Electronic supplementary information for

I_2–TBHP-catalyzed one-pot highly efficient synthesis of 4,3-fused 1,2,4-triazoles from *N*-tosylhydrazones and aromatic *N*-heterocycles *via* intermolecular formal 1,3-dipolar cycloaddition

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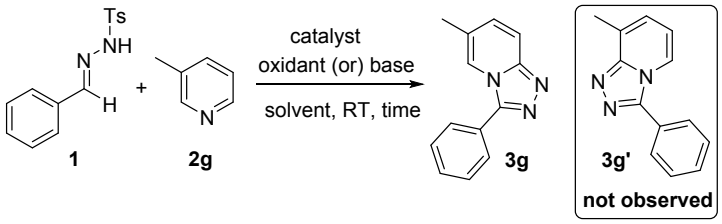
Table of contents

General experimental methods	S2
Optimization of reaction conditions	S3-S4
General procedure for the preparation of *N*-tosylhydrazones	S5
Characterization data of new *N*-tosylhydrazones	S5-S6
Experimental procedure for compounds **3a-r**, **5a-j** & **6a-u**	S7
Experimental procedure for compounds **6v-x**	S7
Characterization data of all synthesized compounds	S8-S30
References	S30
Crystal preparations and X-ray crystal structures of compounds **3h** & **6k**	S31-S32

1. General experimental methods:

All reagents were purchased from commercial suppliers and used without further purification. Solvents were used without drying. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100.5 MHz on Varian NMR spectrometer with $CDCl_3$ (or) DMSO-d_6 as solvent. Chemical shifts were reported in δ ppm using tetramethylsilane (δ 0.00 ppm) as the internal standard when using CDCl3 as solvent in ^{1}H NMR and residual solvent protons as internal standard (δ 2.48 ppm for DMSO-d_6 in ^{1}H-NMR, δ 77.0 ppm for $CDCl_3$ and δ 40.0 ppm for DMSO-d_6 in ^{13}C-NMR). Coupling constants (J) were reported in Hz and refer to apparent peak multiplications. The peak splitting patterns were indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; td, triplet of doublets; quint, quintet; sext, sextet; bs, broad singlet. High resolution mass spectra were obtained on WATERS Q-TOF Premier-HAB213 spectrometer in ESI mode. Melting points were recorded using Buchi melting point apparatus and temperatures were uncorrected. Thin layer chromatography was performed on aluminium plates coated with silica gel 60 with F_{254} indicator. The *N*-tosylhydrazones **1** were synthesized according to the reported procedure.[1]

Table S1: Optimization of reaction conditions.[a]

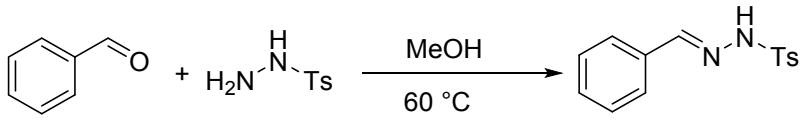


Entry	Catalyst	Oxidant [j] /Base	Solvent	Time [h]	Yield [%][b]
1[c]	I_2		DCM	16	11
2[d]	I_2	Cs_2CO_3	DCM	16	28
3[d]	I_2	DBU	DCM	16	10
4[d]	I_2	K_2CO_3	DCM	16	24
5	I_2	TEMPO	DCM	16	trace
6	I_2	$K_2S_2O_8$	DCM	16	trace
7	I_2	DTBP	DCM	16	8
8	I_2	H_2O_2	DCM	12	52
9	I_2	BPO[k]	DCM	12	41
10[e]	I_2	TBHP	DCM	8	68
11	**I_2**	**TBHP**	**DCM**	**6**	**85**
12		TBHP	DCM	16	0
13	I_2		DCM	16	trace
14	PhI	TBHP	DCM	16	0
15	NaI	TBHP	DCM	7	70
16	KI	TBHP	DCM	7	72
17	NIS	TBHP	DCM	10	51
18	TBAI	TBHP	DCM	10	53
19	I_2	TBHP	THF	16	40
20	I_2	TBHP	1,4-dioxane	16	45
21	I_2	TBHP	1,2-DCE	10	70
22	I_2	TBHP	DMF	16	15
23[f]	I_2	TBHP	DCM	12	69
24[g]	I_2	TBHP	DCM	4	73
25[h]	I_2	TBHP	DCM	2	47
26[i]	I_2	TBHP	DCM	10	64

Reaction conditions: [a] **1** (0.5 mmol), **2g** (1.0 mmol), catalyst (20 mol%), oxidant (1.0 mmol) in CH_2Cl_2 (3.0 mL), RT (24–25 °C), open air. [b] Isolated yields. [c] I_2 (0.5 mmol). [d] I_2 (0.5 mmol), base (0.5 mmol). [e] TBHP (70% aqueous). [f] I_2 (10 mol%). [g] I_2 (40 mol%). [h] At 40 °C. [i] **2g** (0.7 mmol). [j] TBHP (5–6 M in decane). [k] BPO (benzoyl peroxide).

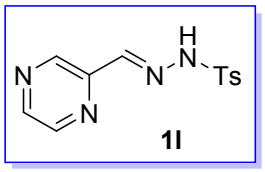
We initially began our investigation reaction between *N′*-benzylidene-4-methylbenzenesulfonohydrazide **1** and 3-methylpyridine **2g** using I_2 (1 equiv) in DCM at room temperature (Table S1, entry 1). To our delight, the desired compound **3g** was obtained in 11% yield over a period of 16 h with complete regioselectivity (confirmed by ^{1}H NMR) along with the recovery of the un-reacted starting materials as indicated by TLC. The optimization results are summarized in Table S1. Our study began by screening of external base (1 equiv, such as Cs_2CO_3, DBU and K_2CO_3), however none of them improved the yields significantly (Table S1, entries 2–4). Next, we sought to test the feasibility of the reaction with various oxidants and catalytic I_2 (20 mol%). It was noteworthy to metion that the desired product **3g** was achieved in 85% yield in 6 h using 2 equiv of *tert*-butyl hydroperoxide [TBHP (5–6 M) in decane] in DCM at room temperature (Table S1, entry 11). The reaction failed to proceed in absence of I_2 or TBHP over a period of 16 h (Table S1, entries 12 and 13) suggesting the crucial roles of both I_2 and TBHP together for the formation of **3g**. The reaction proceeded less efficiently in other iodine sources such as PhI, NaI, KI, NIS and TBAI even after prolonging the reaction time (Table S1, entries 14–18). Moreover, from the solvent screening results, DCM proved to be the best choice (Table S1, entries 19–22). In order to optimize the I_2 loading, it was found that either lowering the I_2 loading to 10 mol% or increasing to 40 mol% did not improve the yield of **3g** (Table S1, entries 23 and 24). Finally, the effect of temperature was examined and it was found that increasing the temperature up to 40 ^{0}C lowered the yield of **3g** (Table S1, entry 25). A reduction in yield of **3g** was observed while lowering the amount of **2g** to 1.4 equiv even after increasing the reaction time up to 10 h (Table S1, entry 26). Thus, the optimized catalytic system was established as: **1** (1 equiv), **2g** (2 equiv), I_2 (20 mol%), TBHP (2 equiv) in DCM at room temperature (Table S1, entry 11).

