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TBAF-Catalyzed Tandem Synthesis of Triazolo[4,5-*c*]quinolines at Ambient Temperature

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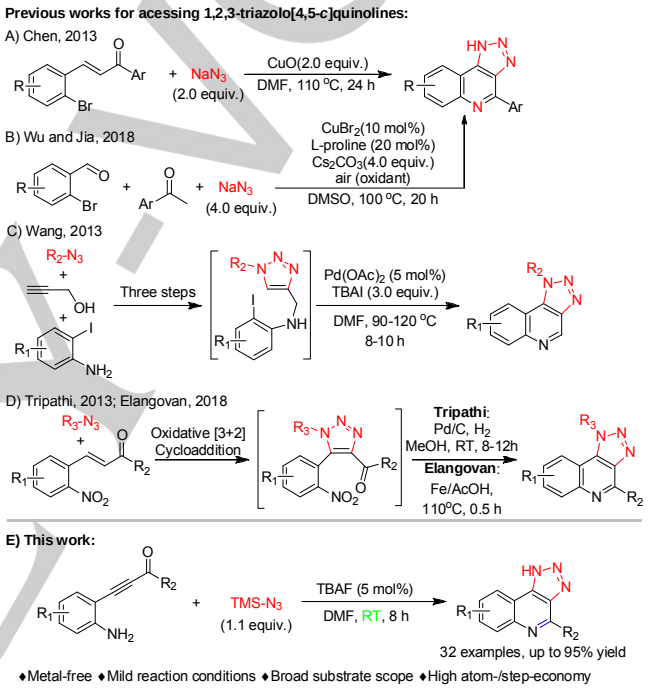
Abstract: A mild, efficient and metal-free synthetic method for 1*H*-[1,2,3]triazolo[4,5-*c*]quinolines has been developed *via* intermolecular [3+2] cycloaddition of β-(2-aminoaryl)-α,β-ynones and TMS-N_3, followed by intramolecular dehydration annulation sequential reactions. With 5 mmol% of TBAF as catalyst, the reaction can smoothly proceed in DMF at ambient temperature to afford a wide range of functionalized 1*H*-[1,2,3]triazolo[4,5-*c*]quinolines in good to excellent yields.

Introduction

Heterocycles play a center role in drug discovery and medicinal chemistry.[1] Notably, about 80% of the currently global best-selling pharmaceuticals are heterocyclic compounds.[2] 1,2,3-Triazolo[4,5-*c*]quinoline is a kind of structurally novel tricyclic fused heterocycle condensed by 1,2,3-triazole and quinoline frameworks. Owing to the great medicinal value of both 1,2,3-triazoles[3] and quinolines,[4] this class of heterocyclic compounds are considered as promising candidates for the generation of new chemical therapeutic agents. Up to date, several related synthetic methods have been reported, which include CuO-promoted tandem S_NAr and cyclization of *(E)*-3-(2-bromoaryl)-1-arylprop-2-en-1-ones and sodium azide (Scheme 1A),[5] CuBr-catalyzed and aerobic oxdative three-component tandem reaction of 2-bromobenzaldehydes, aryl methyl ketones, and sodium azide (Scheme 1B),[6] $Pd(OAc)_2$-catalyzed intramolecular cyclization of 2-iodo-((1*H*-1,2,3-triazol-4-yl)methyl)benzenamines followed by TBAI-mediated oxidation (Scheme 1C),[7] and Pd/C-catalyzed[8] or Fe/AcOH-mediated[9] intramolecular reductive cyclization of 4-benzoyl-5-(2-nitrophenyl)-1,2,3-triazoles (Scheme 1D). These methods made considerable contributions for the access of 1,2,3-triazolo[4,5-*c*]quinolines and their *N*-substituted derivatives, all of them, however, relied on the use of transition metals as catalysts or stoichiometric reductants. The removal of the residual transition metals remaining in the final products as well as the cost would be great challenges if these methods were practically applied in pharmaceuticals production.[10] In addition, these methods were also suffered from some other drawbacks such as harsh reaction conditions, limited functional group tolerance, and poor availability of special prefunctionalizated substrates. Therefore, the development of a new approach for diverse 1,2,3-triazolo[4,5-*c*]quinoline compounds from readily available substrates under mild and metal-free conditions remains highly desirable.

α,β-Ynones are valuable synthons in modern synthetic organic



Scheme 1. Synthetic strategies for 1,2,3-triazolo[4,5-*c*]quinolones.

chemistry and can be conveniently derived from simple materials by a variety of methods.[11] Both the carbonyl group and the polarized alkyne group render this class of compounds highly reactive to undergo 1,4-conjugated addition, cycloaddition, isomerization, carbonyl addition and many other transformations. An early work reported by Marinelli's group attracted our attention.[12] In their extensive study on tandem synthesizing quinoline derivatives from β-(2-aminoaryl)-α,β-ynones,[13] it was found that an *N*-aryl substituted 1,2,3-triazolo[4,5-*c*]quinoline derivative, 4-(naphthalen-2-yl)-3-(4-nitrophenyl)-3*H*-[1,2,3]triazolo [4,5-*c*]quinoline, can be obtained in 63% yield after refluxing 3-(2-aminophenyl)-1-(naphthalen-1-yl)prop-2-yn-1-one and 4-nitrophenylazide in 1,1,2,2-tetrachloroethane for 6 hours. The reaction was assumed to proceed *via* the sequential 1,3-dipolar cycloaddition of ynone and organic azide followed by intramolecular dehydration annulation reactions. Unfortunately, this method was demonstrated only by this special example. Moreover, the reaction was carried out under rather harsh conditions (~150 °C) with unsatisfied yield, most likely due to the low reactivity of organic azides toward ynones. However, this

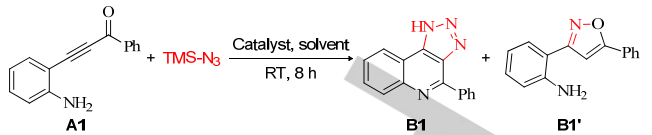
simple protocol inspired us to develop a more promising and general approach for 1,2,3-triazolo[4,5-*c*]quinolines from β-(2-aminoaryl)-α,β-ynones, envisaging that the cycloaddition reaction between ynones and organic azides could be improved by employing an alternative azide reagent. Trimethylsilyl azide (TMS-N_3) is a safe, powerful and commercially available azide reagent widely used in the synthesis of diverse nitrogen-containing molecules.[14] In analogy with organic azides, TMS-N_3 can behave as a 1,3-dipole toward acetylenes, olefins and nitriles to give corresponding triazoles and tetrazoles.[15] Recently, Vaccaro and co-workers reported that such cycloaddition reactions can be promoted by catalysis of tetrabutylammonium fluoride (TBAF).[16] Herein, we presented our findings that a broad range of functionalized 1*H*-[1,2,3]-triazolo[4,5-c]quinolines can be delivered from β-(2-aminoaryl)-α,β-ynones in good to excellent yields at ambient temperature with TMS-N_3 as an azidation source and TBAF as catalyst in DMF (Scheme 1E).

