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Azide-Triggered Bicyclization of *o*-Alkynylisocyanobenzenes: Synthesis of Tetrazolo[1,5-*a*]quinolines

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Abstract: An efficient and rapid synthetic approach for the synthesis of tetrazolo[1,5-*a*]quinolines has been developed employing the reaction of *o*-alkynylisocyanobenzenes with sodium azide. The present strategy involved nucleophilic addition of azide to isocyanide followed by 6-*endo* cyclization. The reaction gives access to a collection of tetrazolo[1,5-*a*]quinolines with broad functional group in moderate to high yields under metal-, and base-free conditions.

Introduction

Nitrogen-containing heterocycles are prevalent structural motifs found in naturally occurring compounds and biologically active molecules and they have been associated with the pharmaceutical and agrochemical industries.[1] Among many privileged classes of the aza-heterocycles, tetrazolo[1,5-*a*]quinolines contain unique structural features and can be found in pharmaceutically relevant compounds exhibiting antibacterial,[2a] anti-inflammatory,[2a] antimicrobial,[2b] anticancer,[2c] HMG-CoA reductase inhibitory,[2d] antihypertensive[2e] and antituberculosis[2f] activities (Figure 1). In addition to their pharmacological significance, the tetrazolo[1,5-*a*]quinolines are also important intermediates for the synthesis of indoxyl-fused pyridines,[3a] quinolinotriazoles,[3b] 2-aminoquinolines,[3c] and α-carbolines.[3d]

Due to the biological and synthetic utilities of tetrazolo[1,5-*a*]quinolines, their syntheses received much attention and are of particular interest. The previously reported methods to access tetrazolo[1,5-*a*]quinolines involve the reaction of sodium azide or $TMSN_3$ with 2-chloroquinolines,[2,4] as well as other alternative approaches starting from quinoline *N*-oxides,[5] 1-aryltetrazoles,[3c,6] and other substrates.[7] Although there are several approaches existing toward the synthesis of tetrazolo[1,5-*a*]quinoline scaffolds, the development of alternative synthetic methods toward the preparation of tetrazolo[1,5-*a*]quinolines under mild and convenient experimental procedures is still desirable.

Over the past few decades, nucleophile-triggered cyclization of *o*-alkynylisocyanobenzenes has emerged as efficient and atom-economical synthetic strategy for the synthesis of 2-substituted quinolines and indoles.[8] Our group interested in the tandem cyclization toward the synthesis of *N*-heterocycles.[9] Recently, we reported the utilization of water, sulfinate sodium salts, and ammonium thiocyanate as nucleophile to react with *o*-alkynylisocyanobenzenes to access quinolin-2(1*H*)-ones, 2-sulfonyl- and 2-thiocyanato quinolines, respectively.[10] As a part of our on-going program, we now report the synthesis of tetrazolo[1,5-*a*]quinoline derivatives from the reaction of *o*-alkynylisocyanobenzenes **2** and sodium azide (**3**) (Scheme 1).

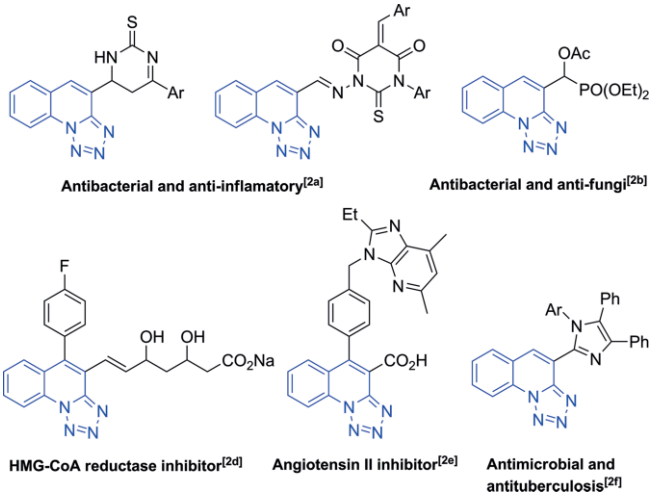
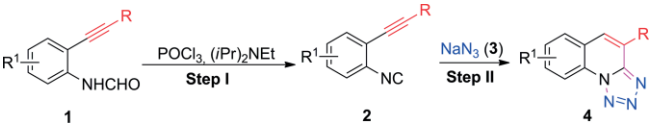


Figure 1. Some selected examples of bioactive molecules containing tetrazolo[1,5-*a*]quinoline motif.



Scheme 1. Synthetic approach to access tetrazolo[1,5-*a*]quinolines **4**.

Results and Discussion

Primarily, the reaction between *o*-(phenylethynyl)isocyanobenzene (**2a**) and sodium azide (**3**) was examined under various

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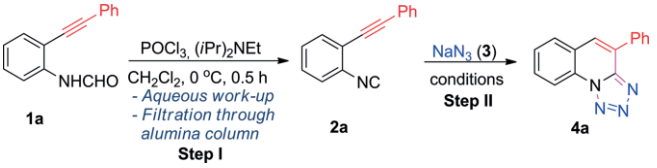
reaction parameters in order to screen for the optimum reaction conditions and the results are summarized in Table 1. It is worth to emphasize that **2a** was readily obtained from its corresponding *N*-(2-(phenylethynyl)phenyl)formamide (**1a**) upon treatment with $POCl_3$, iPr_2NEt in CH_2Cl_2 at 0 °C for 0.5 h (Step I).[11] Compound **2a** is inherently unstable, therefore after aqueous work-up, it was filtered through a short-path column (aluminium oxide, Type E) eluted with EtOAc. After solvent removal, the obtained crude compound **2a** was treated with sodium azide (**3**, 2 equiv.) in DMF at room temperature (30–32 °C) for overnight (18 h) (Table 1, entry 1) (Step II). Gratifyingly, the desired 4-phenyltetrazolo[1,5-*a*]quinoline (**4a**) was obtained in high yield (82 % yield). It is should be emphasized here that the yield of **4a** was based on the starting compound **1a**. The yield was not significantly improved at elevated temperature (60–100 °C) (Table 1, entries 2–4). Additionally, an increase or decrease of the amount of sodium azide employed (1–3 equivalents) did not have a profound effect on the yields of **4a** (Table 1, entry 1 vs. entries 5–7). Therefore, we decided to employ a slight excess amount of sodium azide with respect to the starting compound **1a**. After the reaction temperature and the stoichiometry of sodium azide were chosen (room temperature and 1.5 equivalents, respectively), it was found that the reaction time can be shortened from 18 h to 2 h (Table 1, entry 1 vs. entries 8–10). Solvents, including dimethyl sulfoxide (DMSO), toluene, dichloromethane (DCM) and water, were evaluated (Table 1, entries 11–14). Among solvents screened, only DMSO gave comparable results to those obtained when DMF was employed as the solvent; others failed to provide the expected product **4a**. After extensive experimentation, the optimal reaction conditions were identified as follows: **1** (0.5 mmol) and sodium azide (**3**, 1.5 equiv.) in DMF at room temperature, 2 h (Table 1, entry 9).

