Synthesis of Tetrazolo[1,5-*a*]pyridines Utilizing Trimethylsilyl Azide and Tetrabutylammonium Fluoride Hydrate

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Abstract: A method for the preparation of tetrazolo[1,5-*a*]pyridines from 2-halopyridines, utilizing trimethylsilyl azide in the presence of tetrabutylammonium fluoride hydrate, is described. In addition, 8-bromotetrazolo[1,5-*a*]pyridine is further transformed into a variety of novel tetrazolo[1,5-*a*]pyridine derivatives.

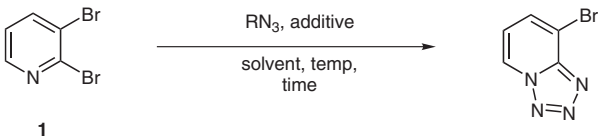
Key words: tetrazolo[1,5-*a*]pyridines, 2-halopyridines, trimethylsilyl azide, tetrabutylammonium fluoride hydrate, palladium coupling

Tetrazolo[1,5-*a*]pyridines are an interesting class of heterocycles that have been utilized to synthesize 2-cyanopyrroles,[1a] substituted 1,3-diazepines,[1b] pyrido-2,3-furoxanes,[1c,d] and 2-aminopyridines.[1e] In some cases the tetrazolo[1,5-*a*]pyridines exist in equilibrium with the corresponding 2-azidopyridines.[2] Substituents on the heterocyclic ring can influence this equilibrium, but in most instances the tetrazole is either the predominant or the exclusive species.

Tetrazolo[1,5-*a*]pyridines are prepared either by heating 2-halopyridines with sodium azide in a polar solvent,[3] or by allowing pyridine *N*-oxides to react with toluenesulfonyl azide,[4] or diphenyl phosphoryl azide,[5,6] or by treatment of *N*-(methylsulfonyloxy)pyridinium chlorides generated in situ with trimethysilyl azide ($TMSN_3$).[7] Generally, high temperatures are required to facilitate the nucleophilic displacement of the halogen by azide ion. The synthesis of tetrazolo[1,5-*a*]pyridines from pyridine *N*-oxides also suffers from several disadvantages, including the need for high temperature and a lack of regioselectivity. Interestingly, during the synthesis of tetrazol-5-yl pyridines from *N*-fluoropyridinium fluorides generated in situ in the presence of $TMSN_3$ and isonitriles, tetrazolo[1,5-*a*]pyridines were produced as minor byproducts.[8] Herein we report a convenient method for the preparation of tetrazolo[1,5-*a*]pyridines from 2-halopyridines. In addition, one of the tetrazolo[1,5-*a*]pyridine products is further transformed into a variety of novel tetrazolo[1,5-*a*]pyridine derivatives.

2,3-Dibromopyridine (**1**) was chosen as the starting material for the initial optimization reaction because a bromide at the 2-position of the pyridine ring could facilitate nucleophilic displacement and the additional bromide at the 3-position could serve as a synthetic handle for further functionalization of the tetrazolo[1,5-*a*]pyridine. The reaction of **1** with either sodium, tetrabutylammonium or trimethylsilyl azide utilizing various additives, solvents, temperatures and times was examined.

Table 1 Conversion of **1** into **2** under Various Conditions



1 **2**

Entry	R[a]	Additive[b]	Solvent	Temp (°C)	Time (h)	Yield (%)
1	Na	–	DMF	60	24	0
2	Na	–	DMF	95	70	25[c]
3	Na	18-crown-6	DMF	95	24	40[c]
4	Na	Bu_4NBr	DMF	95	24	40[c]
5	Na	Bu_4NBr	MeOH	60	18	0
6	Na	–	DMF–H_2O (4:1)	95	24	50[d]
7	Na	Bu_4NBr	DMF–H_2O (4:1)	95	24	75[d]
8	Bu_4N[b]	–	DMF	95	24	40[c]
9	TMS	–	DMF	95	60	48[c]
10	TMS	TBAF·xH_2O	DMF (1.5 M)	85	24	90[d]
11	TMS	TBAF·xH_2O	–	85	24	90[c] 100[d]

[a] 2 equiv.
[b] 1 equiv.
[c] Isolated yield.
[d] Conversion determined by reverse-phase HPLC analysis.

