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3-(2-Pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridines. An experimental and theoretical (DFT) study of the ring–chain isomerization

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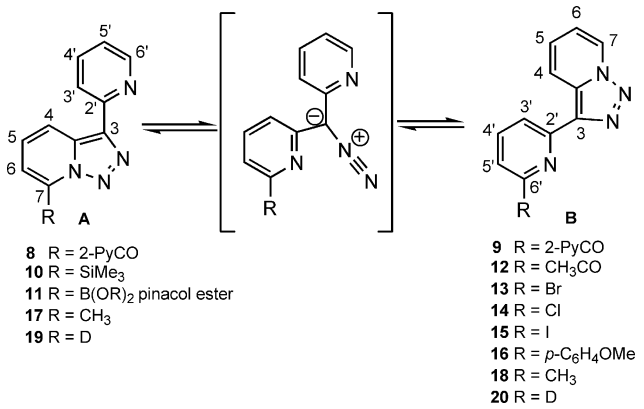
An experimental (^{1}H NMR) and theoretical (DFT) study of the ring–chain–ring isomerization of 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyrid-7-yl derivatives (**A**) into 6-{[1,2,3]triazolo[1,5-*a*]pyrid-3-yl}-2-pyridyl derivatives (**B**) has been carried out. Based on the calculations, a mechanism of several steps will be proposed. The experimental results as well as the calculations lead to the conclusion that the **A**–**B** ratio depends on the electronic properties of the substituents.

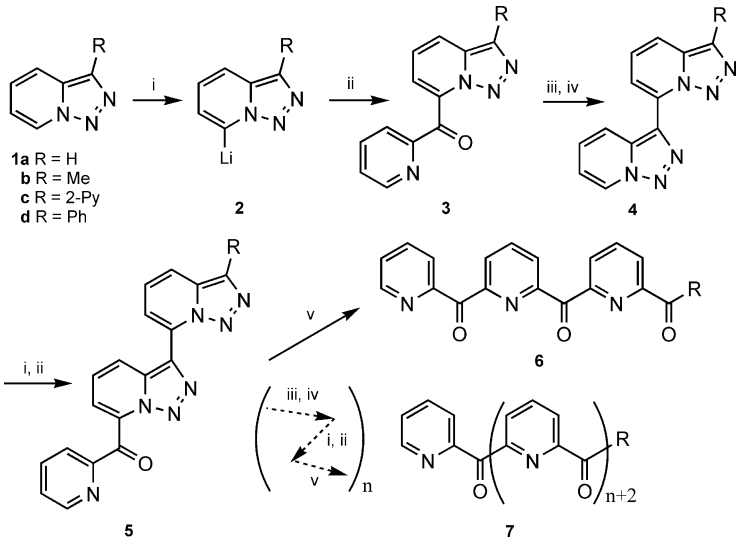
Introduction

During our research on the chemistry of [1,2,3]triazolo[1,5-*a*]pyridines **1**, we were interested in synthesising 2-pyridyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-ylmethanones **3**,[1] to use them as starting materials to prepare polypyridylcarbonylpyridines **6** and **7**, polynitrogenated ligands able to make helicates, a versatile family of supramolecular complexes.[2] Compounds **3** can be synthesised from triazolopyridines **1a–d** by regioselective lithiation at −40 °C giving **2** and subsequent reaction with the adequate electrophile.[1,3,4] Reaction of **3** with N_2H_4 followed by oxidation with MnO_2, or with $TsNHNH_2$ and aqueous sodium hydroxide, gave the corresponding compounds **4**.[1] The new ligands **6** and **7** can be accessed if the methodology summarised above is applied several times, followed by triazolo ring opening with loss of dinitrogen (Scheme 1). In this context we had found an interesting structural feature for the compound so-called **3c**, (from now on **8**). Its ^{1}H NMR spectrum demonstrates that it exists almost entirely as its isomer **9**.[1] To account for this structure we assumed that, in solution, the first formed compound **8**, a type **A** isomer, 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyrid-7-yl derivative, is in equilibrium with the diazo form; this intermediate may undergo a new ring–chain isomerisation,[5,6] giving **9**, a type **B** isomer, 6-{[1,2,3]triazolo[1,5-*a*]pyrid-3-yl}-2-pyridyl derivative (Scheme 2).



