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Triazolopyridines. Part 24: New polynitrogenated potential helicating ligands☆

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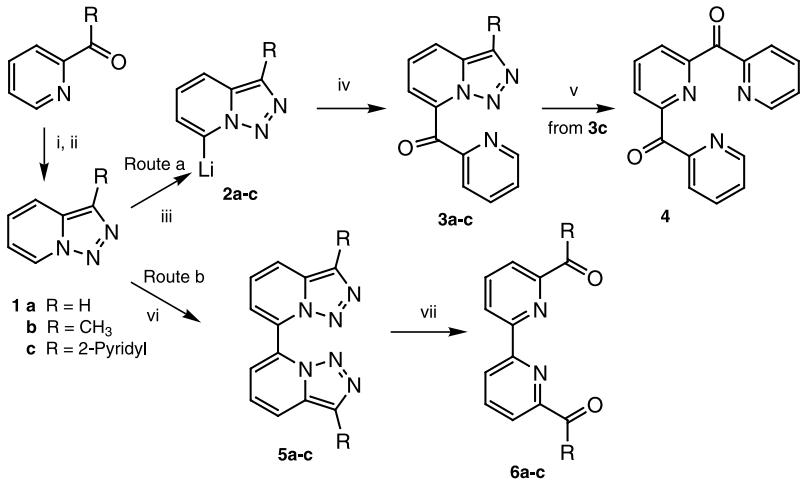
Abstract—The synthesis of novel 7-{[1,2,3]triazolo[1,5-*a*]pyridin-3-yl}-[1,2,3]triazolo[1,5-*a*]pyridines **7**, 2-pyridyl-[1,2,3]triazolo[1,5-*a*]-pyrid-7-ylmethanols **11**, 3-(6-substituted-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridines **12**, and 7,7′-disubstituted-3,3′-[1,2,3]triazolo[1,5-*a*]-pyridine **20**, interesting polynitrogenated ligands as potential helicating compounds or luminescent sensors, from [1,2,3]triazolo[1,5-*a*]-pyridines is described.

1. Introduction

The synthetic chemical mimicry of the double-helix structural motif is an interesting area of research with intense activity in recent years.[2] The formation of helicates, term introduced by Lehn and co-workers in 1987 for the description of a polymetallic helical double-stranded complex,[3] has become an important synthetic tool. Oligo-pyridines and related compounds are very useful helicating ligands.[2,4] We have recently discovered a facile route to new potential helicating ligands **3c**, **4**, **5a-c**, and **6a-c** from triazolopyridines **1a-c**,[5] (obtained by reaction of the corresponding acylpyridine with N_2H_4 and then oxidation with MnO_2), by regioselective lithiation at −40 °C, subsequent reaction with electrophiles and then triazolo ring opening with loss of dinitrogen,[6,7] (route a, Scheme 1) or by lithiation at −70 °C, giving 7,7′-bitriazolopyridines and then opening of the triazolo ring to produce 2,2′-bipyridines,[8] (route b, Scheme 1). Following this study we have designed new ligands **7**-**10**, which can be



Scheme 1. (i) N_2H_4; (ii) MnO_2, CL_2CH_2; (iii) LDA, THF, −40 °C; (iv) 2-PyCHO/air; (v) SeO_2; (vi) LDA, THF, −70 °C; (vii) SeO_2.

☆ See Ref. 1.

Keywords: Nitrogenated heterocycles; Helicating ligands; Lithiation; Luminescent sensors.
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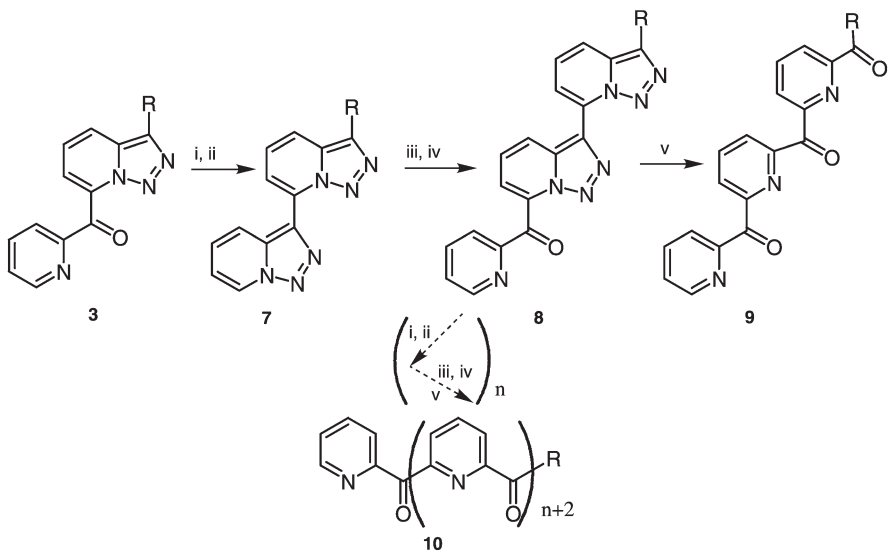
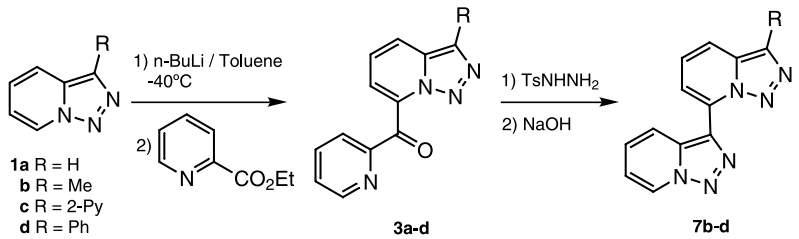


Scheme 2. (i) N_2H_4; (ii) MnO_2,Cl_2CH_2; (iii) LDA, −40 °C; (iv) 2-Py-CHO/air; (v) SeO_2.

easily accessible from compounds **3** if the methodology summarised above in route a is applicable (see Scheme 2). The understanding that the availability of **3** is important to success, led us to attempt to improve the reported yield.[9] We wish to report here our new results in this project, that allow us to synthesize the novel polynitrogenated ligands **7b**,**d**, **7c′**, **11b**,**d**, **11c′**, **12**-**14**, **16**, **18**-**20**, liable to make helicates as versatile supramolecular complexes.[10] These compounds have other potential fields of applications based on its rich photophysical and photo-chemical properties,[11] or as luminescent molecular sensors.[12]



Scheme 3.