Heating a mixture of **1** and sodium azide at 60 °C in DMF for 24 hours did not produce any product (Table 1, entry 1). However, elevating the temperature to 95 °C and prolonging the reaction time to 70 hours gave **2**[9] in 25% yield (entry 2). Addition of the phase-transfer reagents 18-crown-6 or tetrabutylammonium bromide (TBAB) increased the yield to 40% (entries 3 and 4). Utilizing methanol as solvent was detrimental (entry 5), but using a

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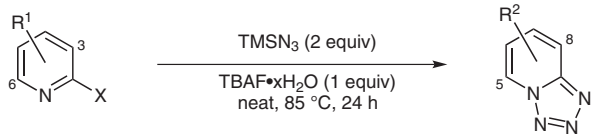
mixture of DMF–H_2O (4:1) without an additive (entry 6) or in the presence of TBAB (entry 7) resulted in 50% and 75% conversion of **1** into **2**, respectively. Tetrabutylammonium azide (entry 8) resulted in a conversion yield similar to that obtained using a combination of TBAB and sodium azide. $TMSN_3$ proved to be better as an azide source (entry 9). Furthermore, $TMSN_3$ in the presence of tetrabutylammonium fluoride hydrate (TBAF·xH_2O) in DMF at 85 °C for 24 hours gave a 90% conversion of **1** into **2** (entry 10). Parenthetically, heating **1** in the presence of TBAF·xH_2O (1 equiv) in DMF at 95 °C for 24 hours did not result in exchange of the 2-bromo substituent with fluoride, although such a reaction has been reported for a different 2-bromopyridine derivative at higher temperature and in the presence of 20 equivalents of anhydrous TBAF.[10] Also, heating a solution of 2-fluoro-3-bromopyridine in $TMSN_3$ at 95 °C for 24 hours did not yield **2**. These two observations suggest that the 2-fluoropyridine derivative is not participating as an intermediate in the transformation of **1** into **2** in the presence of $TMSN_3$ and TBAF·xH_2O. Finally, utilizing $TMSN_3$ (2.0 equiv) in the presence of TBAF·xH_2O (1.0 equiv) *without* solvent, at 85 °C for 24 hours, gave a 100% conversion and a 90% isolated yield of **2** (entry 11).[11] Two equivalents of $TMSN_3$ was necessary; one equivalent resulted in a significant amount of unreacted **1** remaining after 24 hours.

Table 2 Synthesis of Tetrazolo[1,5-*a*]pyridines



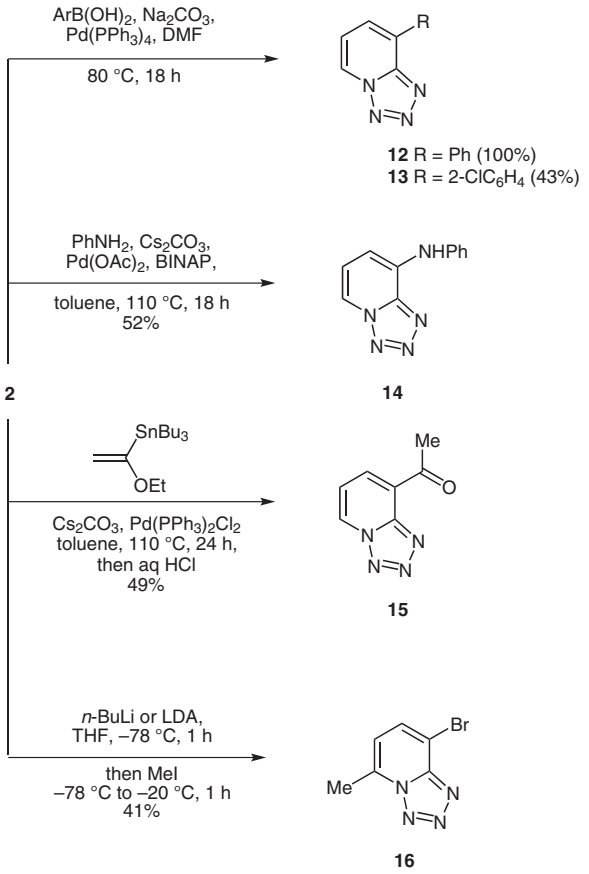
Entry	X	R^1	Product (% yield)	R^2
1	Br	3-Br	**2** (90)	8-Br
2	Br	–	**3** (91)	–
3	Br	4-Br	**4** (12) **5** (37)[a]	7-Br 7-N_3
4	Br	5-Br	**6** (85)	6-Br
5	Br	6-Br	–	–
6	Br	6-*N*-Boc-Pip[b]	–	–
7	Br	6-Me	**7** (76)	5-Me
8	Cl	3-Br	**2** (83)	8-Br
9	Cl	5,6-benzo	**8** (88)	5,6-benzo
10	Cl	3,4-benzo	**9** (95)	7,8-benzo
11	Cl	3-CO_2Et	**10** (81)	8-CO_2Et
12	Cl	3-Cl-5-CF_3	**11** (78)[c]	8-Cl-6-CF_3