Results and Discussion

We first selected our studies by choosing the reaction of 3-(2-aminophenyl)-1-phenylprop-2-yn-1-one **A1** and TMS-N_3 (1.1 equiv.) as a template reaction to explore the feasibility of the protocol (Table 1). In the initial attempt, the reaction was carried out in THF with 5 mol% TBAF as catalyst. Excitingly, after stirred at room temperature for 8 h, the starting material **A1** was totally consumed and the desired product 4-phenyl-*1H*-[1,2,3]triazolo[4,5-*c*]quinolines (**B1**) was obtained in 54% yields, along with 14% of 2-(5-phenylisoxazol-3-yl)aniline (**B1'**) as the main by-product by HPLC analysis (entry 1, Table 1). Recently, this competitive isoxazoles formation between α,β-ynones and TMS-N_3 *via* tandem hydroazidation/denitrogenation/cyclization reactions has been disclosed by Reddy and co-workers, and its chemo-selectivity was reported to be strongly solvent-dependent.[17] To restrain this competitive side reaction as well as improve the yield of **B1**, a wide range of organic solvents were subsequently screened. The change of THF to either dioxane, toluene, EtOH, CH_3CN, DCM or TCE brought no improvement in the reaction outcome (entries 2-7, Table 1). However, on the other hand, the competitive by-product **B1'** was significantly depressed to less than 5%, and the target product **B1** was obtained in excellent yields when we switched to aprotonic dipolar solvents, such as, DMSO, DMF, DMAc and NMP (entries 8-11, Table 1). In particular, with DMF as reaction medium, the isolated yield of **B1** reached to 90% (entry 9, Table 1). After that, the catalytic activity of other F^- source, such as NH_4F, KF and NaF, on this transformation was tested. Unfortunately, all of them were far inferior to TBAF, which was most likely ascribed to their insolubility in DMF (entries 12-14, Table 1). Further optimization by varying the amount of TBAF catalyst and reaction time did not provide better results (entries 15-18, Table 1). Finally, the optimal reaction conditions for this transformation were obtained as follows: TBAF (5 mmol%) as catalyst in DMF at room temperature for 8 h.

With the optimal conditions in hand, we started to evaluate the substrate scope of this protocol. At first, the reaction scope with respect to substituted phenyl on the carbonyl terminal of ynones was investigated. As the results summarized in Table 2, a variety of *para*-substituted phenyl ynones **A2-A7** either attached

Table 1. Optimizing the reaction conditions[a)]



A1 B1 B1'

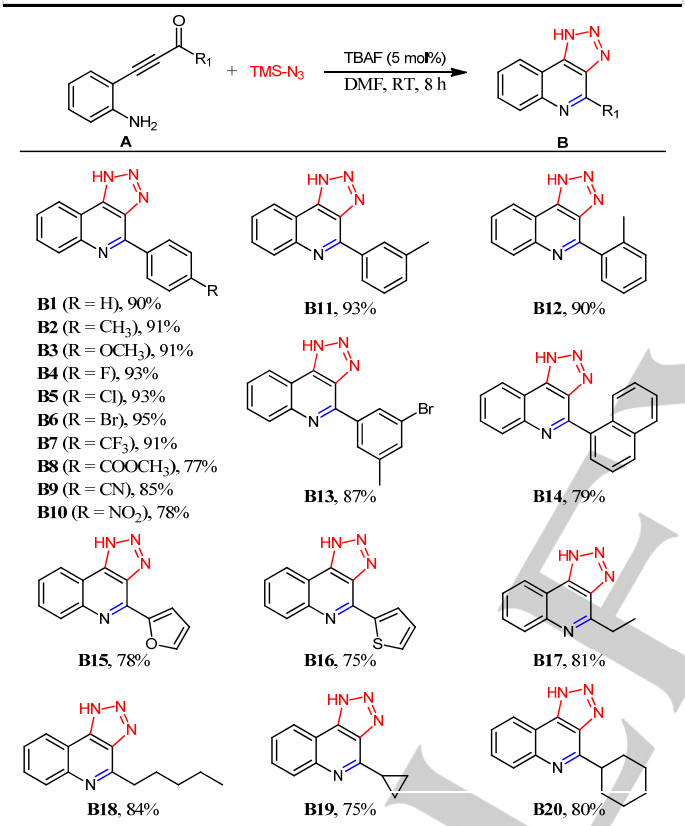
Entry	Solvent	Catalyst (x mol%)	Yields (%)[b]	
			B1	**B1'**
1	THF	TBAF (5)	54	15
2	dioxane	TBAF (5)	52	15
3	toluene	TBAF (5)	20	31
4	EtOH	TBAF (5)	23	12
5	CH_3CN	TBAF (5)	27	42
6	DCE	TBAF (5)	19	44
7	TCE	TBAF (5)	14	74(68)
8	DMSO	TBAF (5)	88	4
9	DMF	TBAF (5)	93(90)	2
10	DMAc	TBAF (5)	91	5
11	NMP	TBAF (5)	92	3
12	DMF	NH_4F (5)	79	5
13	DMF	KF (5)	75	3
14	DMF	NaF (5)	75	2
15	DMF	TBAF (10)	93	2
16	DMF	TBAF (3)	89	2
17	DMF	-	56	4
18[c]	DMF	TBAF (5)	84	2

[a] *Reaction conditions:* 3-(2-aminophenyl)-1-phenylprop-2-yn-1-one 1a (0.5 mmol), TMS-N_3 (0.55 mmol), catalyst (0-10 mol%) and solvent (5 ml) at room temperature (25-30 °C) for 8h. THF = tetrahydrofuran, DCE = dichloroethane, TCE = trichloroethylene, DMF = *N*,*N*-dimethyl formamide, DMAc = *N*,*N*-dimethyl acetamide, NMP = *N*-methyl-2-pyrrolidone. [b] Determined by HPLC analyses, the yields were obtained with a standard curve method and the data in parentheses were isolated yields. [c] Reacted at RT for 6 h.

with electron-donating group (Me and OMe) or moderated electron-withdrawing group (F, Cl, Br and CF_3) exhibited similar reaction activity to the basic substrate **A1** and corresponding products (**B2**-**B7**) were obtained in excellent yields (91-95%) under the identified reaction conditions. Whereas, for the reaction of highly electron-withdrawing group ($COOCH_3$, CN and NO_2) substituted phenyl ynone analogues **A8**-**A10**, a slight lower yields (77-85%) were resulted, which was ascribed to their reduced nucleophilicity of the carbonyl group affecting the efficiency of this transformation (retarding the intramolecular dehydration annulation to form quinoline cycle). Noteworthy, most of these functionalized products can be further derived. It seemed that the position of the substituents attached on the phenyl ring had little influence on the reaction efficiency, since no obvious difference in yield was observed for the reactions of

ortho- and *mata*-methyl substituted phenyl ynones (**A11** and **A12)** with its *para*-substituted analogue (**A2**). Furthermore, ynones possessing multiple-substituted phenyl group (3-bromo-5-methyl phenyl), fused aromatic group (naphthyl) or heteroaryl group (furyl and thienyl) were employed and the desired products **B13**-**B16** were obtained in 87%, 79%, 78% and 75% yields, respectively. In addition to aromatic ynones, alkyl ynones also showed good compatibility with this transformation affording the corresponding 4-alkyl 1*H*-[1,2,3]triazolo[4,5-*c*]quinolines **B17**-**B20** in good to excellent yields (75-84%). It is noteworthy to point out that these type of products cannot be acquired by previous reported methods.

