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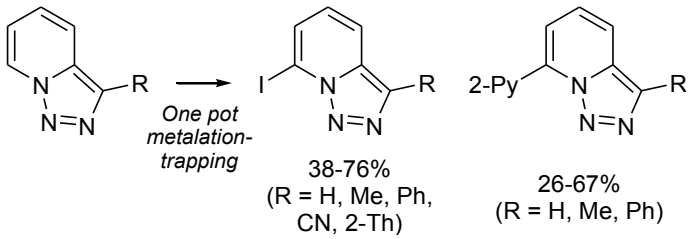


Abstract:

[1,2,3]Triazolo[1,5-*a*]pyridine and 3-substituted derivatives were regioselectively metalated at the 7 position using either Bu_3MgLi or $(TMP)_3CdLi$, the former at –10 °C and the latter at room temperature. The lithium arylmagnesates (R = H, Me, Ph) proved to react with iodine (34-75%) or 3,4,5-trimethoxybenzaldehyde (32-51%). Attempts to obtain the cross-couplings products using 2-bromopyridine under palladium catalysis failed, a result attributed to the low stability of these compounds. The corresponding lithium arylzincates reacted in 17 to 60% yield under the same reaction conditions. The lithium arylcadmates were either trapped with iodine (38-76%, R = H, Me, Ph, CN, 2-thienyl) or involved in palladium-catalyzed cross-coupling reactions with 2-bromopyridine (26-67%, R = H, Me, Ph). For R = 2-pyridyl, 3-(6-iodo-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine was isolated in 73% yield. $(TMP)_3CdLi$ also proved suitable for the clean dideprotonation of two substrates (R = H, 2-thienyl), a result demonstrated by quenching with iodine (66-75%).

Introduction

The deprotonative metalation of aromatic rings has been widely used as a powerful method for regioselective functionalization. The methodology using alkyllithiums and lithium dialkylamides have been largely employed for this purpose.[1] Nevertheless their use is limited to substrates with C-H acidity enhanced by directing groups and generally requires low reaction temperatures due to the high reactivity of the corresponding aryllithiums. In addition, unlike organoboron, organotin, organozinc and organomagnesium compounds, organolithiums can hardly be involved in cross-coupling reactions.[2]

Mixed alkaline organobimetallic mixtures such as those described by Schlosser[3] and Lochmann[4] exhibit powerful basic properties that cannot be attained by the homometallic compounds on their own, but low chemoselectivities. Organobimetallic mixtures containing only one alkali atom display a large panel of reactivities depending on both the non-alkali metal and the groups connected to it. R_nMLi–type ate compounds, present in stoichiometric[5] or catalytic[6] amounts in these mixtures, are in general supposed to be responsible for the exhibited reactivities ("synergy").

In the framework of studies dealing with triazolopyridine systems,[7] we have been interested in the development of new strategies to functionalize [1,2,3]triazolo[1,5-*a*]pyridines. Among the methods used,[8] deprotonative metalation reactions using lithium bases have been developed, and prove efficient in the absence of reactive functional groups, provided that very low reaction temperatures are used.

Herein, we report the first regio-controlled functionalization of [1,2,3]triazolo[1,5-*a*]pyridines using lithium-magnesium and lithium-cadmium organobimetallic bases.

Results and Discussion

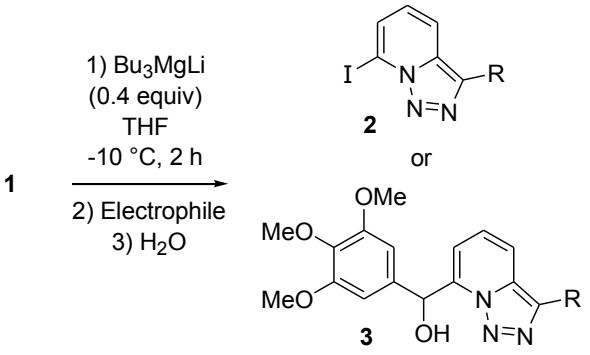
To develop new deprotonation reactions of [1,2,3]triazolo[1,5-*a*]pyridines, our approach first capitalized on the good reactivity of magnesates. Since 1999, Mulvey has documented the preparation of mixed alkali metal-magnesium amides for the site selective deprotonation of benzene,[9] toluene,[10] ferrocene,[11] ruthenocene,[12] osmocene,[12] bis(arene)chromium,[13] and furan.[14] At the same time, we studied the deprotonative metalation of pyridines,[15] thiophenes,[16] oxazoles,[17] and furans[18] using easily available lithium magnesates, the obtained arylmagnesates being either trapped with electrophiles or involved in palladium-catalyzed cross-couplings.

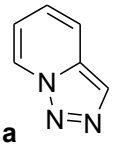
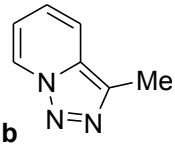
First studies about the lithiation of [1,2,3]triazolo[1,5-*a*]pyridine (**1a**) have been reported from 1980, and showed butyllithium and lithium diisopropylamide (LiDA) are suitable for a regioselective metalation at the 7 position when used in ethereal solvents (the best yields being obtained in tetrahydrofuran) provided that the reaction temperature is kept below –40 °C.[19] Similar reaction

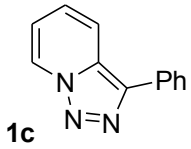
conditions can be used for 3-methyl and 3-phenyl derivatives **1b**,**c**.[19] Above this temperature, the corresponding 7,7'-dimers form.[20] Metalation yields were improved in 1987 by using butyllithium in toluene at –40 °C.[21]