Scheme 2

Probably the position of the **A**–**B** equilibrium depends on some characteristics of the substituents. To verify this hypothesis, we have carried out a ^{1}H NMR study of a series of



Scheme 1 *Reagents and conditions*: (i) *n*-BuLi–toluene, −40 °C; (ii) 2-Py–CO_2Et; (iii) N_2H_4; (iv) MnO_2, Cl_2CH_2; (v) SeO_2.

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Table 1 ^{1}H NMR (in $CDCl_3$). *J* values are given in Hertz (Hz)

	R	H4	H5	H6	H7	H3′	H4′	H5′	H6′	Other
1c	H Ref. 1	8.69m	7.28dd $J_1 = 9.0$ $J_2 = 6.6$	6.96dd $J_1 = 6.6$ $J_2 = 7.3$	8.69m	8.27d $J = 8.0$	7.71dd $J_1 = 8.0$ $J_2 = 7.5$	7.13dd $J_1 = 5.1$ $J_2 = 7.5$	8.69m	
9	2-PyCO Ref. 1	8.01d $J = 9.0$	7.10dd $J_1 = 9.0$ $J_2 = 6.0$	6.95dd $J_1 = 6.9$ $J_2 = 6.0$	8.65d $J = 6.9$	8.40d $J = 7.6$	7.92dd $J_1 = 7.6$ $J_2 = 7.7$	7.98d $J = 7.7$		8.73d, H6″ 8.01d, H3″ 7.85dd, H4″ 7.47dd, H5″
10	$SiMe_3$ Ref. 3	8.61d $J = 9.1$	7.20dd $J_1 = 9.1$ $J_2 = 6.6$	7.01d $J = 6.6$		8.27 $J = 8.0$	7.69dd $J_1 = 8.0$ $J_2 = 7.6$	7.10dd $J_1 = 5.1$ $J_2 = 7.6$	8.57d $J = 5.1$	0.45s, $3CH_3$
11	$B(OR)_2$[a] Ref. 7	8.76d $J = 8.9$	7.26dd $J_1 = 8.9$ $J_2 = 6.6$	7.46d $J = 6.6$		8.32d $J = 7.9$	7.72dd $J_1 = 7.7$ $J_2 = 7.7$	7.14dd $J_1 = 4.9$ $J_2 = 7.5$	8.59d $J = 4.9$	1.38s, $4CH_3$
12	CH_3CO	8.71d $J = 9$	7.46 dd $J_1 = 9.0$ $J_2 = 6.9$	7.10ddd $J_1 = 6.9$ $J_2 = 6.9$ $J_3 = 1.2$	8.80d $J = 6.9$	8.55dd $J_1 = 6.9$ $J_2 = 2.4$	7.98–7.92 m	7.98–7.92 m		2.867s, CH_3
13	Br	8.65d $J = 9.0$	7.43dd $J_1 = 9.0$ $J_2 = 6.9$	7.07dd $J_1 = 7.2$ $J_2 = 6.6$	8.75d $J = 6.9$	8.28d $J = 7.8$	7.63dd $J_1 = 7.8$ $J_2 = 7.8$	7.37dd $J = 8.1$		
14	Cl	8.66d $J = 9$	7.40ddd $J_1 = 8.7$ $J_2 = 6.9$ $J_3 = 0.9$	7.04ddd $J_1 = 6.9$ $J_2 = 6.9$ $J_3 = 1.2$	8.72d $J = 6.9$	8.22d $J = 7.8$	7.70dd $J_1 = 7.8$ $J_2 = 7.8$	7.19dd $J_1 = 7.8$ $J_2 = 0.6$		
15	I	8.61d $J = 9.0$	7.43dd $J_1 = 9.0$ $J_2 = 6.9$	7.07dd $J_1 = 6.9$ $J_2 = 6.9$	8.76d $J = 6.9$	8.29d $J = 7.8$	7.38dd $J_1 = 7.8$ $J_2 = 7.8$	7.61d $J = 7.8$		
16	*p*-C_6H_4OMe	8.61d $J = 9.0$	6.99dd $J_1 = 9.0$ $J_2 = 6.9$	7.34dd $J_1 = 6.9$ $J_2 = 6.9$	8.70d $J = 6.9$	8.19d $J = 7.8$	7.76dd $J_1 = 7.8$ $J_2 = 7.8$	7.56d $J = 7.8$		7.98d, 2H 6.99d, 2H 3.9s, OCH_3
17	Me 75%	8.61d $J = 9.0$	7.32dd $J_1 = 9.0$ $J_2 = 6.9$	6.89d $J = 6.9$		8.37d $J = 8.1$	7.78dd $J_1 = 7.8$ $J_2 = 7.8$	7.20ddd $J_1 = 7.5$ $J_2 = 4.8$ $J_3 = 0.9$	8.66d $J = 4.8$	2.92s, CH_3
18	Me 25%	8.76–8.72 m	7.38–7.73 m	7.04dd $J_1 = 6.9$ $J_2 = 7.2$	8.76–8.72 m	8.13d $J = 7.8$	7.67d $J_1 = 7.5$ $J_2 = 7.8$	7.07d $J = 7.8$		2.62s, CH_3