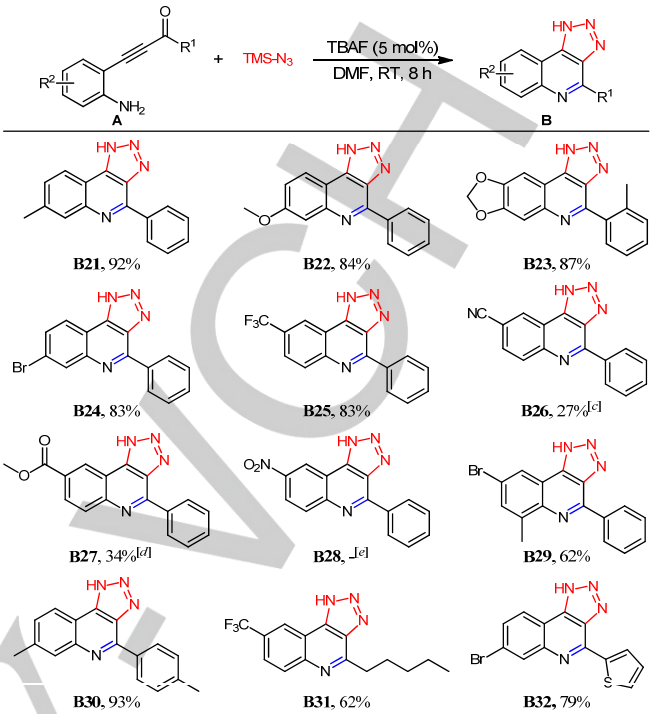
Table 2. Substrate scope of β-(2-aminoaryl)-α,β-ynones with varying substitutions at the carbonyl terminal.[a, b]



[a] *Reaction conditions*: **A** (0.5 mmol), TMS-N_3 (0.55 mmol), TBAF (0.025 mmol) in DMF (5 mL) at room temperature for 8 h. [b] The data in parentheses were isolated yields.

Various substituted 2-aminoaryls at the alkyne terminal of ynones were explored to further extend the substrate scope (Table 3). The substrates attached with either electron-donating group (alkyl and alkoxy) or moderate electron-withdrawing group (Br and CF_3) at 2-aminoaryl were high productive, and delivered the corresponding cyclized products **B21-B25** in good to excellent yields (83-92%) under the identified reaction conditions. However, for the substrates with high electron-withdrawing groups, the reaction tended to form isoxazoles instead of 1*H*-[1,2,3]triazolo[4,5-*c*]quinolines. For instance, when $COOCH_3$- and CN-substituted 2-aminoaryl ynones were subjected to the standard conditions, the expected products **B26** and **B27** were obtained only in 27% and 34% yields, respectively. On the contrary, about 69% of 3-(2-amino-5-cyanophenyl)-5-phenyl

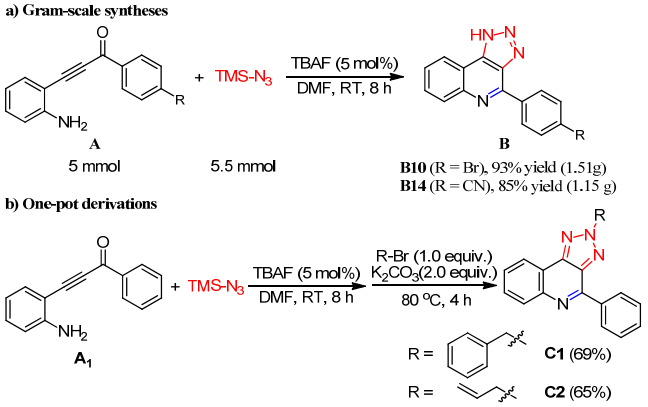
Table 3. Substrate scope of β-(2-aminoaryl)-α,β-ynones with different substituted 2-aminoaryls.[a, b]



[a] *Reaction conditions*: **A** (0.5 mmol), TMS-N_3 (0.55 mmol), TBAF (0.025 mmol) in DMF (5 mL) at room temperature for 8 h. [b] The data in parentheses were isolated yields. [c] 69% of 3-(2-amino-5-cyanophenyl)-5-phenylisoxazole was obtained. [d] 55% of 3-(2-amino-5-methoxycarbonyl-phenyl)-5-phenylisoxazole was obtained. [e] 87% of 3-(2-amino-5-nitrophenyl)-5-phenylisoxazole was obtained.

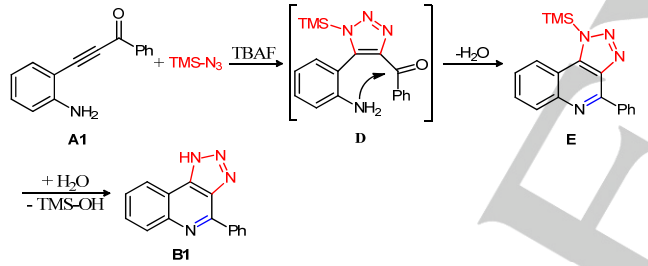
isoxazole (**B26'**) and 55% of 3-(2-amino-5-methoxycarbonyl-phenyl)-5-phenyl isoxazole (**B27'**) were isolated. Furthermore, when NO_2 substituted 2-aminoaryl ynone was employed, the reaction exclusively gave rise to 3-(2-amino-5-nitrophenyl)-5-phenyl isoxazole (**B28'**) up to an 87% isolated yield. Finally, with various alkyne and carbonyl terminal substituted ynones as substrates, we efficiently synthesized a diversity of multi-substituted 1*H*-[1,2,3]Triazolo[4,5-*c*]quinolines **B29-B32**.

To further demonstrate the practicability of the newly developed method, two selected reactions on a gram scale (5 mmol of substrates) were carried out. Delightedly, no obvious change in yields was found, which indicates that this reaction can be scaled up (Scheme 2a). Considering that 1*H*-[1,2,3]triazolo[4,5-*c*]quinolines can undergo nucleophilic substitution reaction with alkyl halides to form *N*2-alkylated derivatives,[18] the one-pot alkylation without the isolation of formed 1*H*-[1,2,3]triazolo[4,5-*c*]quinolines was carried out, too. Firstly, 3-(2-aminophenyl)-1-phenylprop-2-yn-1-one (**A1**) reacted with TMS-N_3 under the previous standard reaction conditions to generate 4-phenyl-1*H*-[1,2,3]triazolo[4,5-*c*]quinoline (**B1**). Then 1.0 equiv. of benzyl bromide and 2.0 equiv. of K_2CO_3 was added. After further heated at 80 °C for 4h, the desired 2-benzyl-4-phenyl-2*H*-[1,2,3]triazolo[4,5-*c*]quinoline (**C1**) was isolated in 69% total yield in this one-pot procedure (Scheme 2b). Similarly, with allyl bromide as an alkylating agent, 2-allyl-4-phenyl-2*H*-[1,2,3]triazolo[4,5-*c*]quinoline (**C2**) was obtained in 65% total yield (Scheme 2b).



Scheme 2. Gram-scale reactions and one-pot derivation to synthesize *N*2-alkyl substituted 1,2,3-triazolo[4,5-*c*]quinolines

On the basis of the reported works[16b, 19] and our experimental results, a plausible mechanism is proposed in Scheme 3. Initially, under the catalysis of TBAF, ynone **A1** and TMS-N_3 proceeded [3+2] cycloaddition to form triazole **D**, followed by subsequent intermolecular dehydration annulation to afford the correponding *N*-TMS substituted triazole-quinoline **E**. The *N-Si* bond of **E** was instable and tended to occur protonation with the *in-situ* releasing H_2O molecule, and finally furnished the target product **B1**.



Scheme 3. Plausible reaction mechanism

Conclusion

In conclusion, we demonstrated an effcient and promising protocol for the tandem synthesis of 1*H*-[1,2,3]triazolo[4,5-*c*]quinolines from β-(2-aminoaryl)-α,β-ynones and TMS-N_3. With TBAF as catalyst and DMF as reaction medium, the reaction smoothly proceeded with high selectivity under ambient conditions. Salient features of this protocol included metal-free, mild reaction conditions, broad substrate scope, and high atom-/step-economy, which made it a more practical alternative to the existing methods. Moreover, this protocol also enabled further derivation for *N*2-substituted 1,2,3-triazolo[4,5-*c*]quinolines in one-pot. Further studies related to biological activity of the synthesized 1,2,3-triazolo[4,5-*c*]quinoline derivatives are in progress in our laboratory.