Table 1. Optimization of reaction conditions.[a]

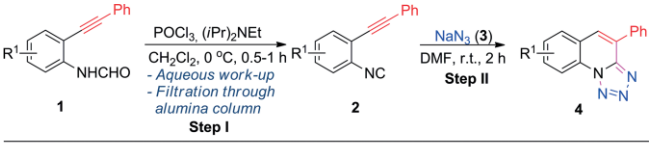


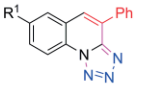
Entry	**3** (equiv.)	Solvent	Temp (°C)	Time [h]	Yield [%][b]
1	2	DMF	r.t.	18	82
2	2	DMF	60	18	82
3	2	DMF	80	18	81
4	2	DMF	100	18	85
5	1.5	DMF	r.t.	18	88
6	1	DMF	r.t.	18	80
7	3	DMF	r.t.	18	88
8	1.5	DMF	r.t.	6	85
9	**1.5**	**DMF**	**r.t.**	**2**	**88**
10	1.5	DMF	r.t.	1	83
11	1.5	DMSO	r.t.	2	78
12	1.5	Toluene	r.t.	2	N.D.
13	1.5	DCM	r.t.	2	N.D.
14	1.5	H_2O	r.t.	2	N.D.

[a] Reaction conditions: Step I: **1a** (0.5 mmol), $POCl_3$ (0.75 mmol), $(iPr)_2NEt$ (4.0 mmol), CH_2Cl_2 (4 mL), 0 °C, 0.5 h; after aqueous work-up and evaporation to dryness the crude mixture was diluted with EtOAc, filtered by a short-path column chromatography (aluminium oxide, Type E) and eluted with EtOAc. Step II: **2a** (freshly prepared from **1a**) was treated with NaN_3 (**3**) in the solvent (2 mL) under various reaction conditions. [b] Isolated yields after chromatographic purification (SiO_2 column chromatography).

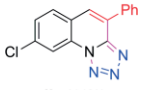
After having the optimized reaction conditions in hand, we next evaluated the generality of the present transformation on structurally different *o*-alkynylisocyanobenzenes **2** (freshly prepared from the corresponding formamides **1**) and the results are summarized in Table 2. First, the effect of the substitution on the aryl ring attached with the isocyanide moiety of the *o*-alkynylisocyanobenzenes **2** was evaluated. Substrates **2** bearing a substituent located at the *para* position with respect to the isocyanide moiety were first examined. The *p*-methyl-substituted substrate gave the corresponding product **4b** in 66 % yield. Substrates with *para* electron attracting substituent (CF_3, F, Cl, Br) yielded the corresponding products **4c**–**4f** with the yields ranging from 40 %–76 % yields. Unfortunately, under the standard reaction conditions, the *p*-nitro substituted substrate **1g** was consumed but did not provide the desired product. Finally, the *m*-chloro substrate delivered product **4h** in 44 % yield.

Table 2. Reaction of *o*-alkynylisocyanobenzenes **2a**–**2h**.[a]





4a, R^1 = H (88%)
4b, R^1 = CH_3 (66%)
4c, R^1 = CF_3 (40%)
4d, R^1 = F (76%)
4e, R^1 = Cl (57%)
4f, R^1 = Br (56%)
4g, R^1 = NO_2 (trace)



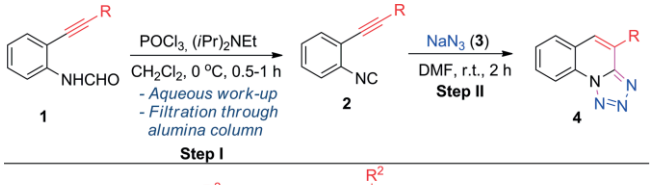
4h, (44%)

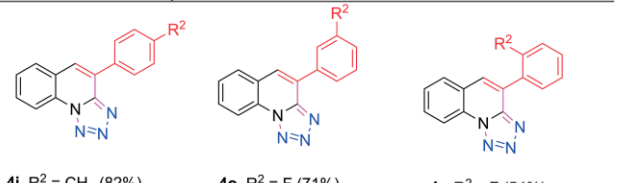
[a] Reaction conditions: Step I: **1** (0.5 mmol), $POCl_3$ (0.75 mmol), $(iPr)_2NEt$ (4.0 mmol), CH_2Cl_2 (4 mL), 0 °C, 0.5–1 h; after aqueous work-up and evaporation to dryness the crude mixture was diluted with EtOAc, filtered by a short-path column chromatography (aluminium oxide, Type E) and eluted with EtOAc. Step II: **2** (freshly prepared from **1**), NaN_3 (**3**, 1.5 equiv.) in DMF (2 mL), r.t. (30–32 °C), 2 h. In parenthesis: isolated yields after chromatographic purification (SiO_2 column chromatography).

Next, the reactions of *o*-alkynylisocyanobenzenes **2** bearing different substituent R on the alkynyl moiety were evaluated and the results are summarized in Table 3. Substrates **2i**–**2n** bearing a substituent (R^2) located at the *para* position with respect to the arylethynyl moiety of **2** were first tested. Substrates **2i** and **2j** with electron-donating groups in *para* position (CH_3 and OCH_3) gave the desired products **4i** and **4j** in 82 % and 87 % yields, respectively. While the *para*-halogen-substituted substrates **2k**–**2m** delivered their corresponding products **4k**–**4m** in good to high yields, limitation was again observed with the *p*-nitro substrate. The reactions of substrates with a substituent at *meta* position (*m*-F, *m*-Cl, and *m*-Br) readily proceeded and gave the corresponding products with the yields ranging from 59–71 % yields. Apparently, the steric effect on the reac-

tion efficiency was noticed. Substrates **2r** and **2s** bearing substituent at the *ortho* position (*o*-F and *o*-Cl) gave products **4r** and **4s** in 54 % and 29 % yields, respectively. The steric effect was further emphasized when **4t** and **4u** were obtained in much lower yields (8 % and 16 % yields, respectively). Extending the reaction time from 2 h to 18 h raised the yield of **4t** to 33 % yield. Although **4w** was obtained in low yield (20 % yield) when a terminal alkynyl substrate was employed, the present reaction can accommodate *o*-alkylnylisocyanobenzenes bearing heterocycle (R = 2-thienyl) and aliphatic substituent (R = *n*-butyl, *n*-hexyl, isopentyl and cyclopropyl) and furnished the corresponding products with the yields ranging from 53–76 % yields.