[a] Pinacol ester.

pyridyltriazolo–pyridines **1c** and **9–20** in order to study the influence of the substituents on the equilibrium and on the ring–chain isomerisation and hence on the structure of these products. We have also carried out DFT/B3LYP/6-31G* calculations on some of these compounds. We wish to report here the results of this research.

Results and discussion

Trimethyl[3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyrid-7-yl]silane **10**, and 2-[3-(2-pyridyl)-7-[1,2,3]triazolo[1,5-*a*]pyridyl]-4,4,5,5-tetramethyl[1,3,2]dioxaborolane **11**, have been synthesised previously.[3,7] Pyridyltriazolopyridines **12–18** are new compounds. Compound **12** was synthesised using the standard procedure by lithiation of [1,2,3]triazolo[1,5-*a*]pyridines and reaction with esters,[1] using ethyl acetate as co-reagent. The bromo- and chloro-derivatives **13** and **14** were prepared by the method described by some of us for the halogenation of 3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine,[8] lithiation reaction followed by treatment with 1,2-dibromotetrachloroethane or hexachloroethane respectively, using toluene as solvent in the step of lithiation.[4] The iodo-derivative **15** was prepared by lithiation with LDA in THF,[9] and then treatment with I_2. A Suzuki coupling reaction between **15** and 4-methoxyphenylboronic acid, using dioxane as solvent and Na_2CO_3 as base, gave the *p*-methoxyphenyl derivative **16** in good yield. To synthesise compound **17** we used a general procedure for the synthesis of triazolopyridines, reaction of an acylpyridine with $N_2H_4{\cdot}H_2O$ and, without isolation of the corresponding hydrazone, oxidation with MnO_2.[10] The starting material was 6-methyl-2-pyridyl-2-pyridylmethanone **21**.

Table 1 reports the ^{1}H NMR data of series **1c**, **9–18**. The δ and *J* values for all of them prove that they have a pyridyltriazolo–pyridine structure. In compounds **10** and **11**, which contain a 3,7-disubstituted triazolopyridine and a 2-substituted pyridine, the presence of a proton with a coupling constant of $J = 4.9$–5.1 Hz is significant, corresponding to a H2 or H6 pyridine proton. On the other hand, for compounds **9** and **12–16** which have a 3-substituted triazolopyridine and a 2,6-disubstituted pyridine, there is always a H7 triazolopyridine proton present in these six compounds as is proved by signals at $\delta = 8.65$–8.80 (d) with $J = 6.9$ Hz, characteristic of this type of protons. We can conclude that those compounds that have electron-donating substituents (**10**, **11**) have the equilibrium shifted to the left, these are type **A** isomers, while in those with electron-withdrawing substituents (**9**, **12–16**), the equilibrium is shifted to the right, being type **B** isomers (Scheme 2). When the substituent is a methyl group, the NMR spectrum corresponds to a mixture of both isomers **17** and **18**, 75 : 25 in favour of **17**.

In the parent compound 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **1c**, this type of isomerization can take place, but it would be a degenerate rearrangement and the product would be structurally identical to the starting material. The existence of degenerate isomers can be detected by use of isotopic labels, thus we have incorporated deuterium in **1c** after lithiation and treatment with D_2O. The spectrum of the deuterated compound shows that a 50 : 50 mixture of **19** and its isomer **20** is present, because all the signals are at the same δ values and have exactly the same multiplicity as in the **1c** spectrum (see Table 1), but only the multiplets corresponding to H4, H7 and H6′, maintaining the same appearance, have an integral value that shows that the number of hydrogens being detected corresponds to 2.