2. General procedure for the preparation of *N*-tosylhydrazones:[1]



To a stirred solution of $TsNHNH_2$ (5 mmol) in methanol (5 mL) was heated to 60 °C until the $TsNHNH_2$ was completely dissolved. Then carbonyl compounds (5 mmol) were dropped to the mixture slowly (solid reagents were added as a methanol solution or portion wise). After approximately 30 min the mixture was cooled to 0 °C and the precipitated products was removed by filtration. The precipitates were washed by petroleum ether then were dried under vacuum to afford the pure products.

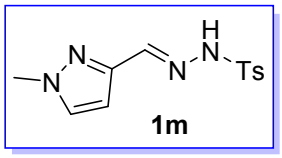
3. Characterization data of new *N*-tosylhydrazones:



1l

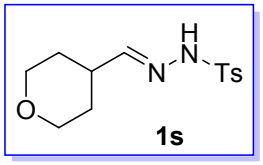
4-methyl-*N*'-(pyrazin-2-ylmethylene)benzenesulfonohydrazide (1l)

Brown solid; Yield: 90%; M.p.: 169-170 °C; R_f = 0.62 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.95 (s, 1H), 8.90 (s, 1H), 8.59 – 8.58 (m, 2H), 7.90 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 148.3, 145.1, 144.8, 144.7, 144.2, 142.0, 136.3, 130.2, 127.6, 21.4. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{12}H_{12}N_4NaO_2S$, 299.0579; found, 299.0579.



4-methyl-*N*'-((1-methyl-1H-pyrazol-3-yl)methylene)benzenesulfonohydrazide (1m)

White solid; Yield: 89%; M.p.: 149-151 °C; R_f = 0.5 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.25 (s, 1H), 7.83 (s, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 1.6 Hz, 1H), 7.37 (d, J = 8.0 Hz, 2H), 6.39 (d, J = 1.2 Hz, 1H), 3.79 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 147.0, 143.8, 142.3, 136.6, 132.8, 130.0, 127.6, 103.2, 39.1, 21.4. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{12}H_{14}N_4NaO_2S$, 301.0735; found, 301.0737.



4-methyl-N'-((tetrahydro-2H-pyran-4-yl)methylene)benzenesulfonohydrazide (1s)

White solid; Yield: 86%; M.p.: 119-121 °C; R_f = 0.72 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.84 (s, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 4.4 Hz, 1H), 3.73 – 3.70 (m, 2H), 3.28 – 3.27 (m, 0.5H), 3.23 – 3.22 (m, 1.5H), 2.36 (s, 3H), 2.33 – 2.29 (m, 1H), 1.51 – 1.48 (m, 2H), 1.33 – 1.23 (m, 2H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 154.2, 143.6, 136.6, 129.9, 127.6, 66.5, 37.4, 29.6, 21.4. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{13}H_{18}N_2NaO_3S$, 305.0936; found, 305.0938.

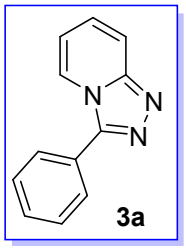
4. Experimental procedure for compounds 3a-r, 5a-j & 6a-u:

To a stirred solution of N-sulfonylhydrazones (0.5 mmol, 1 equiv) and aromatic *N*-heterocycles (1.0 mmol, 2 equiv) in DCM (3.0 mL) was added 5 6 M solution of TBHP in decane (1.0 mmol, 2 equiv) and iodine (20 mol %). The reaction mixture was stirred at room temperature as monitored by TLC. After completion, the reaction mixture was quenched with 10% aqueous $Na_2S_2O_3$ solution (2.5 mL) and extracted with DCM (2x10 mL), the combined organic layers were dried over Na_2SO_4, filtered, and evaporated under vacuum. The crude products were purified by flash column chromatography on silica gel using ethyl acetate (EtOAc) and hexane to give the fused triazoles **3a-l, 3o-q, 5a-j & 6a-u**.

5. Experimental procedure for compounds 6v-x:

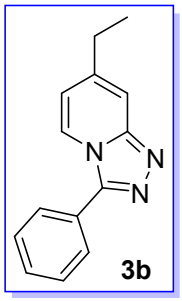
To a stirred solution of $TsNHNH_2$ (0.5 mmol) in dichloromethane (3 mL) was added carbonyl compounds (0.5 mmol) at room temperature. This reaction mixture was stirred at room temperature for 1 hour. After this time, was added 3-methylpyridine (1.0 mmol, 2 equiv) followed by added 5 6 M solution of TBHP in decane (1.0 mmol, 2 equiv) and iodine (20 mol %) to the above reaction mixture. The reaction mixture was stirred at room temperature for 2 hours as monitored by TLC. After completion, the reaction mixture was quenched with 10% aqueous $Na_2S_2O_3$ solution (2.5 mL) and extracted with DCM (2x10 mL), the combined organic layers were dried over Na_2SO_4, filtered, and evaporated under vacuum. The crude products were purified by flash column chromatography on silica gel using ethyl acetate and hexane to give the fused triazoles **6v-x**.

6. Characterization data of all synthesized compounds:



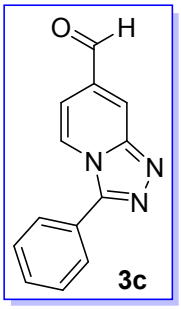
3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (3a)

White solid; Yield: 85%; M.p.: 175-176 °C (lit: 172-174 °C,[2] 172 °C,[3] 172-173 °C[4]); R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, *J* = 7.2 Hz, 1H), 7.84 – 7.83 (m, 3H), 7.61 – 7.53 (m, 3H), 7.30 – 7.28 (m, 1H), 6.86 (t, *J* = 6.8 Hz, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 150.5, 146.7, 130.1, 129.2, 128.2, 126.9, 126.6, 122.5, 116.8, 114.1. ESI-MS $[M+H]^+$ *m/z* 196.1.



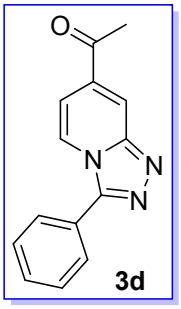
7-ethyl-3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (3b)

White solid; Yield: 87%; M.p.: 74-75 °C; R_f = 0.42 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 7.2 Hz, 1H), 7.82 (d, *J* = 6.8 Hz, 2H), 7.59 – 7.51 (m, 4H), 6.71 (d, *J* = 6.4 Hz, 1H), 2.73 (q, *J* = 7.6 Hz, 2H), 1.31 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 151.2, 146.2, 144.1, 129.9, 129.2, 128.1, 126.8, 121.8, 116.2, 112.9, 28.3, 13.8. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{13}N_3Na$, 246.1007; found, 246.1006.



