reflux for 12 h. After completion of the reaction, the solvent was concentrated and the resulting precipitate was filtered, washed with water (2 × 20 mL) and recrystallised from EtOAc and *n*-hexane. Yellow powder; yield 90%; m.p. 160–162 °C; ^{1}H NMR ($CDCl_3$): δ 3.08 (s, 3H, CH_3), 5.72 (s, 2H, CH_2N), 7.31–7.39 (m, 3H, Ar-H), 7.46–7.48 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 20.2, 50.5, 128.4, 128.8, 129.1, 134.1, 134.8, 150.0, 158.3, 165.2; IR (KBr) ν_{max}/cm^{-1}: 3434, 3359, 3297, 3258, 3056, 2925, 2872, 1659, 1587, 1496, 1455; MS: *m/z* 249 (M^+), 157 ($M^+ - C_7H_7$); Anal. calcd for $C_{12}H_{13}ClN_4$: C, 57.95; H, 5.27; N, 22.53; found: C, 57.90; H, 5.22; N, 22.48%.

3-Benzyl-5-chloro-7-methyl-3H-[1,2,3]triazolo[4,5-d]pyrimidine (**3**)

To a stirring mixture of *N⁴*-benzyl-2-chloro-6-methylpyridine-4,5-diamine **2** (4 mmol, 1.0 g) and concentrated HCl (2 mL) solution in water (2 mL), a solution of $NaNO_2$ (8 mmol, 0.6 g) in water (3 mL) was added dropwise in an ice-water bath. After the completion of the reaction which was monitored by TLC using $CHCl_3$/MeOH (30:1), water was added and the resulting precipitate was filtered off, washed with water (2 × 20 mL) and recrystallised from EtOH. Yellow solid; yield 70%; m.p. 140–143 °C; ^{1}H NMR ($CDCl_3$): δ 3.03 (s, 3H, CH_3), 5.83 (s, 2H, CH_2N), 7.29–7.41 (m, 3H, Ar-H), 7.47–7.49 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 20.4, 50.8, 128.5, 128.8, 129.0, 134.0, 134.9, 150.1, 158.5, 165.5; MS: *m/z* 259 (M^+), 168 ($M^+ - C_7H_7$); Anal. calcd for $C_{12}H_{10}ClN_5$: C, 55.50; H, 3.88; N, 26.97; found: C, 55.45; H, 3.85; N, 26.94%.

3-Benzyl-5-hydrazinyl-7-methyl-3H-[1,2,3]triazolo[4,5-d]pyrimidine (**4**)

To a solution of 3-benzyl-5-chloro-7-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine **3** (1 mmol, 0.3 g) in EtOH (5 mL), hydrazine hydrate (1 mL) was added and the solution was refluxed for 5 h. After completion of the reaction, the solution was cooled and the resulting solid was filtered off, washed with water (2 × 20 mL) and recrystallised from EtOH. White solid; yield 85%; m.p. 140–142 °C; ^{1}H NMR ($CDCl_3$): δ 2.02 (s, 2H, NH_2), 2.90 (s, 3H, CH_3), 5.76 (s, 2H, CH_2N), 7.30–7.43 (m, 5H, Ar-H), 8.20 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 25.8, 49.7, 128.1, 128.2, 128.7, 132.3, 135.2, 150.7, 158.2, 164.2; IR (KBr) ν_{max}/cm^{-1}: 3448, 3274, 3060, 3029, 2937, 1610, 1559, 1469, 1449; MS: *m/z* 255 (M^+), 164 ($M^+ - C_7H_7$); Anal. calcd for $C_{12}H_{13}N_7$: C, 56.46; H, 5.13; N, 38.41; found: C, 56.40; H, 5.09; N, 38.37%.