[a] 94% pure as determined by reverse-phase HPLC analysis.
[b] Pip = piperazinyl.
[c] Tetrazole–azide (3:1) in $CDCl_3$ as determined by ^{1}H NMR.

The scope of the reaction under the optimized conditions was then examined by employing an array of 2-halopyridines, as well as 2-chloroquinoline and 1-chloroisoquinoline, to give a variety of substituted tetrazolo[1,5-*a*]pyridines, tetrazolo[1,5-*a*]quinoline and tetrazolo[5,1-*a*]isoquinoline, respectively. For example, 2-bromopyridine readily underwent cyclization to give **3**[1d] in 91% yield (Table 2, entry 2). Interestingly, 2-bromopyridines with an additional bromide in the 4- or 6-positions were poor substrates. In the case of 2,4-dibromopyridine (entry 3), tetrazole **4** was isolated in only 12% yield along with 7-azidotetrazolo[1,5-*a*]pyridine (**5**), in 37% yield, which was produced by addition of a second equivalent of azide. In the case of 2,6-dibromopyridine, no tetrazole product was isolated (entry 5). Similarly, a 2-bromo-6-piperizinepyridine derivative also did not afford any tetrazole (entry 6). However, 2-bromo-6-methylpyridine gave the corresponding tetrazole **7**[1a] in 76% (entry 7). On the other hand, 2,5-dibromopyridine was an excellent substrate, giving **6**[2c] in 85% yield (entry 4). 2-Chloropyridine derivatives could also be utilized as substrates. For example, 3-bromo-2-chloropyridine gave **2** in 83% yield (entry 8). Pyridine substrates containing a fused ring, such as 2-chloroquinoline and 2-cholorisoquinoline, formed fused tetrazolo[1,5-*a*]pyridines[12,13] in excellent yields (entries 9 and 10). Finally, the optimized reaction conditions were also found to be compatible with other functional groups. For example, ethyl 2-chloronicotinate and 2,3-dichloro-5-trifluoromethylpyridine afforded **10**[1c] and **11**[2a] in 81% and 78% yields, respectively (entries 11 and 12).

Reactions of tetrazolo[1,5-*a*]pyridines have been limited to a few examples, such as reduction of the pyridine ring to give aliphatic tetrazoles,[14] and alkylation[15] or arylation[16] of the tetrazole to give N-substituted bicyclic tetrazoles. Therefore, the reactivity of 8-bromotetrazolo[1,5-*a*]pyridine was studied in order to further explore the chemistry of this interesting heterocycle (Scheme 1). For example, arylation of **2** with phenylboronic acid or 2-chlorophenylboronic acid under Suzuki reaction conditions[15] gave **12** or **13** in 100% and 43% yields, respectively. Arylamination of **2** with aniline utilizing a palladium-mediated reaction gave **14** in 52% yield.[18] Functional group transformation of the aryl bromide to an acetyl group was achieved utilizing a Stille coupling with tributyl(1-ethoxyvinyl)tin, followed by hydrolysis in situ to afford **15** in 49% yield.[19] Finally, anion generation with *n*-BuLi or LDA at –78 °C, followed by addition of methyl iodide, gave **16** in 41% isolated yield (based on recovered starting material).[20] Hydrogenation of **16** using 10% Pd/C gave **7** in 54% yield, providing further structural confirmation of **16**.