Table 3. Reaction of *o*-alkynylisocyanobenzenes **2i**–**2z** and **2a'**.[a]

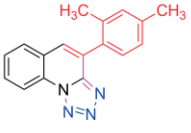




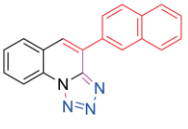
4i, R^2 = CH_3 (82%)
4j, R^2 = OCH_3 (87%)
4k, R^2 = F (85%)
4l, R^2 = Cl (68%)
4m, R^2 = Br (72%)
4n, R^2 = NO_2 (trace)

4o, R^2 = F (71%)
4p, R^2 = Cl (69%)
4q, R^2 = Br (59%)

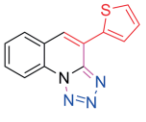
4r, R^2 = F (54%)
4s, R^2 = Cl (29%)



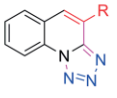
4t, (8%) (33%)[b]



4u, (16%)



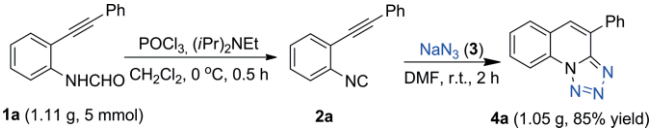
4v, (54%)



4w, R = H (20%)
4x, R = $(CH_2)_3CH_3$ (53%)
4y, R = $(CH_2)_5CH_3$ (76%)
4z, R = $(CH_2)_2CH(CH_3)_2$ (61%)
4a', R = cyclopropyl (54%)

[a] Reaction conditions: Step I: **1** (0.5 mmol), $POCl_3$ (0.75 mmol), $(iPr)_2NEt$ (4.0 mmol), CH_2Cl_2 (4 mL), 0 °C, 0.5–1 h; after aqueous work-up and evaporation to dryness the crude mixture was diluted with EtOAc, filtered by a short-path column chromatography (aluminium oxide, Type E) and eluted with EtOAc. Step II: **2** (freshly prepared from **1**), NaN_3 (**3**, 1.5 equiv.) in DMF (2 mL), r.t. (30–32 °C) for 2 h. In parenthesis: isolated yields after chromatographic purification (SiO_2 column chromatography). [b] Reaction time = 18 h.

The synthetic applicability of the present reaction to a gram-scale reaction was also evaluated. Under standard reaction conditions, **2a** freshly prepared from **1a** (1.11 g, 5 mmol) was treated with sodium azide (0.49 g, 7.5 mmol) to provide **4a** (1.05 g, 85 % yields) (Scheme 2). Finally, synthetic utility of the tetrazolo[1,5-*a*]quinoline adduct to access 2-aminoquinoline was also demonstrated. By modifying the previously reported procedure, denitrogenation reaction of **4a** took place in the presence of $Cu(OAc)_2 \cdot H_2O$ (2 equiv.) in DMF to provide 3-phenylquinolin-2-amine (**5**) in 51 % yield (Scheme 3).[3c]



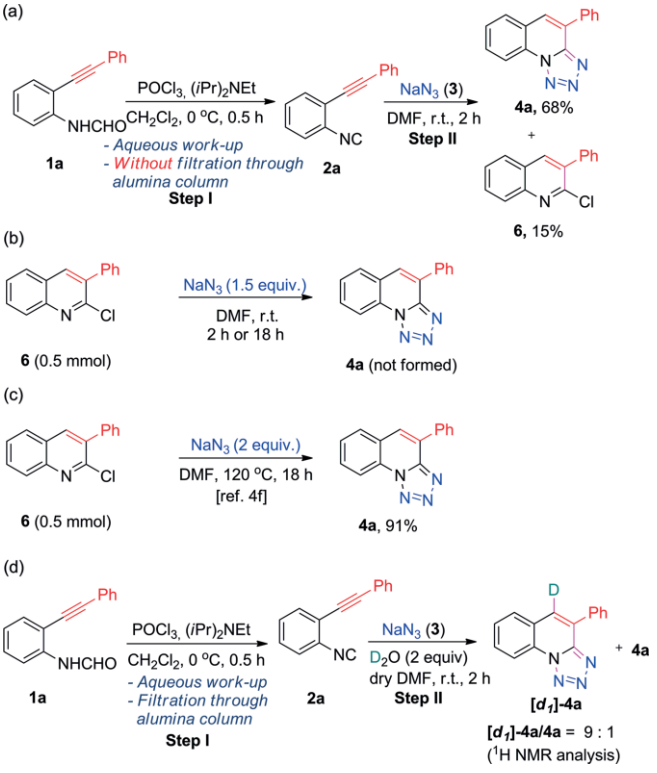
1a (1.11 g, 5 mmol) **2a** **4a** (1.05 g, 85% yield)

Scheme 2. Gram-scale synthesis of 4-phenyltetrazolo[1,5-*a*]quinoline (**4a**).

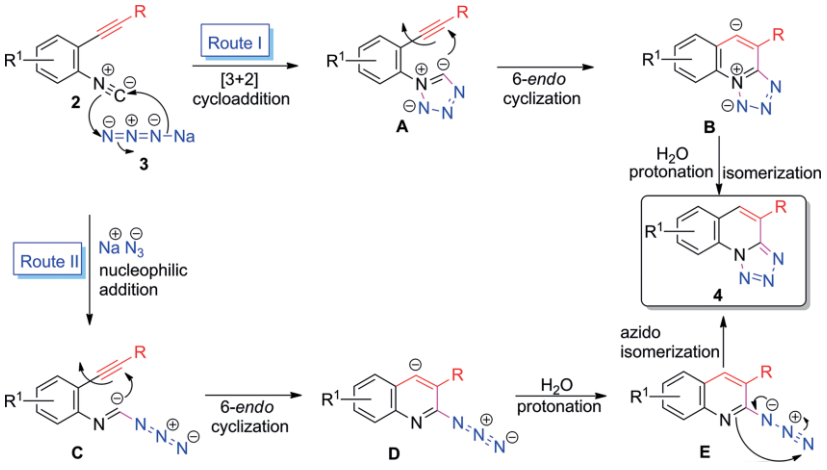
4a **5**, 51% 19%

Scheme 3. Synthetic application of 4-phenyltetrazolo[1,5-*a*]quinoline (**4a**).