3-Benzyl-9-methyl-3H-[1,2,3]triazolo[4,5-d][1,2,4]triazolo[4,3-a]pyrimidine-7(6H)-thione (**5**)

To a stirred solution of 3-benzyl-5-hydrazinyl-7-methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine **4** (1 mmol, 0.3 g) in pyridine (5 mL), CS_2 (2 mmol, 0.12 mL) was added and the solution was heated under reflux for 7 h. After completion of the reaction, which was monitored by TLC using $CHCl_3$/MeOH (5:1), the solvent was removed under reduced pressure. The resulting solid was washed with water (10 mL) and recrystallised from EtOH. Pale brown powder; yield 76%; m.p. 220–222 °C; ^{1}H NMR ($CDCl_3$): δ 2.91 (s, 3H, CH_3), 5.75 (s, 2H, CH_2N), 7.31–7.44 (m, 5H, Ar-H), 7.66 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 25.8, 49.7, 128.1, 128.2, 128.7, 132.3, 135.2, 150.7, 158.2, 164.2, 165.4; IR (KBr) ν_{max}/cm^{-1}: 3100, 3067, 3039, 2929, 1631, 1587, 1554, 1498, 1452, 1432; MS: *m/z* 297 (M^+), 206 ($M^+ - C_7H_7$); Anal. calcd for $C_{13}H_{11}N_7S$: C, 52.51; H, 3.73; N, 32.97; S, 10.78; found; C, 52.47; H, 3.69; N, 32.92, S, 10.69%.

Synthesis of [1,2,3]triazolo[4,5-d][1,2,4]triazolo[4,3-a]pyrimidine (**6a–e**)*; general procedure*

To a solution of compound **5** (1 mmol, 0.3 g) and an appropriate alkyl halide (1 mmol) in CH_3CN (10 mL), Et_3N (1 mmol, 0.1 mL) was added and the solution was refluxed for about 6 h. After completion of the reaction, which was monitored by TLC using $CHCl_3$/MeOH (9:1), the solvent was removed under reduced pressure. The resulting solid was washed with water (2 × 10 mL) and recrystallised from EtOH.

*7-Methylthio-3-benzyl-9-methyl-3*H*-[1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine* (**6a**): White solid; yield 70%; m.p. 140–143 °C; ^{1}H NMR ($CDCl_3$): δ 2.65 (s, 3H, CH_3), 3.29 (s, 3H, CH_3S), 5.83 (s, 2H, CH_2N), 7.31–7.36 (m, 3H, Ar-H), 7.50–7.55 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 15.6, 16.5, 38.8, 128.6, 128.7, 129.0, 130.6, 156.5, 165.9, 185.3; IR (KBr) ν_{max}/cm^{-1}: 3064, 3039, 2929, 1631, 1587, 1554, 1498; MS: *m/z* 311 (M^+), 192 ($M^+ - C_7H_7N_2$); Anal. calcd. for $C_{14}H_{13}N_7S$: C, 54.00; H, 4.21; N, 31.49; S, 10.30; found: C, 53.95; H, 4.18; N, 31.40; S, 10.23%.

*7-Ethylthio-3-benzyl-9-methyl-3*H*-[1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine* (**6b**): White solid; yield 65%; m.p. 130–134 °C; ^{1}H NMR ($CDCl_3$): δ 1.51 (t, *J* = 6.0 Hz, 3H, CH_3), 3.29 (s, 3H, CH_3), 3.37 (q, *J* = 6.0 Hz, 2H, CH_2), 5.84 (s, 2H, CH_2N), 7.31–7.34 (m, 3H, Ar-H), 7.50–7.55 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 13.9, 15.2, 25.8, 50.6, 128.7, 128.9, 129.2, 134.4, 142.9, 146.9, 155.8, 172.5;

IR (KBr) ν_{max}/cm^{-1}: 3035, 2970, 2921, 1632, 1589, 1552, 1492; MS: *m/z* 325 (M^+), 234 ($M^+ - C_7H_7$); Anal. calcd for $C_{15}H_{15}N_7S$: C, 55.37; H, 4.65; N, 30.13; S, 9.85; found: C, 55.46; H, 4.7; N, 29.98, S, 9.79%.

*7-Propylthio-3-benzyl-9-methyl-3*H-*[1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine* (**6c**): White solid; yield 60%; m.p. 180–185 °C; ^{1}H NMR ($CDCl_3$): δ 1.09 (t, *J* = 7.2 Hz, 3H, CH_3), 1.87 (sextet, *J* = 7.2 Hz, 2H, CH_2), 3.28 (s, 3H, CH_3), 3.35 (q, *J* = 7.2 Hz, 2H, CH_2S), 5.83 (s, 2H, CH_2N), 7.30–7.36 (m, 3H, Ar-H), 7.51–7.54 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 13.3, 13.9, 23.2, 33.3, 50.5, 128.7, 128.9, 129.2, 134.4, 142.0, 146.9, 155.8, 172.8; IR (KBr) ν_{max}/cm^{-1}: 3064, 3027, 2962, 2929, 2876, 1629, 1588; 1550, 1496; MS: *m/z* 339 (M^+), 310 (M^+-C_2H_5), 264 ($M^+ - C_3H_7S$), 206 ($M^+ - C_7H_7N_3$); Anal. calcd for $C_{16}H_{17}N_7S$: C, 56.62; H, 5.05; N, 28.89; S, 9.45: found: C, 56.57; H, 5.01; N, 28.84; S, 9.39%.