All of the products synthesized herein existed exclusively in the tetrazole form in the solid state. IR spectra on KBr plates for all the products, with the exception of **5** which incorporates a second equivalent of azide, lacked absorption in the azide diagnostic region (2120–2160 cm^{-1}). Similarly, ^{1}H NMR spectra of the products recorded in two different solvents ($CDCl_3$ and DMSO-d_6) indicated



Scheme 1 Tetrazolo[1,5-*a*]pyridines prepared from **2**

the presence of only one form in solution, except in the case of **11**,[2a] which was in equilibrium with the azide form (tetrazole/azide = 3:1 in $CDCl_3$; Table 2, entry 12). Attempts to trap the azido form of **12** in solution through the reaction with triphenylphosphine, via a Staudinger reaction, were unsuccessful and only resulted in recovered starting material. These results are consistent with predominance of the tetrazole form. In addition, compound **12** demonstrated remarkable stability in strong acid, which is again indicative of the tetrazole form and is in accordance with the literature.[2d] In the case of compound **11**, treatment with triphenylphosphine gave 3-chloro-5-trifluoromethyl-*N*-(triphenylphosphoranylidene)-2-pyridinamine (**17**) in 98% yield, which confirms the presence of the azide form in solution.

In summary, a method for the preparation of tetrazolo[1,5-*a*]pyridines from 2-halopyridines, utilizing trimethylsilyl azide in the presence of tetrabutylammonium fluoride hydrate, has been developed. One derivative, 8-bromotetrazolo[1,5-*a*]pyridine (**2**), was further transformed into a variety of novel tetrazolo[1,5-*a*]pyridine derivatives. These methods will facilitate the synthesis of additional tetrazolo[1,5-*a*]pyridine derivatives that can be used for various applications, including screening for biological activities.

Unless otherwise noted, all reagents and solvents were purchased from commercial sources and used without further purification. Degassed solvents were used in all of the palladium-coupling reactions and performed under positive pressure of argon. NMR spectra were obtained using a Varian 500 MHz spectrometer. All ^1H NMR spectra are reported in δ units (ppm) and referenced to tetramethylsilane (TMS). All ^{13}C NMR spectra are reported in δ units (ppm) and referenced to the central line of the $CDCl_3$ triplet at δ = 77.23 ppm. Column chromatography was performed on a CombiFlash Sg 100c separation system (ISCO) with disposable silica gel columns (Luknova). IR spectra were recorded on a Perkin-Elmer System 2000 FT-IR spectrophotometer. High-resolution mass spectra were carried out on an Agilent 6210 Time-of-Flight LC/MS with ESI+ mode using direct flow injection. Elemental analyses were performed by Perkin-Elmer 2400 CHN analyzer. Melting points were recorded on a Mel-Temp® melting point apparatus and are uncorrected.

Tetrazolo[1,5-*a*]pyridines; Typical Procedure for 8-Bromotetrazolo[1,5-*a*]pyridine (2)[9]

Into a screw-capped vial equipped with a magnetic stirring bar were added **1** (237 mg, 1.00 mmol) and TBAF·xH_2O (262 mg, 1.00 mmol). $TMSN_3$ (230 mg, 2.00 mmol) was then added slowly to the solid mixture (**CAUTION**: exothermic reaction). After the vigorous reaction subsided, the vial was sealed and heated under vigorous stirring at 85 °C for 24 h. The heterogeneous mixture was transferred to a flask using a mixture of 2 N NH_3 in MeOH–CH_2Cl_2 (2:98) and then concentrated under reduced pressure. EtOAc (40 mL) was added to the residue and the solution was washed sequentially with H_2O (2 × 10 mL) and brine (1 × 10 mL), dried with anhyd Na_2SO_4, filtered and concentrated to give a crude product that was purified by column chromatography (silica gel; 0–2% 2 N NH_3 in MeOH–CH_2Cl_2, 2:98) to give **2**.[9]

Yield: 180 mg (90%); pale-yellow solid; mp 217–219 °C.

IR (KBr): 939, 1101, 1406, 1480, 3024–3110 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.14 (t, *J* = 7.0 Hz, 1 H), 7.89 (d, *J* = 7.0 Hz, 1 H), 8.81 (d, *J* = 7.0 Hz, 1 H).

Anal. Calcd for $C_5H_3BrN_4$: C, 30.18; H, 1.52; N, 28.15. Found: C, 30.39; H, 1.47; N, 27.95.

Tetrazolo[1,5-*a*]pyridine (3)[1d]

Yield: 91%; pale-yellow solid; mp 161–163 °C.

IR (KBr): 1492, 3033–3127 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.24–7.26 (m, 1 H), 7.67–7.71 (m, 1 H), 8.07 (d, *J* = 9.0 Hz, 1 H), 8.85 (d, *J* = 9.0 Hz, 1 H).