To gain better insight into the reaction mechanism, some control experiments were carried out (Scheme 4). After an aqueous work-up but without prior filtration through a short-path column (aluminium oxide, Type E), a freshly prepared **2a** was allowed to react with sodium azide (**3**) under standard reaction conditions (Scheme 4a). It was found that 2-chloro-3-phenylquinoline (**6**) was competitively formed in 15 % yield and **4a** was obtained in lower yield (68 % yield). Therefore, in this work, it is necessary that the crude *o*-alkynylisocyanobenzenes **2** were filtered through a short-path aluminium oxide column prior to treatment with sodium azide. As previously mentioned, tetrazolo[1,5-*a*]quinolines can generally be prepared by the re-



Scheme 4. Control experiments.



Scheme 5. Plausible reaction mechanisms.

action of 2-chloroquinolines and sodium azide.[2,4] In order to exclude the possibility that **4a** formed from 2-chloro-3-phenylquinoline (**6**) under standard reaction conditions, **6** was treated with NaN_3 (1.5 equiv.) and the reaction was allowed to stand at room temperature for 2 h and 18 h (Scheme 4b). It was found that **4a** was not formed and **6** was recovered (93–96 % yields). Thus, in the present work, formation of **4a** from **6** can be excluded. Nevertheless, under forcing conditions (120 °C, 18 h), **6** can be converted to **4a** in 91 % yield (Scheme 4c). Finally, when D_2O (2 equiv.) was added into the reaction of **2a** and **3**, a mixture of products **[*d*$_1$]-4a** and **4a** (**[*d*$_1$]-4a**/**4a** = 9:1, ^{1}H NMR analysis, see Supporting Information) was obtained (Scheme 4d). The results imply that proton source from water or D_2O served as a proton donor.

According to the experimental results as well as control experiments, two plausible reaction mechanisms were proposed as shown in Scheme 5. In Route I, a [3+2] cycloaddition of the azido anion to an isocyanide moiety in compound **2** occurs leading to intermediate **A**. The intermediate **A** undergoes 6-*endo* cyclization to provide intermediate **B**. Subsequent protonation and isomerization will lead to the obtained tetrazolo[1,5-*a*]quinolines **4**. An alternative mechanism (Route II) which cannot be excluded involves nucleophilic addition of an azide anion to the isocyano carbon atom to generate the corresponding imidoyl anion intermediate **C**. Next, **C** undergoes 6-*endo* cyclization leading to intermediate **D**. The subsequent protonation generates **E**, in which the azido group undergoes ring-chain azido-isomerization to furnish the tetrazolo[1,5-*a*]quinolines **4**.[4h,8,10]

Conclusions

In summary, we have developed an alternative strategy for the synthesis of tetrazolo[1,5-*a*]quinolines from the reaction of *o*-alkynylisocyanobenzenes with sodium azide. The salient features of the present method include the consecutive formation of two heterocyclic rings via a one-pot process, mild reaction conditions (room temperature), a broad scope, scalability as well as the robustness of the reaction. Structurally different kinds of tetrazolo[1,5-*a*]quinolines could be prepared in moderate to good yields. The present method should be found as an attractive synthetic approach for a direct diversification of tetrazolo[1,5-*a*]quinolines in both chemical and pharmaceutical research and other related disciplines.

Experimental Section

General information. ^{1}H NMR spectra were recorded with a Bruker AVANCE 400 spectrometer (400 MHz) in $CDCl_3$ by using tetramethylsilane (δ = 0 ppm) or residual non-deuterated solvent peak as an internal standard. ^{13}C NMR spectra were recorded with a Bruker AVANCE 400 (100 MHz) spectrometer. Infrared spectra were recorded with a Bruker ALPHA FT-IR spectrometer and only partial data were listed. High-Resolution Mass Spectra (HRMS) were recorded with a Bruker micro TOF spectrometer in the ESI mode. Melting points were recorded with a Sanyo Gallenkamp apparatus. Reactions were monitored by Thin-Layer Chromatography and visualized by UV and a solution of $KMnO_4$. *N*-(2-Arylethynyl)phenyl)-formamides and *N*-(2-alkylethynyl)phenyl)formamides were synthesized according to literature procedures. The structures of known compounds were confirmed by comparing their ^{1}H NMR and ^{13}C NMR data with those in the literature. All reagents and solvents were obtained from commercial sources and used without further purification. Column chromatography was performed by using Merck silica gel 60 (Art 7734).

General procedure for the synthesis of *N*-(2-(arylethynyl)phenyl)formamides and *N*-(2-(alkylethynyl)phenyl)formamides 1. To a round-bottom flask filled with formic acid (1.5 mL) was added Ac_2O (2 mL) at room temperature, and the resulting mixture was stirred for 10 min. To this mixture was added the solution of 2-iodoaniline derivatives (10 mmol) in CH_2Cl_2 (10 mL) then the reaction chamber was stirred for 2 h at room temperature. After completion, the reaction was quenched with H_2O (5 mL) and the resulting mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), filtered, and concentrated (aspirator). Crude product was purified by column chromatography on silica gel (hexanes/ethyl acetate) to yield the corresponding *N*-(2-iodoaryl)formamide. The obtained *N*-(2-iodoaryl)formamide was subjected to coupling reaction in the next step. To the two-neck flask containing *N*-(2-iodoaryl)formamide (10 mmol), $PdCl_2(PPh_3)_2$ (0.13 mmol), and CuI (0.1 mmol) was added THF (10 mL) and NEt_3 (10 mL) under argon atmosphere. Then, monosubstituted acetylene (11 mmol) was added dropwise

to the reaction mixture. The reaction was allowed to stir at room temperature under Ar atmosphere for overnight. After completion, the reaction was quenched with dilute HCl solution (20 mL) and the resulting mixture was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$, filtered, and concentrated (aspirator). Crude product was purified by column chromatography on silica gel (hexane/ethyl acetate) to provide the corresponding *N*-(2-(arylethynyl)phenyl)-formamide or *N*-(2-(alkylethynyl)phenyl)formamide **1**.

