

Triazolopyridines. Part 29.¹ Direct arylation reactions with [1,2,3]triazolo[1,5-*a*]pyridines

Belén Abarca,* Rosa Adam, Rafael Ballesteros,* Leonardo Chiassai and Cristina Gamón

Departamento de Química Orgánica, Facultad de Farmacia, Universidad de Valencia, Avda. Vicente Andrés Estellés s/n, 46100 Burjassot (Valencia), Spain

E-mail: belen.abarca@uv.es

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Abstract

[1,2,3]Triazolo[1,5-*a*]pyridine reacts with aryl halides in presence of catalytic amounts of Pd(OAc)₂ and PPh₃ in DMF to give, in medium or low yield, direct arylations in C3 and pyridyl aryl ketones. Thiazole and benzothiazole have been directly arylated using 7-halotriazolopyridines. These behaviours are unprecedented in the chemistry of [1,2,3]triazolo[1,5-*a*]pyridines.

Keywords: Nitrogenated heterocycles, triazolopyridines, direct arylations, palladium catalyst

Introduction

[1,2,3]Triazolo[1,5-*a*]pyridines **1** are simple fused heterocycles, readily accessible by mild oxidation of pyridyl-ketone or pyridyl-aldehyde hydrazones.^{2a} Their chemistry has been studied by Jones and ourselves.² This system is used as building blocks of pyridines 2,6-disubstituted not available by other synthetic methodology.³ Indolizines,⁴ and bipyridines,⁵ have also been synthesized using [1,2,3]triazolo[1,5-*a*]pyridines as synthons. Their coordination chemistry⁶ as well as their application in the field of magnetic materials have been reported.^{6d,7} One very interesting property of this system is the fluorescence of triazolopyridines 3 or 7 substituted by aryl or heteroaryl groups.⁸ This property provides molecular chemosensors for metal ions, anions, and amino acids.^{1,9}

Fluorescent aryltriazolopyridines were synthesized with a triazolopyridine halide and an aryl or heteroaryl boronic acid,⁸ by cross-coupling reactions,¹⁰ especially the Suzuki-Miyaura reaction.¹¹ However, the 3-halotriazolopyridines used as starting materials were obtained in very low yield.¹²

The reaction involving a triazolopyridyl boronic acid and an aryl halide was not successful. It was possible to synthesize and characterize some 7-triazolopyridyl

boronic acids and esters that are stable when stored, but in solution under the various Suzuki reaction conditions experimented, were not stable and underwent protodeboronation.¹³ On the other hand, it was impossible to prepare 3-triazolopyridyl boronic acid.¹²

The requisite of triazolopyridine preactivation, such as halide or boronic acid, involves several manipulations prior to the cross-coupling reaction. In recent years, direct arylation reactions catalysed by palladium in a single step, have emerged as a very attractive alternative *via* to traditional cross-coupling methods for the functionalisation of unactivated C-H bonds in heterocycles.¹⁴ Although direct arylations have been studied with a great number of heterocycles,^{14a,h} no reports of this type of reaction involving triazolopyridines have been published to date.^{15,2d} Thus, we decided to explore the possibility of direct arylation of triazolopyridines.