Anal. Calcd for $C_5H_4N_4$: C, 50.00; H, 3.36; N, 46.65. Found: C, 49.88; H, 3.09; N, 46.33.

7-Bromotetrazolo[1,5-*a*]pyridine (4)

Yield: 12%; pale-yellow solid; mp 152–154 °C.

IR (KBr): 1099, 1471, 1621, 3018–3111 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 9.0 Hz, 1 H), 8.25 (s, 1 H), 8.71 (d, *J* = 9.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 118.5, 121.0, 125.7, 126.7.

Anal. Calcd for $C_5H_3BrN_4$: C, 30.18; H, 1.52; N, 28.15. Found: C, 30.04; H, 1.59; N, 27.86.

7-Azidotetrazolo[1,5-*a*]pyridine (5)

Yield: 37%; yellow solid; mp 175 °C (dec.).

IR (KBr): 1232, 1450, 1642, 2142, 3037–3116 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.23 (d, *J* = 7.5 Hz, 1 H), 7.98 (s, 1 H), 9.31 (d, *J* = 7.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 102.8, 112.5, 128.1, 146.0, 149.7.

Bulk material was 94% pure as determined by reverse-phase HPLC analysis (column: Zorbax SB-C8, 4.6 x 30 mm, 3.5 micron; injection volume: 5 μL; sample concentration: 1 mg/mL in MeCN; λ = 254 nm; gradient: 5% MeCN in H_2O to 95% MeCN in H_2O over 2.5 min; total run time: 2.5 min; elution rate: 3 mL/min). An analytically pure sample was prepared after several purifications using silica gel chromatography.

Anal. Calcd for $C_5H_3N_7$: C, 37.27; H, 1.88; N, 60.85. Found: C, 37.55; H, 2.08; N, 60.58.

6-Bromotetrazolo[1,5-*a*]pyridine (6)[2c]
Yield: 85%; white solid; mp 156–158 °C.

IR (KBr): 1480, 3069–3114 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 9.0 Hz, 1 H), 7.97 (d, *J* = 9.0 Hz, 1 H), 9.00 (br s, 1 H).

Anal. Calcd for $C_5H_3BrN_4$: C, 30.18; H, 1.52; N, 28.15. Found: C, 30.50; H, 1.59; N, 28.00.

5-Methyltetrazolo[1,5-*a*]pyridine (7)[1a]
Yield: 76%; white solid; mp 157–159 °C.

IR (KBr): 803, 1509, 1639, 3066–3101 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.96 (s, 3 H), 7.01 (d, *J* = 7.0 Hz, 1 H), 7.61 (dd, *J* = 9.0, 7.0 Hz, 1 H), 7.92 (d, *J* = 7.0 Hz, 1 H).

Anal. Calcd for $C_6H_6N_4$: C, 53.72; H, 4.51; N, 41.77. Found: C, 53.51; H, 4.28; N, 42.03.

Tetrazolo[1,5-*a*]quinoline (8)[12]
Yield: 88%; white solid; mp 157–159 °C.

IR (KBr): 763, 823, 1611 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.74 (t, *J* = 7.0 Hz, 1 H), 7.88–7.92 (m, 2 H), 7.96–8.00 (m, 2 H), 8.73 (d, *J* = 8.0 Hz, 1 H).

Anal. Calcd for $C_9H_6N_4$: C, 63.52; H, 3.55; N, 32.92. Found: C, 63.44; H, 3.65; N, 33.06.

Tetrazolo[5,1-*a*]isoquinoline (9)[13]
Yield: 95%; white solid; mp 146–148 °C.

IR (KBr): 792 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 8.5 Hz, 1 H), 7.85–7.87 (m, 2 H), 7.93–7.95 (m, 1 H), 8.57 (d, *J* = 7.5 Hz, 1 H), 8.79–8.81 (m, 1 H).

Anal. Calcd for $C_9H_6N_4$: C, 63.52; H, 3.55; N, 32.92. Found: C, 63.42; H, 3.42; N, 32.67.

Ethyl Tetrazolo[1,5-*a*]pyridine-8-carboxylate (10)[1c]
Yield: 81%; white solid; mp 124–126 °C.

