Ru-Catalyzed Selective C–H Functionalization of Pyridotriazoles with Acrylates

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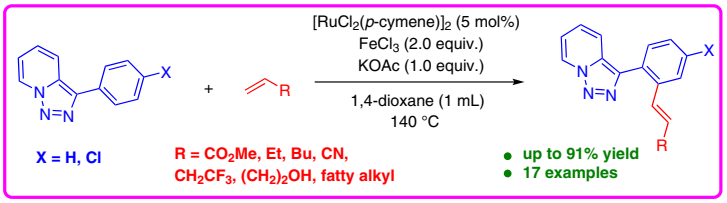

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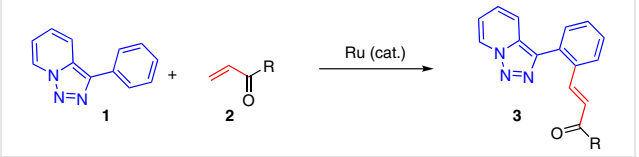
Abstract Ruthenium-catalyzed efficient and selective C–H alkenylation of pyridotriazoles with acrylates is described. The combination of metals (Ru and Fe) plays a crucial role in achieving quantitative yields of the desired products. The reaction is proposed to involve the formation of a ruthenium cyclometalated intermediate.

Key words C–H functionalization, pyridotriazoles, acrylates

Transition-metal-catalyzed C–H bond activation has emerged as a new tool in organic synthesis for the functionalization of arenes.[1] In general, selective C–H functionalization is controlled by the directing/functional groups present on the substrates. Therefore, the use of directing groups by transition-metal-catalyzed C–H functionalization has aroused much attention in recent years.[2] Directing groups such as carboxyl,[3] carbonyl,[4] cyano,[5] and hydroxyl[6] are well-known for various transition-metal-catalyzed C–H functionalizations of arenes.

Pyridotriazole is an important scaffold in organic chemistry and plays an important role in several transition-metal-catalyzed denitrogenative transannelation reactions to generate diverse heterocycles.[7,8] However, to the best of our knowledge, C–H alkenylation reaction using the pyridotriazole as a directing group to form C(sp^2)–C(sp^2) bonds has never been attempted. In continuation of our works on the transannelation of pyridotriazoles,[8] we herein describe the ruthenium-catalyzed regioselective alkenylation of pyridotriazoles (Scheme 1).

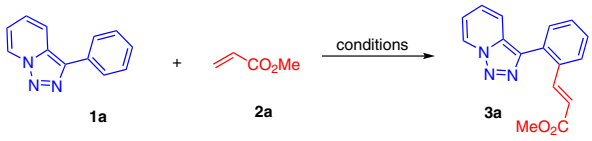


Scheme 1 Alkenylation of pyridotriazoles

Initially, we focused on the optimization of reaction conditions for the selective alkenylation of pyridotriazole **1a** with **2a** in the presence of [$RuCl_2$(*p*-cymene)]$_2$ (5 mol%) as the catalyst with 2.0 equiv. of potassium acetate at 140 °C in 1,4-dioxane (1 mL) for 36 h (Table 1). Under these conditions, a trace amount of product **3a** formation was observed (entry 1). With $Cu(OAc)_2$ (0.5 equiv.) as an additive in the absence of base, 20% yield of **3a** was obtained (entry 2).

When the reaction was performed without any catalyst, no product formation was observed (entry 3). When the reaction was performed with 5 mol% [$RuCl_2$(*p*-cymene)]$_2$, 0.5 equiv. of $Cu(OAc)_2$, and 2.0 equiv. of KOAc, a 42% yield of **3a** was obtained after 48 h (entry 4). After screening various solvents (DCE, toluene, DMF, and DMSO) as well as different catalysts (Co, Ni, and Pd) either no reaction or no improvement in yield was observed (entries 5–12). On increasing the amount of additive $Cu(OAc)_2$, to one and two equivalents, the yield of the product was increased to 62% (entries 13 and 14). Performing the reaction with two equivalents of $ZnCl_2$ and $FeCl_3$ as additives 36% and 73% yields of desired product were obtained, respectively (entries 15 and 16). With $FeCl_3$ as additive, the amount of base (KOAc) was decreased to 1.0 equiv., and under these conditions the desired product **3a** was obtained in 90% yield (entry 17). On decreasing the base to 0.5 equiv. the yield was reduced to 74% (entry 18). The best yield of **3a** was thus obtained un-