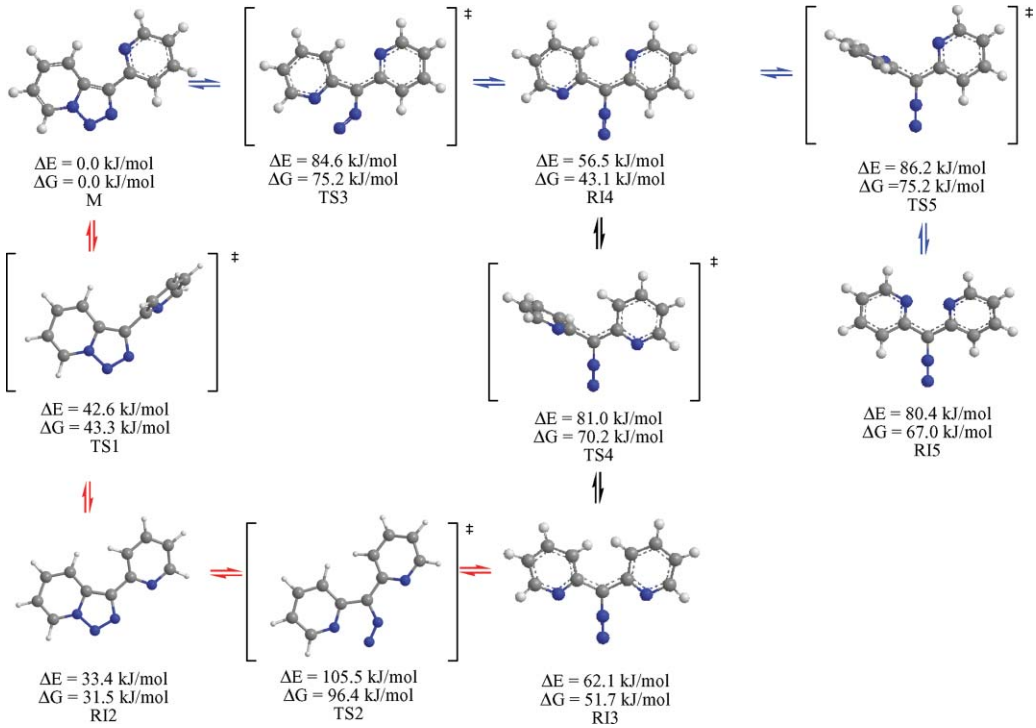


Fig. 1

In summary, we have proved that structures **A** and **B** are in equilibrium (*i.e.*, the isomerization barrier should be low) and the **A**–**B** ratio depends on the electronic properties of the R substituent. Electron-donating substituents [$SiMe_3$, $B(OR)_2$] favour the **A** form, electron-withdrawing substituents [COMe, Br, Cl, I, *p*-MeOPh] favour the **B** form, and only in the case where R = Me are both forms present (75% of **A**, 25% of **B**).

Computational results

(a) Part concerning the reaction profile (1c, Scheme 1, R′ = H)

The reaction path is more complex than was initially thought (Fig. 1 and Scheme 3). In the case of **1c**, the degenerate nature of the process allows the representation of only one half of the mechanism in Fig. 1 (in Scheme 3 it is complete). We will distinguish three pathways:

The red pathway starts by a rotation of the pyridyl ring about the C–C bond of the minimum **M**. It then goes through the "orthogonal" transition state **TS1** to a second minimum **R12**, where both nitrogen atoms are on the same side. The "planar" transition state (not represented) connects **R12** with its enantiomer (ΔE = 37.3 and ΔG = 38.8 kJ mol^{-1}). From **R12** to **R13** there is a TS of 96.4 kJ mol^{-1}. From the reaction intermediate **R13**, both minima **M** can be reached.

The blue pathway starts from **M** to **RI4** (**TS3**, ΔG = 75.2 kJ mol^{-1}) and **RI4** with **RI5** (TS, ΔG = 75.2 kJ mol^{-1}). From the reaction intermediate **RI5**, both minima **M** can be reached.