Table 1. ^{1}H NMR data for compounds **3a**-**d**

	H4	H5	H6	H7	H3′	H4′	H5′	H6′	Others
3a	7.84, dd, J_1=8.85 Hz, J_2=1.50 Hz	7.29, dd, J_1=8.85 Hz, J_2=6.78 Hz	7.37, dd, J_1=6.78 Hz, J_2=1.50 Hz	—	8.15, ddd, J_1=7.71 Hz, J_2=1.10 Hz, J_3=0.93 Hz	7.88, ddd, J_1=J_2=7.71 Hz, J_3=1.68 Hz	7.43, ddd, J_1=7.71 Hz, J_2=4.71 Hz, J_3=1.10 Hz	8.44, ddd, J_1=4.71 Hz, J_2=1.68 Hz, J_3=0.93 Hz	8.37, s, H3
3b	7.73, dd, J_1=8.85 Hz, J_2=1.50 Hz	7.23, dd, J_1=8.85 Hz, J_2=6.78 Hz	7.34, dd, J_1=6.78 Hz, J_2=1.50 Hz	—	8.15, ddd, J_1=7.71 Hz, J_2=1.10 Hz, J_3=0.93 Hz	7.88, ddd, J_1=J_2=7.71 Hz, J_3=1.68 Hz	7.43, ddd, J_1=7.71 Hz, J_2=4.71 Hz, J_3=1.10 Hz	8.45, ddd, J_1=4.71 Hz, J_2=1.68 Hz, J_3=0.93 Hz	2.57, s, CH_3
3c	8.01, ddd, J_1=9.0 Hz, J_2=1.1 Hz, J_3=0.9 Hz	7.10, ddd, J_1=6.0 Hz, J_2=9.0 Hz, J_3=0.9 Hz	6.95, ddd, J_1=6.9 Hz, J_2=6.0 Hz, J_3=1.1 Hz	8.65, ddd, J_1=6.9 Hz, J_2=J_3=0.9 Hz	8.01, ddd, J_1=7.5 Hz, J_2=1.3 Hz, J_3=0.9 Hz	7.85, ddd, J_1=7.3 Hz, J_2=7.5 Hz, J_3=1.6 Hz	7.47, ddd, J_1=7.3 Hz, J_2=4.8 Hz, J_3=1.3 Hz	8.73, ddd, J_1=4.8 Hz, J_2=1.6 Hz, J_3=0.9 Hz	8.40, dd, J_1=7.6 Hz, J_2=1.3 Hz, H3″, 7.92, dd, J_1=7.6 Hz, J_2=7.7 Hz, H4″, 7.98, dd, J_1=7.7 Hz, J_2=1.3 Hz, H5″
3d	7.90–7.87, m, 3H*	7.37–7.35, m, 3H* *	7.90–7.87, m, 3H*	—	8.17, ddd, J=7.92 Hz	7.90–7.87, m, 3H*	7.44–7.41, m, 3H* * *	8.46, d, J=4.71 Hz	8.11–8.08, m, 1H, (H_p), 7.44–7.41, m, 3H, ($2H_o$* * *), 7.37–7.35, m, 3H, ($2H_m$* *)

*, * *, * * * Assigned by COSY experiments.

2. Results and discussion

We had reported that reaction of triazolopyridine **1c** in THF solution at −40 °C with LDA gave the 7-lithio derivative **2c** which reacted with 2-pyridine carbaldehyde to form an unstable diarylmethyl alkoxide intermediate, which provides rapid access to ketone **3c** by spontaneous air oxidation in work-up, with 35% yield.[5] Since we had found later that lithiation reactions of triazolopyridines **1** give better results using toluene as solvent and *n*-BuLi as lithiating agent, we thought that under these conditions, and with 2-cyanopyridine as co-reagent, we would be able to improve the yield of **3c**. However the new reaction gave, as only characterised product, the compound **3c** in almost the same yield. This type of reaction was also performed with compounds **1a**,**b**. In the conditions above indicated, the 7-lithio derivatives **2a**,**b** were formed. Subsequent reactions with 2-cyanopyridine gave the corresponding 7-pyridylcarbonyl derivatives **3a**,**b** in low yields.[9] We have now improved the results using as co-reagent ethyl picolinate, and compounds **3a**-**d** are obtained in 78, 75, 90 and 78% yield, respectively (Scheme 3).

After a carefully study of the 300 MHz ^{1}H NMR data of these compounds, compiled in Table 1, we realized that the δ and J values for the compound obtained in the reaction from **1c** don't fit properly with the structure **3c** that we proposed.[5,9] If we look the δ and J values for protons in acylpyridine (H3′, H4′, H5′, H6′) and triazolopyridine (H4, H5, H6) part of the compounds **3a**,**b**,**d**, there are the expected similarity in all of them, nevertheless for the so-called **3c** there are protons corresponding to an acylpyridyl group, but there are interesting features in the rest of data. Signals at δ 8.65 (1H, ddd, J_1=6.9 Hz, J_2=J_3=0.9 Hz, H7), 6.95 (1H, ddd, J_1=6.9 Hz, J_2=6.0 Hz, J_3=1.1 Hz, H6), 7.10 (1H, ddd, J_1=9.0 Hz, J_2=6.0 Hz, J_3=0.9 Hz, H5), 8.01 (1H, ddd, J_1=9.0 Hz, J_2=0.9 Hz, J_3=1.1 Hz, H4) for a 3-substituted triazolopyridine and 8.40 (1H, dd, J_1=7.6 Hz, J_2=1.3 Hz, H3″), 7.92 (1H, dd, J_1=7.6 Hz, J_2=7.7 Hz, H4″), 7.98 (1H, dd, J_1=7.7 Hz, J_2=1.3 Hz, H5″) for a 2,6-disubstituted pyridine are more in agreement with structure **3c′**. To account for this structure we assume that, in solution, the first formed **3c** is in equilibrium with the diazo form **A**, this intermediate may undergo a new ring-chain isomerization,[13,14] giving **3c′** (Scheme 4). A X-ray study of this compound is in progress.

To obtain compounds **7** from **3** we tried the 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.[15] When **3b** was the starting material compound **7b** (20%) was obtained together with a surprising alcohol **11b** (20%), and **3b** (25%) (Scheme 5). From **3c** the only identified compound was an alcohol, in the isomeric form **11c′**, and compound **3d** gave also an alcohol in the form **11d** (Fig. 1).