Table 1 Optimization of Reaction Conditions for **3a**[a]



1a + **2a** → **3a**

Entry	Catalyst (5 mol%)	Additive (equiv.)	Base (equiv.)	Solvent (1 mL)	Yield (%)[b]
1	$[RuCl_2(p\text{-cymene})]_2$	–	KOAc (2.0)	1,4-dioxane	trace
2	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$ (0.5)	–	1,4-dioxane	20
3	–	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	1,4-dioxane	nr
4	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	1,4-dioxane	42
5	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	DCE	nr
6	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	toluene	nr
7	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	DMF	nr
8	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	DMSO	nr
9	$Pd(OAc)_2$	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	1,4-dioxane	26
10	PdI_2	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	1,4-dioxane	20
11	$Co(OAc)_2$	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	1,4-dioxane	nr
12	$Ni(acac)_2$	$Cu(OAc)_2$ (0.5)	KOAc (2.0)	1,4-dioxane	nr
13	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$ (1.0)	KOAc (2.0)	1,4-dioxane	53
14	$[RuCl_2(p\text{-cymene})]_2$	$Cu(OAc)_2$ (2.0)	KOAc (2.0)	1,4-dioxane	62
15	$[RuCl_2(p\text{-cymene})]_2$	$ZnCl_2$ (2.0)	KOAc (2.0)	1,4-dioxane	36
16	$[RuCl_2(p\text{-cymene})]_2$	$FeCl_3$ (2.0)	KOAc (2.0)	1,4-dioxane	73
17	$[RuCl_2(p\text{-cymene})]_2$	$FeCl_3$ (2.0)	KOAc (1.0)	1,4-dioxane	90
18	$[RuCl_2(p\text{-cymene})]_2$	$FeCl_3$ (2.0)	KOAc (0.5)	1,4-dioxane	74

[a] Conditions: **1a** (0.25 mmol), **2a** (0.5 mmol), catalyst, additive, base, solvent (1 mL), in an oil bath at 140 °C for 24 h.
[b] Isolated yield.

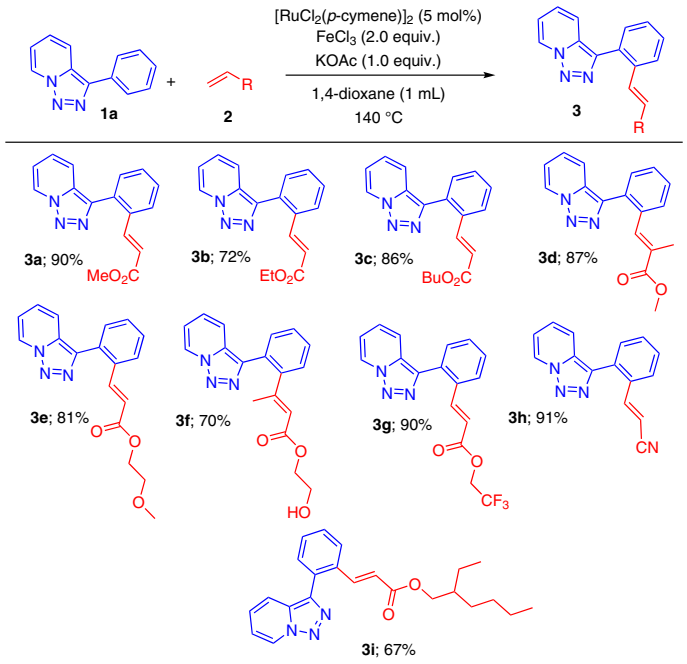
der the conditions of entry 17; hence these parameters were set as optimum for further alkenylations of pyridotriazoles with different acrylates (Table 1).

With this set of optimized conditions, the C–H functionalization of 3-phenyl[1,2,3]triazolo[1,5-*a*]pyridine (**1a**) with different acrylates was examined (Scheme 2).