*7-Butylthio-3-benzyl-9-methyl-3*H-*[1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine* (**6d**): White solid; yield 80%; m.p. 160–164 °C; ^{1}H NMR ($CDCl_3$): δ 0.97 (t, *J* = 7.5 Hz, 3H, CH_3), 1.48–1.56 (m, 2H, CH_2), 1.77 (quint., *J* = 7.2 Hz, 2H, CH_2), 3.29 (s, 3H, CH_3), 3.35 (t, *J* = 7.5 Hz, 2H, CH_2S), 5.84 (s, 2H, CH_2N), 7.30–7.36 (m, 3H, Ar-H), 7.50–7.54 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 13.6, 13.9, 21.9, 31.1, 31.7, 50.5, 128.7, 128.9, 129.2, 134.4, 142.8, 146.9, 155.3, 155.8, 172.0; IR (KBr) ν_{max}/cm^{-1}: 3060, 3031, 2957, 2929, 2870, 1631, 1587, 1552, 1496; MS: *m/z* 353 (M^+), 262 ($M^+ - C_7H_7$), 234 ($M^+ - C_7H_7N_2$); Anal. calcd for $C_{17}H_{19}N_7S$: C, 57.77; H, 5.42; N, 27.74; S, 9.07; found: C, 57.71; H, 5.39; N, 27.70; S, 9.01%.

*7-Benzylthio-3-benzyl-9-methyl-3*H-*[1,2,3]triazolo[4,5-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine* (**6e**): White solid; yield 69%; m.p. 174–180 °C; ^{1}H NMR ($CDCl_3$): δ 3.29 (s, 3H, CH_3), 4.59 (s, 2H, CH_2S), 5.84 (s, 2H, CH_2N), 7.31–7.55 (m, 10H, Ar-H); ^{13}C NMR ($CDCl_3$): δ 37.6, 38.5, 54.1, 128.1, 128.4, 128.7, 128.8, 128.9, 129.1, 129.2, 134.7, 135.2, 135.8, 155.1, 164.8, 185.8; IR (KBr) ν_{max}/cm^{-1}: 3067, 3031, 2932, 2074, 1631, 1586, 1551, 1490; MS: *m/z* 387 (M^+), 296 ($M^+ - C_7H_7$), 264 ($M^+ - C_7H_7S$); Anal. calcd for $C_{20}H_{17}N_7S$: C, 62.00; H, 4.42; N, 25.30; S, 8.28; found: C, 61.94; H, 4.36; N, 25.24; S, 8.21%.

Computational details

All optimisation, frequency and NMR calculations were performed with the Gaussian 09 Rev. A.01 package.[33] All computational models were geometrically optimised without any symmetric restriction by using B3LYP DFT code[34] and choosing the 6-311+g(2d,p) basis set for all atoms. Cartesian coordinates of geometrically optimised models are available in the supplementary information. Frequency calculations were done at the same level of theory to make sure that optimised models were in their local minimum energy as long as no imaginary frequency was observed. In order to perform accurate and precise ^{1}H NMR GIAO calculations, the WP04 method[35] and *aug*-cc-pVDZ as the basis set were used as reported by Jain *et al*. so that no further scaling operation was necessary at this level of calculation.[36] Also, ^{1}H NMR GIAO chemical shift calculations were performed *via* SCRF with the PCM model[37] to consider the solvent effect (chloroform). Geometrical optimisation and the computation of isotropic magnetic shielding tensors for TMS as reference were performed at the same level of calculation.

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Electronic supplementary information

^{1}H and ^{13}C NMR data and NOESY spectra for **6b** are given in the electronic supplementary information which is available through:
stl.publisher.ingentaconnect.com/content/stl/jcr/supp-data

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