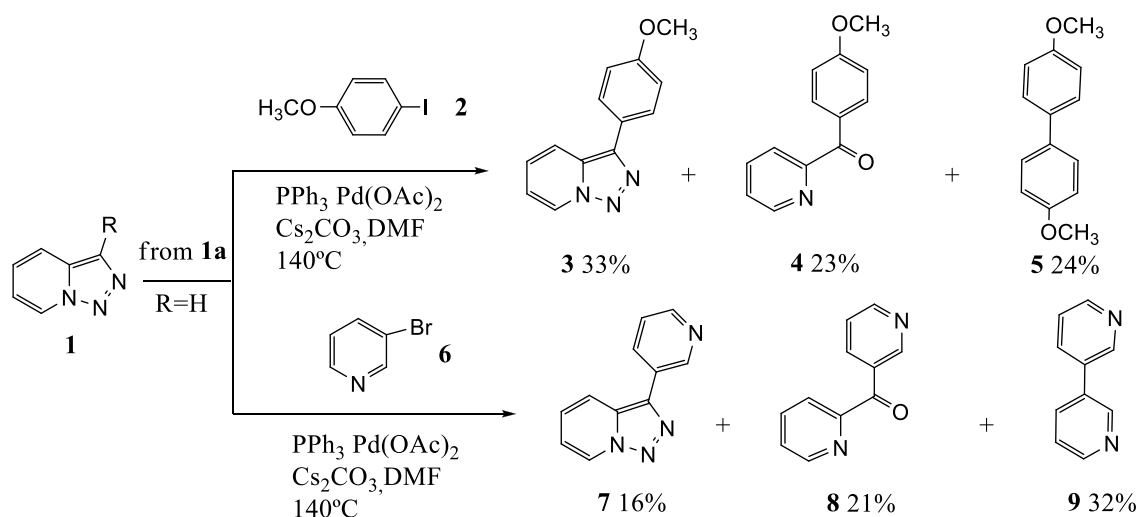
In this context, we report the first results on the study of this reaction with [1,2,3]triazolo[1,5-*a*]pyridine **1a**, and the application of 7-halo-[1,2,3]triazolo[1,5-*a*]pyridines for direct arylation of thiazole and benzothiazole.

Results and Discussion

Electrophilic aromatic substitution was initially proposed by Miura as a possible mechanism for direct arylation reactions,^{16a} since then distinct mechanisms have been proposed: C-H activation,^{16b,c} cross-coupling,^{16a} and Heck-type arylation.^{14d} For palladium catalysed arylation of electron-rich heterocycles, the mechanistic pathway proposed by Miura^{16a} has often been considered as the most probable mechanism for arylation of heterocycles,^{14d} and has been strongly supported by a combination of experimental and computational data.¹⁷ Nevertheless, the potential involvement of other aforementioned pathways or mixed mechanisms could not be completely ruled out.^{14d}

It is known that in [1,2,3]triazolo[1,5-*a*]pyridine **1a** the most acid hydrogen is the one in the C3 position, and that **1a** reacts with electrophiles in two contrasting ways.^{2a} In cases of Vilsmeier formylation or nitration, 3-substituted triazolopyridines are obtained, and with other electrophiles (acids, acetic anhydride, SeO₂, etc) products resulting from a triazolo ring opening reaction losing dinitrogen are given. Thus, we decided to explore the possibility of direct arylation of triazolopyridine in the C3 position using Miura conditions.^{16a}

We first examined the reaction between triazolopyridine **1a** and 2 equivalents of 4-iodoanisole **2** in DMF at 140 °C, in the presence of 0.05 equivalents of Pd(OAc)₂, 0.1 equivalents of triphenylphosphine as ligand, and 2 equivalents of caesium carbonate as base. The reaction was completed after 3 days, and three compounds were isolated in moderate to low yields (Table 1, entry 1): 3-substituted triazolopyridine **3** (33%), 2-pyridyl 4-methoxyphenyl ketone **4** (23%) and 4,4'-dimethoxybiphenyl **5** (24%) (Scheme 1).



Scheme 1

Triazolopyridine **3** is the first example of a compound obtained by direct arylation of a triazolopyridine system. Compound **3** was obtained previously by some of us, by Suzuki reaction of 3-iodotriazolopyridine and 4-methoxyphenyl boronic acid, in a global yield of only 13.7%.⁸ An interesting feature is the attainment of ketone **4**, it must be formed from **3** by a triazolo ring opening reaction with the loss of N_2 .¹⁸ The formation of the biaryl derivative **5** can be explained by a homocoupling reaction of **2**.¹⁹

Several attempts to improve these results have been made modifying the reaction conditions. We modified the reaction time and temperature (Table 1, entry 2), the ligand and reaction time (entries 3²⁰-5), the catalyst (entry 6), yet we always obtained mixtures of difficult handling and unfavourable results. As reported by Bellina *et al.*, the addition of copper(I) iodide (CuI) dramatically improved reaction efficiency of some direct arylations,^{16b,c,21c} thus we investigated the activity of this transition element in our reaction. However no arylation product was found, (entry 7). Fagnou *et al.* developed a palladium-pivalic acid co-catalyst combination exhibiting unprecedented reactivity in direct arylation,^{22a} that provides highly variable outcomes depending on the choice of base and the presence /absence of pivalic acid.^{22b} They also established broadly applicable reaction conditions associated with the use of substoichiometric quantities of pivalic acid (*in situ* generated potassium pivalate) to accelerate direct arylation.^{22c} Using some of these conditions, we tried to achieve better results, yet without success (entry 8).