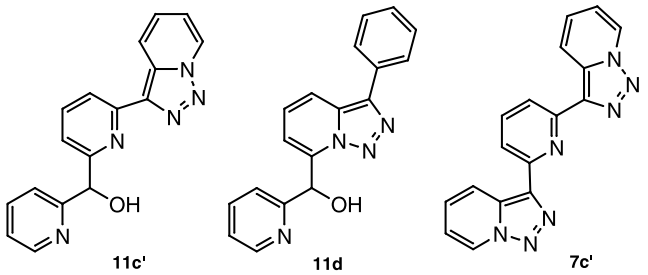
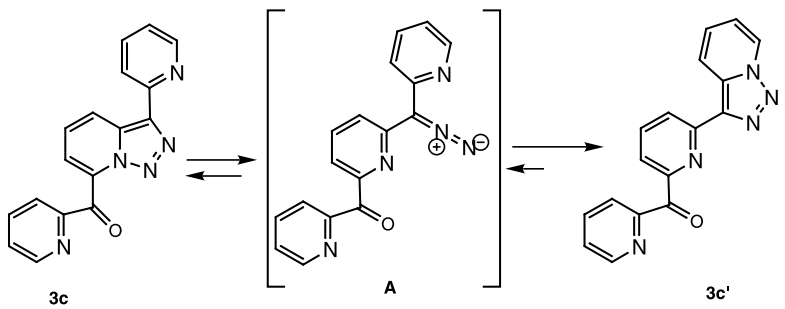
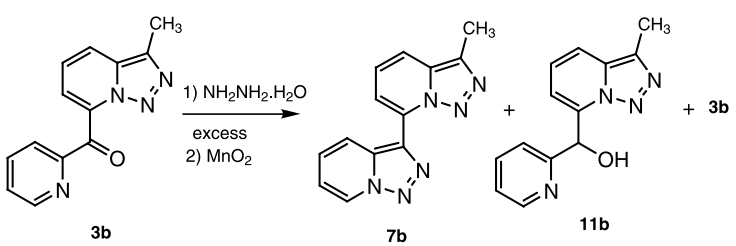


Figure 1.

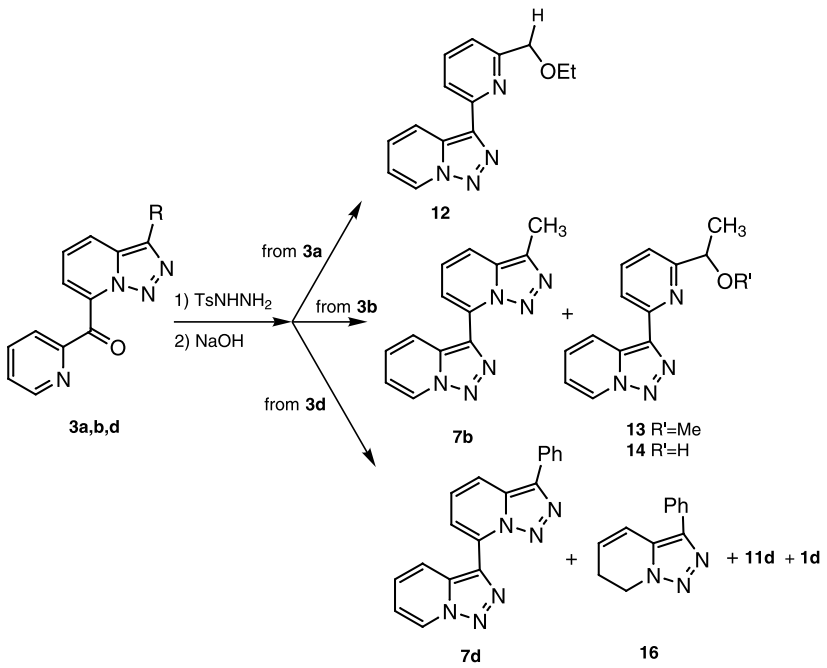
The formation of alcohols **11** is not easy to explain on treatment with an oxidizer. To check when they are formed we analysed the crude of the reaction with hydrazine, alcohols **11** are the only isolated compounds almost in quantitative yield. To account for its formation we believe that the hydrazones are formed and transformed to the diazo compounds by oxidation due to molecular oxygen,[16] that before to lie the equilibrium to triazolopyridines, loose nitrogen to form a carbene,[17] that is trapped by water to



Scheme 4.



Scheme 5.



Scheme 6.

form the alcohols.[18] We tried to avoid oxidation of the hydrazone to the diazo compound carrying out the reaction with **3b** under a nitrogen atmosphere but, a new reaction occurs giving two major products, triazolopyridine **1b** and an acylpyridine derivative.

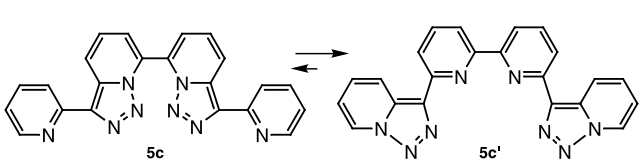
When $TsNHNH_2$ was used as co-reagent and the reaction work-up with aqueous sodium hydroxide,[19] compounds **7b**-**d** were finally synthesized in low or excellent yields, different secondary compounds were formed depending of the starting material. From **3a** in ethanol as solvent, an intractable mixture was formed from which could only be identified compound **12**. From **3b** in methanol as solvent, compounds **7b** (15%), **13** (15%), and **14** (15%) were isolated and identified (Scheme 6).

The formation of **12**, **13**, and **14** from the corresponding **7a**, or **7b** may be explained by the equilibrium between bitriazolopyrines **7a**,**b** and triazolopyridylpyridyl-diazoalkanes **15a**,**b** that could loose nitrogen to form a carbene trapped by solvents (ethanol, methanol, water) (Scheme 7).

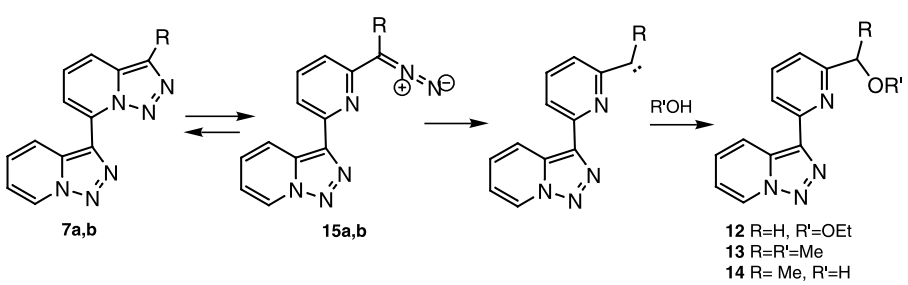
Best result was found with **3c**′, an unique product was formed in very good yield (96%). This compound shows a molecular ion of 313.1039 corresponding to a molecular formula of $C_{17}H_{11}N_7$. A carefully study of its ^1H and ^{13}C NMR data suggest a very symmetric structure with two 3-substituted triazolopyridines and a 2,6-disubstituted pyridine. We propose the structure **7c**′ for it (Fig. 1). That structure is resembling to terpyridines and the quelating properties could be similar.[4] Finally compound **3d** gave a mixture of **7d** (2%), **11d** (45%), **1d** (15%) and **16** (38%) (Scheme 6). Interesting the formation of **16**, we have verified that it is formed from **11d** in basic medium. A research is in progress to elucidate the mechanism and the scope of this transformation.