Experimental Section

General Information: All chemicals and organic solvents were commercially available and directly used without further purification. All proton and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AVANCE III 500 MHz or a Bruker Magnet System 400/600 MHz spectrometer in deuterated solvents with tetramethylsilane (TMS) as internal standard. High resolution mass spectra were recorded in the EI mode on Waters GCT Premier TOF mass spectrometer with an Agilent 6890 gas chromatography using a DB-XLB column (30 m x 0.25 mm (i.d.), 0.25 μ) or ESI mode on an Agilent 6210 LC/TOF mass spectrometer. Melting points (uncorrected) were determined on a BUCHI M-565 apparatus. High performance liquid chromatography (HPLC) analyses were performed on Shimadzu LC-20ADXR using a Insertsil ODS-3 column (4.6 mm x 250 mm x 5 μm). Flash column chromatography was performed on silica gel (200-300 mesh) with petroleum ether/ethyl acetate as eluents.

General procedure for the synthesis of *1H*-[1,2,3]triazolo[4,5-*c*]quinolones: To a 15 mL of Young tube were added β-(2-aminoaryl)-α,β-ynones **A** (0.5 mmol), TMS-N_3 (0.55 mmol), TBAF (0.025 mmol, 1mol/L in THF) and DMF (5 mL). The resulting mixture was stirred at room temperature (25-30 °C) for 8 h. Upon completion, the crude reaction mixture was poured into saturated brine (10.0 mL) and extracted with ethyl acetate (3 × 5 mL). The extractions were combined, dried over anhydrous Na_2SO_4, filtrated and removed the solvent under reduced pressure. The residual was purified by flash chromatography on silica to afford the desired products.

4-Phenyl-1H-[1,2,3]triazolo[4,5-c]quinoline B1 (CAS No.: 1537188-84-3): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 90% yield (110 mg); white solid; m.p. 216.2 °C (lit.[6] m.p.: 219-221 °C); ^1H NMR (DMSO-d_6, 500 MHz): δ = 16.97 (br, 1H), 8.86 (s, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 7.90-7.85 (m, 1H), 7.82-7.77 (m, 1H), 7.68-7.63 (m, 2H), 7.63-7.59 (m, 1H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 149.5, 144.1, 136.5, 130.5, 129.8, 129.7, 129.3, 128.6, 127.4, 122.7, 115.3. IR (KBr): ν = 3460.1, 3064.3, 2794.5, 2688.3, 1576.8, 1519.6, 1458.3, 1417.5, 1327.6, 1241.8, 1135.5, 972.1, 955.7, 763.7, 698.3 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{15}H_{11}N_4$ $[M+H]^+$, 247.0978, found 247.0989.

4-(p-Tolyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B2 (CAS No.: 1537188-85-4): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 91% yield (118 mg); yellowish solid; m.p. 218.1 °C (lit.[6] m.p.: 210-212 °C); ^1H NMR (DMSO-d_6, 500 MHz): δ = 16.93 (br, 1H), 8.79 (s, 2H), 8.41 (d, *J* = 8.1 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.88-7.83 (m, 1H), 7.79-7.74 (m, 1H), 7.45 (d, *J* = 8.1 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 149. 4, 144.1, 140.3, 133.8, 129.8, 129.6, 129.2, 129.2, 127.2, 122.7, 115.2, 21.1. IR (KBr): ν = 3442.1, 3084.7, 2917.4, 2651.5, 1634.1, 1609.5, 1527.8, 1511.5, 1356.2, 1209.1, 1180.5, 984.3, 829.0, 763.7 730.9 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{13}N_4$ $[M+H]^+$, 261.1140, found 261.1161.

4-(4-Methoxyphenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B3 (CAS No.: 1417697-01-8): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 91% yield (126 mg); white solid; m.p. 208.7 °C (lit.[5] m.p.: 206-208 °C); ^1H NMR (DMSO-d_6, 500 MHz): δ = 16.84 (br, 1H), 8.87 (d, *J* = 8.3 Hz, 2H), 8.38 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 7.86-7.78 (m, 1H), 7.76-7.68 (m, 1H), 7.19 (d, *J* = 9.0 Hz, 2H), 3.88 (s, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 161.3, 149.1, 144.2, 137.1, 131.3, 130.9, 129.7, 129.5, 129.0, 126.9, 122.7, 114.0, 113.8, 55.3. IR (KBr): ν = 3389.0, 3082.6, 2920.2, 2759.6, 1637.6, 1601.4, 1503.3, 1458.1, 1362.0, 1254.0, 1173.9, 1030.8, 983.7, 835.9, 765.4 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{13}N_4O$ $[M+H]^+$, 277.1089, found 277.1105.

4-(4-Fluorophenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B4 (CAS No.: 1537188-87-6): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 93% yield (123 mg); white solid; m.p. 246.9 °C (lit.[6] m.p.: 234-236 °C); ^1H NMR (DMSO-d_6, 500 MHz): δ = 16.97 (br, 1H), 8.95 (s, 2H), 8.42 (d, *J* = 7.9 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.90-

7.85 (m, 1H), 7.82-7.76 (m, 1H), 7.52-7.45 (m, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 163.6 (d, J = 247.7 Hz, $^{1}J_{CF}$), 148.3, 144.0, 137.4, 132.9 (d, J = 2.4 Hz, $^{4}J_{CF}$), 131.5 (d, J = 8.8 Hz, $^{3}J_{CF}$), 129.8, 129.7, 127.4, 122.7, 115.6 (d, J = 21.5 Hz, $^{2}J_{CF}$). IR (KBr): ν = 3482.0, 3044.8, 2936.7, 2827.4, 1638.1, 1603.1, 1503.3, 1356.3, 1233.6, 1158.8, 1085.1, 996.7, 842.4, 764.6, 664.4 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{15}H_{10}N_4F$ $[M+H]^+$, 265.0889, found 265.0903.

4-(4-Chlorophenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B5 (CAS No.: 1537188-88-7): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 93% yield (131 mg); white solid; m.p. 251.9 °C (lit.[6] m.p.: 252-254 °C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.90 (br, 1H), 8.85 (d, J = 8.4 Hz, 2H), 8.35 (d, J = 7.9 Hz, 1H), 8.18 (d, J = 8.3 Hz, 1H), 7.84-7.79 (m, 1H), 7.77-7.72 (m, 1H), 7.66 (d, J = 8.7 Hz, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 148.0, 143.9, 135.4, 135.2, 130.8, 129.8, 129.7, 128.7, 127.6, 122.7, 115.3. IR (KBr): ν = 3444.2, 3135.1, 2932.5, 2870.6, 1646.3, 1593.5, 1491.8, 1460.7, 1354.9, 1236.7, 1090.0, 997.0, 837.1, 760.9 664.0 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{15}H_{10}ClN_4$ $[M+H]^+$, 281.0589, found 281.0596.

4-(4-Bromophenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B6 (CAS No.: 1537188-89-8): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 95% yield (155 mg); white Solid; m.p. 252.4 °C (lit.[6] m.p.: 247-249 °C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 17.00 (br, 1H), 8.84 (d, J = 5.5 Hz, 2H), 8.43 (d, J = 8.1 Hz, 1H), 8.26 (d, J = 8.1 Hz, 1H), 7.91-7.85 (m, 3H), 7.84-7.78 (m, 1H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 148.2, 144.0, 135.5, 131.7, 131.1, 129.9, 129.8, 127.7, 124.4, 122.8, 115.5. IR (KBr): ν = 3372.9, 3091.2, 2920.1, 2855.6, 2663.1, 1638.1, 1585.0, 1486.9, 1421.9, 1356.0, 1209.0, 1070.2, 984.3, 834.3, 761.6 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{15}H_{10}BrN_4$ $[M+H]^+$, 325.0083, found 325.0094.