Table 1 Synthesis of 3-aryl-[1,2,3]triazolo[1,5-*a*]pyridines

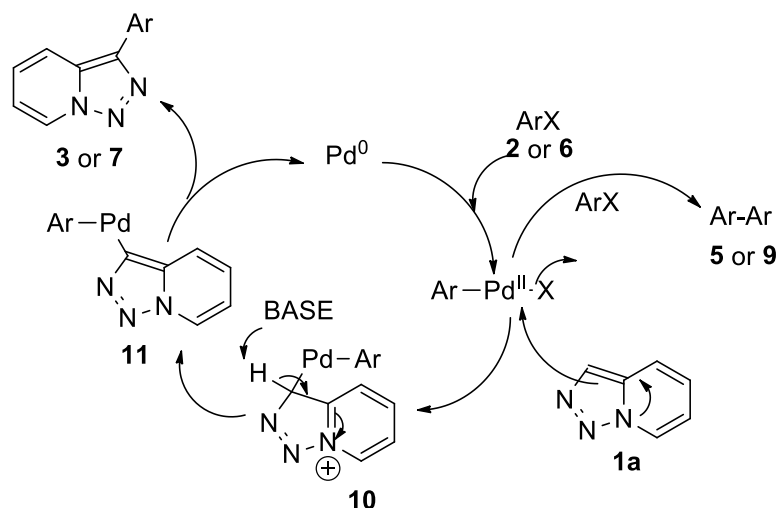
Entry	Ar-X / (equiv)	Catalyst / (equiv)	Ligand / Additive (equiv)	Base / (equiv)	Solvent / (mL)	T ^a (°C)	Time (h)	Products (%)
1	2 / (2)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	72	3 (33%) 4 (23%) 5 (24%)
2	2 / (2)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1)	Cs ₂ CO ₃ / (2)	DMF / (5)	160	24	4 (17,4%) 5 (8,4%)
3	2 / (2)	Pd(OAc) ₂ / (0.05)	P(<i>o</i> -Tol) ₃ / (0.1)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	72	3 (7,1%)
4	2 / (2)	Pd(OAc) ₂ / (0.05)	P(<i>o</i> -Tol) ₃ / (0.45)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	96	4 (6,1%) 5 (9,3%)
5	2 / (2)	Pd(OAc) ₂ / (0.05)	Xanphos / (0.05)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	96	3 (9,8%)
6	2 / (2)	PdCl ₂ (PPh) ₃ / (0.05)	PPh ₃ / (0.1)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	72	4 (traces)
7	2 / (2)	Pd(OAc) ₂ / (0.05) CuI / (2)	PPh ₃ / (0.1)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	72	3 (traces) 4 (traces)
8	2 / (2)	Pd(AcO) ₂ / PivOH / 0,02/0,3	PCy ₃ .HBF ₄	K ₂ CO ₃ (1,5)	DMA / (5)	100	72	3 (3%) 4 (10%)
9	6 / (1,1)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	48	7 (16%) 8 (21%) 9 (32%)

When 3-bromopyridine **6** was used as co-reagent in cited Miura conditions,^{16a} triazolopyridine **7**, (16%), ketone **8** (21%), and 3,3'-bipyridine **9** (32%) were obtained (Scheme 1, entry 9). These compounds are analogous to **3**, **4**, and **5**.

Some experiments were also carried using microwave conditions at a frequency of 2.45 GHz, however no reaction was observed.