The structures proposed for **3c**′ and **7c**′ make us to turn to the structure of **5c**,[5] studying a more sensitive ^1H NMR spectrum we realised that the data fit better whit two 3-substituted triazolopyridines and one 6,6′-disubstituted-2,2′-bipyridine as in structure **5c**′ (Scheme 8).

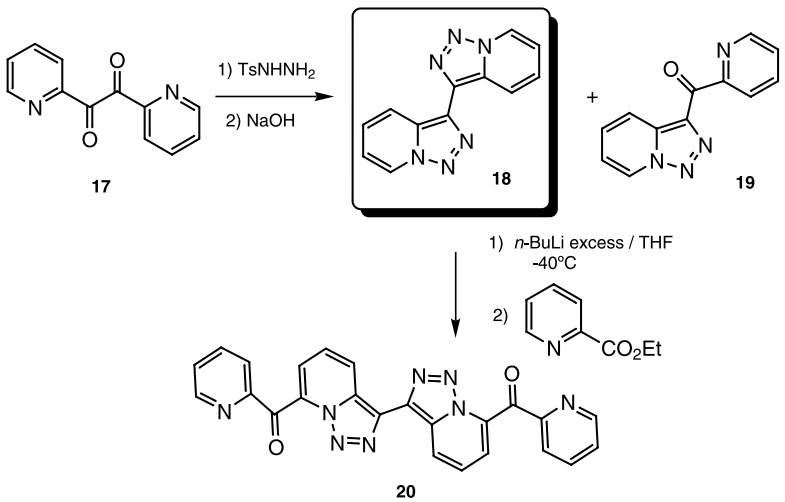
From 1,2-di(2-pyridyl)-1,2-ethanodione **17** by reaction



Scheme 8.



Scheme 7.



Scheme 9.

with $TsNHNH_2$ in basic medium we have synthesized 3,3′-bitriazolopyridine **18**. A secondary product was formed in this reaction that was identified as **19**. We have studied the behaviour of **18** with lithiating agents. Compound **18** is insoluble in toluene, we used THF as solvent and *n*-BuLi as co-reagent, after quenching with D_2O a 7,7′-dideuterio-3,3′-bitriazolopyridine was formed indicating the previous formation of a dilithium derivative. This intermediate is trapped by electrophiles. Reaction with two moles of ethyl picolinate gave **20** in 66% yield (Scheme 9). We have tried the lithiation of compound **7c′** in the same conditions, the 7,7′-dideuterio derivative have been identified after treatment of the dilithium derivative with D_2O, nevertheless reaction of dilithium compound with ethyl picolinate gave only polymeric compounds.

All new synthesized compounds have interesting ligand structures and should be able to form polynuclear complexes with different metal ions. We have studied the coordinating behaviour of **1b** with Cu(II),[20] and the spin crossover behaviour of some complex formed with **1c** and Fe(II).[21] We are at the present investigating the luminescence properties of **5c′** and **7c′** and their use as chemosensors.

3. 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. Ultraviolet spectra were recorded on a Shimazu UV-2101 instrument. All the lithiation reactions were done under inert atmosphere and dry solvents.[22]

[1,2,3]Triazolo[1,5-*a*]pyridine **1a**, 3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine **1b**, 3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]-pyridine **1c**, and 3-phenyl-[1,2,3]triazolo[1,5-*a*]pyridine **1d**. Prepared as described elsewhere.[13,19,23]

3.1. General procedure for lithiation of [1,2,3]triazolo-[1,5-*a*]pyridines 1a-d and reaction with ethyl picolinate

To a solution of the corresponding [1,2,3]triazolo[1,5-*a*]-pyridine **1** in anhydrous toluene at −40 °C, a solution of *n*-butyllithium in hexane (2.5 M) (20% excess) was added with stirring. A deep red colour developed. The mixture was kept at −40 °C (4 h). Treatment with a dry toluene solution (10 mL) of ethyl picolinate (20% excess) produced a colour change to yellow. The mixture was left at −40 °C (2 h) and allowed at room temperature overnight, then was treated with a saturated solution of ammonium chloride. The organic layer was separated and the aqueous layer extracted with dichloromethane. After dried over anhydrous Na_2SO_4 and evaporation of the organic solvents, a residue was obtained. Precipitation with ethyl acetate gave compounds **3a-d** as brown or yellow solids. In same cases the filtrate was evaporated to dryness and the residue purified by chromatotron with ethyl acetate/hexane as eluent, to obtain additional amount of compound **3**. The yield and conditions of purification are given for each compound.

3.1.1. 2-Pyridyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-ylmethanone 3a. *Compound* **1a** (1 g, 8.4 mmol), toluene (40 mL), *n*-BuLi (4 mL), ethyl picolinate (1.5 mL), (78%). Purification by recrystallization from ethyl acetate. Mp 158–160 °C. Lit.[9] 158–160 °C.

3.1.2. 2-Pyridyl-3-methyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-ylmethanone 3b. *Compound* **1b** (0.5 g, 3.75 mmol), toluene (20 mL), *n*-BuLi (1.9 mL), ethyl picolinate (0.7 mL), (75%). Purification by recrystallization from ethyl acetate. Mp 165–167 °C. Lit.[9] 165–167 °C.

3.1.3. 2-Pyridyl-6-[1,2,3]triazolo[1,5-*a*]pyrid-3-yl-2-pyridylmethanone 3c′. *Compound* **1c** (0.5 g, 2.5 mmol), toluene (20 mL), *n*-BuLi (1.6 mL), ethyl picolinate (0.4 mL), (90%). Purification by recrystallization from ethyl acetate/hexane give two crystalline phases. At 194–195 °C there is a phase transition forming needles that melt at 220–221 °C.[9] Lit.[5] 194–195 °C.

3.1.4. 2-Pyridyl-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-ylmethanone 3d. *Compound* **1d** (1 g, 5.13 mmol), toluene (40 mL), *n*-BuLi (4 mL), ethyl picolinate (1.5 mL), (78%). Purification by recrystallization from ethyl acetate/hexane. Mp 169–171 °C. HRMS found for M^+ 300.0993; $C_{18}H_{12}N_4O$ requires 300.1011. ν_{max} (KBr) (cm^{-1}) 1689 (CO), 1584, 1313, 1293, 1063, 758, 693. λ_{max} (nm) (log ε) (EtOH) 293.5 (4.04), 381.5 (3.58). ^{13}C NMR δ 188.40 (CO), 153.08 (C), 149.25 (CH), 138.09 (C), 137.36 (CH), 135.12 (C), 131.15 (C), 130.74 (C), 129.03 (2CH), 128.10 (CH), 127.72 (CH), 126.90 (2CH), 125.00 (CH), 123.75 (CH), 121.10 (CH), 118.15 (CH). MS *m*/*z* (%) 300 (6), 272 (100), 271 (59), 243 (41), 194 (25), 166 (41), 78 (49).