The black pathway connects **M** with **RI4** (**TS3**, ΔG = 75.2 kJ mol^{-1}) and **RI4** with **RI3** through a second TS (**TS4**, ΔG = 70.2 kJ mol^{-1}). The differences between the blue and black pathways are very small (compare **TS4** with **TS5**) and besides the limiting step, common to both, is the transformation of **M** into **RI4** through **TS3**.

The red process corresponds to a ring–ring–chain–ring–ring tautomerism while the black and blue ones are of a ring–chain–chain–chain–ring type. In these last two cases, the higher barrier involved, about 75 kJ mol^{-1}, explains why in the cases of R = D (**19**/**20**) and R = CH_3 (**17**/**18**), an equilibrium was observed in solution.

(b) Part concerning the A–B ratio

We have selected different R groups (Scheme 2), some of them corresponding to those studied experimentally. In the case of R = H, E = −642.960693 hartree. For the other substituents, the difference in energy between the **A** and **B** isomers are (in kJ mol^{-1}): NO_2 (−53.8), F (−40.7), Cl (−30.5), Br (−26.2), OMe (−22.0), CN (−18.8), OH (−17.9), NMe_2 (−17.8), COMe (−14.0), CHO (−11.0), NH_2 (−4.9), *t*Bu (−2.3), CH_3 (6.4), SiH_3 (15.1), $SiMe_3$ (20.7) and $B(OH)_2$ (29.2). The sign always coincides with the isolated isomer. In the case of R = CH_3, 6.4 kJ mol^{-1} corresponds to 93% of **A** and 7% of **B**, while the experimental result is 75% **A**/25% **B**, which are in an acceptable agreement.

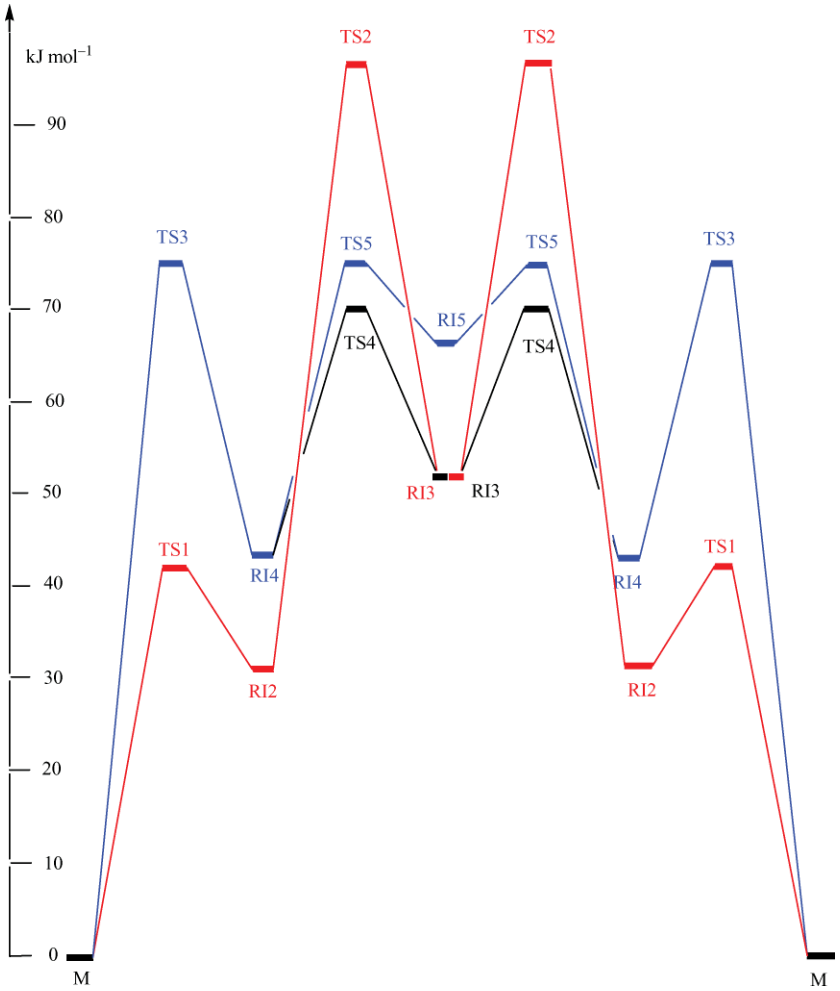
If we situate the seven experimental values in a 10 to −10 scale, to be consistent with the calculations it is necessary that Cl **14** = −10, Br **13** = −9, COMe **12** = −5, H **1c** = 0, Me **17**/**18** = 2, $SiMe_3$ **10** = 7 and $B(OR)_2$ **11** = 10. These values are ordered from electron-withdrawing to electron-releasing substituents but none is linearly related to any Hammett or Taft coefficients nor to gas-phase basicity (PA) of 2-substituted pyridines (NIST data). Only the combined use of σ_m, σ_p and MR (molar refractivity as a steric coefficient) yields an acceptable correlation coefficient (r^2 = 0.955).