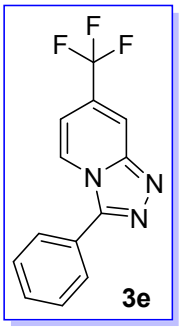
3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine-7-carbaldehyde (3c)

White solid; Yield: 89%; M.p.: 182-184 °C; R_f = 0.37 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.05 (s, 1H), 8.35 – 8.33 (m, 2H), 7.87 – 7.84 (m, 2H), 7.63 – 7.61 (m, 3H), 7.36 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 189.0, 150.0, 148.1, 134.7, 130.8, 129.5, 128.3, 125.8, 123.7, 123.5, 110.1. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{13}H_{10}N_3O$, 224.0824; found, 224.0825.



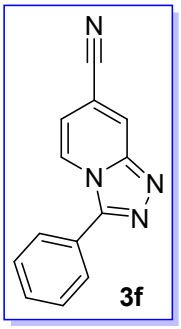
1-(3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridin-7-yl)ethanone (3d)

White solid; Yield: 92%; M.p.: 253-254 °C; R_f = 0.38 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.61 – 8.57 (m, 2H), 7.92 – 7.90 (m, 2H), 7.64 – 7.58 (m, 3H), 7.31 (d, J = 7.6 Hz, 1H), 2.67 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 196.6, 150.3, 147.4, 135.4, 130.7, 129.7, 128.6, 126.6, 124.4, 118.8, 111.8, 26.7. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{12}N_3O$, 238.0980; found, 238.0987.



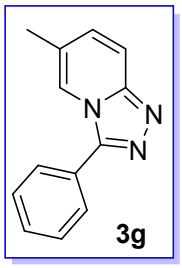
3-phenyl-7-(trifluoromethyl)-[1,2,4]triazolo[4,3-*a*]pyridine (3e)

White solid; Yield: 46%; M.p.: 225-226 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (d, J = 7.6 Hz, 1H), 8.16 (s, 1H), 7.84 (d, J = 5.6 Hz, 2H), 7.62 – 7.61 (m, 3H), 7.01 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 148.9, 147.7, 130.8, 129.5, 129.2 (q, $J_{C\text{-}F}$ = 34.4 Hz), 128.3, 125.8, 123.9, 122.5 (q, $J_{C\text{-}F}$ = 273.3 Hz), 115.4 (q, $J_{C\text{-}F}$ = 5.0 Hz), 110.1 (d, $J_{C\text{-}F}$ = 2.3 Hz). HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{13}H_8F_3N_3Na$, 286.0568; found, 286.0565.



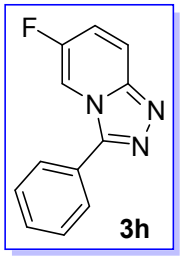
3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine-7-carbonitrile (3f)

Brown solid; Yield: 41%; M.p.: 225-226 °C; R_f = 0.38 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (d, J = 7.2 Hz, 1H), 8.26 (s, 1H), 7.83 – 7.82 (m, 2H), 7.62 – 7.61 (m, 3H), 6.97 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 148.6, 148.1, 131.0, 129.5, 128.3, 125.4, 124.0, 123.9, 116.3, 113.8, 110.7. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{13}H_9N_4$, 221.0827; found, 221.0826.



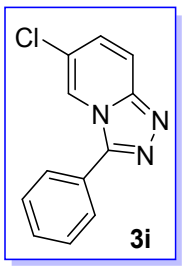
6-methyl-3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (3g)[5]

White solid; Yield: 85%; M.p.: 155-156 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.73 (d, *J* = 10.0 Hz, 1H), 7.60 – 7.52 (m, 3H), 7.13 (d, *J* = 9.6 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 149.9, 146.3, 130.4, 129.9, 129.2, 128.2, 126.9, 124.0, 119.5, 115.9, 18.2. ESI-MS $[M+H]^+$ *m/z* 210.1.



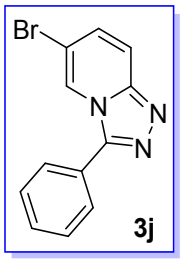
6-fluoro-3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (3h)

White solid; Yield: 65%; M.p.: 162-163 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.85 – 7.80 (m, 3H), 7.62 – 7.54 (m, 3H), 7.23 – 7.21 (m, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 154.0 (d, $J_{C\text{-}F}$ = 242.9 Hz), 148.6, 147.7, 130.4, 129.4, 128.0, 126.2, 120.2 (d, $J_{C\text{-}F}$ = 27.2 Hz), 117.7 (d, $J_{C\text{-}F}$ = 9.3 Hz), 109.0 (d, $J_{C\text{-}F}$ = 41.2 Hz). HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{12}H_9FN_3$, 214.0781; found, 214.0780.



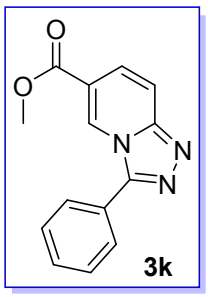
6-chloro-3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (3i)

White solid; Yield: 68%; M.p.: 154-156 °C (lit: 154-156 °C[2]); R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.67 (s, 1H), 7.92 – 7.90 (m, 3H), 7.61 – 7.57 (m, 3H), 7.47 (d, J = 9.6 Hz, 1H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.1, 146.8, 130.6, 129.7, 129.4, 128.6, 126.5, 122.3, 121.9, 117.0. ESI-MS $[M+H]^+$ *m/z* 230.1.



6-bromo-3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine (3j)

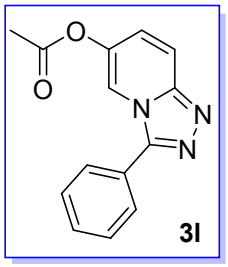
White solid; Yield: 71%; M.p.: 171-173 °C (lit: 174-175 °C[6]); R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (s, 1H), 7.81 (d, J = 6.0 Hz, 2H), 7.73 (d, J = 9.6 Hz, 1H), 7.63 – 7.56 (m, 3H), 7.33 (d, J = 9.6 Hz, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 149.0, 146.6, 130.7, 130.5, 129.4, 128.2, 126.0, 122.5, 117.4, 109.4. ESI-MS $[M+H]^+$ *m/z* 274.0.



methyl 3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridine-6-carboxylate (3k)

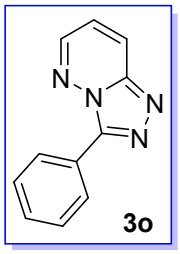
White solid; Yield: 68%; M.p.: 155-157 °C; R_f = 0.38 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.99 (s, 1H), 7.85 – 7.79 (m, 4H), 7.65 – 7.58 (m, 3H), 3.96 (s, 3H); ^{13}C NMR

(100.5 MHz, $CDCl_3$): δ 164.3, 150.4, 147.8, 130.6, 129.5, 128.4, 127.1, 126.4, 125.9, 118.6, 116.2, 52.7. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{11}N_3NaO_2$, 276.0749; found, 276.0750.