We assume that the mechanism of these direct arylation reactions could be an electrophilic attack of the arylhalopalladium(II) species, which is formed by oxidative addition of aryl halide to the palladium (0) generated *in situ*, onto the triazolopyridine **1a** generating intermediate **10**, that by deprotonation gives aryl(triazolopyridyl)

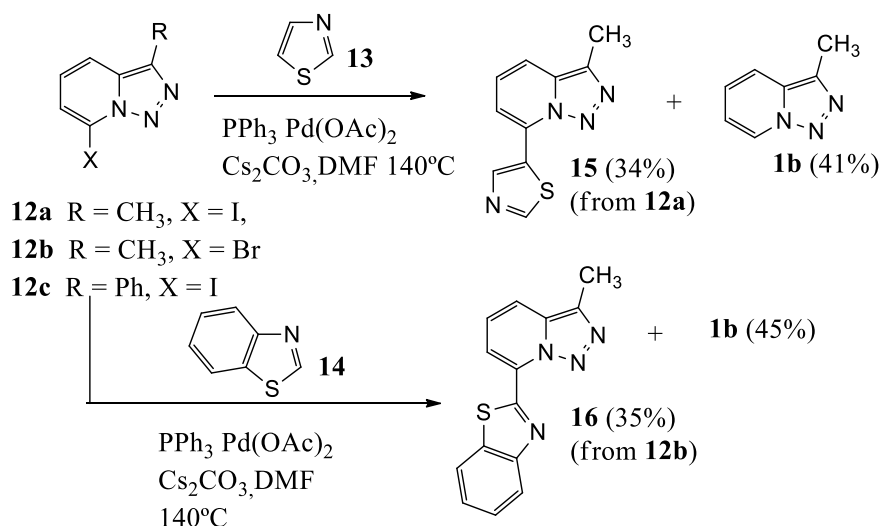
palladium(II) intermediate **11**. By reductive palladium elimination the new triazolopyridines **3** or **7** could be formed (Scheme 2).



Scheme 2

Direct arylation reactions of thiazole **13** and benzothiazole **14** with 7-iodo- or 7-bromo-3-substituted triazolopyridines **12** were also studied, under the same conditions as those that Miura *et al.*^{16a} used for direct arylation of 1,3-azoles and benzoazoles (Table 2).

7-Halotriazolopyridines **12** are available products from regioselective lithiation of triazolopyridine (*n*-BuLi/toluene, -40 °C) and iodine,¹² dibromotetrachloroethane (DBTCE),²³ or tetrachloroethane (TCE)¹² in good yield. By reaction of 7-iodo-3-methyltriazolopyridine **12a** with thiazole in presence of Pd(OAc)₂ (0.05 eq.), PPh₃ (0.1 eq.) in DMF at 140 °C using caesium carbonate (2 eq.) as base, we obtained 7-(5-thiazolyl)-3-methyltriazolopyridine **15** in 34% yield. This reaction gave regioselective arylation in C5 of the thiazole ring, (Scheme 3) (Table 2, entry 1). The dehalogenated product 3-methyltriazolopyridine **1b** was also obtained in 41% yield. In contrast, when 7-bromo-3-methyltriazolopyridine **12b** was used, triazolopyridine **1b** was obtained (60%) and only traces of compound **15** (entry 2). The reactions of 3-substituted-7-halotriazolopyridines with benzothiazole gave different result depending on the substituent in C3 (Scheme 3). With compound **12b**, 7-(2-benzothiazolyl)-3-methyltriazolopyridine **16** (35%), and triazolopyridine **1b** (45%) were obtained (entry 3). However, with R = phenyl, compound **12c**, no reaction was observed with or without CuI as additive.