3.2. General procedure for reaction of 2-pyridyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-yl methanones 3b-d with hydrazine hydrate

Procedure A. A solution of the corresponding 2-pyridyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-ylmethanone in ethanol was added to an excess of hydrazine hydrate, and was heated under reflux. Then water (10 mL) was added and extracted with dichroromethane (3×10 mL). The organic layer was dried and evaporated, the residue was dissolved in chloroform (5 mL). Manganese oxide (50% excess) was added and the mixture heated to reflux, then was filtered and the solvent was evaporated. The residue was purified by chromatotron using hexane/ethyl acetate as eluent.

Procedure B. A solution of the corresponding 2-pyridyl-[1,2,3]triazolo[1,5-*a*]pyridin-7-ylmethanone in a organic solvent was added to an excess of hydrazine hydrate, and was heated under reflux. Then water (10 mL) was added and extracted with dichroromethane (3×10 mL). The organic layer was dried and evaporated. The residue was purified by chromatotron using hexane/ethyl acetate as eluent.

3.2.1. 3-Methyl-7-{[1,2,3]triazolo[1,5-*a*]pyrid-3-yl}-[1,2,3]triazolo[1,5-*a*]pyridine 7b. The title compound was obtained by procedure A from **3b** (100 mg, 0.42 mmol), refluxed 24 h and after addition of the oxidant an additional time (1 h 30 m) was refluxed, **7b** was the first eluted product (20%). Mp 218–220 °C (AcOEt). HRMS found M^+ 250.0971; $C_{13}H_{10}N_6$ requires 250.0966. ν_{max} (KBr) (cm^{-1}) 3110, 1643, 1627, 1536, 1407, 1218, 1162, 780, 740. λ_{max} (nm) (log ε) (Cl_2CH_2) 229 (4.08), 283 (4.08), 349.5 (3.96). ^1H NMR δ 8.74 (d, J=6.96 Hz, 1H, H7′), 8.41 (d, J=9.24 Hz, 1H, H4), 7.68 (dd, J_1=6.75 Hz, J_2=1.14 Hz, 1H, H6), 7.62 (dd, J_1=8.67 Hz, J_2=1.14 Hz, 1H, H4′), 7.31 (m, 2H, H5, H5′), 7.04 (ddd, J_1=6.96 Hz, J_2=6.78 Hz, J=1.14 Hz, 1H, H6′), 2.63 (s, 3H, CH_3). ^{13}C NMR δ 134.87 (C), 132.49 (C), 130.39 (C), 130.34 (C), 130.24 (C), 126.10 (CH), 125.35 (CH), 124.29 (CH), 122.49 (CH), 116.26 (CH), 115.92 (CH), 115.67 (CH), 10.51 (CH_3). MS *m*/*z* (%) 250 (29), 222 (12), 194 (33), 193 (100), 192 (31), 179 (16), 166 (12). Then starting material **3b** (25%) was eluted, further elution gave 2-pyridyl-3-methyl-[1,2,3]-triazolo-[1,5-*a*]pyrid-7-ylmethanol **11b** (20%). Mp 113–115 °C. Lit.[24] 113–115 °C (CH_2Cl_2/hexane).

3.2.2. 2-Pyridyl-3-methyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-ylmethanol 11b. The title compound was obtained by procedure B from **3b** (10 mg, 0.042 mmol), solvent *n*-BuOH, refluxed 30 min, almost pure in quantitative yield.

3.2.3. 2-Pyridyl-6-{[1,2,3]triazolo[1,5-*a*]pyrid-3-yl}-2-pyridylmethanol 11c′. The title compound was obtained by procedure B from **3c′** (10 mg, 0.039 mmol), solvent *n*-BuOH, refluxed 30 m, almost pure in quantitative yield. Mp 124–126 °C (cyclohexane). HRMS found for M^+ 303.1122; $C_{17}H_{13}N_5O$ requires 303.1120. ν_{max} (KBr) (cm^{-1}) 3324, 3182, 1590, 1055, 745. λ_{max} (nm) (log ε) (EtOH) 207 (4.36), 268 (4.20), 326 (4.14). ^1H NMR δ 8.70 (d, J=6.99 Hz, 1H, H7), 8.53 (m, 2H, H4, H6″), 8.19 (dd, J_1=7.92 Hz, J_2=0.96 Hz, 1H, H5′), 7.73 (dd, J_1=7.92 Hz, J_2=7.71 Hz, 1H, H4′), 7.63 (ddd, J_1=7.71 Hz, J_2=7.92 Hz, J_3=1.5 Hz, 1H, H4″), 7.49 (d, J=7.92 Hz, 1H, H3″), 7.41 (d, J=7.71 Hz, 1H, H3′), 7.33 (ddd, J_1=6.78 Hz, J_2=9.06 Hz, J_3=0.96 Hz, 1H, H5), 7.19 (ddd, J_1=7.71 Hz, J_2=5.1 Hz, J_3=1.14 Hz, 1H, H5″), 7.00 (ddd, J_1=6.99 Hz, J_2=6.78 Hz, J_3=1.32 Hz, 1H, H6), 5.98 (s, 1H, *CH*–OH), 2.1 (brs, 1H, OH). ^{13}C NMR δ 160.72 (C), 151.19 (C), 147.91 (CH), 138.18 (CH), 137.99 (CH), 137.50 (C), 132.36 (C), 126.96 (CH), 125.78 (CH), 123.31 (CH), 123.32 (C), 122.11 (CH), 121.36 (CH), 119.93 (CH), 119.89 (CH), 116.25 (CH), 75.63 (CH–OH).