The deprotonation of [1,2,3]triazolo[1,5-*a*]pyridine[22] (**1a**) was attempted using 1/3 equiv of lithium tributylmagnesate[23] (Bu_3MgLi) in THF at –10 °C. Addition to the reaction mixture of iodine or 3,4,5-trimethoxybenzaldehyde after 2 h afforded iodide **2a**[24] and alcohol **3a**, respectively, in moderate yields (Table 1, entries 1,2). When treated under the same reaction conditions, 3-methyl[25] and 3-phenyl[26] derivatives **1b**,**c** furnished the corresponding iodides **2b**,**c** and alcohols **3b**,**c** in better yields ranging from 40 to 75% (Table 1, entries 3-6). Heterocycles being more efficiently deprotonated using Bu_3MgLi in THF containing TMEDA,[16] a reaction involving 3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine (**1b**) was attempted with this change, but without improvement.

TABLE 1. Deprotonation of 1a-c using Bu_3MgLi (0.4 equiv) Followed by Electrophilic Trapping.



entry	**substrate**	**product** (R)	yield (%)
1	 **1a**	**2a** (H)	34
2		**3a** (H)	32
3	 **1b**	**2b** (Me)	40 (23)[a]
4		**3b** (Me)	61 (60)[b]

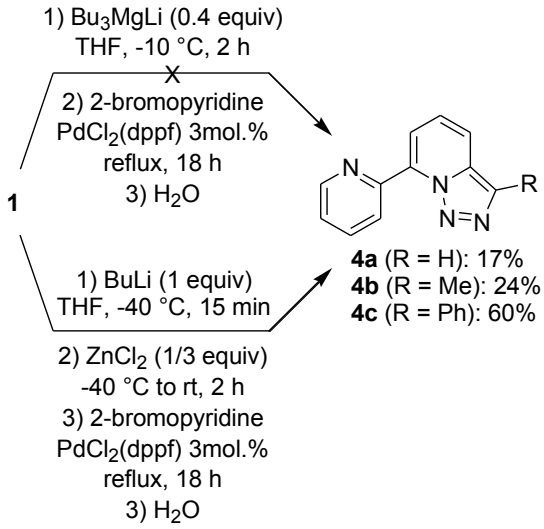
5		**2c** (Ph)	75
6		**3c** (Ph)	51

1c

[a] Using BuLi, THF, -40 °C.[27] [b] Reaction carried out in the presence of TMEDA (0.4 equiv).

In order to synthesize bisheterocycles, cross-coupling reactions between the [1,2,3]triazolo[1,5-*a*]pyridines **1a**,**b** magnesates and 2-bromopyridine were attempted under palladium catalysis using 1,1'-bis(diphenylphosphino)ferrocene (dppf) as ligand,[28] but without success. To know if this result could be related to the moderate stability of the heterocyclic organomagnesium compounds, we decided to involve the corresponding lithium zincates in similar reactions.[29] To this purpose, the [1,2,3]triazolo[1,5-*a*]pyridines **1a-c** were successively treated with butyllithium in tetrahydrofuran at –40 °C for 15 min[30] and zinc chloride (1/3 equivalent) before heating with 2-bromopyridine in the presence of the catalyst. This protocol allowed the compounds **4a-c** to be obtained in yields ranging from 17% to 60% (Scheme 1).

SCHEME 1. Deprotonation of 1a-c Followed by Cross-coupling.

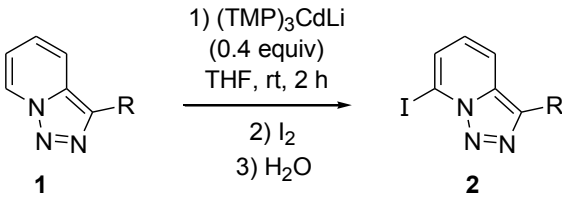


In order to avoid butyllithium which hardly tolerates functional groups, and requires low temperatures which can be difficult to realize on an industrial scale, we investigated the deproto-metalation using a still efficient but more chemoselective ate compound. By combining LiTMP (TMP = 2,2,6,6-tetramethylpiperidino) with soft organometallic compounds, ate bases such as $^{t}Bu_2Zn(TMP)Li$,[29f,31] $^{i}Bu_3Al(TMP)Li$,[32] $(Me_3SiCH_2)_2Mn(TMP)Li\cdot TMEDA$[33] and $MeCu(TMP)(CN)Li_2$[34] have been prepared and used to generate functionalized aromatic compounds. When performed in tetrahydrofuran (THF), the reactions proved to be chemoselective, but require 1 or 2 equiv of base. We reported very recently a new basic mixture ("TMP-cadmate"), prepared by mixing LiTMP (3 equivalents) and $CdCl_2\cdot TMEDA$,[35] that combines both efficiency and chemoselectivity.[36] The method based on the handling of cadmium salts, for which the toxicity is reported,[37] was used for the functionalization of the sensitive [1,2,3]triazolo[1,5-*a*]pyridines.

When substrates **1a** and **1c** were successively treated by in situ prepared $(TMP)_3CdLi$ (0.4 equiv) in THF at room temperature for 2 h, and iodine, the expected iodides **2a** and **2c** were provided in 71 to 72% yields (Table 2, entries 1 and 3). The iodide **2b** was obtained similarly from **1b** in 76% yield (Table 2, entry 2), but using $(TMP)_3CdLi$ (1 equiv). These satisfying results encouraged us to attempt the reaction with more elaborated substrates.