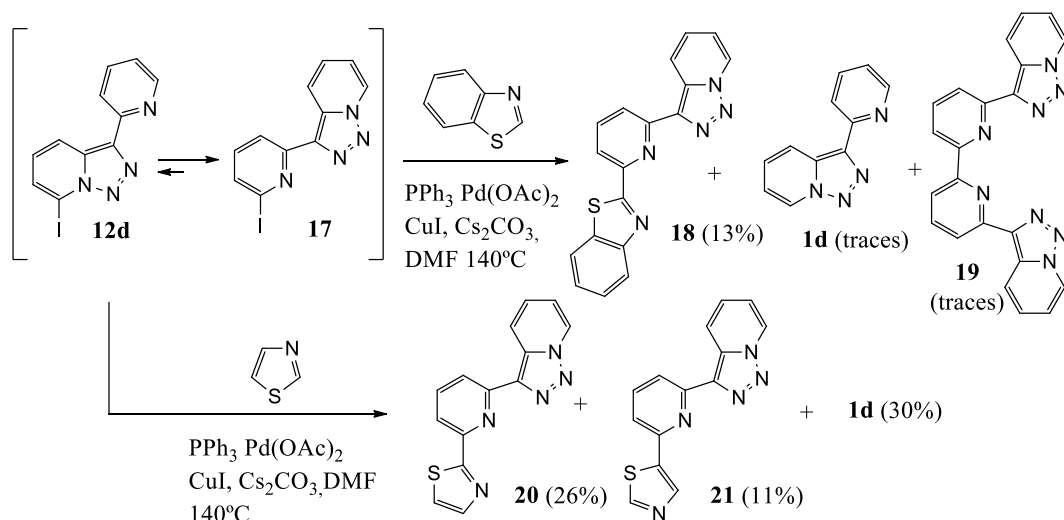


Scheme 3

Table 2. Reactions of 7-halo-[1,2,3]triazolo[1,5-*a*]pyridines with thiazole and benzothiazole

Entry	Starting material TP-X/ (equiv)	Aromatic co-reactive/ (equiv)	Catalyst/ (equiv)	Ligand, Additive / (equiv)	Base / (equiv)	Solvent t/ (mL)	T ^a (°C)	Time (h)	Products (%)
1	12a / (1)	13 / (2)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	2	1b (41%) 15 (34%)
2	12b / (1)	13 / (2)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	2	1b (60%) 15 (traces)
3	12b / (1)	14 / (2)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1) CuI/ (0.02)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	2	1b (45%) 16 (35%)
4	17 / (1)	14 / (2)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	2	1d (traces) 18 (13%)
5	17 / (1)	14 / (2)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1) CuI/ (0.02)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	2	1d (58%) 18 (13%)
6	17 / (1)	14 / (2)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1) CuI/ (0.02)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	4	1d (traces) 18 (10%) 19 (traces)
7	17 / (1)	13 / (2)	Pd(OAc) ₂ / (0.05)	PPh ₃ / (0.1) CuI/ (0.02)	Cs ₂ CO ₃ / (2)	DMF / (5)	140	2	1d (30%) 20 (26%) 21 (11%)

When trying to synthesize compound **12** with R=2-pyridyl and X=I, **12d** was not obtained, instead the compound found had the structure of their isomer **17**, due to the ring-chain-ring isomerism in 3-(2-pyridyl)-7-substituted triazolopyridines previously described by our group (Scheme 4).²⁴



Scheme 4

When the reaction with 3-(6-iodopyridin-2-yl)-[1,2,3]triazolo[1,5-*a*]pyridine **17** and benzothiazole was studied, direct arylation was found giving **18** in low yield. In this case, product of dehalogenation **1d** was also observed, (Table 2, entry 4). Similar results were found adding CuI (entries 5, 6). In conditions of entry 6, the dimer **19** was also formed,²⁵ (Scheme 4). Compound **18** is a new polynitrogenated tridentate ligand that has fluorescent properties. We are at the moment studying its potential application as sensor of cations and anions due to its structural similarity to another compound with this property described by some of us.^{9b}

In conditions of entry 5, compound **17** reacts with thiazole (entry 7) to give, in low yield, two thiazolylpyridyltriazolopyridines, **20** (26%) and **21** (11%). Also the triazolopyridine **1d** was formed (scheme 4).

Conclusions

[1,2,3]Triazolo[1,5-*a*]pyridine reacts with aryl halides in presence of palladium acetate and PPh_3 to give, in medium or low yield, direct arylations in the C3 position, and pyridyl aryl ketones. Thiazole and benzothiazole give direct arylations with 7-halotriazolopyridines in Miura conditions, also in low yields. These behaviours are unprecedented in the chemistry of [1,2,3]triazolo[1,5-*a*]pyridines.