3.2.4. 2-Pyridyl-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-ylmethanol 11d. The title compound was obtained by procedure B from **3d** (50 mg, 0.19 mmol), solvent ethanol, refluxed 2 h, in 53% yield. Mp 157–158 °C (hexane). HRMS found for M^+ 302.1163; $C_{18}H_{14}N_4O$ requires 302.1167. ν_{max} (KBr) (cm^{-1}) 3201, 1591, 1549, 1477, 1451, 1263, 1223, 1182, 1080, 995, 790, 705. λ_{max} (nm) (log ε) (EtOH) 301.5 (4.01), 322 (3.93). ^1H NMR δ 8.46 (d, J=4.71 Hz, 1H, H6′), 7.81–7.88 (m, 4H, 2H*o*, H4, H3′), 7.58 (ddd, J_1=7.92 Hz, J_2=7.53 Hz, J_3=1.71 Hz, 1H, H4′), 7.38–7.44 (m, 2H, H*m*), 7.31 (ddd, J_1=7.32 Hz, J_2=J_3=1.32 Hz, 1H, H*p*), 7.24 (dd, J_1=J_2=8.85 Hz, 1H, H5), 7.15 (ddd, J_1=7.53 Hz, J_2=4.71 Hz, J_3=0.93 Hz, 1H, H5), 7.10 (d, J=6.78 Hz, 1H, H6), 6.68 (brs, 1H, CH), 5.75 (brs, 1H, OH). ^{13}C NMR δ 157.31 (C), 148.42 (CH), 140.15 (C), 138.12 (C), 137.18 (CH), 131.31 (C), 130.93 (C), 128.95 (2CH), 127.88 (CH), 126.63 (2CH), 126.10 (CH), 123.46 (CH), 122.16 (CH), 117.08 (CH), 112.84 (CH), 70.01 (CH). MS *m*/*z* (%) 302 (8), 274 (48), 257 (100), 168 (37), 78 (19).

3.3. General procedure for reaction of 2-pyridyl-[1,2,3]-triazolo[1,5-*a*]pyrid-7-yl methanones 3a-d with tosylhydrazine

A solution of the corresponding 2-pyridyl-[1,2,3]triazolo-[1,5-*a*]pyrid-7-ylmethanone in suitable alcohol was added to an equimolar solution of tosylhydrazine in ethanol, the mixture was boiled under reflux for 5 h, and then was treated with aqueous sodium hydroxide and refluxed for an additional time (1 h). The mixture was concentrated under reduced pressure to 10–15 mL and, in some cases, after cooling a precipitate was formed that was filtered and identified. The filtrate was extracted with an organic solvent (3×10 mL). The organic layer was dried (Na_2SO_4), evaporated, and the crude purified by chromatotron eluting with ethyl acetate/hexane. The yield and conditions of purification are given for each compound.

3.3.1. 3-[6-(1-Ethoxyethyl)-2-pyridyl]-[1,2,3]triazolo-[1,5-*a*]pyridine 12. *Compound* **3a** (0.1 g, 0.45 mmol), tosylhydrazine (0.11 g, 0.6 mmol), ethanol (50 mL), NaOH (3 mL, 2 N). No precipitate was formed, and the solution was extracted with dichloromethane. The only isolated compound as an oil was identified as 3-[6-(1-ethoxiethyl)-2-pyridyl]-[1,2,3]triazolo[1,5-*a*]pyridine **12** (26 mg, 23%). HRMS found for M^+ 254.1127; $C_{14}H_{14}N_4O$ requires 254.1167. ^{1}H NMR δ 8.67 (d, J=6.59 Hz, 1H, H7), 8.65 (d, J=8.29 Hz, 1H, H4), 8.16 (d, J_1=7.91 Hz, 1H, H5′), 7.73 (dd, J_1=7.91 Hz, J_2=7.70 Hz, 1H, 4H′), 7.32–7.27 (m, 2H, H5, H3′), 6.96 (ddd, J_1=6.97 Hz, J_2=6.59 Hz, J_3=1.32 Hz, 1H, H6), 4.65(s, 2H, CH2), 3.60 (c, J=6.97 Hz, 2H, CH2), 1.35 (t, J=6.97 Hz, 3H, CH_3). ^{13}C NMR δ 158.42 (C), 151.25 (C), 137.28 (CH), 136.57 (C), 132.00 (C), 126.23 (CH), 125.20 (CH), 120.53 (CH), 119.44 (CH), 118.92 (CH), 115.83 (CH), 73.82 (CH_2), 66.44 (CH_3), 15.32 (CH_3). MS *m/z* (%) 254 (22), 226 (39), 181 (100), 169 (16), 142 (10), 78 (11).

3.3.2. 3-Methyl-7-{[1,2,3]triazolo[1,5-*a*]pyrid-3-yl}-[1,2,3]triazolo[1,5-*a*]pyridine 7b. *Compound* **3b** (0.1 g, 0.44 mmol), tosylhydrazine (0.08 g, 0.42 mmol), methanol (10 mL), NaOH (7 mL, 2 N). The precipitate was 3-methyl-{7-[1,2,3]triazolo[1,5-*a*]pyridin-3-yl}-[1,2,3]triazolo[1,5-*a*]-pyridine **7b** almost pure (15 mg, 14%). The filtrate was extracting with ether (3×10 mL). The organic layer was dried (Na_2SO_4), evaporated, and the crude (66 mg) purified by chromatotron eluting with ethyl acetate/hexane. First was eluted 3-[6-(1-methoxyethyl)-2-pyridyl]-[1,2,3]triazolo[1,5-*a*]pyridine **13** (15 mg, 15%) as an oil. HRMS found for M^+ 254.1130; $C_{14}H_{14}N_4O$ requires 254.1167. ^{1}H NMR δ 8.68 (m, 2H, H4, H7), 8.17 (dd, J_1=7.92 Hz, J_2=0.96 Hz, 1H, H5′), 7.74 (dd, J_1=7.92 Hz, J_2=7.74 Hz, 1H, H4′), 7.30 (ddd, J_1=8.85 Hz, J_2=6.88 Hz, J_3=1.14 Hz, 1H, H5), 7.26 (dd, J_1=7.74 Hz, J_2=0.96 Hz, 1H, H3′), 6.97 (ddd, J_1=6.96 Hz, J_2=6.88 Hz, J_3=1.14 Hz, 1H, H6), 4.46 (c, J=6.57 Hz, 1H, CH), 3.31 (s, OCH_3) 2.50 (d, J=6.57 Hz, 3H, CH_3). ^{13}C NMR δ 162.44 (C), 151.28 (C), 137.40 (CH), 136.56 (C), 132.08 (C), 126.28 (CH), 125.20 (CH), 121.51 (CH), 118.94 (CH), 118.18 (CH), 115.83 (CH), 80.85 (CH), 56.96 (OCH_2), 22.18 (CH_3). MS *m/z* (%) 254 (24), 226 (50), 211 (45), 195 (100), 181 (37), 169 (14), 168 (37), 78 (19). The second fraction was an oil identified as 3-[6-(1-hydroxyethyl)-2-pyridyl]-[1,2,3]triazolo[1,5-*a*]pyridine **14** (16 mg, 15%). HRMS found M^+ 240.1022; $C_{13}H_{12}N_4O$ requires 240.1011. ^{1}H NMR δ 8.71 (d, J=7.17 Hz, 1H, H7), 8.52 (d, J=9.03 Hz, 1H, H4), 8.21 (d, J=7.74 Hz, 1H, H5′), 7.76 (dd, J_1=J_2=7.74 Hz, 1H, H4′), 7.34 (ddd, J_1=9.03 Hz, J_2=6.96 Hz, J_3=0.96 Hz, 1H, H5), 7.17 (d, J=7.74 Hz, 1H, H3′), 7.01 (ddd, J_1=6.96 Hz, J_2=7.17 Hz, J_3=1.14 Hz, 1H, H6), 4.94 (c, J=6.42 Hz, 1H, CH), 3.60 (brs, 1OH), 1.54 (d, J=6.42 Hz, 3H, CH_3). ^{13}C NMR δ 162.58 (C), 150.59 (C), 137.68 (CH), 137.07 (C), 131.87 (C), 126.66 (CH), 125.43 (CH), 120.74 (CH), 119.23 (CH), 118.17 (CH), 115.89 (CH), 69.22 (CH), 24.34 (CH_3). MS *m/z* (%) 240 (46), 212 (73), 197 (100), 169 (89), 78 (20).