General procedure for the synthesis of *o*-alkynylisocyanobenzenes 2. To a solution of *N*-(2-(arylethynyl)phenyl)formamide or *N*-(2-(alkylethynyl)phenyl)formamide **1** (0.5 mmol) and diisopropylethylamine (0.70 mL, 4.0 mmol) in CH_2Cl_2 (4 mL) was added dropwise $POCl_3$ (0.07 mL, 0.75 mmol) at 0 °C under argon atmosphere. The reaction mixture was stirred at 0 °C for 0.5–1 h. After completion, the reaction was quenched with $NaHCO_3$ (5 mL) and the resulting mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), filtered, and concentrated (aspirator). The crude product was filtered through a short-path column (aluminium oxide, Type E), eluted with 100 % ethyl acetate, and was concentrated (aspirator) to provide the corresponding *o*-alkynylisocyanobenzene **2** which were subsequently used in the next step without prior purification.

General procedure for the synthesis of tetrazolo[1,5-*a*]quinoline derivatives 4. To a round-bottomed flask filled with *o*-alkynylisocyanobenzene **2** [freshly prepared from the corresponding *N*-(2-(arylethynyl)phenyl)formamide or *N*-(2-(alkynyl)phenyl)-formamide (0.5 mmol)] was diluted with DMF (2 mL). To this mixture was added sodium azide (0.049 g, 0.75 mmol, 1.5 equiv.). The reaction mixture was stirred at room temperature for 2 h. After completion, the reaction mixture was diluted with H_2O (5 mL) and the resulting mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), filtered, and concentrated (aspirator). Crude product was purified by column chromatography on silica gel (hexanes/ethyl acetate or hexanes/dichloromethane) to yield the corresponding tetrazolo[1,5-*a*]quinoline derivatives **4**.

4-Phenyltetrazolo[1,5-*a*]quinoline (4a):[7c] white solid (108 mg, 88 % yield); m.p. 154.4–156.4 °C (from CH_2Cl_2/hexanes) (lit.[7c] m.p. 175 °C). IR (neat): $\tilde{\nu}$ = 3051, 1699, 1525, 1457, 1443 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.68 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 7.6 Hz, 2H), 8.06 (s, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.84 (t, *J* = 7.2 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.51–7.47 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.3, 133.8, 130.6, 129.9, 129.54, 129.46, 129.0, 128.9, 128.5, 128.1, 126.5, 124.3, 116.8 ppm. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd. for $C_{15}H_{11}N_4$: 247.0978, found 247.0980.

7-Methyl-4-phenyltetrazolo[1,5-*a*]quinoline (4b): colorless needle (86 mg, 66 % yield); m.p. 177.5–179.3 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3068, 1657, 1579, 1524, 1442 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.37 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 7.2 Hz, 2H), 7.84 (s, 1H), 7.60 (s, 1H), 7.51–7.44 (m, 3H), 7.43–7.41 (m, 1H), 2.49 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 146.8, 138.3, 133.7, 131.9, 129.3, 129.1, 128.8, 128.3, 128.2, 127.7, 125.9, 124.1, 116.1, 21.3 ppm. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd. for $C_{16}H_{13}N_4$: 261.1135, found 261.1137.

4-Phenyl-7-(trifluoromethyl)tetrazolo[1,5-*a*]quinoline (4c): pale yellow needle (63 mg, 40 % yield); m.p. 226.0–228.0 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3069, 1630, 1523, 1499, 1442 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.86 (d, *J* = 8.8 Hz, 1H), 8.34 (s, 1H), 8.18 (d, *J* = 7.2 Hz, 2H), 8.14 (s, 1H), 8.09 (d, *J* = 8.8 Hz, 1H), 7.62–7.53 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.8, 133.2, 131.5, 130.5 (q, $J_{C,F}$ = 32.9 Hz), 130.1, 129.2, 128.8, 128.6, 128.5, 126.9 (q, $J_{C,F}$ = 3.3 Hz), 126.5 (q, $J_{C,F}$ = 3.9 Hz), 124.2, 123.4 (q, $J_{C,F}$ = 271.0 Hz), 117.9 ppm. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd. for $C_{16}H_9F_3N_4Na$: 337.0672, found 337.0671.

7-Fluoro-4-phenyltetrazolo[1,5-*a*]quinoline (4d): pale brown solid (100 mg, 76 % yield); m.p. 193.9–195.9 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3053, 1629, 1575, 1527, 1464 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.73–8.70 (m, 1H), 8.15 (d, *J* = 7.2 Hz, 2H), 8.01 (s, 1H), 7.68 (dd, *J* = 8.2, 2.6 Hz, 1H), 7.62–7.50 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.4 (d, $J_{C,F}$ = 248.1 Hz), 147.1, 133.5, 129.9, 129.1, 128.6, 128.5 (d, $J_{C,F}$ = 3.0 Hz), 128.0, 126.6, 125.9, 119.2 (d, $J_{C,F}$ = 24.4 Hz), 119.0, 113.8 (d, $J_{C,F}$ = 23.2 Hz) ppm. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd. for $C_{15}H_{10}FN_4$: 265.0884, found 265.0881.

7-Chloro-4-phenyltetrazolo[1,5-*a*]quinoline (4e): colorless needle (80 mg, 57 % yield); m.p. 228.5–230.4 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3054, 1660, 1602, 1522, 1439 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.66 (d, *J* = 9.2 Hz, 1H), 8.16–8.13 (m, 2H), 8.01 (d, *J* = 2.0 Hz, 1H), 7.99 (s, 1H), 7.81 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.60–7.50 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.3, 134.1, 133.4, 131.0, 129.9, 129.1, 128.6, 128.3, 128.2, 128.0, 125.5, 118.4 ppm. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd. for $C_{15}H_{10}ClN_4$: 281.0589, found 281.0588.

7-Bromo-4-phenyltetrazolo[1,5-*a*]quinoline (4f): white solid (91 mg, 56 % yield); m.p. 243.7–245.2 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3051, 1674, 1593, 1518, 1441 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.59 (d, *J* = 8.8 Hz, 1H), 8.18–8.13 (m, 3H), 7.98 (s, 1H), 7.95 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.60–7.50 (m, 3H) ppm.^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.3, 133.7, 133.4, 131.2, 130.0, 129.1, 128.7, 128.6, 128.1, 125.8, 121.8, 118.5 ppm. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd. for $C_{15}H_9NBrNa$: 346.9903, found 346.9904.