Experimental Section

General. Melting points were determined on a Kofler heated stage and are uncorrected. NMR spectra were recorded on a Bruker AC300MHz with CDCl₃ as solvent. COSY experiments were carried out for all compounds. HRMS Electron Impact (EI) or ElectroSpray (ES) determinations were made using a VG Autospec Trio 1000 (Fisons). All lithiation reactions were performed under inert atmosphere and with dry solvents.²⁶ [1,2,3]Triazolo[1,5-*a*]pyridine **1a**,²⁷ 7-iodo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine **12a**,²⁸ 7-bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine **12b**,²³ 7-Iodo-3-phenyl-[1,2,3]triazolo[1,5-*a*]pyridine **12c**,²⁸ and 3-(6-iodo-pyridin-2-yl)-[1,2,3]triazolo[1,5-*a*]pyridine **17**,^{24a} were prepared as described elsewhere.

General procedure for the preparation of 3-aryl-[1,2,3]triazolo[1,5-*a*]pyridines

A mixture of [1,2,3]triazolo[1,5-*a*]pyridine **1a** (1 equiv), and aryl halide **2** or **6** (2 equiv.), Pd(OAc)₂ (0.05 equiv.), triphenylphosphine (0.1equiv.), and caesium carbonate (2equiv) in DMF (5 mL) was heated at 140 °C whilst being vigorously stirred under argon atmosphere. The progress of the reaction was followed by TLC. An aqueous solution of sodium hydroxide was added at room temperature until reaching basic pH, and the mixture was extracted with dichloromethane. The organic layer was dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude reaction mixture was purified by chromatotron, using ethyl acetate/hexane as solvent in increasing amounts.

3-(4-Methoxyphenyl)-[1,2,3]triazolo[1,5-*a*]pyridine (3). [1,2,3]Triazolo[1,5-*a*]pyridine **1a** (0.10 g, 0.84 mmol) and 4-iodoanisole **2** (0.39 g, 1.68 mmol). In the purification 4,4'-dimethoxybiphenyl **5** (43 mg, 24%) was first eluted. The second fraction was a yellow oil identified as 4-methoxyphenyl 2-pyridyl ketone **4**,²⁹ (30 mg, 23%). The third fraction was a white solid identified as 3-(4-methoxyphenyl)-[1,2,3]triazolo[1,5-*a*]pyridine **3** (10 mg, 33%), mp (AcOEt/Hexane) 132-134 °C, lit.⁸ 132-134 °C. The last fraction was starting material **1a** (37 mg).

3-(3-Pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine (7). [1,2,3]Triazolo[1,5-*a*]pyridine **1a** (0.20 g, 0.84 mmol) and 3-bromopyridine **6** (0.29 g, 1.85 mmol). In the purification 3-pyridyl 2-pyridyl ketone **8** (65 mg, 21%) was first eluted as a yellow oil.³⁰ The second fraction was triphenylphosphine oxide (51 mg), and further a white solid was eluted identified as 3-(3-pyridyl)-[1,2,3]triazolo[1,5-*a*]pyridine **7** (53 mg, 16%), mp (AcOEt/Hexane) 146-148 °C, lit.⁸ 146-148 °C. The last fraction was 3,3'-bipyridyl **9** (26 mg, 32%).³¹

General procedure for the reactions of 7-halo-[1,2,3]triazolo[1,5-*a*]pyridines with thiazole or benzothiazole

A mixture of the corresponding 7-halo-[1,2,3]triazolo[1,5-*a*]pyridine **12a,b** or **17** (1 equiv), thiazole **13** or benzothiazole **14** (2 equiv.), Pd(OAc)₂ (0.05 equiv.), triphenylphosphine (0.1 equiv.), in some cases CuI (0.02 equiv), and caesium carbonate (dried at 150 °C 2 h in vacuo) (2 equiv) in dry DMF (5 mL), was heated at 140 °C in

argon atmosphere whilst being vigorously stirred. The progress of the reaction was followed by TLC for 2 hours. The mixture was evaporated at reduced pressure and treated with an aqueous solution of sodium hydroxide until reaching basic pH, and later extracted with dichloromethane (3x25 mL). The organic layer was dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude reaction mixture was purified by chromatotron using ethyl acetate/hexane as solvent in increasing amounts.