IR (KBr): 1713, 3061–3089 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.51 (t, *J* = 7.0 Hz, 3 H), 4.60 (q, *J* = 7.0 Hz, 2 H), 7.35 (t, *J* = 7.0 Hz, 1 H), 8.44 (d, *J* = 7.0 Hz, 1 H), 9.01 (d, *J* = 7.0 Hz, 1 H).

Anal. Calcd for $C_8H_8N_4O_2$: C, 50.00; H, 4.20; N, 29.15. Found: C, 49.96; H, 4.15; N, 29.09.

8-Chloro-6-trifluoromethyltetrazolo[1,5-*a*]pyridine (11)[2a]
Yield: 78%; viscous liquid.

IR (KBr): 1197, 1335, 3043–3103 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): $\delta_{tetrazole}$ = 7.85 (br s, 1 H), 9.13 (br s, 1 H); δ_{azide} = 7.88 (br s, 1 H), 8.50 (br s, 1 H).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_6H_2ClF_3N_4$: 222.9992; found: 222.9996.

8-Phenyltetrazolo[1,5-*a*]pyridine (12)
A mixture of **2** (70 mg, 0.35 mmol), phenylboronic acid (52 mg, 0.42 mmol), $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), and Na_2CO_3 (56 mg, 0.53 mmol, dissolved in minimum amount of H_2O) in DMF (3.5 mL) was heated at 80 °C for 18 h under an argon atmosphere. The solvent was removed under reduced pressure and excess EtOAc (30 mL) was added to the solid residue. The organic layer was washed sequentially with H_2O (2 × 5 mL) and brine (1 × 5 mL), dried over anhyd Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (silica gel; 0–2% 2 N NH_3 in MeOH–CH_2Cl_2, 1:99) to give **12**.

Yield: 68 mg (100%); white solid; mp 118–120 °C.

IR (KBr): 762, 3056–3114 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (t, *J* = 6.0 Hz, 1 H), 7.51–7.53 (m, 1 H), 7.57 (t, *J* = 7.0 Hz, 2 H), 7.83 (d, *J* = 6.0 Hz, 1 H), 8.14 (d, *J* = 7.0 Hz, 2 H), 8.81 (d, *J* = 6.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 117.2, 124.0, 128.7, 128.8, 129.3, 130.0, 130.1, 133.7, 148.2.

Anal. Calcd for $C_{11}H_8N_4$: C, 67.34; H, 4.11; N, 28.55. Found: C, 67.03; H, 4.06; N, 28.55.

8-(2-Chlorophenyl)tetrazolo[1,5-*a*]pyridine (13)
Prepared in the same manner as **12**, except using 2-chlorophenylboronic acid.

Yield: 43%; white solid; mp 156–158 °C.

IR (KBr): 753, 3072–3104 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33 (t, *J* = 6.5 Hz, 1 H), 7.44–7.46 (m, 2 H), 7.58–7.60 (m, 1 H), 7.64–7.66 (m, 1 H), 7.75 (d, *J* = 6.5 Hz, 1 H), 8.86 (d, *J* = 6.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 116.6, 124.8, 127.3, 128.0, 130.6, 130.8, 131.9, 132.5, 132.7, 133.2, 148.4.

Anal. Calcd for $C_{11}H_7ClN_4$: C, 57.28; H, 3.06; N, 24.29. Found: C, 57.41; H, 3.17; N, 24.36.

8-Phenylaminotetrazolo[1,5-*a*]pyridine (14)
A mixture of **2** (100 mg, 0.500 mmol), aniline (56.0 mg, 0.600 mmol), $Pd(OAc)_2$ (12.0 mg, 0.0500 mmol), BINAP (63.0 mg, 0.100 mmol), and Cs_2CO_3 (244 mg, 0.750 mmol) in toluene (5 mL) was heated at 110 °C for 20 h under an argon atmosphere. The solvent was removed under reduced pressure and excess EtOAc (30 mL) was added to the solid residue. The organic layer was washed sequentially with H_2O (2 × 5 mL) and brine (1 × 5 mL), dried over anhyd Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (silica gel; 0–2% 2 N NH_3 in MeOH–CH_2Cl_2, 2:98) to give **14**.

Yield: 55 mg (52%); yellow solid; mp 135–137 °C.