We thus turned to 3-cyano-[1,2,3]triazolo[1,5-*a*]pyridine[38] (**1d**) for which the deproto-lithiation only gives a complex mixture of derivatives.[38] When submitted successively to the mixed lithium-cadmium base and iodine under the conditions used for **1a-c**, the expected iodide **2d**[39] was isolated in a satisfying 65% yield (Table 2, entry 4). 3-(2-Pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine (**1e**) and 3-(2-thienyl)-[1,2,3]triazolo[1,5-*a*]pyridine (**1f**) have previously been metalated using LiDA in THF.[40] The protocol here developed allowed the iodides **2'e** and **2f** to be obtained (Table 2, entries 5,6). The formation of **2'e**[39] instead of expected **2e** can be rationalized as previously reported (Scheme 2).[40]

TABLE 2. Deprotonation of 1a-f using in Situ Prepared $(TMP)_3CdLi$ (0.4 equiv)[a] Followed by Trapping with I_2.

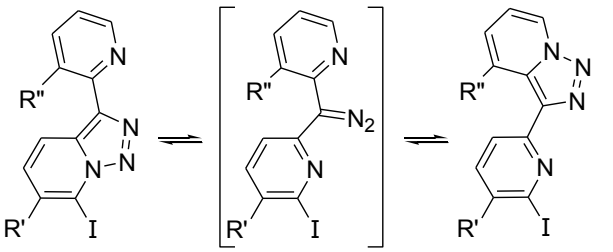


1 **2**

entry	**1**	R	**product**,	yield (%)
1	**1a**	H	**2a**,	72
2	**1b**	Me	**2b**,	76[a] (23)[b]
3	**1c**	Ph	**2c**,	71
4	**1d**	CN	**2d**,	65
5	**1e**	2-pyridyl	**2e ➔ 2'e**,	73 (49)[c]
6	**1f**	2-thienyl	**2f**,	38

[a] 1 equiv of base was used for substrate **1b**. [b] Using BuLi, THF, -40 °C.[27] [c] Using LDA, THF, -40 °C.[40]

SCHEME 2. Isomerization of 7-iodo-3-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridines 2e, 5e and 6e.

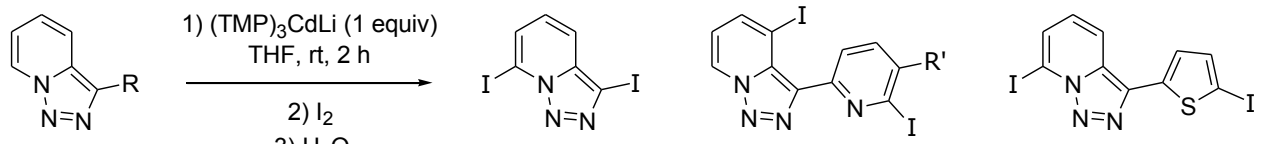


2e: R' = R" = H
5e: R' = H, R" = I
6e: R' = R" = I

2'e: R' = R" = H
5'e: R' = H, R" = I
6'e: R' = R" = I

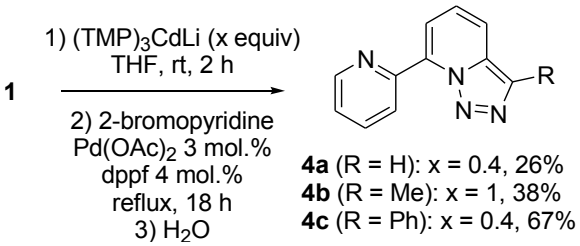
The basic mixture "TMP-cadmate" being able to dideprotonate substrates such as pyrazine, thiazole, *N*-Boc pyrrole and thiophenes,[36] we decided to attempt the access to diiodo derivatives of [1,2,3]triazolo[1,5-*a*]pyridines using 1 equivalent of base. Starting from **1a**, the 3,7-diiodo derivative **5a** was isolated in 66% yield (Scheme 3). Unexpectedly, a mixture of the diiodide **5'e** and the triiodide **6'e**,[41] from which the latter was isolated in 30% yield, was obtained from **1e** using the same protocol. The iodides **5'e** and **6'e** probably result from isomerization of the compounds **5e** and **6e**, as described above (Scheme 2). The precursor **5e** could be formed by dideprotonation at both 7 (the more activated position of [1,2,3]triazolo[1,5-*a*]pyridine) and 3' (induced by the neighboring triazole ring) positions.[42] The triiodide **6e** could be generated by metalation of **5e** during the trapping with iodine (excess of base). The formation of the diiodide **5f** is less unexpected, and logically results from a dideprotonation at the more activated positions of the [1,2,3]triazolo[1,5-*a*]pyridine and thiophene rings (Scheme 3).

SCHEME 3. Polydeprotonation of 1a, 1e and 1f using in Situ Prepared $(TMP)_3CdLi$ (1 equiv) Followed by Trapping with I_2.



Even if cross-coupling reactions using cadmium compounds have mostly been described starting from organocadmium chlorides,[43] reactions from substrates **1a-e** were attempted. Preliminary results[36] showing that palladium catalysis using dppf as ligand was appropriate, the metalated intermediates were subjected to reaction with 2-bromopyridine at the reflux temperature of THF. Whereas no reaction was observed in the presence of an electron-withdrawing group at the 3 position of the [1,2,3]triazolo[1,5-*a*]pyridine ring (substrates **1d**,**e**) under these conditions, the bis(heterocycles) **4a-c** were isolated in yields ranging from 26 to 67% (Scheme 4).