8-Chloro-4-phenyltetrazolo[1,5-*a*]quinoline (4h): white solid (62 mg, 44 % yield); m.p. 230.9–232.3 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3046, 1659, 1601, 1520, 1448 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.73 (d, *J* = 2.0 Hz, 1H), 8.16–8.13 (m, 2H), 8.05 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.69 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.60–7.50 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.4, 136.9, 133.5, 130.3, 130.1, 129.8, 129.1, 129.0, 128.7, 128.5, 126.9, 122.8, 116.9 ppm. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd. for $C_{15}H_{10}ClN_4$: 281.0589, found 281.0591.

4-(*p*-Tolyl)tetrazolo[1,5-*a*]quinoline (4i): white solid (107 mg, 82 % yield); m.p. 159.9–161.8 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3049, 1678, 1527, 1514, 1454, cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.62 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.98 (s, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.78 (t, *J* = 8.2 Hz, 1H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 2.42 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.2, 139.6, 130.8, 130.3, 129.6, 128.74, 128.70, 128.2, 128.0, 126.3, 124.3, 116.6, 21.3 ppm. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd. for $C_{16}H_{13}N_4$: 261.1135, found 261.1138.

4-(4-Methoxyphenyl)tetrazolo[1,5-*a*]quinoline (4j): pale brown solid (120 mg, 87 % yield); m.p. 164.0–165.9 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3073, 1681, 1605, 1511, 1452 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.69 (d, *J* = 8.0 Hz, 1H), 8.17–8.14 (m, 2H), 8.01– 7.98 (m, 2H), 7.82 (t, *J* = 8.4 Hz, 1H), 7.70 (t, *J* = 8.2 Hz, 1H), 7.10–7.08 (m, 2H), 3.90 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 160.7, 147.3, 130.2, 129.8, 129.5, 128.7, 128.00, 127.96, 126.1, 126.0, 124.5, 116.7, 114.3, 55.4 ppm. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd. for $C_{16}H_{12}N_2ONa$: 299.0903, found 299.0905.

4-(4-Fluorophenyl)tetrazolo[1,5-*a*]quinoline (4k): pale brown solid (112 mg, 85 % yield); m.p. 230.0–231.4 °C (from CH_2Cl_2/hex-

anes). IR (neat): $\tilde{\nu}$ = 3066, 1687, 1600, 1508, 1465 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.72 (d, J = 8.4 Hz, 1H), 8.20–8.17 (m, 2H), 8.05–8.02 (m, 2H), 7.87 (d, J = 8.2 Hz, 1H), 7.74 (t, J = 7.2 Hz, 1H), 7.29–7.25 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.6 (d, $J_{C,F}$ = 248.8 Hz), 147.2, 130.8, 130.5 (d, $J_{C,F}$ = 8.3 Hz), 130.0, 129.3, 128.9, 128.2, 125.6, 124.3, 116.9, 116.1 (d, $J_{C,F}$ = 21.6 Hz) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd. for $C_{15}H_9FN_4Na$: 287.0706, found 287.0703.

4-(4-Chlorophenyl)tetrazolo[1,5-*a*]quinoline (4l): pale brown solid (95 mg, 68 % yield); m.p. 229.7–231.3 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3063, 1678, 1525, 1493, 1464 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.71 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.8 Hz, 2H), 8.08 (s, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.84 (t, J = 7.6 Hz, 1H), 7.54 (d, J = 8.4 Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.1, 135.8, 132.2, 131.0, 130.1, 129.8, 129.5, 129.3, 129.0, 128.3, 125.4, 124.3, 116.9 ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd. for $C_{15}H_{10}ClN_4$: 281.0589, found 281.0588.

4-(4-Bromophenyl)tetrazolo[1,5-*a*]quinoline (4m): colorless needle (117 mg, 72 % yield); m.p. 235.5–237.5 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3054, 1670, 1522, 1490, 1463 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.71 (d, J = 8.4 Hz, 1H), 8.08–8.06 (m, 3H), 8.03 (d, J = 8.0 Hz, 1H), 7.88 (t, J = 7.2 Hz, 1H), 7.76–7.69 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.0, 132.7, 132.2, 131.0, 130.0, 129.5, 129.0, 128.3, 125.4, 124.3, 124.1, 116.9 ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd. for $C_{15}H_9BrN_4Na$: 346.9908, found 346.9902.

4-(3-Fluorophenyl)tetrazolo[1,5-*a*]quinoline (4o): white solid (94 mg, 71 % yield); m.p. 208.9–209.8 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3058, 1692, 1583, 1528, 1461 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.63 (d, J = 8.0 Hz, 1H), 8.09 (s, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.98–7.97 (m, 1H), 7.96–7.92 (m, 2H), 7.75–7.71 (m, 1H), 7.54–7.51 (m, 1H), 7.194–7.186 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 163.0 (d, $J_{C,F}$ = 245.1 Hz), 147.0, 135.8 (d, $J_{C,F}$ = 7.9 Hz), 131.1, 130.5 (d, $J_{C,F}$ = 8.3 Hz), 130.1, 129.9, 129.1, 128.3, 125.2, 124.2 (d, $J_{C,F}$ = 2.8 Hz), 124.1, 116.8, 116.5 (d, $J_{C,F}$ = 21.1 Hz), 115.6 (d, $J_{C,F}$ = 23.3 Hz) ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd. for $C_{15}H_9FN_4Na$: 287.0703, found 287.0709.

4-(3-Chlorophenyl)tetrazolo[1,5-*a*]quinoline (4p): pale brown solid (97 mg, 69 % yield); m.p. 182.5–184.3 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3053, 1681, 1567, 1526, 1464 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.69 (d, J = 8.4 Hz, 1H), 8.12–8.08 (m, 3H), 8.03 (d, J = 8.0 Hz, 1H), 7.87 (t, J = 7.8 Hz, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.51–7.45 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.0, 135.5, 135.0, 131.1, 130.2, 130.1, 130.0, 129.6, 129.1, 128.4, 128.3, 126.8, 125.1, 124.1, 116.8 ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd. for $C_{15}H_{10}ClN_4$: 281.0589, found 281.0586.

4-(3-Bromophenyl)tetrazolo[1,5-*a*]quinoline (4q): pale brown solid (96 mg, 59 %); m.p. 226.0–227.9 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3055, 1648, 1586, 1523, 1493 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.68 (d, J = 8.4 Hz, 1H), 8.26 (s, 1H), 8.14 (d, J = 8.0 Hz, 1H), 8.06 (s, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.87 (t, J = 7.8 Hz, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.0, 135.7, 132.5, 131.2, 131.1, 130.4, 130.1, 130.0, 129.1, 128.3, 127.3, 124.9, 124.1, 123.0, 116.8 ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd. for $C_{15}H_9BrN_4Na$: 346.9903, found 346.9906.