Experimental

Melting points were determined on a Kofler heated stage and are uncorrected. NMR spectra were recorded on a Bruker AC 300 MHz in $CDCl_3$ as solvent. COSY experiments were done for all compounds. HRMS (EI) determinations were made using a VG Autospec Trio 1000 (Fisons). Infrared spectra were recorded in KBr discs on a Bio-Rad FTS-7. All the lithiation reactions were done under an inert atmosphere and in dry solvents.[11]

3-(2-Pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine 1c, 2-pyridyl-6-[1,2,3]triazolo[1,5-*a*]pyrid-3-yl-2-pyridylmethanone 9, trimethyl[3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyrid-7-yl]silane 10, and 2-[3-(2-pyridyl)-7-[1,2,3]triazolo[1,5-*a*]pyridyl]-4,4,5,5-tetramethyl[1,3,2]dioxaborolane 11

Prepared as described.[3,7]



Scheme 3

3-(6-Acyl-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine 12

To a solution of 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **1c** (0.24 g, 1.22 mmol) in anhydrous toluene (20 mL) at −40 °C, a solution of *n*-butyllithium in hexane (0.75 mL, 2.5 M) was added with stirring. A deep red colour developed. The mixture was kept at −40 °C (4 h). Treatment with dry ethyl acetate (1 mL) produced a colour change to yellow. The mixture was left at −40 °C (2 h) and allowed to warm to room temperature overnight, and was then treated with a saturated solution of ammonium chloride. The organic layer was separated and the aqueous layer extracted with dichloromethane. After being dried over anhydrous Na_2SO_4 and evaporation of the organic solvents, the obtained residue was purified by chromatotron with hexane and increasing polarity with ethyl acetate as eluent, to obtain 3-(6-acyl-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **12** (20 mg, 8.6% over recovered starting material). Mp 189–192 °C (CH_2Cl_2–hexane). HRMS found for M^+ 238.0857; $C_{13}H_{10}N_4O$ requires 238.0854. ν_{max} (KBr)(cm^{-1}) 3086, 3041, 2924, 2853, 1686, 1633, 1592, 1529. ^{13}C NMR δ($CDCl_3$) 199.74 (CO), 152.89 (C), 151.30 (C), 137.60 (CH), 136.67 (C), 132.00 (C), 126.92 (CH), 125.48 (CH), 123.81 (CH), 120.64 (CH), 119.87 (CH), 115.98 (CH), 26.26 (CH_3). Then 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **1c** (50 mg) was recovered, and further elution gave 7,7′-bi[1,2,3]triazolo[1,5-*a*]pyridine (70 mg). Mp >350 °C, lit.[3] >350 °C.

3-(6-Bromo-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine 13

To a solution of 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **1c** (0.48 g, 2.44 mmol) in anhydrous toluene (30 mL) at −40 °C, a solution of *n*-butyllithium in hexane (1.5 mL, 2.5 M) was added with stirring. A deep red colour developed. The mixture was kept at −40 °C (4 h). Treatment with a dry toluene (5 mL) solution of 1,2-dibromotetrachloroethane (2.0 g, 6.12 mmol) produced a colour change to yellow. The mixture was left at −40 °C (2 h) and allowed to warm to room temperature overnight, and was then treated with a saturated solution of ammonium chloride. The organic layer was separated and the aqueous layer extracted with dichloromethane. After being dried over anhydrous Na_2SO_4 and evaporation of the organic solvents, the obtained residue was purified by chromatotron with hexane–ethyl acetate (increasing the polarity gradually) as eluent, to obtain 3-(6-bromo-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **13** (50 mg, 10.5% based on recovered starting material). Mp 199–201 °C (CH_2Cl_2–hexane). HRMS found for M^+ 273.9869/275.9851; $C_{11}H_7BrN_4$ requires 273.9854/275.9833. ν_{max} (KBr)(cm^{-1}) 3105, 3044, 2926, 1633, 1587, 1555, 1536, 1031. ^{13}C NMR δ($CDCl_3$) 152.67 (C), 141.41 (C), 138.93 (CH), 135.80 (C), 132.10 (C), 126.98 (CH), 125.96 (CH), 125.23 (CH), 121.05 (CH), 118.74 (CH), 116.06 (CH). Then starting material 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **1c** (140 mg) was eluted, and further elution gave 7,7′-bi[1,2,3]triazolo[1,5-*a*]pyridine (250 mg).[3]