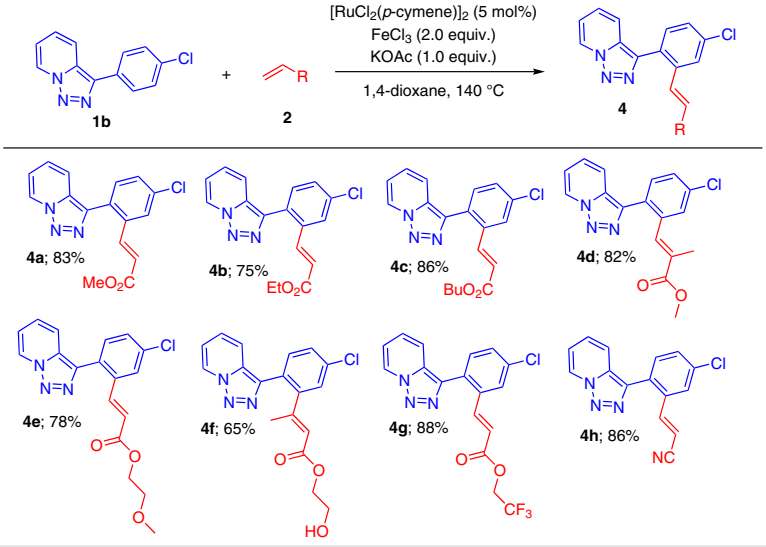
Acrylates bearing Me, Et, and Bu groups at the terminal position reacted smoothly with 3-phenyl-[1,2,3]triazolo[1,5-*a*]pyridine (**1a**) to afford the corresponding alkenylated products **3a–c** in good to excellent yields (72–90%). The reaction of methyl methacrylate also gave the corresponding functionalized product **3d** in good yield (87%). Other acrylates such as 2-methoxyethyl acrylate, 2-hydroxyethyl (*Z*)-but-2-enoate, and 2,2,2-trifluoroethyl acrylate reacted well under the optimized conditions and afforded the corresponding products **3e–g** in good to excellent yields (70–90%). Under the same conditions, 3-[(allyloxy)methyl]heptane and acrylonitrile afforded the corresponding products **3h** and **3i** in 91% and 67% yields, respectively. As is evident from the yields of products **3f–i**, effects associated with electron-donating or electron-withdrawing substituents on the acrylate moiety do not affect the efficiency of the transformation.

This transformation is not limited to the 3-phenyl[1,2,3]triazolo[1,5-*a*]pyridine (**1a**); indeed, the triazole bearing a chlorine substituent at the 4-position of the phenyl ring 3-(4-chlorophenyl)-[1,2,3]triazolo[1,5-*a*]pyridine (**1b**) proved to be amenable to this procedure under the same optimized conditions. Similar reactivities of a range of acrylates were observed with **1b** and afford the differently functionalized products **4a–h** in good yields ranging from 65–88% (Scheme 3).

To gain insight into the reaction mechanism, some control experiments were performed (Scheme 4). Initially, the reaction was conducted by the addition of the radical scavenger TEMPO under the optimized conditions to establish whether the reaction proceeds via a radical or ionic pathway (Scheme 4a). Under these conditions, no adduct formation was observed, indicating that the reaction does not proceed through a radical pathway. However, 2-benzoyl pyridine (**5**) was observed as a side product. To establish

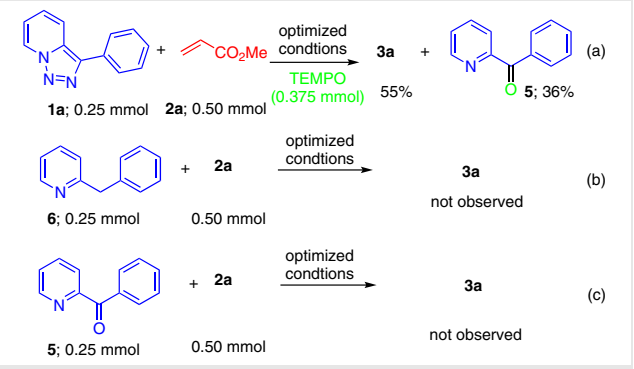


Scheme 2 Substrate scope of triazolo[1,5-*a*]pyridines. *Reagents and conditions*: **1a** (0.25 mmol), **2** (0.5 mmol), catalyst (5 mol%), additive (2.0 equiv.), base (1.0 equiv.), solvent (1 mL), in an oil bath, isolated yield.