4-(4-(Trifluoromethyl)phenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B7: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 91% yield (143 mg); yellowish solid; m.p. 224.2 °C; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 17.05 (br, 1H), 9.06 (d, J = 6.8 Hz, 2H), 8.45 (d, J = 7.6 Hz, 1H), 8.30 (d, J = 8.1 Hz, 1H), 8.03 (d, J = 8.3 Hz, 1H), 7.93-7.88 (m, 1H), 7.86-7.82 (m, 1H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 147.7, 143.9, 140.1, 137.2, 130.2 (q, J = 31.9 Hz, $^{2}J_{CF}$), 129.9, 129.9, 129.8, 128.0, 125.5 (q, J = 3.8 Hz, $^{3}J_{CF}$), 124.2 (q, J = 272.3 Hz, $^{1}J_{CF}$), 122.7. IR (KBr): ν = 3374.8, 3088.7, 2766.0, 2659.7, 1634.1, 1564.6, 1523.7, 1425.7, 1319.4, 1164.1, 1127.4, 1057.9, 980.3, 853.6, 767.8 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{10}F_3N_4$ $[M+H]^+$, 315.0852, found 315.0864.

4-(4-Methoxycarbonylphenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B8: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:2); 77% yield (117 mg); yellowish solid; m.p. 249.7 °C; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.97 (br, 1H), 8.95 (d, J = 6.8 Hz, 2H), 8.40 (d, J = 6.3 Hz, 1H), 8.24 (d, J = 7.4 Hz, 1H), 8.20-8.14 (m, 2H), 7.89-7.83 (m, 1H), 7.82-7.76 (m, 1H), 3.91 (s, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 166.0 148.1, 144.0, 140.6, 137.2, 130.9, 129.9, 129.9, 129.4, 127.9, 122.8, 115.5, 52.3. IR (KBr): ν = 3203.5, 3020.7, 2953.6, 2845.3, 1687.2, 1607.8, 1491.1, 1442.0, 1323.5, 1286.7, 1200.3, 1114.1, 948.3, 775.2, 726.9 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{17}H_{13}N_4O_2$ $[M+H]^+$, 305.1033, found 305.1040.

4-(4-Cyanophenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B9: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:2); 85% yield (115 mg); white solid; m.p. 263.5 °C; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.79 (br, 1H), 8.93 (d, J = 8.4 Hz, 2H), 8.34 (d, J = 8.0 Hz, 1H), 8.17 (d, J = 8.6 Hz, 1H), 8.02 (d, J = 8.5 Hz, 2H), 7.85-7.80 (m, 1H), 7.79-7.73 (m, 1H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 147.2, 143.8, 140.3, 137.1, 132.5, 129.9, 129.6, 128.1, 122.7, 118.7, 115.4, 112.6. IR (KBr): ν = 3480.2, 3198.9, 2922.8, 2864.3, 2185.6, 1617.8, 1563.9, 1492.1, 1322.1, 1286.7, 1202.7, 1161.8, 1008.3, 852.2, 749.8 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{10}N_5$ $[M+H]^+$, 272.0936, found 272.0951.

4-(4-Nitrophenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B10 (CAS No.: 1537188-91-2): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:2); 78% yield (113 mg); white solid; m.p. 263.5 °C (lit.[5] m.p.: 256-258 °C); ^{1}H NMR (DMSO-d_6, 600 MHz): δ = 9.10 (s, 2H), 8.47 (d, J = 8.2Hz, 2H), 8.43 (d, J = 7.8Hz, 1H), 8.28 (d, J = 8.7Hz, 1H), 7.93-7.81 (m, 2H). ^{13}C NMR (DMSO-d_6, 150 MHz): δ = 148.2, 146.7, 143.7, 142.0, 137.1, 130.1, 129.9, 128.2, 123.6, 122.7, 115.5. IR (KBr): ν = 3386.5, 3088.8, 2924.8, 2840.5, 1640.3, 1607.1, 1571.9, 1500.5, 1452.7, 1339.0, 1294.9, 1099.1, 914.3, 831.2, 693.9 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_9N_5O_2$ $[M+H]^+$, 292.0756, found 292.0760.

4-(3-Methylphenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B11: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 93% yield (121 mg); orange solid; m.p. 197.6 °C; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.02 (br, 1H), 8.65 (s, 2H), 8.42 (d, J = 8.1 Hz, 1H), 8.25 (d, J = 8.2 Hz, 1H), 7.89-7.83 (m, 1H), 7.80-7.75 (m, 1H), 7.55-7.50 m, 1H), 7.41 (d, J = 7.4 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 149.5, 144.1, 137.7, 136.5, 131.1, 129.7, 129.7, 129.6, 128.5, 127.3, 126.6, 122.7, 21.2. IR (KBr): ν = 3510.0, 3150.1, 2937.6, 2864.0, 1630.0, 1585.0, 1515.6, 1446.1, 1343.9, 1209.1, 1074.2, 984.3, 771.9, 735.1, 694.2 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{13}N_4$ $[M+H]^+$, 261.1140, found 261.1160.

4-(2-Methylphenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B12: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 90% yield (117 mg); white solid; m.p. 225.4 °C; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.68 (br, 1H), 8.45 (d, J = 7.8 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.86-7.81 (m, 1H), 7.80-7.75 (m, 1H), 7.70 (d, J = 7.4 Hz, 1H), 7.47-7.36 (m, 3H), 2.34 (s, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 152.9, 144.1, 136.6, 136.6, 130.7, 130.5, 129.6, 129.2, 127.6, 125.6, 122.7, 115.3, 20.2. IR (KBr): ν = 3248.1, 2921.2, 2627.0, 2553.5, 2492.2, 1642.2, 1564.6, 1523.7, 1462.4, 1360.3, 1230.0, 1200.9, 976.2, 767.7, 730.9 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{13}N_4$ $[M+H]^+$, 261.1135, found 261.1145.

4-(3-Bromo-5-methylphenyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B13: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 87% yield (148 mg); white solid; m.p. 281.0 °C; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.91 (br, 1H), 8.81 (s, 1H), 8.64 (s, 1H), 8.38 (d, J = 7.8 Hz, 1H), 8.23 (d, J = 8.2 Hz, 1H), 7.87-7.83 (m, 1H), 7.79-7.76 (m, 1H), 7.60 (s, 1H) , 2.47 (s, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 147.6, 143.8, 140.6, 138.5, 133.5, 129.9, 129.8, 128.8, 128.6, 127.7, 122.7, 121.7, 20.9. IR (KBr): ν = 3442.1, 3052.8, 2923.7, 2550.3, 1637.2, 1590.8, 1498.6, 1454.5, 1296.0, 1216.2, 1171.2, 1096.1, 959.9, 775.9, 747.4 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{12}N_4Br$ $[M+H]^+$, 339.0245, found 339.0256.

4-(Naphthalen-1-yl)-1H-[1,2,3]triazolo[4,5-c]quinoline B14 (CAS No.: 2251704-60-4): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 79% yield (117 mg); orange solid; m.p. 227.2 °C (lit.[6] mp: 235-237 °C); ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.93 (br, 1H), 8.51 (s, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.2 Hz, 2H), 8.01 (d, J = 7.3 Hz, 1H), 7.92-7.82 (m, 2H), 7.76-7.71 (m, 1H), 7.60-7.56 (m, 1H), 7.51-7.45 (m, 1H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 144.2, 134.1, 133.5, 132.9, 131.0, 130.7, 129.7, 128.6, 128.3, 127.7, 127.5, 126.6, 126.2, 126.1, 125.7, 125.5, 125.2, 124.9, 122.9. IR (KBr): ν = 3446.5, 3102.7, 2973.4, 2755.3, 1627.4, 1600.2, 1595.1, 1510.0, 1458.5, 1394.4, 1259.1, 1164.3, 957.7, 779.0, 732.2 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{19}H_{13}N_4$ $[M+H]^+$, 297.1135, found 297.1138.