SCHEME 4. Deprotonation of 1a-c using in Situ Prepared $(TMP)_3CdLi$ (x equiv) Followed by Cross-coupling.



Conclusion

Modification of organometallic compounds in order to get more chemoselective bases for the deprotonation of sensitive substrates is a challenging area. Combining lithium and magnesium organometallics in lithium triorganomagnesate (Bu_3MgLi) resulted in a good chemoselectivity when compared with lithium bases, allowing reactions to be carried out in similar yields at -10 °C instead of -40 °C using classical lithium bases.[19a,21a,27,40,44] Using cadmium instead of magnesium and TMP instead of butyl groups afforded an efficient and chemoselective base, able to regioselectively deprotonate [1,2,3]triazolo[1,5-*a*]pyridines substituted or not at the 3 position. Polydeprotonation also proved possible in some cases. The heterocyclic lithium cadmates were evidenced using iodine as electrophile. Trapping was also attempted using 2-bromopyridine to give the expected coupling products under palladium catalysis. Compared to the previously described methods for the synthesis of similar bisheterocycles,[7d,45] the procedure described here has the advantage of being 'one pot' from the corresponding triazolopyridines.

Due to the toxicity of cadmium compounds,[37] we actually try hard to develop basic mixtures containing cadmium salts as catalysts. We already observed using anisole as substrate that $(TMP)_3CdLi$ does not behave as an efficient catalyst when the reaction was performed using a mixture of LiTMP (1.5 equivalents) and $ZnCl_2 \cdot TMEDA$ (0.5 equivalents) in THF at room temperature,[46] but other

catalysis experiments are under investigation. Works in order to develop new mixed lithium-metal bases of ate type still efficient and chemoselective but less toxic are in parallel under investigation.

Experimental Section

General Procedure A (deprotonation using 0.4 equiv Bu_3MgLi followed by trapping using I_2). To a stirred cooled (–10 °C) freshly prepared solution of $MgBr_2$[47] (0.8 mmol) in THF (5 mL) were added BuLi (1.6 M hexanes solution, 2.4 mmol) and, 1 h later, the substrate (2.0 mmol). After 2 h at this temperature, a solution of I_2 (0.61 g, 2.4 mmol) in THF (5 mL) was added. The mixture was stirred overnight before addition of an aq saturated solution of $Na_2S_2O_3$ (10 mL) and extraction with EtOAc (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure.

General Procedure A' (deprotonation using 0.4 equiv Bu_3MgLi followed by trapping using 3,4,5-trimethoxybenzaldehyde). To a stirred cooled (–10 °C) freshly prepared solution of $MgBr_2$[47] (0.8 mmol) in THF (5 mL) were added BuLi (1.6 M hexanes solution, 2.4 mmol) and, 1 h later, the substrate (2.0 mmol). After 2 h at this temperature, 3,4,5-trimethoxybenzaldehyde (0.48 g, 2.4 mmol) was added. The mixture was stirred overnight before addition of water (10 mL) and extraction with EtOAc (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure.

General Procedure B (deprotonation using 0.4 equiv $CdCl_2$·TMEDA and 1.2 equiv LiTMP followed by trapping using I_2). To a stirred cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.42 mL, 2.4 mmol) in THF (5 mL) were added BuLi (1.6 M hexanes solution, 2.4 mmol) and, 5 min later, $CdCl_2$·TMEDA[35] (0.24 g, 0.8 mmol). The mixture was stirred for 10 min at 0 °C before introduction of the substrate (2.0 mmol). After 2 h at room temperature, a solution of I_2 (0.61 g, 2.4 mmol) in THF (5 mL) was added. The mixture was stirred overnight before addition of an aq saturated

solution of $Na_2S_2O_3$ (10 mL) and extraction with EtOAc (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure.

General Procedure C (deprotonation using 1.0 equiv $CdCl_2$·TMEDA and 3.0 equiv LiTMP followed by trapping using I_2). To a stirred cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (1.1 mL, 6.0 mmol) in THF (5 mL) were successively added BuLi (1.6 M hexanes solution, 6.0 mmol) and, 5 min later, $CdCl_2$·TMEDA[35] (0.60 g, 2.0 mmol). The mixture was stirred for 10 min at 0 °C before introduction of the substrate (2.0 mmol). After 2 h at room temperature, a solution of I_2 (1.5 g, 6.0 mmol) in THF (5 mL) was added. The mixture was stirred overnight before addition of an aq saturated solution of $Na_2S_2O_3$ (10 mL) and extraction with EtOAc (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure.

General Procedure D (deprotonation using 1 equiv BuLi followed by transmetalation using $ZnCl_2$ and cross-coupling). To a stirred cooled (–40 °C) solution of the substrate (2.0 mmol) in THF (4 mL) were added BuLi (1.6 M hexanes solution, 2.4 mmol) and, 15 min later, a solution of $ZnCl_2$ (0.12 g, 0.8 mmol) in THF (3 mL). After 2 h at room temperature, the mixture thus obtained was added dropwise to a solution of 2-bromopyridine (0.19 mL, 2.0 mmol) and $PdCl_2$(dppf) (49 mg, 60 μmol), and the resulting mixture was heated at reflux for 18 h before addition of water saturated with NH_4Cl (0.5 mL) and AcOEt (30 mL). After drying over $MgSO_4$, the organic phase was filtered and concentrated under reduced pressure.