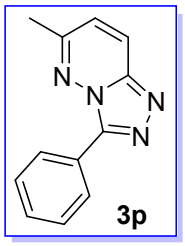
3-phenyl-[1,2,4]triazolo[4,3-*a*]pyridin-6-yl acetate (3l)

Colorless oil; Yield: 73%; R_f = 0.35 (EtOAc/hexane = 3:1); ^1H NMR (400 MHz, $CDCl_3$): δ 8.28 (s, 1H), 7.83 – 7.81 (m, 3H), 7.60 – 7.55 (m, 3H), 7.12 (dd, *J* = 10, 1.6 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 168.7, 148.9, 147.5, 140.7, 130.3, 129.3, 128.1, 126.3, 124.6, 116.7, 115.0, 20.8. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{11}N_3NaO_2$, 276.0749; found, 276.0750.



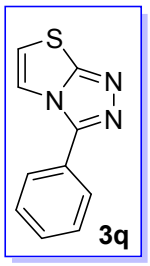
3-phenyl-[1,2,4]triazolo[4,3-*b*]pyridazine (3o)[7]

Brown solid; Yield: 73%; M.p.: 152-153 °C; R_f = 0.3 (EtOAc/hexane = 3:1); ^1H NMR (400 MHz, $CDCl_3$): δ 8.49 – 8.45 (m, 3H), 8.20 (d, *J* = 9.2 Hz, 1H), 7.58 – 7.50 (m, 3H), 7.14 (dd, *J* = 9.2, 4.0 Hz, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 148.1, 145.0, 144.8, 130.2, 128.6, 127.7, 126.1, 125.4, 119.2. ESI-MS $[M+H]^+$ *m/z* 197.1.



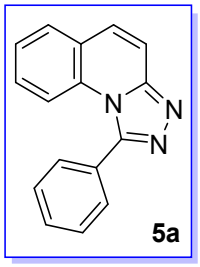
6-methyl-3-phenyl-[1,2,4]triazolo[4,3-*b*]pyridazine (3p)

Brown solid; Yield: 69%; M.p.: 154-155 °C; R_f = 0.3 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 – 8.49 (m, 2H), 8.06 (d, J = 9.6 Hz, 1H), 7.57 – 7.48 (m, 3H), 7.01 (d, J = 9.6 Hz, 1H), 2.66 (s, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 154.4, 147.7, 144.2, 130.0, 128.5, 127.6, 126.4, 124.6, 121.6, 21.9. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{12}H_{10}N_4Na$, 233.0803; found, 233.0804.



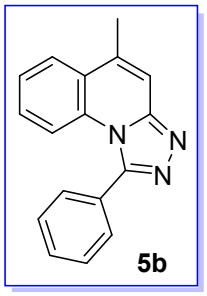
3-phenylthiazolo[2,3-*c*][1,2,4]triazole (3q)

Brown solid; Yield: 32%; M.p.: 159-160 °C; R_f = 0.28 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.26 (d, J = 4.0 Hz, 1H), 7.94 (d, J = 6.8 Hz, 2H), 7.56 – 7.52 (m, 4H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 158.5, 146.8, 130.2, 129.6, 127.0, 126.6, 119.5, 118.3. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{10}H_7N_3NaS$, 224.0258; found, 224.0261.



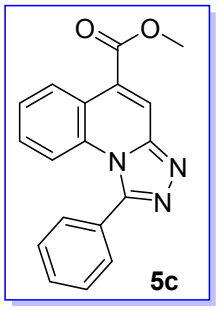
1-phenyl-[1,2,4]triazolo[4,3-*a*]quinoline (5a)

White solid; Yield: 80%; M.p.: 136-138 °C (lit: 135-137 °C[2]); R_f = 0.42 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.97 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 9.2 Hz, 1H), 7.73 – 7.61 (m, 6H), 7.48 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H) ; ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.5, 148.8, 131.8, 130.9, 130.3, 130.3, 130.1, 130.0, 129.5, 129.4, 126.5, 124.6, 116.3, 115.0. ESI-MS $[M+H]^+$ *m/z* 246.1.



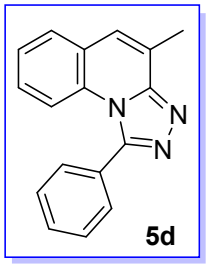
5-methyl-1-phenyl-[1,2,4]triazolo[4,3-*a*]quinoline (5b)

White solid; Yield: 90%; M.p.: 153-154 °C (lit: 152-153 °C[8]); R_f = 0.42 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.02 (d, J = 8.0 Hz, 1H), 7.70 – 7.62 (m, 6H), 7.54 (t, J = 7.2 Hz, 1H), 7.46 – 7.40 (m, 2H), 2.60 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.2, 148.4, 137.2, 131.6, 130.9, 130.3, 130.2, 129.5, 129.3, 126.7, 126.4, 124.9, 116.5, 113.7, 19.3. ESI-MS $[M+H]^+$ *m/z* 260.1.



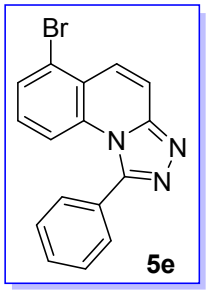
methyl 1-phenyl-[1,2,4]triazolo[4,3-*a*]quinoline-5-carboxylate (5c)

White solid; Yield: 56%; M.p.: 191-193 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (d, J = 8.4 Hz, 1H), 8.40 (s, 1H), 7.70 – 7.59 (m, 6H), 7.52 (t, J = 7.8 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 4.05 (s, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 165.5, 149.8, 148.5, 131.9, 130.7, 129.8, 129.7, 129.2, 129.1, 129.0, 128.6, 128.1, 126.6, 121.7, 119.8, 116.9, 52.8. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{18}H_{14}N_3O_2$, 304.1086; found, 304.1082.



4-methyl-1-phenyl-[1,2,4]triazolo[4,3-*a*]quinoline (5d)

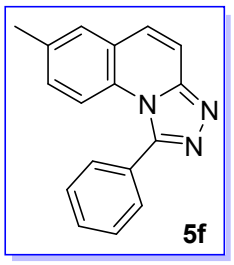
White solid; Yield: 96%; M.p.: 179-180 °C; R_f = 0.42 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.89 (d, J = 7.6 Hz, 1H), 7.71 – 7.62 (m, 5H), 7.60 (s, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.37 – 7.29 (m, 2H), 2.59 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 150.2, 149.3, 130.9, 130.9, 130.3, 130.1, 129.5, 129.1, 128.3, 127.5, 126.4, 125.0, 124.5, 116.1, 16.8. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{14}N_3$, 260.1188; found, 260.1186.



6-bromo-1-phenyl-[1,2,4]triazolo[4,3-*a*]quinoline (5e)

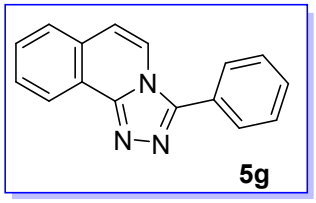
Brown solid; Yield: 57%; M.p.: 171-172 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 9.6 Hz, 1H), 7.77 (d, J = 9.6 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.67 – 7.51 (m, 6H), 7.16 (t, J = 8.2 Hz, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 149.5, 149.1, 132.9,

130.6, 130.3, 129.8, 129.3, 129.2, 129.1, 128.5, 123.9, 123.8, 116.4, 116.2. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{11}BrN_3$, 324.0136; found, 324.0139.