3-Methyl-7-thiazol-5-yl-[1,2,3]triazolo[1,5-a]pyridine (15). 7-Iodo-3-methyl-[1,2,3]triazolo[1,5-a]pyridine **12a** (0.10 g, 0.38 mmol) and thiazole (0.05 mL, 0.70 mmol). In the purification 3-methyl-[1,2,3]triazolo[1,5-a]pyridine **1b** (13 mg) was first eluted, then triphenylphosphine oxide (21 mg), and the last fraction was a yellow oil identified as **15**, (20 mg, 34%). HRMS found for M⁺ 216.0475, C₁₀H₈N₄S requires 216.0469. ¹H NMR δ 8.95 (s, 1H), 8.89 (s, 1H), 7.60 (dd, J₁ = 8.7 Hz, J₂ = 1.2 Hz, 1H), 7.35 (dd, J₁ = 7.2 Hz, J₂ = 1.2 Hz, 1H), 7.21 (dd, J₁ = 8.7 Hz, J₂ = 7.2 Hz, 1H), 2.62 (s, 3H). ¹³C NMR δ 154.5 (CH), 143.5 (CH), 122.7 (CH), 115.6 (CH), 112.7 (CH), 9.5 (CH₃). MS (EI) *m/z* (%) 216 (2); 188 (100); 187 (27); 162 (39).

3-Methyl-7-benzothiazol-2-yl-[1,2,3]triazolo[1,5-a]pyridine (16). 7-Bromo-3-methyl-[1,2,3]triazolo[1,5-a]pyridine **12b** (0.20 g, 0.94 mmol), and benzothiazole (0.21 mL, 1.9 mmol). In the purification benzothiazole (108 mg) was first eluted, then 3-methyl-[1,2,3]triazolo[1,5-a]pyridine **1b** (20 mg), and finally a yellow oil identified as **16** (35%). HRMS found for M⁺ 266.0620, C₁₄H₁₀N₄S requires 266.0626. ¹H NMR δ 8.29 (d, J = 7.2 Hz, 1H), 8.08 (d, J = 8.1 Hz, 1H), 7.98 (d, J = 7.4 Hz, 1H), 7.71 (d, J = 8.7 Hz, 1H), 7.49 (ddd, J₁ = J₂ = 9.0 Hz, J₃ = 1.2 Hz, 1H), 7.39 (ddd, J₁ = J₂ = 8.1 Hz, J₃ = 1.2 Hz, 1H), 7.32 (dd, J₁ = 7.2 Hz, J₂ = 8.7 Hz, 1H). ¹³C NMR δ 156.69 (C), 152.10 (C), 137.10 (C), 135.74 (C), 132.49 (C), 130.87 (C), 126.66 (CH), 125.77 (CH), 123.72 (CH), 123.38 (CH), 121.77 (CH), 118.61 (CH), 115.96 (CH), 10.52 (CH₃). MS(EI) *m/z* (%) 266 (9); 238 (100); 237 (49); 212 (34).

3-(6-Benzothiazol-2-yl-pyridin-2-yl)-[1,2,3]triazolo[1,5-a]pyridine (18). 3-(6-Iodopyridin-2-yl)-[1,2,3]triazolo[1,5-a]pyridine **17** (0.10 g, 0.31 mmol) and benzothiazole (0.77 mL, 0.62 mmol). In the purification Cl₂CH₂/ethyl acetate was used as eluent. Starting material **17** (11 mg) was first eluted, then 3-(2-pyridyl)-[1,2,3]triazolo[1,5-a]pyridine **1d** (30 mg), and the last product eluted was a fluorescent yellow oil identified as **18** (13 mg, 13%). HRMS found for [M+H]⁺ 330.0806, C₁₈H₁₂N₅S requires 330.0813. ¹H NMR δ 8.93 (d, J = 9.0 Hz, 1H), 8.80 (d, J = 6.9 Hz, 1H), 8.47 (dd, J₁ = 7.8 Hz, J₂ = 0.9 Hz, 1H), 8.28 (dd, J₁ = 7.8 Hz, J₂ = 0.9 Hz, 1H), 8.12 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.96 (t, J = 7.8 Hz, 1H), 7.53 (dd, J₁ = 7.2 Hz, J₂ = 6.8 Hz, 2H), 7.43 (ddd, J₁ = 9.0 Hz, J₂ = 7.2 Hz, J₃ = 1.3 Hz, 1H), 7.11 (ddd, J₁ = J₂ = 6.9 Hz, J₃ = 1.2 Hz, 1H). ¹³C NMR δ 169.8 (C), 154.6 (C), 152.1 (C), 138.0 (CH), 136.8 (C), 136.1 (C), 132.4 (C), 131.1 (C), 127.2 (CH), 126.6 (CH), 125.9 (CH), 125.6 (CH), 123.9 (CH), 122.2 (CH), 122.1 (CH), 121.4 (CH), 119.0 (CH), 116.2 (CH).