General Procedure E (deprotonation using 0.4 equiv $CdCl_2$·TMEDA and 1.2 equiv LiTMP followed by cross-coupling). To a stirred cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.42 mL, 2.4 mmol) in THF (5 mL) were added BuLi (1.6 M hexanes solution, 2.4 mmol) and, 5 min later, $CdCl_2$·TMEDA[35] (0.24 g, 0.8 mmol). The mixture was stirred for 10 min at 0 °C before introduction of the substrate (2.0 mmol). After 2 h at room temperature, the mixture was treated with $Pd(OAc)_2$ (13 mg, 60 μmol), dppf (44 mg, 80 μmol) and 2-bromopyridine (0.19 mL, 2.0 mmol). The mixture was

heated under reflux for 18 h before addition of water (0.5 mL) and AcOEt (30 mL). After drying over $MgSO_4$, the organic phase was filtered and concentrated under reduced pressure.

General Procedure E' (deprotonation using 1 equiv $CdCl_2$·TMEDA and 3 equiv LiTMP followed by cross-coupling). To a stirred cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (1.1 mL, 6.0 mmol) in THF (5 mL) were added BuLi (1.6 M hexanes solution, 6.0 mmol) and, 5 min later, $CdCl_2$·TMEDA[35] (0.60 g, 2.0 mmol). The mixture was stirred for 10 min at 0 °C before introduction of the substrate (2.0 mmol). After 2 h at room temperature, the mixture was treated with $Pd(OAc)_2$ (13 mg, 60 μmol), dppf (44 mg, 80 μmol) and 2-bromopyridine (0.19 mL, 2.0 mmol). The mixture was heated under reflux for 18 h before addition of water (0.5 mL) and AcOEt (30 mL). After drying over $MgSO_4$, the organic phase was filtered and concentrated under reduced pressure.

7-Iodo-[1,2,3]triazolo[1,5-*a*]pyridine (2a). 2a was obtained according to the general procedure A (0.17 g, 34%) or B (0.35 g, 72%), and isolated after purification by flash chromatography on silica gel (CH_2Cl_2/AcOEt: 95/5) as a white powder: mp 148–150 °C; ^{1}H NMR ($CDCl_3$) δ 6.99 (dd, 1H, J = 8.5 and 7.2), 7.46 (d, 1H, J = 6.9), 7.72 (d, 1H, J = 8.8), 8.24 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 86.0 (C), 117.8 (CH), 126.1 (CH), 127.3 (CH), 127.7 (CH), 134.3 (C); IR (KBr) ν 1618, 1533, 1480, 1410, 1350, 1308, 1298, 1261, 1228, 1204, 1144, 1095, 1036, 970, 932, 802, 780, 722, 677, 630 and 580 cm^{-1}. HRMS: calcd for $C_6H_4IN_3$ ($M^{+\bullet}$) 244.9450, found 244.9406. Anal. Calcd for $C_6H_4IN_3$ (245.02): C, 29.41; H, 1.65; N, 17.15. Found: C, 29.05; H, 1.99; N, 17.13.

7-Iodo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine (2b). 2b was obtained according to the general procedure A (0.21 g, 40%) or C (0.39 g, 76%), and isolated after purification by flash chromatography on silica gel (CH_2Cl_2/AcOEt: 80/20) as a beige powder: mp 135 °C; ^{1}H NMR ($CDCl_3$) δ 2.59 (s, 3H), 6.92 (t, 1H, J = 7.8), 7.41 (d, 1H, J = 6.8), 7.60 (d, 1H, J = 8.7); ^{13}C NMR ($CDCl_3$): δ 11.0 (CH_3), 86.0 (C), 117.4 (CH), 124.5 (CH), 127.0 (CH), 132.3 (C), 136.6 (C); IR (KBr) ν 3066, 2962, 2922, 1622, 1532, 1505, 1458, 1428, 1397, 1335, 1298, 1261, 1225, 1203, 1127, 1103, 1035, 925, 806, 768, 722,

672, 610, 551 and 497 cm^{-1}. HRMS: calcd for $C_7H_6IN_3$ ($M^{+\bullet}$) 258.9606, found 258.9586. Anal. Calcd for $C_7H_6IN_3$ (259.05): C, 32.46; H, 2.33; N, 16.22. Found: C, 32.66; H, 2.49; N, 15.82.

7-Iodo-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyridine (2c). 2c was obtained according to the general procedure A (0.48 g, 75%) or B (0.46 g, 71%), and isolated after purification by flash chromatography on silica gel (heptane/CH_2Cl_2: 50/50) as a yellow powder: mp 139 °C; ^{1}H NMR ($CDCl_3$) δ 7.03 (dd, 1H, *J* = 8.8 and 7.0), 7.39 (t, 1H, *J* = 7.4), 7.47-7.52 (m, 3H), 7.91-7.98 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 86.6 (C), 118.2 (CH), 126.3 (CH), 126.9 (2CH), 127.4 (CH), 128.2 (CH), 129.1 (2CH), 131.2 (C), 131.5 (C), 140.0 (C); IR (KBr) ν 3087, 3052, 1614, 1509, 1484, 1448, 1418, 1345, 1291, 1267, 1215, 1184, 1134, 1073, 1039, 1007, 929, 804, 789, 767, 729, 696, 688, 610 and 538 cm^{-1}. HRMS: calcd for $C_{12}H_8IN_3$ ($M^{+\bullet}$) 320.9763, found 320.9763. Anal. Calcd for $C_{12}H_8IN_3$ (321.12): C, 44.88; H, 2.51; N, 13.09. Found: C, 44.59; H, 2.56; N, 12.99.