3.3.3. 3-{6-([1,2,3]Triazolo[1,5-*a*]pyrid-3-yl)-2-pyridyl}-[1,2,3]triazolo[1,5-*a*]pyridine 7c′. *Compound* **3c′** (0.1 g, 0.33 mmol), ethanol (50 mL), tosylhydrazine (0.08 g, 0.42 mmol), ethanol (50 mL), NaOH (3 mL, 2 N). The precipitate was compound **7c′** almost pure (90 mg). The filtrate was extracting with dichloromethane (50 mL). The organic layer was dried (Na_2SO_4) and evaporated giving a crude, that was treated with ethanol (10 mL) and compound **7c′** was precipitated (10 mg) (total yield 96%). Mp 279–281 °C (EtOH/H_2O). HRMS found for M^+ 313.1039; $C_{17}H_{11}N_7$ requires 313.1075. ν_{max} (KBr) (cm^{-1}) 3087, 1631, 1595, 1570, 1529, 1448, 1402, 1162, 821, 740. λ_{max} (nm) (log ε) (EtOH) 294 (5.56), 336.5 (5.53). ^{1}H NMR δ 8.74 (ddd, J_1=6.99 Hz, J_2=J_3=0.93 Hz, 2H, H7, H7′), 8.54 (ddd, J_1=8.85 Hz, J_2=J_3=1.32 Hz, 2H, H4, H4′), 8.19 (d, J=7.71 Hz, 1H, H4″), 7.88 (t, J=7.71 Hz, 2H, H3″, H5″), 7.30 (ddd, J_1=8.85 Hz, J_2=6.78 Hz, J_3=0.93 Hz, 2H, H5, H5′), 7.01 (ddd, J_1=6.99 Hz, J_2=6.78 Hz, J_3=1.32 Hz, 2H, H6, H6′). ^{13}C NMR δ 151.39 (2C), 137.90 (2C), 137.58 (CH), 131.89 (2C), 126.34 (2CH), 125.59 (2CH), 120.49 (2CH), 119.62 (2CH), 115.77 (2CH). MS *m/z* (%), 313 (32), 285 (10), 257 (95), 256 (100), 229 (23), 179 (78), 78(13).

3.3.4. 3-Phenyl-7-{[1,2,3]triazolo[1,5-*a*]pyrid-3-yl}-[1,2,3]triazolo[1,5-*a*]pyridine 7d. *Compound* **3d** (0.2 g, 0.66 mmol), tosylhydrazine (0.36 g, 1.98 mmol), ethanol (110 mL), NaOH (6 mL, 2 N). A yellow solid was filtrated, identified as compound **7d** (4 mg, 2%) almost pure. Mp 218–220 °C (EtOH/H_2O). HRMS found for M^+ 312.1077; $C_{18}H_{12}N_6$ requires 312.1123. ^{1}H NMR δ 8.77 (ddd, J_1=6.96 Hz, J_2=1.14 Hz, J_3=0.93 Hz, 1H, H7′), 8.48 (ddd, J_1=9.21 Hz, J_2=1.14 Hz, J_3=0.93 Hz, 1H, H4′), 8.02 (dd, J_1=8.85 Hz, J_2=1.14 Hz, 1H, H4), 7.97–794 (m, 2H, H*o*), 7.78 (dd, J_1=6.96 Hz, J_2=1.14 Hz, 1H, H6), 7.54–7.41 (m, 3H, H5, 2H*m*), 7.39–7.33 (m, 2H, H5′, H*p*) 7.07 (ddd, J_1=6.96 Hz, J_2=6.78 Hz, J_3=1.14 Hz, 1H, H6′). MS *m/z*(%) 312 (8), 284 (9), 256 (58), 255 (100), 230 (8), 152 (5), 78 (6). First fraction eluted from chromatotron was 3-phenyl-[1,2,3]triazolo[1,5-*a*]pyridine **1d** (19 mg, 15%). The second fraction was a yellow solid identified as 3-phenyl-6,7-dihydro[1,2,3]triazolo[1,5-*a*]pyridine **16** (50 mg, 38%). Mp 100–102 °C (hexane). HRMS found for M^+ 197.0870; $C_{12}H_{11}N_3$ requires 197.0953. ^{1}H NMR δ 7.75 (dd, J_1=7.14 Hz, J_2=1.5 Hz, 2H, H*o*), 7.45 (dd, J_1=J_2=7.14 Hz, 2H, H*m*), 7.36 (dd, J_1=7.14 Hz, J_2=1.5 Hz, 1H, H*p*), 6.78 (ddd, J_1=9.99 Hz, J_2=J_3=1.89 Hz, 1H, H4), 6.19 (ddd, J_1=9.99 Hz, J_2=J_3=4.35 Hz, 1H, H5), 4.45 (t, J=7.74 Hz, 2H, H7, H7′), 2.67 (m, 2H, H6, H6′). ^{13}C NMR δ 142.06 (C), 131.23 (C), 128.85 (2CH), 127.97 (CH), 127.58 (CH), 126.93 (2CH), 126.17 (C), 116.25 (CH), 44.09 (CH_2), 23.92 (CH_2). MS *m/z* (%) 197 (58), 169 (100), 168 (93), 154 (50), 141 (46), 115 (36), 104 (20), 77 (12), 66 (44). The last fraction was 2-pyridy-3-phenyl-[1,2,3]triazolo-[1,5-*a*]pyridin-7-ylmethanol **11d** (89 mg, 45%).