4-(2-Fluorophenyl)tetrazolo[1,5-*a*]quinoline (4r): colorless crystal (71 mg, 54 % yield); m.p. 186.7–187.8 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3085, 1618, 1527, 1491, 1461 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.70 (d, J = 8.0 Hz, 1H), 8.13 (s, 1H), 8.08–8.04 (m, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.87 (t, J = 8.2 Hz, 1H), 7.72 (t, J = 7.2 Hz, 1H), 7.51–7.45 (m, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.30–7.25 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 160.1 (d, $J_{C,F}$ = 248.9 Hz), 147.2, 132.9 (d, $J_{C,F}$ = 6.0 Hz), 131.8, 131.2, 131.1, 130.1, 129.1, 128.1, 124.6 (d, $J_{C,F}$ = 3.5 Hz), 124.0, 121.7 (d, $J_{C,F}$ = 12.5 Hz), 120.9, 116.8, 116.4 (d, $J_{C,F}$ = 22.1 Hz) ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd. for $C_{15}H_{10}FN_4$: 265.0884, found 265.0883.

4-(2-Chlorophenyl)tetrazolo[1,5-*a*]quinoline (4s): pale yellow solid (41 mg, 29 % yield); m.p. 182.5–183.2 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3074, 1620, 1523, 1483, 1458 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.74 (d, J = 8.4 Hz, 1H), 8.03–8.01 (m, 2H), 7.90 (t, J = 7.6 Hz, 1H), 7.74 (t, J = 7.4 Hz, 1H), 7.68–7.65 (m, 1H), 7.60–7.58 (m, 1H), 7.46–7.43 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.4, 133.3, 132.9, 131.8, 131.2, 130.6, 130.4, 129.1, 128.2, 127.1, 124.4, 123.9, 116.9 ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd. for $C_{15}H_{10}ClN_4$: 281.0589, found 281.0588.

4-(2,4-Dimethylphenyl)tetrazolo[1,5-*a*]quinoline (4t): pale yellow solid (45 mg, 33 % yield); m.p. 166.0–168.0 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3073, 1666, 1523, 1501, 1461 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.74 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.88 (t, J = 7.2 Hz, 1H), 7.81 (s, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.21 (s, 1H), 7.15 (d, J = 7.6 Hz, 1H), 2.41 (s, 3H), 2.26 (s, 3H) ppm ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.7, 139.3, 136.5, 132.0, 131.6, 131.1, 130.6, 130.1, 128.8, 128.0, 127.6, 126.9, 124.2, 116.9, 21.2, 20.3 ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd. for $C_{17}H_{15}N_4$: 275.1291, found 275.1293.

4-(Naphthalen-2-yl)tetrazolo[1,5-*a*]quinoline (4u): pale yellow solid (24 mg, 16 % yield); m.p. 183.9–185.9 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3046, 1687, 1523, 1507, 1449 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.80 (d, J = 8.4 Hz, 1H), 8.04–7.91 (m, 5H), 7.79–7.71 (m, 3H), 7.63 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H) ppm ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.2, 134.0, 133.2, 131.8, 131.4, 131.0, 130.3, 129.9, 129.0, 128.7, 128.3, 128.2, 126.7, 126.3, 126.0, 125.3, 125.0, 124.2, 117.0 ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd. for $C_{19}H_{13}N_4$: 297.1135, found 297.1136.

4-(Thiophen-2-yl)tetrazolo[1,5-*a*]quinoline (4v): pale yellow solid (68 mg, 54 % yield); m.p. 179.4–180.5 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3078, 1679, 1599, 1538, 1453 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.52 (d, J = 8.0 Hz, 1H), 8.34 (dd, J = 3.8, 1.0 Hz, 1H), 7.93 (s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.72 (t, J = 8.4 Hz, 1H), 7.60 (t, J = 8.2 Hz, 1H), 7.43 (dd, J = 5.0, 1.0 Hz, 1H), 7.17–7.15 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 146.0, 135.9, 130.3, 129.7, 129.3, 128.6, 128.5, 128.1, 127.4, 126.4, 124.1, 120.3, 116.6 ppm; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd. for $C_{13}H_8N_4SNa$: 275.0362, found 275.0364.

Tetrazolo[1,5-*a*]quinoline (4w):[5a–5b] pale yellow needle (17 mg, 20 % yield); m.p. 147.6–149.9 °C (from CH_2Cl_2/hexanes) (lit.[5a] m.p. 156–157 °C). IR (neat): $\tilde{\nu}$ = 3075, 1697, 1529, 1448 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.68 (d, J = 8.4 Hz, 1H), 7.98–7.94 (m, 2H), 7.89–7.84 (m, 2H), 7.71 (t, J = 7.6 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.4, 133.3, 131.2, 130.8, 128.9, 128.0, 123.8, 116.8, 112.6 ppm. HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd. for $C_9H_6N_4Na$: 193.0485, found 193.0487.

4-Butyltetrazolo[1,5-*a*]quinoline (4x): pale brown solid (60 mg, 53 % yield); m.p. 83.9–85.9 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3058, 2961, 1691, 1614, 1529, 1461 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.57 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.4 Hz, 1H), 7.63 (t, J = 8.0 Hz, 2H), 3.11 (t, J = 7.8 Hz, 2H), 1.89–1.81 (m, 2H), 1.50–1.41 m, 2H), 0.68 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.0, 129.8, 129.6, 129.5, 128.2, 128.1, 127.8, 124.3, 116.5, 31.0, 30.7, 22.4, 13.7 ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd. for $C_{13}H_{14}N_4Na$: 249.1111, found 249.1107.

4-Hexyltetrazolo[1,5-*a*]quinoline (4y): pale yellow solid (97 mg, 76 % yield); m.p. 73.4–75.2 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3098, 2929, 1674, 1610, 1524, 1458 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.54 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.63–7.59 (m, 2H), 3.08 (t, *J* = 7.8 Hz, 1H), 1.88–1.81 (m, 2H), 1.43–1.38 (m, 2H), 1.35–1.25 (m, 4H), 0.86–0.83 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.0, 129.7, 129.5, 129.4, 128.1, 128.0, 127.7, 124.3, 116.4, 31.4, 31.2, 28.9, 28.5, 22.4, 13.9 ppm. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd. for $C_{15}H_{18}N_4Na$: 277.1424, found 277.1422.