3-Cyano-7-iodo-[1,2,3]triazolo[1,5-*a*]pyridine (2d). 2d was obtained according to the general procedure B (0.35 g, 65%), and isolated after purification by flash chromatography on silica gel (CH_2Cl_2) as a white powder: mp 202 °C; ^{1}H NMR ($(CD_3)_2SO$) δ 7.51 (t, 1H, *J* = 7.8), 7.92 (d, 1H, *J* = 6.9), 8.18 (d, 1H, *J* = 8.6); ^{1}H NMR ($CDCl_3$) δ 7.26 (dd, 1H, *J* = 8.8 and 7.2), 7.60 (dd, 1H, *J* = 7.1 and 0.9), 7.83 (dd, 1H, *J* = 8.7 and 0.9); ^{13}C NMR ($(CD_3)_2SO$): δ 91.8 (C), 112.0 (C), 112.6 (C), 116.3 (CH), 129.1 (CH), 131.6 (CH), 137.0 (C). Anal. Calcd for $C_7H_3IN_4$ (270.03): C, 31.14; H, 1.12; N, 20.75. Found: C, 31.20; H, 1.21; N, 20.54.

3-(6-Iodo-2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine (2'e).[40] **2'e** was obtained according to the general procedure B (0.47 g, 73%), and isolated after purification by flash chromatography on silica gel (CH_2Cl_2/AcOEt: 80/20) as a beige powder: mp 191 °C; ^{1}H NMR ($CDCl_3$) δ 7.06 (td, 1H, *J* = 6.8 and 0.8), 7.37-7.44 (m, 2H), 7.60 (d, 1H, *J* = 7.6), 8.27 (d, 1H, *J* = 7.8), 8.59 (d, 1H, *J* = 8.9), 8.74 (d, 1H, *J* = 7.0); ^{13}C NMR ($CDCl_3$): δ 116.2 (CH), 117.4 (C), 119.2 (CH), 121.0 (CH), 125.4 (CH), 127.1 (CH),

132.2 (C), 132.8 (CH), 135.9 (C), 138.2 (CH), 153.2 (C). Anal. Calcd for $C_{11}H_7IN_4$ (322.10): C, 41.02; H, 2.19; N, 17.39. Found: C, 40.98; H, 2.32; N, 17.52.

7-Iodo-3-(2-thienyl)-[1,2,3]triazolo[1,5-*a*]pyridine (2f). 2f was obtained according to the general procedure B (0.25 g, 38%), and isolated after purification by flash chromatography on silica gel (CH_2Cl_2/AcOEt: 80/20) as a beige powder: mp 134 °C; ^{1}H NMR ($CDCl_3$) δ 6.95 (dd, 1H, *J* = 8.8 and 7.0), 7.05 (dd, 1H, *J* = 5.0 and 3.6), 7.28 (dd, 1H, *J* = 5.0 and 1.0), 7.38 (dd, 1H, *J* = 6.9 and 0.8), 7.45 (dd, 1H, *J* = 3.6 and 1.0), 7.85 (dd, 1H, *J* = 8.9 and 0.8); ^{13}C NMR ($CDCl_3$): δ 86.6 (C), 118.1 (CH), 124.4 (CH), 125.5 (CH), 126.4 (CH), 127.6 (CH), 127.9 (CH), 130.4 (C), 133.3 (C), 135.5 (C). Anal. Calcd for $C_{10}H_6IN_3S$ (327.14): C, 36.71; H, 1.85; N, 12.84; S, 9.80. Found: C, 36.46; H, 1.98; N, 12.41; S, 10.08.

([1,2,3]Triazolo[1,5-*a*]pyrid-7-yl) (3,4,5-trimethoxyphenyl) methanol (3a). 3a was obtained according to the general procedure A' (0.20 g, 32%), and isolated after purification by flash chromatography on silica gel (AcOEt/cyclohexane: 80/20) as a yellow powder: mp < 50 °C; ^{1}H NMR ($CDCl_3$) δ 3.72 (s, 9H), 6.48 (s, 1H), 6.74 (s, 2H), 6.83 (d, 1H, *J* = 7.0), 7.17 (dd, 1H, *J* = 9.0 and 7.0), 7.58 (d, 1H, *J* = 9.0), 7.99 (s, 1H), OH not seen; ^{13}C NMR ($CDCl_3$): δ 153.6 (2C), 140.8 (C), 138.0 (C), 135.0 (C), 134.4 (C), 126.3 (CH), 126.1 (CH), 117.2 (CH), 113.3 (CH), 104.5 (2CH), 71.2 (CH), 61.2 (CH_3), 56.4 ($2CH_3$); IR (KBr) ν 3274, 3007, 2938, 2839, 1638, 1594, 1506, 1463, 1421, 1327, 1234, 1184, 1127, 1005, 967, 815, 754, 700, 665 and 577 cm^{-1}. HRMS: calcd for $C_{16}H_{17}N_3O_4$ ($M^{+\bullet}$) 315.1219, found 315.1225.