3-(6-Thiazol-2-yl-pyridin-2-yl)-[1,2,3]triazolo[1,5-a]pyridine 20, and 3-(6-Thiazol-5-yl-pyridin-2-yl)-[1,2,3]triazolo[1,5-a]pyridine (21). 3-(6-Iodopyridin-2-yl)-[1,2,3]triazolo[1,5-a]pyridine **17** (0.20 g, 0.31 mmol) and thiazole (0.11 mg, 1.2 mmol). In the purification toluene/ethyl acetate (8:1) was used as eluent. 3-(2-Pyridyl)-[1,2,3]

triazolo[1,5-*a*]pyridine **1d** (30 mg, 15%) was first eluted, then a yellow solid identified as **20** (45 mg, 26%). Mp. (AcOEt/ Hexane) 181-183 °C. HRMS found for $[M+H]^+$ 280.0656, $C_{14}H_{10}N_5S$ requires 280.0657. 1H NMR δ 8.77-8.71 (m, 2H), 8.34 (dd, $J_1 = 7.8$, $J_2 = 1.2$ Hz, 1H), 8.05 (dd, $J_1 = 7.8$, $J_2 = 0.9$ Hz, 1H), 7.91 (d, $J = 3$ Hz, 1H), 7.88 (dd, $J_1 = J_2 = 7.8$ Hz, 1H), 7.43 (d, $J = 3$ Hz, 1H), 7.41 (ddd, $J_1 = 9$ Hz, $J_2 = 6.9$ Hz, $J_3 = 0.9$ Hz, 1H), 7.03 (ddd, $J_1 = J_2 = 6.9$ Hz, $J_3 = 1.2$ Hz, 1H). ^{13}C NMR δ 169.73(C), 151.67 (C), 150.59 (C), 144.24 (CH), 137.85 (CH), 136.68 (C), 132.17 (C), 126.88 (CH), 125.39 (CH), 121.15 (CH), 121.13 (CH), 121.10 (CH), 117.71 (CH), 116.02 (CH), and the last product eluted was a fluorescent yellow solid identified as **21** (25 mg, 11%). Mp. (AcOEt) 211-213 °C. HRMS found for $[M+H]^+$ 280.0662, $C_{14}H_{10}N_5S$ requires 280.0657. 1H NMR δ 8.80 (s, 1H), 8.70 (d, $J = 6.9$ Hz, 2H), 8.66 (d, $J = 9.2$, 1H), 8.32 (s, 1H), 8.2 (d, $J = 8$ Hz, 1H), 7.76 (dd, $J_1 = J_2 = 8$ Hz, 1H), 7.53 (d, $J = 8$ Hz, 1H), 7.39-7.35 (m, 1H), 7.01 (ddd, $J_1 = J_2 = 6.9$ Hz, $J_3 = 1.2$ Hz, 1H). ^{13}C NMR δ 154.32 (CH), 152.14 (C), 149.67 (C), 141.01 (C), 140.26 (CH), 138.72 (CH), 136.81 (C), 132.21 (C), 126.94 (CH), 125.47 (CH), 121.20 (CH), 119.49 (CH), 117.89 (CH), 116.10 (CH).

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