4-(Furan-2-yl)-1H-[1,2,3]triazolo[4,5-c]quinoline B15: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 78% yield (92 mg); brown solid; m.p. 281.9 °C; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.94 (br, 1H), 8.38 (s, 1H), 8.19 (d, J = 8.3 Hz, 1H), 8.09 (s, 1H), 8.05 (s, 1H), 7.87-7.81 (m, 1H), 7.78-7.72 (m, 1H), 6.88-6.83 (m, 1H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 150.0, 146.0, 144.2, 129.9, 129.4, 127.3, 122.7, 112.7. IR (KBr): ν = 3395.4, 3150.1, 2924.1, 2856.5, 1608.3, 1556.9, 1445.9, 1389.9, 1255.0, 1156.8, 1040.0, 1004.1, 916.8, 844.9,

741.1 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{13}H_9N_4O$ $[M+H]^+$, 236.0698, found 236.0705.

4-(Thiophen-2-yl)-1H-[1,2,3]triazolo[4,5-c]quinoline B16 (CAS No.: 2251704-61-5): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 75% yield (95 mg); yellowish solid; m.p. 285.3 °C (lit.[6] m.p.: 279-281 °C); ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.92 (br, 1H), 8.82 (d, *J* = 2.42 Hz, 1H), 8.34 (d, *J* = 7.8 Hz, 1H), 8.11 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 5.0 Hz, 1H), 7.82-7.77 (m, 1H), 7.73-7.68 (m, 1H), 7.38-7.33 (m, 1H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 145.1, 144.1, 141.5, 135.9, 131.5, 130.8, 129. 9, 129.1, 128.8, 127.1, 122.8, 115.2. IR (KBr): ν = 3472.9, 3080.7, 2958.0, 2786.4, 1625.9, 1580.9, 1564.6, 1531.9, 1450.2, 1360.3, 1205.0, 1045.6, 976.2, 759.6, 714.6 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{13}H_9N_4S$ $[M+H]^+$, 253.0542, found 253.0543.

4-Ethyl-1H-[1,2,3]triazolo[4,5-c]quinoline B17: Flash column chromatography eluent (petroleum ether/ethyl acetate = 10:1); 81% yield (80 mg); light yellowish solid; m.p. 236.5 °C; ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.70 (br, 1H), 8.37 (d, *J* = 7.9 Hz, 1H), 8.12 (d, *J* = 8.3 Hz, 1H), 7.882-7.77 (m, 1H), 7.75-7.70 (m, 1H), 3.34 (q, *J* = 7.6 Hz, 4H), 1.46 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 156.3, 143.9, 136.6, 129.1, 128.9, 126.8, 122.6, 115.7, 27.7, 12.2. IR (KBr): ν = 3435.2, 3088.0, 2974.3, 2796.2, 1639.2, 1605.5, 1529.2, 1421.6, 1368.4, 1205.1, 1074.2, 1017.6, 988.4, 861.8, 763.7 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{11}H_{11}N_4$ $[M+H]^+$, 199.0978, found 199.0983.

4-Pentyl-1H-[1,2,3]triazolo[4,5-c]quinoline B18: Flash column chromatography eluent (petroleum ether/ethyl acetate = 10:1); 84% yield (101 mg); yellowish solid; m.p. 181.4 °C; ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.57 (br, 1H), 8.35 (d, *J* = 7.7 Hz, 1H), 8.09 (d, *J* = 7.9 Hz, 1H), 7.78-7.72 (m, 1H), 7.71-7.65 (m, 1H), 3.27 (t, *J* = 7.7 Hz, 2H), 1.87-1.94 (m, 2H), 1.26-1.38 (m, 4H), 0.82 (t, *J* = 6.97 Hz, 3H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 155.7, 143.9, 136.9, 129.1, 128.9, 126.7, 122.6, 115.7, 34.4, 31.2, 27.5, 21.9, 13.8. IR (KBr): ν = 3450.5, 3020.5, 2953.8, 2854.8, 1661.8, 1593.2, 1552.4, 1502.1, 1464.5, 1433.2, 1356.9, 1185.2, 755.5, 708.7, 624.5 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{14}H_{17}N_4$ $[M+H]^+$, 240.1375, found 240.1382.

4-Cyclopropyl-1H-[1,2,3]triazolo[4,5-c]quinoline B19: Flash column chromatography eluent (petroleum ether/ethyl acetate = 10:1); 75% yield (79 mg); yellowish solid; m.p. 180.9 °C; ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.69 (br, 1H), 8.31 (d, *J* = 7.9 Hz, 1H), 7.98 (d, *J* = 8.7 Hz, 1H), 7.75-7.69 (m, 1H), 7.67-7.60 (m, 1H), 2.95-2.87 (m, 1H), 1.41 (s, 2H), 1.26-1.91 (m, 2H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 157.0, 144.1, 129.3, 128.6, 126.2, 122.7, 115.1, 99.6, 14.3, 10.8. IR (KBr): ν = 3567.1, 3002.1, 2655.4, 1661.6, 1615.8, 1589.3, 1468.1, 1423.0, 1346.7, 1170.0, 1074.1, 987.1, 919.9, 766.8, 707.9 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{12}H_{11}N_4$ $[M+H]^+$, 211.0984, found 211.1004.

4-Cyclohexyl-1H-[1,2,3]triazolo[4,5-c]quinoline B20: Flash column chromatography eluent (petroleum ether/ethyl acetate = 10:1); 80% yield (101 mg); yellowish solid; m.p. 207.3 °C; ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.46 (br, 1H), 8.35 (d, *J* = 7.8 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.77-7.71 (m, 1H), 7.70-7.64 (m, 1H), 3.50 (t, *J* = 11.3 Hz, 1H), 2.02 (t, *J* = 11.1 Hz, 2H), 1.80-1.92 (m, 4H), 1.73 (d, *J* = 12.5 Hz, 1H), 1.40-1.52 (m, 2H), 1.25-1.36 (m, 1H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 159.1, 143.9, 129.1, 128.8, 128.1, 126.7, 125.2, 122.5, 115.6, 43.1, 31.0, 25.9, 25.7. IR (KBr): ν = 3480.0, 2925.3, 2851.8, 1658.6, 1585.0, 1507.4, 1458.3, 1421.6, 1356.2, 1188.6, 1002.2, 980.3, 755.5, 686.0, 637.0 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{15}H_{17}N_4$ $[M+H]^+$, 254.1453, found 253.1455.

7-Methyl-4-phenyl-1H-[1,2,3]triazolo[4,5-c]quinoline B21 (CAS No.: 2251704-64-8): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 92% yield (120 mg); white solid; m.p. 253.6 °C (lit.[6] m.p.: 245-247 °C); ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.77 (br, 1H), 8.82 (d, *J* = 5.6 Hz, 2H), 8.21 (d, *J* = 8.2 Hz, 1H), 7.97 (s, 1H), 7.65-7.60 (m, 2H), 7.60-7.55 (m, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 2.52 (s, 3H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 149.3, 144.3, 139.6, 137.3, 136.6, 134.2, 130.4, 129.2, 129.1, 129.0, 128.5, 122.3, 112.2, 21.3. IR (KBr): ν = 3476.5, 3019.3, 2868.1, 2823.2, 1638.1, 1560.5, 1519.6, 1486.9, 1458.3, 1343.9, 1254.0, 1090.6, 996.6, 771.8, 686.0 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{13}N_4$ $[M+H]^+$, 261.1135, found 261.1142.