(3-Methyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-yl) (3,4,5-trimethoxyphenyl) methanol (3b). 3b was obtained according to the general procedure A' (0.40 g, 61%), and isolated after purification by flash chromatography on silica gel (AcOEt/cyclohexane: 80/20) as a yellow powder: mp 144–146 °C; ^{1}H NMR ($CDCl_3$) δ 2.62 (s, 3H), 3.82 (s, 9H), 6.48 (s, 1H), 6.72 (d, 1H, *J* = 7.0), 6.80 (s, 2H), 7.17 (dd, 1H, *J* = 9.0 and 6.8), 7.58 (d, 1H, *J* = 9.0), OH not seen; ^{13}C NMR ($CDCl_3$): δ 153.8 (2C), 140.1 (C),

138.3 (C), 135.4 (C), 134.3 (C), 132.5 (C), 124.6 (CH), 117.0 (CH), 113.6 (CH), 104.5 (2CH), 71.9 (CH), 61.3 (CH_3), 56.5 ($2CH_3$), 10.8 (CH_3); IR (KBr) ν 3468, 2943, 2831, 1639, 1595, 1509, 1450, 1422, 1332, 1224, 1176, 1129, 1076, 1002, 957, 833, 798, 771, 736, 696, 665, 582, 530 and 492 cm^{-1}. HRMS: calcd for $C_{17}H_{19}N_3O_4$ ($M^{+\bullet}$) 329.1376, found 329.1357.

(3-Phenyl-[1,2,3]triazolo[1,5-*a*]pyrid-7-yl) (3,4,5-trimethoxyphenyl) methanol (3c). 3c was obtained according to the general procedure A' (0.40 g, 51%), and isolated after purification by flash chromatography on silica gel (AcOEt/cyclohexane: 80/20) as a yellow powder: mp < 50 °C; ^1H NMR ($CDCl_3$) δ 3.74 (s, 9H), 4.95 (s, 1H), 6.48 (s, 1H), 6.75 (s, 2H), 6.79 (d, 1H, *J* = 6.8), 7.20 (dd, 1H, *J* = 8.9 and 6.8), 7.30 (m, 1H), 7.40 (m, 2H), 7.84 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 152.2 (2C), 139.6 (C), 137.3 (C), 135.8 (C), 133.3 (C), 130.1 (C), 129.9 (C), 128.0 (2CH), 127.1 (CH), 125.7 (2CH), 125.1 (CH), 116.2 (CH), 112.2 (CH), 103.1 (2CH), 70.0 (CH), 59.8 (CH_3), 54.9 ($2CH_3$); IR (KBr) ν 3370, 2937, 2836, 1635, 1593, 1547, 1506, 1462, 1421, 1329, 1233, 1184, 1126, 1075, 1004, 959, 832, 799, 778, 738, 694, 665 and 583 cm^{-1}. HRMS: calcd for $C_{22}H_{21}N_3O_4$ ($M^{+\bullet}$) 391.1532, found 391.1578.

3,7-Diiodo-[1,2,3]triazolo[1,5-*a*]pyridine (5a). 5a was obtained according to the general procedure C (0.49 g, 66%), and isolated after purification by flash chromatography on silica gel (heptane/AcOEt: 50/50) as a beige powder: mp 144 °C; ^1H NMR ($CDCl_3$) δ 7.08 (dd, 1H, *J* = 8.7 and 6.8), 7.53 (d, 1H, *J* = 5.9), 7.60 (d, 1H, *J* = 8.8); ^{13}C NMR ($CDCl_3$): δ 80.9 (C), 86.4 (C), 117.9 (CH), 127.1 (CH), 128.1 (CH), 136.7 (C); Anal. Calcd for $C_6H_3I_2N_3$ (370.92): C, 19.43; H, 0.82; N, 11.33. Found: C, 19.74; H, 0.97; N, 11.18.

3-(5,6-Diiodo-2-pyridyl)-4-iodo-[1,2,3]triazolo[1,5-*a*]pyridine (6'e). 6'e was obtained according to the general procedure C (0.34 g, 30%), and isolated after purification by flash chromatography on silica gel (CH_2Cl_2/AcOEt: 95/5) as a white powder: mp 245 °C; ^1H NMR ($(CD_3)_2SO$) δ 7.03 (t, 1H, *J* = 7.0), 7.76 (d, 1H, *J* = 8.2), 8.00 (dd, 1H, *J* = 7.0 and 0.65), 8.11 (d, 1H, *J* = 8.2), 9.23 (dd, 1H, *J* = 7.0 and 0.65); ^{13}C NMR ($(CD_3)_2SO$): δ 82.0 (C), 101.7 (C), 118.8 (C), 117.2 (CH), 125.9 (CH), 131.9 (C),

136.3 (CH), 137.3 (CH), 139.5 (C), 147.6 (CH), 154.5 (C). Anal. Calcd for $C_{11}H_5I_3N_4$ (573.90): C, 23.02; H, 0.88; N, 9.76. Found: C, 23.31; H, 1.11; N, 9.86.

7-Iodo-3-(5-iodo-2-thienyl)-[1,2,3]triazolo[1,5-*a*]pyridine (5f). 5f was obtained according to the general procedure C (0.68 g, 75%), and isolated after purification by flash chromatography on silica gel (CH_2Cl_2) as a yellow powder: mp 201 °C; ^{1}H NMR ($CDCl_3$) δ 7.09 (dd, 1H, *J* = 9.0 and 6.8), 7.22-7.32 (m, 2H), 7.53 (dd, 1H, *J* = 6.9 and 0.9), 7.92 (dd, 1H, *J* = 9.0 and 1.0); ^{1}H NMR ($(CD_3)_2SO$) δ 7.25 (t, 1H, *J* = 7.9), 7.36-7.41 (m, 2H), 7.75 (d, 1H, *J* = 6.9), 8.21 (d, 1H, *J* = 8.8); ^{13}C NMR ($(CD_3)_2SO$): δ 76.1 (C), 90.0 (C), 117.7 (CH), 125.8 (CH), 127.8 (CH), 127.9 (CH), 129.5 (C), 133.4 (C), 137.9 (CH), 138.8 (C). Anal. Calcd for $C_{10}H_5I_2N_3S$ (453.04): C, 26.51; H, 1.11; N, 9.28; S, 7.08. Found: C, 26.77; H, 1.17; N, 9.27; S, 7.27.