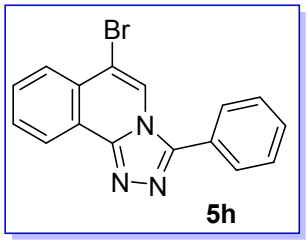
7-methyl-1-phenyl-[1,2,4]triazolo[4,3-*a*]quinoline (5f)

White solid; Yield: 86%; M.p.: 179-181 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 – 7.65 (m, 3H), 7.62 – 7.57 (m, 4H), 7.50 (d, *J* = 10.0 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 149.8, 148.8, 136.0, 130.4, 130.0, 129.9, 129.8, 129.6, 129.5, 129.0, 129.0, 124.6, 116.5, 114.9, 20.8. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{14}N_3$, 260.1188; found, 260.1186.



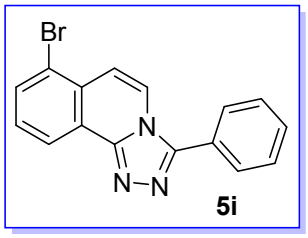
3-phenyl-[1,2,4]triazolo[3,4-*a*]isoquinoline (5g)

White solid; Yield: 87%; M.p.: 189-190 °C (lit: 181-183 °C[2]); R_f = 0.42 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (d, *J* = 7.2 Hz, 1H), 7.99 (d, *J* = 6.8 Hz, 1H), 7.85 (d, *J* = 6.8 Hz, 2H), 7.75 – 7.67 (m, 3H), 7.62 – 7.56 (m, 3H), 7.08 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 149.2, 148.5, 130.2, 130.0, 129.7, 129.2, 129.1, 128.5, 127.0, 126.7, 124.1, 121.7, 119.5, 115.4. ESI-MS $[M+H]^+$ *m/z* 246.1.



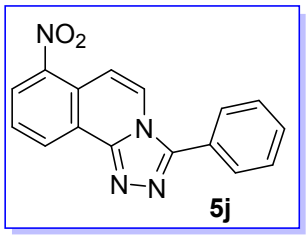
6-bromo-3-phenyl-[1,2,4]triazolo[3,4-*a*]isoquinoline (5h)

White solid; Yield: 88%; M.p.: 158-160 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.64 (d, J = 7.2 Hz, 1H), 8.53 (s, 1H), 8.07 (d, J = 7.6 Hz, 1H), 7.93 – 7.85 (m, 4H), 7.65 – 7.63 (m, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 148.3, 148.1, 131.5, 130.8, 130.7, 129.7, 128.9, 128.4, 127.0, 126.4, 123.9, 122.3, 121.1, 110.5. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{11}BrN_3$, 324.0136; found, 324.0139.



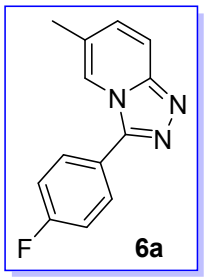
7-bromo-3-phenyl-[1,2,4]triazolo[3,4-*a*]isoquinoline (5i)

White solid; Yield: 84%; M.p.: 211-212 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.79 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 7.6 Hz, 1H), 7.85 (dd, J = 8.0, 1.6 Hz, 2H), 7.64 – 7.51 (m, 5H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 148.6, 133.9, 130.4, 129.8, 129.3, 129.0, 128.5, 126.3, 123.5, 123.3, 121.9, 120.6, 114.1. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{11}BrN_3$, 324.0136; found, 324.0139.



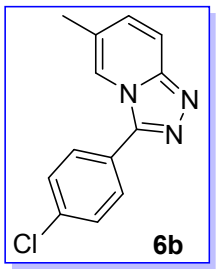
7-nitro-3-phenyl-[1,2,4]triazolo[3,4-*a*]isoquinoline (5j)

Yellow solid; Yield: 65%; M.p.: 237-238 °C; R_f = 0.38 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.15 (d, *J* = 8.0 Hz, 1H), 8.40 (dd, *J* = 8.0, 0.8 Hz, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.87 – 7.82 (m, 3H), 7.66 – 7.59 (m, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 149.1, 147.9, 145.8, 130.8, 129.7, 129.4, 128.6, 128.5, 126.7, 125.8, 123.6, 122.9, 122.7, 109.6. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{11}N_4O_2$, 291.0882; found, 291.0881.



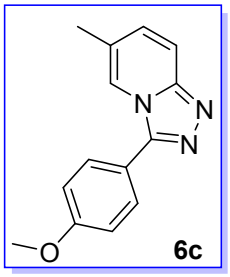
3-(4-fluorophenyl)-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6a)

White solid; Yield: 82%; M.p.: 147-148 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.31 (s, 1H), 7.93 (dd, *J* = 8.4, 2.8 Hz, 2H), 7.75 (d, *J* = 10.0 Hz, 1H), 7.44 (t, *J* = 9.0 Hz, 2H), 7.28 (d, *J* = 9.2 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 163.3 (d, $J_{C\text{-}F}$ = 247.5 Hz), 149.7, 145.2, 131.5, 131.0 (d, $J_{C\text{-}F}$ = 8.6 Hz), 124.4, 123.7, 120.9, 116.7 (d, $J_{C\text{-}F}$ = 21.8 Hz), 115.3, 17.8. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{13}H_{11}FN_3$, 228.0937; found, 228.0938.



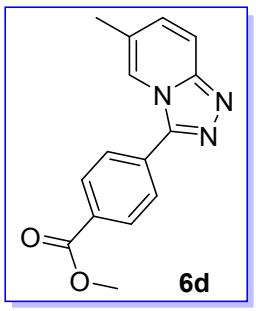
3-(4-chlorophenyl)-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6b)

White solid; Yield: 84%; M.p.: 182-183 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.35 (s, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 9.2 Hz, 1H), 7.66 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 9.6 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.9, 145.0, 134.9, 131.6, 130.2, 129.7, 126.0, 124.6, 121.0, 115.4, 17.9. HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{13}H_{11}ClN_3$, 244.0642; found, 244.0647.



3-(4-methoxyphenyl)-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6c)

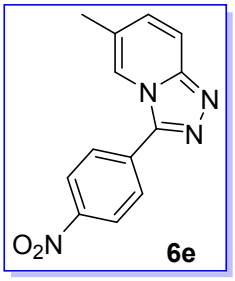
White solid; Yield: 90%; M.p.: 162-163 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.26 (s, 1H), 7.80 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 9.2 Hz, 1H), 7.25 (d, J = 9.6 Hz, 1H), 7.15 (d, J = 8.4 Hz, 2H), 3.84 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 160.8, 149.5, 145.9, 131.2, 130.0, 124.1, 120.8, 119.4, 115.3, 115.0, 55.8, 17.9. HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{14}N_3O$, 240.1137; found, 240.1132.



methyl 4-(6-methyl-[1,2,4]triazolo[4,3-*a*]pyridin-3-yl)benzoate (6d)

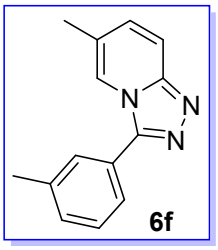
White solid; Yield: 74%; M.p.: 207-208 °C; R_f = 0.38 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.45 (s, 1H), 8.15 (d, J = 8.4 Hz, 2H), 8.07 (d, J = 8.4 Hz, 2H), 7.79 (d, J =

9.2 Hz, 1H), 7.33 (d, J = 9.2 Hz, 1H), 3.90 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 166.1, 150.1, 145.1, 131.8, 131.5, 130.7, 130.3, 128.5, 124.9, 121.2, 115.4, 52.8, 17.9. HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{14}N_3O_2$, 268.1086; found, 268.1086.