3.3.5. 3,3′-Bi[1,2,3]triazolo[1,5-*a*]pyridine 18. A mixture of 1,2-di(2-pyridil)-1,2-ethanodione (1 g, 4.7 mmol) and tosylhydrazine (1.85 g, 9.9 mmol) in ethanol (50 mL) was boiled under reflux (8 h). After treating with aqueous sodium hydroxide (7 mL, 2 N) the reaction was refluxed for 2 h. Then the solvent was concentrated in vacuo to 10–15 mL and a precipitate was obtained. By filtration, compound **18** was separated (0.45 g) almost pure. Mp 262–264 °C (EtOH). Lit.[19] 254–255 °C (EtOH). No spectroscopical data is in the literature. HRMS found for M^+ 236.0806; $C_{12}H_8N_6$ requires 236.0810. ν_{max} (KBr) (cm^{-1}) 3113, 1630, 1530, 1504, 1152, 1015, 755. λ_{max} (nm) (log ε) (EtOH) 294.5 (5.36), 349.5 (5.29). ^{1}H NMR δ 8.71 (ddd,

J_1=6.99 Hz, J_2=J_3=0.96 Hz, 2H, H7, H7′), 8.62 (ddd, J_1=9.03 Hz, J_2=J_3=1.11 Hz, 2H, H4, H4′), 7.32 (ddd, J_1=9.03 Hz, J_2=6.99 Hz, J_3=0.96 Hz, 2H, H5, H5′), 7.01 (ddd, J_1=J_2=6.99 Hz, J_3=1.11 Hz, 2H, H6, H6′). ^{13}C NMR δ 134.22 (C3, C3′), 131.02 (C3a, C3a′), 125.65 (C7, C7′), 125.01 (C4, C4′), 120.50 (C5, C5′), 116.11 (C6, C6′). MS *m/z* (%) 236 (17), 180 (100). The filtrate was extracted with ether (3×25 mL). The organic layer was dried (Na_2SO_4), evaporated, and the crude purified by chromatotron, eluting with ethyl acetate hexane bitriazoplopyridine **18** was first eluted (0.08 g, total yield 48%), the second fraction was 2-pyridyl-[1,2,3]triazolo[1,5-*a*]pyridin-3-ylmethanone **19** (0.081 g, 8%). Mp 150–152 °C (MeOH/H_2O). Lit.[22] 151 °C (acetone). No spectroscopical data are in the literature. HRMS found for M^+ 224.0695; $C_{12}H_8N_4O$ requires 224.0698. ν_{max} (KBr) (cm^{-1}) 3077, 3030, 1655 (CO), 1626, 1514, 1418, 1229, 943, 770. λ_{max} (nm) (log ε) (EtOH) 327 (4.18). ^{1}H NMR δ 8.81 (m, 2H, H6′, H7), 8.48 (ddd, J_1=8.85 Hz, J_2=J_3=1.11 Hz, 1H, H4), 8.33 (ddd, J_1=7.71 Hz, J_2=J_3=0.93 Hz, 1H, H3′), 7.85 (ddd, J_1=J_2=7.71 Hz, J_3=1.68 Hz, 1H, H4′), 7.57 (ddd, J_1=8.85 Hz, J_2=6.78 Hz, J_3=0.93 Hz, 1H, H5), 7.44 (ddd, J_1=7.71 Hz, J_2=4.68 Hz, J_3=1.11 Hz, 1H, H5′), 7.15 (ddd, J_1=J_2=6.78 Hz, J_3=1.11 Hz, 1H, H6). ^{13}C NMR δ 185.40 (CO), 154.41 (C), 149.73 (CH), 136.77 (CH), 136.47 (C), 136.16 (C), 130.40 (CH), 126.36 (CH), 125.86 (CH), 125.42 (CH), 120.48 (CH), 117.04 (CH). MS *m/z* (%) 224 (10), 196 (9), 168 (100), 140 (12), 78 (12).

3.3.6. 7,7′-Di(2-pyridylcarbonyl)-3,3′-bi[1,2,3]triazolo[1,5-*a*]pyridine 20. To a solution of 3,3′-bi[1,2,3]triazolo[1,5-*a*]pyridine **18** (0.1 g, 0.42 mmol) in anhydrous THF (100 mL) at −40 °C, a solution of *n*-butyllithium in hexane (0.7 mL, 2.5 M, 4 equiv.) was added with stirring. A deep red colour developed. The mixture was kept at −40 °C (2 h). Further, a deep orange-yellow colour was developed and a new amount of *n*-BuLi (0.3 mL, 2 equiv.) was added. The mixture was kept at −40 °C (2 h). Then was treated with a dry THF solution (5 mL) of ethyl picolinate (0.2 g, 1.32 mmol, 3 equiv.). The mixture was left at −40 °C (2 h), and treated with a saturated solution of ammonium chloride. The organic layer was separated and the aqueous layer extracted with dichloromethane. After drying over anhydrous Na_2SO_4 and evaporation of the organic solvents, a residue was obtained (0.2 g). Precipitation with ethyl acetate gave the compound **20** as a yellow solid (0.1 g) almost pure. Mp 190–192 °C (AcOEt). HRMS found for M^+-2N_2 390.1137; $C_{24}H_{14}N_4O_2$ requires 390.1116. ν_{max} (KBr) (cm^{-1}) 3095, 3060, 2924, 2859, 1684 (CO), 1581, 1313, 1063, 743. λ_{max} (nm) (log ε) (EtOH) 291 (3.93), 402 (3.61). ^{1}H NMR δ 8.75 (dd, J_1=8.46 Hz, J_2=1.5 Hz, 1H, H4), 8.43 (ddd, J_1=4.71 Hz, J_2=1.68 Hz, J_3=0.75 Hz, 1H, H6′), 8.18 (d, J=7.71 Hz, 1H, H3′), 7.91 (ddd, J_1= J_2=7.71 Hz, J_3=1.68 Hz, 1H, H4′), 7.48–7.39 (m, 3H, H5′, H5, H6). ^{13}C NMR 186.46 (CO), 152.18 (C), 149.57 (CH), 138.11 (CH), 134.34 (C), 130.39 (C), 130.26 (C), 128.60 (CH), 126.91 (CH), 123.37(CH), 121.45 (CH), 118.71 (CH). MS *m/z* (%), 300 (6), 272 (100), 271 (59), 243 (41), 194 (25), 166 (41), 78 (49). The filtrate was evaporated and purified by chromatotron with ethyl acetate/hexane as eluent. An additional amount of compound **20** (0.017 g) was obtained (total yield 66%), ethyl picolinate (0.078 g, 38%) and starting material (0.005 g, 5%).

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