7-(2-Pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine (4a). 4a was obtained according to the general procedure D (67 mg, 17%) or E (0.10 g, 26%), and isolated after purification by flash chromatography on silica gel (CH_2Cl_2/AcOEt: 80/20) as a white powder: mp 94 °C; ^{1}H NMR ($CDCl_3$) δ 7.39-7.45 (m, 2H), 7.82 (dd, 1H, *J* = 8.7 and 1.0), 7.90-7.96 (m, 2H), 8.21 (s, 1H), 8.79-8.80 (m, 1H), 9.00 (d, 1H, *J* = 8.2); ^{13}C NMR ($CDCl_3$): δ 116.7 (CH), 118.0 (CH), 124.5 (CH), 125.3 (CH), 125.7 (CH), 126.2 (CH), 135.1 (C), 136.7 (C), 136.9 (CH), 149.2 (C), 149.9 (CH); IR (KBr) ν 3134, 3059, 2926, 2862, 1634, 1584, 1570, 1510, 1466, 1436, 1417, 1369, 1324, 1262, 1206, 1153, 1102, 1046, 995, 976, 953, 902, 837, 769, 732, 698, 678, 627, 612, 576 and 496 cm^{-1}. HRMS: calcd for $C_{11}H_8N_4$ ($M^{+\bullet}$) 196.0749, found 196.0732. Anal. Calcd for $C_{11}H_8N_4$ (196.21): C, 67.34; H, 4.11; N, 28.55. Found: C, 67.06; H, 4.29; N, 28.29.

3-Methyl-7-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine (4b). 4b was obtained according to the general procedure D (0.10 g, 24%) or E' (0.16 g, 38%), and isolated after purification by flash chromatography on silica gel (CH_2Cl_2/AcOEt: 80/20) as a white powder: mp 68 °C; ^{1}H NMR ($CDCl_3$) δ 2.68 (s, 3H), 7.32 (m, 2H), 7.70 (dd, 1H, *J* = 8.7 and 1.0), 7.89-7.95 (m, 2H), 8.78 (d, 1H, *J* = 4.5),

9.02 (d, 1H, J = 8.1); ^{13}C NMR ($CDCl_3$): δ 10.6 (CH_3), 116.6 (CH), 117.6 (CH), 124.2 (CH), 124.4 (CH), 125.2 (CH), 133.1 (C), 134.8 (C), 136.5 (C), 136.9 (CH), 149.4 (C), 149.8 (CH); IR (KBr) ν 3053, 3010, 2926, 2852, 1630, 1583, 1533, 1467, 1429, 1380, 1343, 1315, 1203, 1155, 1125, 1089, 1045, 990, 947, 808, 777, 731, 696, 676, 616 and 568 cm^{-1}. HRMS: calcd for $C_{12}H_{10}N_4$ ($M^{+\bullet}$) 210.0905, found 210.0869. Anal. Calcd for $C_{12}H_{10}N_4$ (210.23): C, 68.56; H, 4.79; N, 26.65. Found: C, 68.31; H, 4.78; N, 26.53.

3-Phenyl-7-(2-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine (4c). 4c was obtained according to the general procedure D (0.33 g, 60%) or E (0.36 g, 67%), and isolated after purification by flash chromatography on silica gel (heptane/AcOEt: 50/50) and recrystallization from heptane/Et_2O (30/70) as a yellow powder: mp 95–97 °C; ^{1}H NMR ($CDCl_3$) δ 7.39-7.57 (m, 5H), 7.91-8.02 (m, 4H), 8.09 (dd, 1H, J = 8.9 and 1.0), 8.80 (ddd, J = 3.8, 1.6 and 0.8), 9.05 (d, 1H, J = 8.1); ^{13}C NMR ($CDCl_3$): δ 117.0 (CH), 118.4 (CH), 124.5 (CH), 125.4 (CH), 126.1 (CH), 127.0 (2CH), 128.1 (CH), 129.1 (2CH), 131.6 (C), 131.9 (C), 136.8 (CH), 137.0 (C), 138.3 (C), 149.2 (C), 149.9 (CH); IR (KBr) ν 3064, 2989, 1630, 1605, 1571, 1532, 1496, 1466, 1427, 1349, 1318, 1299, 1265, 1220, 1159, 1139, 1117, 1072, 1051, 1008, 990, 916, 802, 782, 748, 736, 696, 616, 599 and 564 cm^{-1}. HRMS: calcd for $C_{17}H_{12}N_4$ ($M^{+\bullet}$) 272.1062, found 272.1026. Anal. Calcd for $C_{17}H_{12}N_4$ (272.30): C, 74.98; H, 4.44; N, 20.58. Found: C, 74.71; H, 4.39; N, 20.33.

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Supporting Information Available: General procedures, X-ray diffraction analysis of compounds **2a**, **2d** and **2'e**, and copies of the ^{1}H and ^{13}C NMR spectra for compounds **2a-d**, **2'e**, **2f**, **3a-c**, **5a**, **6'e**, **5f** and **4a-c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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