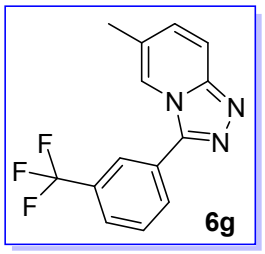
6-methyl-3-(4-nitrophenyl)-[1,2,4]triazolo[4,3-*a*]pyridine (6e)

Yellow solid; Yield: 62%; M.p.: 256-257 °C; R_f = 0.38 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.50 (s, 1H), 8.41 (d, J = 8.0 Hz, 2H), 8.22 (d, J = 8.0 Hz, 2H), 7.83 (d, J = 9.2 Hz, 1H), 7.36 (d, J = 10.0 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 150.3, 148.1, 144.4, 133.3, 132.1, 129.3, 125.2, 124.7, 121.4, 115.4, 17.9. HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{13}H_{11}N_4O_2$, 255.0882; found, 255.0887.



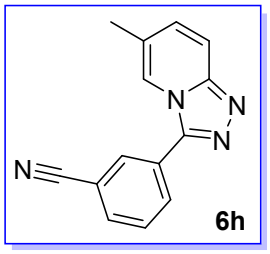
6-methyl-3-(m-tolyl)-[1,2,4]triazolo[4,3-*a*]pyridine (6f)

Colorless oil; Yield: 87%; R_f = 0.42 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.33 (s, 1H), 7.75 (d, J = 9.6 Hz, 1H), 7.67 – 7.65 (m, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.38 (d, J = 7.2 Hz, 1H), 7.28 (d, J = 9.6 Hz, 1H), 2.43 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.7, 146.0, 139.0, 131.4, 130.9, 129.5, 128.9, 127.1, 125.5, 124.4, 120.9, 115.4, 21.4, 17.9. HRMS–ESI (m/z): $[M+Na]^+$ calcd for $C_{14}H_{13}N_3Na$, 246.1007; found, 246.1009.



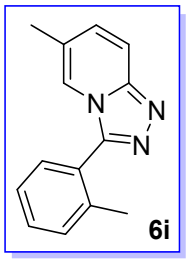
6-methyl-3-(3-(trifluoromethyl)phenyl)-[1,2,4]triazolo[4,3-*a*]pyridine (6g)

White solid; Yield: 75%; M.p.: 145-146 °C; R_f = 0.42 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.38 (s, 1H), 8.22 – 8.19 (m, 2H), 7.93 (d, J = 7.6 Hz, 1H), 7.85 (t, J = 7.8 Hz, 1H), 7.79 (d, J = 10.0 Hz, 1H), 7.32 (d, J = 9.2 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 150.0, 144.8, 132.2, 131.9, 130.8, 130.4 (q, $J_{C\text{-}F}$ = 31.9 Hz), 128.3, 126.7 (d, $J_{C\text{-}F}$ = 3.1 Hz), 125.2 (d, $J_{C\text{-}F}$ = 3.9 Hz), 124.7, 124.3 (q, $J_{C\text{-}F}$ = 272.5 Hz), 121.1, 115.3, 17.9. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{11}F_3N_3$, 278.0905; found, 278.0904.



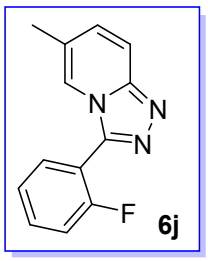
3-(6-methyl-[1,2,4]triazolo[4,3-*a*]pyridin-3-yl)benzonitrile (6h)

White solid; Yield: 73%; M.p.: 212-213 °C; R_f = 0.4 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.47 (s, 1H), 8.35 (s, 1H), 8.23 (d, J = 7.6 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.82 – 7.77 (m, 2H), 7.33 (d, J = 9.6 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 150.0, 144.4, 133.7, 133.2, 131.9, 131.6, 130.8, 128.4, 124.8, 121.3, 118.7, 115.3, 112.8, 17.8. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{10}N_4Na$, 257.0803; found, 257.0805.



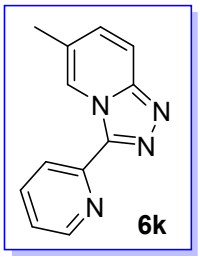
6-methyl-3-(o-tolyl)-[1,2,4]triazolo[4,3-*a*]pyridine (6i)

Colorless oil; Yield: 92%; R_f = 0.42 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.81 (s, 1H), 7.75 (d, J = 9.6 Hz, 1H), 7.53 – 7.46 (m, 3H), 7.40 (t, J = 7.0 Hz, 1H), 7.27 (d, J = 9.2 Hz, 1H), 2.24 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.0, 145.5, 138.4, 131.5, 131.3, 130.7, 126.7, 126.4, 124.3, 120.6, 115.3, 19.8, 17.7. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{13}N_3Na$, 246.1007; found, 246.1008.



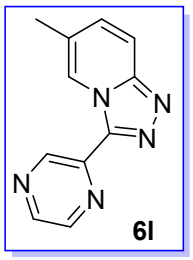
3-(2-fluorophenyl)-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6j)

White solid; Yield: 87%; M.p.: 124-125 °C; R_f = 0.42 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.02 (s, 1H), 7.80 – 7.74 (m, 2H), 7.72 – 7.67 (m, 1H), 7.52 – 7.43 (m, 2H), 7.32 (d, J = 9.2 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 160.0 (d, $J_{C\text{-}F}$ = 249.1 Hz), 149.7, 141.8, 133.2 (d, $J_{C\text{-}F}$ = 7.7 Hz), 132.4, 131.8, 125.7, 124.5, 121.3, 116.9 (d, $J_{C\text{-}F}$ = 21.0 Hz), 115.2, 114.9 (d, $J_{C\text{-}F}$ = 14.7 Hz), 17.7. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{13}H_{11}FN_3$, 228.0937; found, 228.0938.



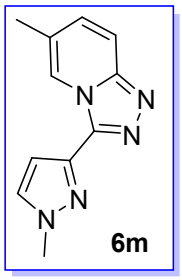
6-methyl-3-(pyridin-2-yl)-[1,2,4]triazolo[4,3-*a*]pyridine (6k)

White solid; Yield: 80%; M.p.: 174-175 °C; R_f = 0.32 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.48 (s, 1H), 8.79 – 8.78 (m, 1H), 8.36 (d, J = 8.0 Hz, 1H), 8.02 (t, J = 7.6 Hz, 1H), 7.84 (d, J = 9.2 Hz, 1H), 7.51 (t, J = 6.2 Hz, 1H), 7.38 (d, J = 9.2 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 150.3, 149.4, 148.2, 143.7, 138.0, 132.0, 124.7, 124.3, 123.8, 122.3, 115.2, 18.2. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{12}H_{11}N_4$, 211.0984; found, 211.0986.