7-Methoxy-4-phenyl-1H-[1,2,3]triazolo[4,5-c]quinoline B22: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 84% yield (116 mg); yellowish solid; m.p. 254.9 °C; ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.75 (br, 1H), 8.87 (d, *J* = 2.9 Hz, 2H), 8.27 (d, *J* = 8.6 Hz, 1H), 7.67 (d, *J* = 2.5 Hz 1H), 7.66-7.62 (m, 2H), 7.61-7.57 (m, 1H), 7.40 (d, *J* = 8.8 Hz, 1H), 3.96 (s, 3H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 160.5, 149.0, 146.0, 136.9, 136.6, 136.3, 130.4, 129.3, 128.6, 123.8, 118.4, 109.8, 55.5. IR (KBr): ν = 3466.5, 3019.5, 2827.2, 1638.1, 1597.3, 1487.0, 1458.3, 1343.9, 1262.2, 1196.8, 1155.9, 1082.4, 996.6, 845.4, 720.8 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{13}N_4O$ $[M+H]^+$, 277.1089, found 277.1091.

4-Phenyl-1H-[1,3]dioxolo[4,5-g][1,2,3]triazolo[4,5-c]quinoline B23 (CAS No.: 2251704-67-1): Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 87% yield (126 mg); yellowish solid; m.p. 268.8 °C (lit.[6] m.p.: 267-269 °C); ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.63 (br, 1H), 8.79 (s, 2H), 7.70 (s,1H), 7.64-7.60 (m, 3H), 7.58-7.54 (m, 1H), 6.26 (s, 2H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 150.1, 147.8, 146.7, 141.4, 136.6, 135.8, 130.1, 128.9, 128.6, 107.2, 102.4, 99.2. IR (KBr): ν = 3450.2, 3035.6, 2868.1, 2827.2, 2670.1, 1646.3, 1495.1, 1462.4, 1348.0, 1262.2, 1033.4, 984.3, 939.4, 861.7, 720.4 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{11}N_4O_2$ $[M+H]^+$, 291.0882, found 291.0887.

7-Bromo-4-phenyl-1H-[1,2,3]triazolo[4,5-c]quinoline B24: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 83% yield (135 mg); yellowish solid; m.p. 279.2 °C; ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.93 (br, 1H), 8.77 (s, 1H), 8.33 (d, *J* = 1.9 Hz, 1H), 8.25 (d, *J* = 8.6 Hz, 1H), 7.87 (d, *J* = 8.7 Hz, 1H), 7.65-7.60 (m, 3H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 150.6, 144.8, 136.0, 132.8, 131.6, 130.8, 130.2, 129.4, 129.2, 128.6, 128.5, 124.5, 122.6. IR (KBr): ν = 3442.5, 3007.0, 2925.3, 2810.9, 1634.1, 1552.3, 1507.4, 1486.9, 1343.9, 1241.8, 1086.5, 992.5, 869.9, 763.7, 681.9 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{15}H_{10}N_4Br$ $[M+H]^+$, 325.0089, found 325.0090.

4-Phenyl-8-(trifluoromethyl)-1H-[1,2,3]triazolo[4,5-c]quinoline B25: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 83% yield (130 mg); white solid; m.p. 275.2 °C; ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.95 (br, 1H), 8.79 (s, 2H), 8.69 (s, 1H), 8.29 (d, *J* = 8.8 Hz, 1H), 8.02 (d, *J* = 8.8 Hz, 1 H), 7.65-7.59 (m, 3H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 151.6, 145.3, 137.3, 135.8, 131.0, 130.8, 129.5, 128.5, 126.7 (q, *J* = 32.5 Hz, $^2J_{CF}$), 125.1 (q, *J* = 3.1 Hz, $^3J_{CF}$), 124.5 (q, *J* = 271.7 Hz, $^1J_{CF}$), 120.5, 120.4, 114.8. IR (KBr): ν = 3446.5, 3072.4, 2757.8, 2688.3, 1618.1, 1593.2, 1450.2, 1331.7, 1294.9, 1160.1, 1127.4, 1061.9, 980.3, 837.2, 767.7 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{10}N_4F_3$ $[M+H]^+$, 315.0858, found 315.0868.

4-Phenyl-8-cyano-1H-[1,2,3]triazolo[4,5-c]quinoline B26: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 27% yield (37 mg); yellowish solid; m.p. 276.3 °C; ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 17.05 (br, 1H), 8.82-8.77 (m, 2H), 8.75 (d, *J* = 1.6 Hz, 1H), 8.26 (d, *J* = 8.8 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.66-7.62 (m, 3H). ^{13}C NMR (DMSO-*d*$_6$, 125 MHz): δ = 152.3, 145.4, 137.3, 135.8, 131.3, 131.2, 130.8, 129.6, 128.7, 128.4, 118.5, 115.7, 109.1. IR (KBr): ν = 3447.8, 3064.4, 2937.2, 2870.3, 2223.4, 1640.7, 1604.5, 1499.6, 1324.7, 1230.9, 1169.2, 1025.2, 913.6, 829.8, 693.8 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{10}N_5$ $[M+H]^+$, 272.0936, found 272.0939.

4-Phenyl-8-methoxycarbonyl-1H-[1,2,3]triazolo[4,5-c]quinoline B27: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 34% yield (52 mg); brown solid; m.p. 278.5 °C; ^{1}H NMR (DMSO-*d*$_6$, 500 MHz): δ = 16.97 (br, 1H), 8.97 (d, *J* = 7.1 Hz, 1H), 8.83 (s, 2H), 8.21

(d, *J* = 6.2 Hz, 2H), 7.69-7.60 (m, 1H), 3.94 (s, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 165.6, 151.6, 146.2, 141.5, 136.0, 131.0, 130.0, 129.5, 129.0, 128.7, 127.5, 125.0, 52.5. IR (KBr): ν = 3476.2, 3141.9, 3060.2, 3027.5, 1687.2, 1642.2, 1515.6, 1446.1, 1352.1, 1290.8, 1192.7, 1025.2, 988.4, 718.7, 686.0 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{17}H_{13}N_4O_2$ $[M+H]^+$, 305.1039, found 305.1044.

8-Bromo-6-methyl-4-phenyl-1H-[1,2,3]triazolo[4,5-c]quinolone B29: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 62% yield (105 mg); yellowish solid; m.p. 275.9 ºC; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.75 (br, 1H), 8.81 (d, *J* = 4.9 Hz, 2H), 8.29 (s, 1H), 8.74 (s, 1H), 7.64-7.57 (m, 3H), 2.75 (s, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 148.1, 141.2, 140.3, 136.5, 132.5, 130.6, 129.2, 128.6, 122.6, 119.7, 116.1, 18.0. IR (KBr): ν = 3433.5, 3064.6, 2917.0, 2847.9, 1631.8, 1573.8, 1516.0, 1491.5, 1350.2, 1184.4, 1076.2, 967.5, 862.9, 770.7, 687.9 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{16}H_{12}N_4Br$ $[M+H]^+$, 339.0245, found 339.0250.

7-Methyl-4-(4-methylphenyl)-1H-[1,2,3]triazolo[4,5-c]quinolone B30: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 93% yield (128 mg); white solid; m.p. 225.3 ºC; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.77 (br, 1H), 8.75 (d, *J* = 6.6 Hz, 2H), 8.24 (d, *J* = 8.4 Hz, 1H), 7.99 (s, 1H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 2.54 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 149.3, 144.3, 140.2, 139.5, 137.1, 133.9, 129.2, 129.1, 129.0, 128.8, 122.3, 21.3, 21.0. IR (KBr): ν = 3468.8, 3145.9, 3019.3, 2835.4, 1642.2, 1605.3, 1503.3, 1458.3, 1348.1, 1213.2, 1180.5, 1090.5, 996.6, 820.9, 792.3 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{17}H_{15}N_4$ $[M+H]^+$, 275.1297, found 275.1313.