4-Isopentyltetrazolo[1,5-*a*]quinoline (4z): pale brown solid (73 mg, 61 % yield); m.p. 60.2–61.4 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3060, 2955, 2865, 1689, 1613, 1534, 1465 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.57 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.74 (t, *J* = 7.8 Hz, 1H), 7.65–7.61 (m, 2H), 3.11 (t, *J* = 8.0 Hz, 2H), 1.78–1.66 (m, 3H), 0.99 (d, *J* = 6.4 Hz, 6H); ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.0, 129.8, 129.6, 129.3, 128.3, 128.2, 127.8, 124.3, 116.5, 37.6, 29.1, 27.8, 22.4 ppm. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd. for $C_{14}H_{16}N_4Na$: 263.1267, found 263.1264.

4-Cyclopropyltetrazolo[1,5-*a*]quinoline (4a′): pale yellow solid (57 mg, 54 % yield); m.p. 129.0–130.9 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3098, 1670, 1525, 1458 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.57 (d, *J* = 8.0 Hz, 1H), 7.82 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.72 (t, *J* = 8.4 Hz, 1H), 7.61 (t, *J* = 8.2 Hz, 1H), 7.44 (s, 1H), 2.55–2.48 (m, 1H), 1.21–1.19 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.9, 130.0, 129.6, 129.2, 128.0, 127.8, 125.9, 124.3, 116.5, 12.4, 8.6 ppm. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd. for $C_{12}H_{10}N_4Na$: 233.0798, found 233.0799.

Synthesis of 3-phenylquinolin-2-amine (5).[12] To a round-bottomed flask filled with 4-phenyltetrazolo[1,5-*a*]quinoline (**4a**) (123 mg, 0.5 mmol) was diluted with DMF (2 mL). To this mixture was added $Cu(OAc)_2{\cdot}H_2O$ (200 mg, 2 equiv.). The reaction mixture was stirred at 130 °C for overnight. The reaction mixture was diluted with H_2O (5 mL) and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), filtered, and concentrated (aspirator). Crude product was purified by column chromatography on silica gel (3:2 v/v, hexanes/ethyl acetate) to yield the corresponding 3-phenylquinolin-2-amine (**5**). Pale yellow solid (56 mg, 51 % yield); m.p. 148.7–150.5 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 3455, 3100, 1430 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.77 (s, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 7.2 Hz, 1H), 7.54–7.47 (m, 4H), 7.44–7.40 (m, 1H), 7.28–7.24 (m, 1H), 5.13 (br s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.2, 147.0, 137.5, 137.3, 129.7, 129.1, 128.9, 128.2, 127.5, 125.4, 125.0, 124.1, 122.8 ppm. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd. for $C_{15}H_{13}N_2$: 221.1073, found 221.1075.

Synthesis of 2-chloro-3-phenylquinoline (6).[8b,8c] To a round-bottomed flask filled with *o*-alkynylisocyanobenzene (**2a**) [freshly prepared from the corresponding *N*-(2-(phenylethynyl)phenyl)formamide (**1a**, 221 mg, 1 mmol)] was diluted with DMF (2 mL). To this mixture was added tetrabutylammonium chloride (556 mg, 2 mmol). The reaction mixture was stirred at room temperature for overnight. After completion, the reaction mixture was diluted with H_2O (5 mL) and the resulting mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), filtered, and concentrated (aspirator). Crude product was purified by column chromatography on silica gel (4:1 v/v, hexanes/ethyl acetate) to yield the corresponding 2-chloro-3-phenylquinoline (**6**). Pale yellow solid (184.6 mg, 77 % yield); m.p. 52.6–54.7 °C (from CH_2Cl_2/hexanes). IR (neat): $\tilde{\nu}$ = 1560, 1396, 1134 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.09 (s, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.54–7.43 (m, 5H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 149.5, 146.8, 138.7, 137.5, 134.7, 130.3, 129.5, 128.2, 127.4, 127.2, 127.1 ppm. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd. for $C_{15}H_{10}ClNNa$: 262.0394, found 262.0396.

General procedure for the synthesis of 4-phenyltetrazolo[1,5-*a*]-quinoline-5-*d* ([d_1]-4a). To the three-neck flask filled with *o*-(phenylethynyl)isocyanobenzene (**2a**), freshly prepared from the corresponding *N*-(2-(phenylethynyl)phenyl)formamide (**1a**, 0.5 mmol), was diluted with dry DMF (2 mL) under argon atmosphere. To this mixture was added sodium azide (0.75 mmol, 1.5 equiv.) and D_2O (0.018 mL, 2 equiv.). The reaction mixture was stirred at room temperature for 2 h. After completion, the reaction mixture was diluted with H_2O (5 mL) and the resulting mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), filtered, and concentrated (aspirator). Crude product was purified by column chromatography on silica gel (hexanes/ethyl acetate) to synthesize the corresponding 4-phenyltetrazolo[1,5-*a*]quinoline-5-*d* (**[d_1]-4a**). The mixture of **([d_1]-4a)** and **4a** (**[d_1]-4a/4a** = 9:1, ^1H NMR analysis)**:** pale yellow solid; IR (neat): $\tilde{\nu}$ = 3055, 1680, 1525, 1455, 1440 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.71 (d, *J* = 8.4 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 2H), 8.07 (s, 0.1H of **4a**), 8.02 (d, *J* = 8.0 Hz, 1H), 7.85 (t, *J* = 7.4 Hz, 1H), 7.72 (t, *J* = 7.4 Hz, 1H), 7.59–7.55 (m, 2H), 7.52–7.48 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 147.3, 133.8, 130.7, 130.0, 129.6, 129.0, 128.9, 128.5, 128.1, 126.5, 124.3, 116.8 ppm.

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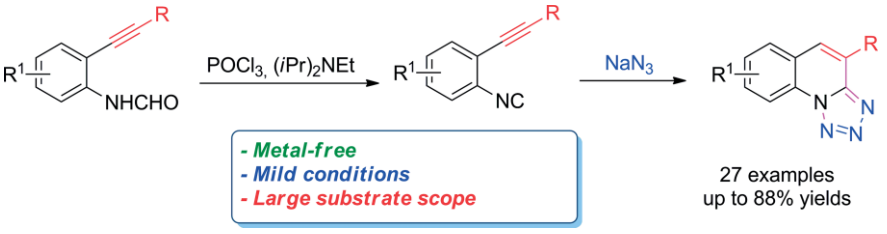
Annulation



An efficient synthesis of tetrazolo[1,5-*a*]-quinolines employing the reaction of *o*-alkynylisocyanobenzenes with sodium azide is described. The reaction proceeds through the nucleophilic addition of the azide to the isocyanide and a subsequent by 6-endo cyclization.

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