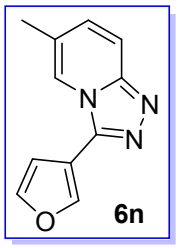
6-methyl-3-(pyrazin-2-yl)-[1,2,4]triazolo[4,3-*a*]pyridine (6l)

White solid; Yield: 85%; M.p.: 184-185 °C; R_f = 0.32 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.54 (s, 1H), 9.30 (s, 1H), 8.82 (s, 1H), 8.73 (s, 1H), 7.89 (d, J = 8.8 Hz, 1H), 7.43 (d, J = 9.6 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 150.5, 144.4, 144.0, 143.8, 143.5, 141.9, 132.5, 125.4, 123.5, 115.4, 18.2. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{11}H_9N_5Na$, 234.0756; found, 234.0756.



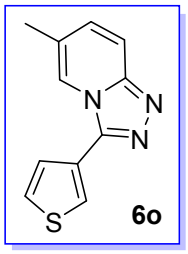
6-methyl-3-(1-methyl-1H-pyrazol-3-yl)-[1,2,4]triazolo[4,3-*a*]pyridine (6m)

White solid; Yield: 75%; M.p.: 167-169 °C; R_f = 0.3 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.97 (s, 1H), 7.93 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.30 (d, J = 9.6 Hz, 1H), 6.91 (s, 1H), 4.01 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.2, 140.7, 140.7, 132.9, 131.4, 124.3, 122.6, 115.1, 105.3, 39.4, 18.1. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{11}H_{11}N_5Na$, 236.0912; found, 236.0918.



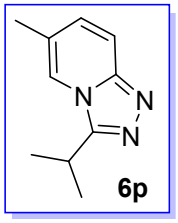
3-(furan-3-yl)-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6n)

White solid; Yield: 77%; M.p.: 186-187 °C; R_f = 0.36 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.64 (s, 1H), 8.33 (s, 1H), 7.94 (s, 1H), 7.74 (d, J = 9.6 Hz, 1H), 7.28 (d, J = 9.6 Hz, 1H), 7.13 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.4, 144.9, 141.6, 140.1, 131.2, 124.6, 121.4, 115.3, 113.4, 109.9, 17.8. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{11}H_9N_3NaO$, 222.0643; found, 222.0641.



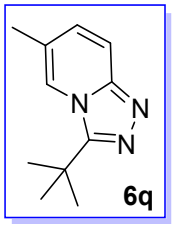
6-methyl-3-(thiophen-3-yl)-[1,2,4]triazolo[4,3-*a*]pyridine (6o)

White solid; Yield: 83%; M.p.: 199-200 °C; R_f = 0.36 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.44 (s, 1H), 8.33 (d, J = 1.2 Hz, 1H), 7.82 (dd, J = 4.8, 2.0 Hz, 1H), 7.76 – 7.72 (m, 2H), 7.28 (d, J = 9.2 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.4, 142.6, 131.3, 128.0, 127.7, 127.5, 125.3, 124.6, 121.3, 115.3, 17.9. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{11}H_{10}N_3S$, 216.0595; found, 216.0596.



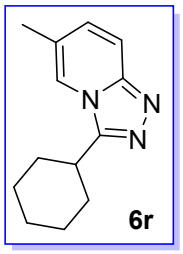
3-isopropyl-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6p)

White solid; Yield: 50%; M.p.: 111-113 °C; R_f = 0.2 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.23 (s, 1H), 7.60 (d, J = 9.2 Hz, 1H), 7.17 (d, J = 9.6 Hz, 1H), 3.47 (heptet, J = 6.8 Hz, 1H), 2.28 (s, 3H), 1.36 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 150.9, 148.9, 130.7, 123.0, 120.8, 115.1, 24.5, 20.6, 17.8. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{10}H_{14}N_3$, 176.1188; found, 176.1182.



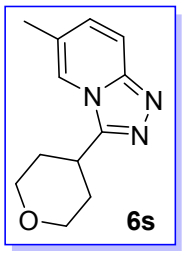
3-(tert-butyl)-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6q)

White solid; Yield: 60%; M.p.: 102-103 °C; R_f = 0.2 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.38 (s, 1H), 7.62 (d, J = 9.6 Hz, 1H), 7.15 (d, J = 9.2 Hz, 1H), 2.30 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 152.4, 150.0, 130.3, 123.1, 122.2, 115.6, 32.5, 27.9, 17.8. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{11}H_{15}N_3Na$, 212.1164; found, 212.1166.



3-cyclohexyl-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6r)

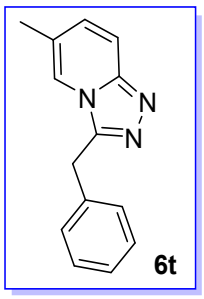
White solid; Yield: 47%; M.p.: 133-135 °C; R_f = 0.24 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.26 (s, 1H), 7.59 (d, J = 9.2 Hz, 1H), 7.16 (d, J = 9.6 Hz, 1H), 3.20 – 3.14 (m, 1H), 2.27 (s, 3H), 1.99 – 1.96 (m, 2H), 1.83 – 1.79 (m, 2H), 1.74 – 1.70 (m, 1H), 1.67 – 1.57 (m, 2H), 1.50 – 1.41 (m, 2H), 1.35 – 1.29 (m, 1H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 150.2, 148.7, 130.6, 122.9, 120.8, 115.1, 33.5, 30.6, 25.9, 25.9, 17.8. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{13}H_{18}N_3$, 216.1501; found, 216.1507.



6-methyl-3-(tetrahydro-2*H*-pyran-4-yl)-[1,2,4]triazolo[4,3-*a*]pyridine (6s)

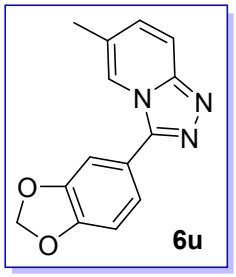
White solid; Yield: 40%; M.p.: 165-167 °C; R_f = 0.22 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.33 (s, 1H), 7.62 (d, J = 9.2 Hz, 1H), 7.19 (d, J = 9.2 Hz, 1H), 3.95 (d, J =

10.8 Hz, 2H), 3.52 (td, J = 11.3, 2.3 Hz, 2H), 3.48 – 3.32 (m, 1H), 2.28 (s, 3H), 1.93 – 1.80 (m, 4H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.1, 148.7, 131.0, 123.1, 120.9, 115.0, 67.0, 30.8, 30.3, 17.8. HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{12}H_{16}N_3O$, 218.1293; found, 218.1296.