3-(6-Chloro-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine 14

To a solution of 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **1c** (0.24 g, 1.22 mmol) in anhydrous toluene (20 mL) at −40 °C, a solution of *n*-butyllithium in hexane (0.75 mL, 2.5 M) was added with stirring. A deep red colour developed. The mixture was kept at −40 °C (4 h). Treatment with a dry toluene solution (5 mL) of hexachloroethane (0.72 g, 3.06 mmol) produced a colour change to yellow. The mixture was left at −40 °C (2 h) and allowed to warm to room temperature overnight, and was

then treated with a saturated solution of ammonium chloride. The organic layer was separated and the aqueous layer extracted with dichloromethane. After being dried over anhydrous Na_2SO_4 and evaporation of the organic solvents, the obtained residue was purified by chromatotron with hexane–ethyl acetate (increasing the polarity gradually) as eluent, to obtain 3-(6-chloro-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **14** (30 mg, 13% over recovered starting material). Mp 178–180 °C (CH_2Cl_2–hexane). HRMS found for M^+ 230.0408/232.0379; $C_{11}H_7ClN_4$ requires 230.0359/232.0329. ν_{max} (KBr)(cm^{-1}) 3105, 3046, 2923, 2853, 1635, 1590, 1527, 1036. ^{13}C NMR δ($CDCl_3$) 152.30 (C), 150.79 (C), 139.22 (CH), 132.13 (C), 131.77 (C), 126.94 (CH), 125.26 (CH), 122.13 (CH), 121.17 (CH), 118.46 (CH), 116.98 (CH). Then starting material 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*] pyridine **1c** (45 mg) was eluted, and further elution gave 7,7′-bi [1,2,3]triazolo[1,5-*a*]pyridine (100 mg).[3]

3-(6-Iodo-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine 15

To a solution of LDA (1.2 eq.) in anhydrous THF (5 mL) at −40 °C, a solution of 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **1c** (0.5 g, 2.6 mmol) in THF (5 mL, 2.5 M) was added with stirring after 30 min. A deep red colour developed. The mixture was kept at −40 °C (4 h) and was then treated with a dry THF solution (5 mL) of iodine (1.2 eq.). The mixture was allowed to warm to room temperature overnight, and was then treated with a saturated solution of ammonium chloride and extracted with dichloromethane. The organic layer was washed with a solution of $NaHSO_3$ 10%, a saturated solution of NaCl and water. After being dried over anhydrous Na_2SO_4 and evaporation of the organic solvents, the obtained solid residue (760 mg) was purified by silica column chromatography with hexane–ethyl acetate (increasing the polarity gradually) as eluent, to obtain 3-(6-iodo-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **15** (415 mg, 1.3 mmol, 49%). Mp 193–195 °C (EtOAc–hexane). HRMS found for M^+ 321.9684; $C_{11}H_7IN_4$ requires 321.9715. ν_{max} (KBr)(cm^{-1}) 3103, 3041, 1633, 1583, 1536, 663. ^{13}C NMR δ($CDCl_3$) 153.32 (C), 138.45 (CH), 136.24 (C), 133.09 (CH), 132.54 (C), 127.39 (CH), 125.67 (CH), 121.33 (CH), 119.54 (CH), 117.70 (C), 116.49 (CH).