4-Pentyl-8-(trifluoromethyl)-1H-[1,2,3]triazolo[4,5-c]quinolone B31: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 62% yield (96 mg); white solid; m.p. 236.1 ºC; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.69 (br, 1H), 8.66 (s, 1H), 8.20 (d, *J* = 8.9 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 3.25 (t, *J* = 7.6 Hz, 2H), 1.94-1.84 (m, 2H), 1.39-1.27 (m, 4H), 0.83 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 158.6, 145.4, 136.6, 130.3, 126.5 (q, *J* = 32.29 Hz, $^2J_{CF}$), 124.8 (q, *J* = 2.81 Hz, $^3J_{CF}$), 124.1 (q, *J* = 274.58 Hz, $^1J_{CF}$), 120.5, 120.4, 115.3, 34.5, 31.2, 27.3, 21.9, 13.8. IR (KBr): ν = 3460.6, 3043.8, 2958.0, 2851.7, 1620.5, 1593.2, 1503.3, 1466.5, 1331.7, 1282.6, 1172.3, 1135.5, 1066.1, 837.2, 714.5 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{15}H_{16}N_4F_3$ $[M+H]^+$, 309.1327, found 309.1330.

7-Bromo-4-(thiophen-2-yl)-1H-[1,2,3]triazolo[4,5-c]quinolone B32: Flash column chromatography eluent (petroleum ether/ethyl acetate = 5:1); 79% yield (131 mg); yellowish solid; m.p. 303.4 ºC; ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 16.84 (br, 1H), 8.76 (s, 1H), 8.23-8.14 (m, 2H), 7.90 (d, *J* = 4.8 Hz, 1H), 7.83-7.77 (m, 1H), 77.37-7.31 (m, 1H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 146.1, 144.9, 141.0, 136.5, 135.9, 132.0, 131.5, 130.9, 129.8, 128.9, 124.5, 122.7, 114.2. IR (KBr): ν = 3458.0, 3084.7, 2998.8, 2823.2, 1638.1, 1531.9, 1503.3, 1433.8, 1352.1, 1233.6, 1057.9, 992.5, 841.3, 784.1, 714.6 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{13}H_8N_4SBr$ $[M+H]^+$, 330.9653, found 330.9656.

One-pot procedure for the synthesis of *N*2-alkyl substituted 4-phenyl-1*H*-[1,2,3]triazolo[4,5-*c*]quinolines (C1 and C2): To a 15 mL of Young tube were added β-(2-aminoaryl)-α,β-ynones (0.5 mmol), TMS-N_3 (0.55 mmol), TBAF (0.025 mmol, 1mol/L in THF) and DMF (5 mL). The resulting mixture was stirred at room temperature for 8 h to get 4-phenyl-*1H*-[1,2,3]triazolo[4,5-*c*]quinolines (**B1**). Then, benzyl bromide or allyl bromide (0.5 mmol) and K_2CO_3 (1.0 mmol) were added. The reaction temperature was raised to 80 ºC in an oil bath and stirred for another 4 h (monitored by TLC). After completion of the reaction, the crude reaction mixture was cooled to room temperature, poured into brine (10 mL) and extracted with ethyl acetate (3 × 5 mL). The extractions were combined, dried over anhydrous Na_2SO_4, filtrated and removed the solvent under reduced pressure. The residual was purified by flash chromatography on silica to afford the desired products **C1** and **C2**.

2-Benzyl-4-phenyl-1H-[1,2,3]triazolo[4,5-c]quinoline C1: Flash column chromatography eluent (petroleum ether/ethyl acetate = 20:1); 69% yield (116 mg); white solid; m.p. 101.0 ºC; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 8.74 (d, *J* = 7.8 Hz, 2H), 8.46 (d, *J* = 7.7 Hz, 1H), 8.26 (d, *J* = 8.8 Hz, 1H), 8.75 (t, *J* = 7.6 Hz, 1H), 7.67-7.52 (m, 4H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.40-7.32 (m, 3H), 6.00 (s, 2H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 151.2, 146.1, 144.7, 138.6, 137.2, 134, 7, 130.5, 130.4, 129.5, 129.1, 128.8, 128.7, 128.4, 127.4, 126.0, 122. 7, 119.3, 60.6 ppm. IR (KBr): ν = 3062.2, 2934.1, 1622.7, 1568.0, 1517.2, 1492.7, 1449.5, 1368.9, 1327.9, 1236.0, 1177.0, 951.7, 770.7, 737.2, 693.2 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{22}H_{17}N_4$ $[M+H]^+$, 337.1453, found 337.1459.

1-Allyl-4-phenyl-1H-[1,2,3]triazolo[4,5-c]quinoline C2: Flash column chromatography eluent (petroleum ether/ethyl acetate = 20:1); 65% yield (93 mg); yellowish oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 8.73 (d, *J* = 8.0 Hz, 2H), 8.46 (d, *J* = 8.0 Hz, 1H), 8.27 (d, *J* = 7.7 Hz, 1H), 7.75 (t, *J* = 6.9 Hz, 1H), 7.65 (t, *J* = 7.0 Hz, 1H), 7.60 (t, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 6.32-6.24 (m, 1H), 5.46-5.40 (m, 4H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 151.2, 145.9, 144.7, 138.4, 137.1, 131.1, 130.5, 130.4, 129.5, 129.3, 128.7, 127.4, 122.6, 120.4, 119.2, 59.2 ppm. IR (KBr): ν = 3057.2, 2926.8, 1620.5, 1566.4, 1515.6, 1493.8, 1448.2, 1362.7, 1323.4, 1235.7, 1182.4, 951.4, 769.7, 728.4, 692.1 cm^{-1}. HRMS (+ESI): m/z calculated for $C_{18}H_{15}N_4$ $[M+H]^+$, 287.1297, found 287.1330.

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Keywords: 1*H*-[1,2,3-triazolo[4,5-*c*]quinolines • β-(2-aminoaryl)-α,β-ynones • TMS-N_3 • TBAF-catalyzed tandem reaction • ambient temperature reaction

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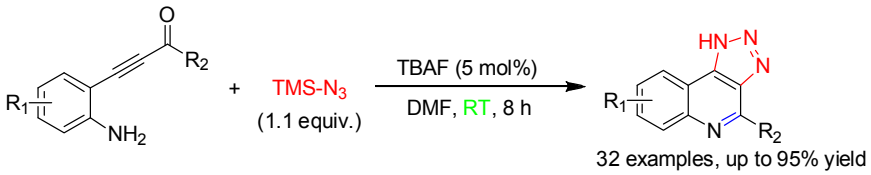
Entry for the Table of Contents

Heterocycle Synthesis:



32 examples, up to 95% yield

♦ Metal-free ♦ Mild reaction conditions ♦ Broad substrate scope ♦ High atom-/step-economy

An efficient and metal-free approach for 1*H*-[1,2,3]triazolo[4,5-*c*]quinolines have been developed based on tandem TBAF-catalyzed intermolecular azide-alkyne [3+2] cycloaddition of β-(2-aminoaryl)-α,β-ynones and TMS-N_3, and intramolecular dehydration annulation reactions. This transformation can smoothly proceed at ambient temperature to provide a broad range of functionalized 1*H*-[1,2,3]triazolo[4,5-*c*]quinolines in up to 95% yield for 32 examples.