IR (KBr): 1563, 3269 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.04 (t, *J* = 7.0 Hz, 1 H), 7.12 (d, *J* = 7.0 Hz, 1 H), 7.17–7.20 (m, 1 H), 7.33–7.35 (m, 2 H), 7.41–7.45 (m, 2 H), 7.49 (br s, 1 H), 8.28 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 105.5, 114.8, 118.3, 121.8, 124.8, 130.0, 133.3, 139.3, 143.8.

Anal. Calcd for $C_{11}H_9N_5$: C, 62.55; H, 4.29; N, 33.16. Found: C, 62.62; H, 4.50; N, 32.84.

1-Tetrazolo[1,5-*a*]pyridin-8-ylethanone (15)
A mixture of **2** (100 mg, 0.500 mmol), tributyl(1-ethoxyvinyl)tin (362 mg, 1.00 mmol), $Pd(PPh_3)_2Cl_2$ (35.0 mg, 0.050 mmol), and Cs_2CO_3 (325 mg, 1.00 mmol) in toluene (3 mL) was heated at

110 °C for 24 h under an argon atmosphere. The reaction mixture was treated with 3 N HCl (2 mL) at r.t. for 4 h. Excess EtOAc (30 mL) was added and the organic layer was separated. The organic layer was washed sequentially with H_2O (2 × 5 mL) and brine (1 × 5 mL), dried over anhyd Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (silica gel; 0–2% 2 N NH_3 in MeOH–CH_2Cl_2, 2:98) to afford **15**.

Yield: 40 mg (49%); off-white solid; mp 134–136 °C.

IR (KBr): 1682, 3064–3112 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.13 (s, 3 H), 7.39 (t, *J* = 7.0 Hz, 1 H), 8.37 (d, *J* = 7.0 Hz, 1 H), 9.02 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 31.3, 116.5, 125.7, 129.2, 134.2, 147.7, 193.8.

Anal. Calcd for $C_7H_6N_4O$: C, 51.85; H, 3.73; N, 34.55. Found: C, 51.63; H, 3.68; N, 34.25.

7-Bromo-8-methyltetrazolo[1,5-*a*]pyridine (16)

A solution of **2** (100 mg, 0.500 mmol) in THF (4 mL) under an argon atmosphere was cooled to –78 °C. *n*-BuLi (0.250 mL, 0.625 mmol, 2.5 M in hexanes) was slowly added and the resulting solution was stirred at –78 °C for 1 h. MeI (142 mg, 1.00 mmol) was added and the reaction mixture was allowed to slowly warm to –20 °C over 1 h. The reaction mixture was quenched with H_2O and then allowed to warm to r.t. Excess EtOAc (30 mL) was added and the organic layer was separated. The organic layer was washed sequentially with H_2O (2 × 5 mL) and brine (1 × 5 mL), dried over anhyd Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (silica gel; hexanes–EtOAc, 3:2) to give **16**.

Yield: 20 mg (41% based on recovered starting material); white solid; mp 179–181 °C.

IR (KBr): 1505 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.92 (s, 3 H), 6.91 (d, *J* = 7.0 Hz, 1 H), 7.81 (d, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.5, 106.3, 116.0, 134.6, 136.3.

Anal. Calcd for $C_6H_5BrN_4$: C, 33.83; H, 2.37; N, 26.30. Found: C, 34.00; H, 2.12; N, 26.11.

Synthesis of 7 via Hydrogenation of 16

A solution of **16** (21 mg, 0.10 mmol) and 10% Pd/C (25 mg) in EtOH–EtOAc (3:1, 4 mL) was stirred at r.t. under a H_2 atmosphere for 18 h. Filtration followed by concentration of the solvent gave **7**.

Yield: 7 mg (54%).

3-Chloro-5-trifluoromethyl-*N*-(triphenylphosphoranylidene)-2-pyridinamine (17)

A solution of **11** (22 mg, 0.10 mmol) and Ph_3P (30 mg, 0.11 mmol) in anhyd $CHCl_3$ (0.5 mL) was heated at 60 °C for 18 h. The reaction mixture was purified by column chromatography (silica gel; hexanes–EtOAc, 3:1) to obtain **17**.

Yield: 45 mg (98%); viscous liquid.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.44–7.47 (m, 6 H), 7.52–7.56 (m, 3 H), 7.64 (s, 1 H), 7.83–7.87 (m, 6 H), 7.93 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 128.6, 128.7, 129.5, 132.1, 132.2, 133.0, 133.3, 133.5, 142.8.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{17}ClF_3N_2P$: 457.0842; found: 457.0841.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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