3-[6-(4-Methoxyphenyl-2-pyridyl)]-[1,2,3]triazolo[1,5-*a*] pyridine 16

To a mixture of 3-(6-iodo-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]-pyridine **15** (160 mg, 0.75 mmol), 4-methoxyphenylboronic acid (130 mg, 0.75 mmol) and $Pd(PPh_3)_4$ (6%), dioxane was added (15 mL) with stirring. The mixture was kept at −40 °C (4 h) and was then treated with a dry THF solution (5 mL) of iodine (1.2 eq.). The mixture was heated to 85 °C with stirring for 8 h, and was then allowed to warm to room temperature, water was added and the mixture was extracted with dichloromethane. The organic layer was dried over anhydrous Na_2SO_4 and the organic solvents evaporated; the obtained solid residue (270 mg) was purified by silica column chromatography with hexane–ethyl acetate (increasing the polarity gradually) as eluent, to obtain 3-[6-(4-methoxyphenyl-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **16** (128 mg, 0.4 mmol, 80%). Mp 213–215 °C (EtOAc–hexane). HRMS found for M^+ 302.1112; $C_{18}H_{14}N_4O$ requires 302.1168. ν_{max} (KBr)(cm^{-1}) 3089, 2926, 1593, 1561, 1244, 1118. ^{13}C NMR δ($CDCl_3$) 160.87 (C), 156.94 (C), 152.02 (C), 138.18 (C), 137.89 (CH), 132.72 (C), 132.47 (C), 128.56 (CH), 126.80 (CH), 125.67 (CH), 121.82 (CH), 118.62 (CH), 118.52 (CH), 116.30 (CH), 55.59 (CH_3).

6-Methyl-2-pyridyl-2-pyridylmethanone 21

To a solution of 2-bromo-6-methylpyridine (0.2 mL, 1.79 mmol) in dry ether (20 mL) at −78 °C under N_2, a solution of *n*-butyllithium in hexane (0.83 mL, 2.5 M) was added gradually. The mixture was kept at −78 °C (75 min), and then was treated with a dry ether solution of ethyl picolinate (0.28 mL), was kept at −78 °C (3 h) and was allowed to warm to room temperature overnight. The reaction mixture was treated with a saturated solution of ammonium chloride, the organic phase was separated and the aqueous phase was extracted with dichloromethane. The combined organic phases were dried with Na_2SO_4 and concentrated. The residue was submitted to column chromatography with hexane–ethyl acetate (2 : 1) as eluent obtaining 6-methyl-2-pyridyl-2-pyridylmethanone **21** (80 mg, 23%).[12]

7-Methyl-3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine 17 and 3-(6-methyl-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine 18

A mixture of 6-methyl-2-pyridyl-2-pyridylmethanone **21** (80 mg) and hydrazine monohydrate (2.5 mL) was heated to 100 °C for 2 h. The reaction mixture was treated with a solution of sodium hydroxide (5 mL, 30%) and then was extracted with CH_2Cl_2. After evaporation of the organic solvent, the residue (68 mg) was refluxed in dried chloroform with activated manganese dioxide (150 mg) for 15 h. The hot solution was filtered over celite. The filtrate was concentrated (75 mg). The crude mixture was purified by chromatotron with hexane–ethyl acetate (increasing the polarity gradually) as eluent, to obtain an isomeric mixture of 7-methyl-3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine (75%) **17** and 3-(6-methyl-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine (25%) **18** (25 mg, 42.8%). Mp 108–110 °C (CH_2Cl_2–hexane). HRMS found for M^+ 210.0889; $C_{12}H_{10}N_4$ requires 210.0905. ν_{max} (KBr)(cm^{-1}) 3053, 2959, 2921, 1641, 1602, 1551, 1535. ^{13}C NMR δ($CDCl_3$) for **17** 152.21 (C), 149.20 (CH), 137.58 (C), 136.48 (CH), 135.79 (C), 132.19 (C), 126.50 (CH), 121.78 (CH), 120.44 (CH), 118.54 (CH), 114.77 (CH), 17.42 (CH_3), for **18** 136.82 (CH), 126.07 (CH), 125.09 (CH), 121.49 (CH), 121.38 (CH), 117.30 (CH), 115.74 (CH), 24.59 (CH_3). Then starting material (25 mg) was eluted.

Computational details

Geometries of the stationary structures **10a** and **13a** were fully optimised at the B3LYP theoretical level,[13,14] with the 6-31G* basis set[15] as implemented in the Gaussian 98 program.[16] Harmonic frequency calculations[17] verified the nature of the stationary points as minima (all real frequencies) and TS (only one imaginary frequency).

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