3-benzyl-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6t)

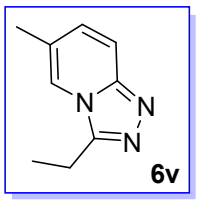
White solid; Yield: 30%; M.p.: 158-160 °C; R_f = 0.28 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.16 (s, 1H), 7.63 (d, J = 9.2 Hz, 1H), 7.31 – 7.26 (m, 4H), 7.22 – 7.17 (m, 2H), 4.48 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 148.9, 145.6, 136.4, 131.1, 129.0, 128.9, 127.2, 123.4, 120.7, 115.0, 30.0, 17.8. HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{14}N_3$, 224.1188; found, 224.1189.



3-(benzo[d][1,3]dioxol-5-yl)-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6u)

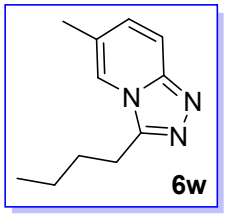
White solid; Yield: 82%; M.p.: 158-160 °C; R_f = 0.38 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.27 (s, 1H), 7.72 (d, J = 9.6 Hz, 1H), 7.39 (s, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 9.2 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 6.14 (s, 2H), 2.28 (s, 3H); ^{13}C NMR (100.5 MHz, DMSO-d_6): δ 149.6, 149.0, 148.3, 145.8, 131.3, 124.2, 122.9, 120.9, 120.7, 115.3, 109.4,

108.8, 102.1, 17.8. HRMS–ESI (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{12}N_3O_2$, 254.0930; found, 254.0932.



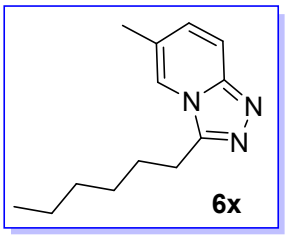
3-ethyl-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6v)

White solid; Yield: 45%; M.p.: 76-78 °C; R_f = 0.22 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.57 (d, *J* = 9.2 Hz, 1H), 7.02 (d, *J* = 9.2 Hz, 1H), 3.01 (q, *J* = 7.6 Hz, 2H), 2.29 (s, 3H), 1.44 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 149.2, 147.2, 129.9, 123.2, 118.8, 115.7, 18.1, 10.8. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_9H_{11}N_3Na$, 184.0851; found, 184.0850.



3-butyl-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6w)

Colorless oil; Yield: 52%; R_f = 0.22 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.57 (d, *J* = 10 Hz, 1H), 7.02 (d, *J* = 9.2 Hz, 1H), 2.99 (t, *J* = 7.8 Hz, 2H), 2.30 (s, 3H), 1.83 (quint, *J* = 7.2 Hz, 2H), 1.43 (sext, *J* = 7.2 Hz, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 149.1, 146.4, 129.9, 123.2, 118.9, 115.7, 28.5, 24.2, 22.3, 18.1, 13.6. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{11}H_{15}N_3Na$, 212.1164; found, 212.1164.



3-hexyl-6-methyl-[1,2,4]triazolo[4,3-*a*]pyridine (6x)

Colorless oil; Yield: 59%; R_f = 0.22 (EtOAc/hexane = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 – 7.62 (m, 2H), 7.06 (d, *J* = 10 Hz, 1H), 3.03 (t, *J* = 7.2 Hz, 2H), 2.34 (s, 3H), 1.89 (quint, *J* = 7.2 Hz, 2H), 1.47 – 1.42 (m, 2H), 1.34 – 1.33 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 149.2, 146.4, 129.8, 123.2, 118.9, 115.8, 31.3, 28.9, 26.4, 24.6, 22.4, 18.1, 13.9. HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{13}H_{19}N_3Na$, 240.1477; found, 240.1479.

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Crystal preparation and X-ray crystal structure of compound 3h.

Compound **3h** (2.5 mg) was dissolved in a mixture of 0.8 mL/0.2 mL of Methanol/Dichloromethane, and it was crystallized to give crystal as colorless prisms after the solvent was slowly volatilized in 2 days at room temperature (~ 25 °C). Structure of **3h** was identified by X-ray diffraction analysis (see Figure S1).

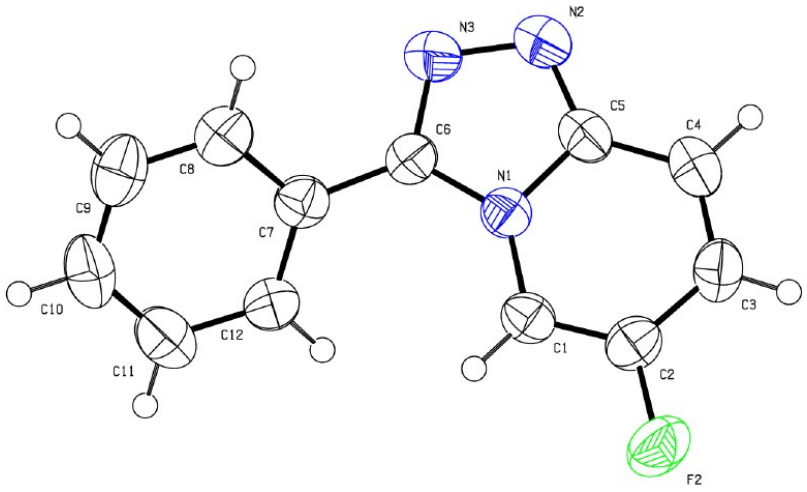

Figure S1. ORTEP X-Ray crystal Structure display of **3h** (CCDC No. 1487670); ellipsoids drawn at 50% probability level

Crystal preparation and X-ray crystal structure of compound 6k.

Compound **6k** (2.5 mg) was dissolved in a mixture of 0.8 mL/0.2 mL of Methanol/Dichloromethane, and it was crystallized to give crystal as colorless prisms after the solvent was slowly volatilized in 2 days at room temperature (~ 25 °C). Structure of **6k** was identified by X-ray diffraction analysis (see Figure S2).

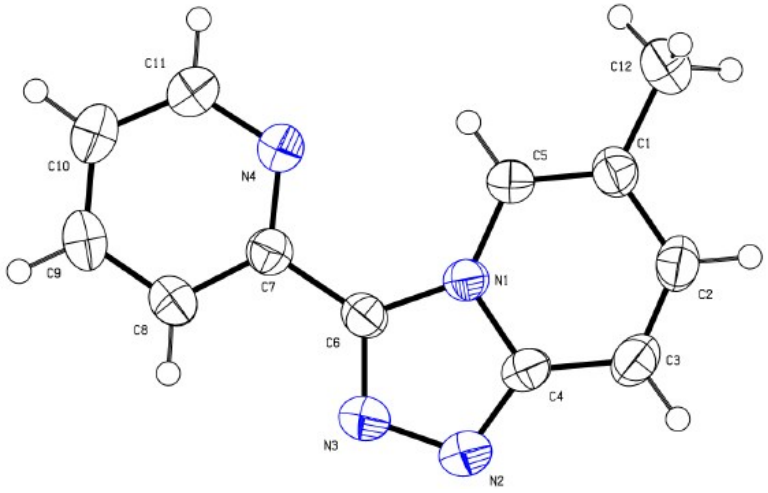

Figure S2. ORTEP X-Ray crystal Structure display of **6k** (CCDC No. 1487669); ellipsoids drawn at 50% probability level