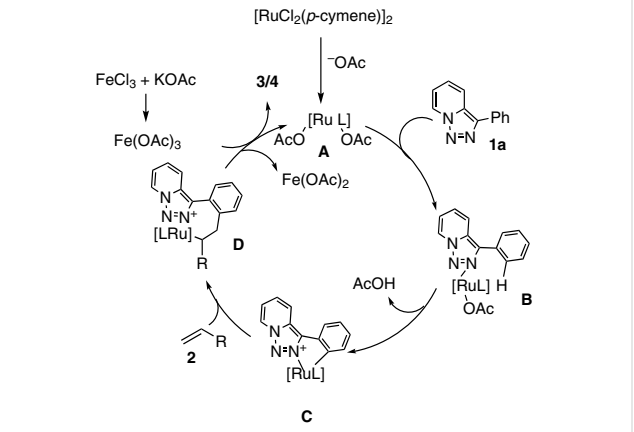
Scheme 3 Substrate scope with 3-(4-chlorophenyl)-[1,2,3]triazolo[1,5-*a*]pyridine. *Reagents and conditions*: **1b** (0.25 mmol), **2** (0.5 mmol), catalyst (5 mol%), additive (2.0 equiv.), base (1.0 equiv.), solvent (1 mL), in carousel reaction station, 48 h, isolated yield.

possible intermediates, 2-benzylpyridine (**6**) was reacted with **2a** under the standard conditions, but the expected product **3a** was not observed (Scheme 4b). Furthermore, when 2-benzoylpyridine (**5**) was reacted with **2a** under the same conditions, it did not yield **3a** (Scheme 4c). These two reactions (Scheme 4b and c) suggest that both **5** and **6** are not intermediates in the reaction pathway.



Scheme 4 Control experiments

Based on the control experiments and literature reports,[9] a plausible reaction mechanism is proposed (Scheme 5). Initially, $[RuCl_2(p\text{-cymene})]_2$ in the presence of base (KOAc) generates the active Ru(II) species **A**, which upon coordination with a nitrogen of the pyridotriazole ring and subsequent ligand-assisted C–H ruthenation via intermediate **B** gives the ruthenacyclic intermediate **C**.



Scheme 5 Plausible reaction mechanism

Coordination of the Ru center of **C** with the addition of the alkene leads to the ruthenacyclic intermediate **D** that, followed by β-hydride elimination, gives the desired alkenylated products **3**/**4**.

In conclusion, we have developed a ruthenium-catalyzed regioselective C–H alkenylation of pyridotriazoles with a range of acrylates.[10] Different acrylates bearing Me, Et, Bu, trifluoroethyl, 2-methoxyethyl acrylate, 2-hydroxyethyl (*Z*)-but-2-enoate, 3-((allyloxy)methyl)heptane, and acrylonitrile reacted smoothly and afforded the corresponding products in good yields. Control experiments suggest that the reaction proceeds through an ionic pathway.

Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-1661-5655.

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(10) **Experimental Section**

All commercially available chemicals and reagents were used without any further purification unless otherwise indicated. ^{1}H and ^{13}C NMR spectra were recorded at 600, 200, 150, and 125 MHz, respectively. Spectra were recorded in $CDCl_3$ as solvent. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), and coupling constants (*J*) are given in Hz. Chemical shifts are reported in ppm relative to TMS as an internal standard. Mass spectra were obtained using electron impact (EI) ionization. Progress of the reactions was monitored by thin-layer chromatography (TLC). All products were purified through column chromatography using silica gel with 100–200 mesh size using ethyl acetate/hexane as eluent unless otherwise stated.

General Procedures(A) Synthesis of Triazolopyridine Derivatives 1

Hydrazine monohydrate (0.30 mmol) and acetic acid (0.02 mmol) were added to a solution of the requisite 2-acylpyridine (0.20 mmol) in ethanol (1.0 mL) at room temperature. The reaction mixture was heated at reflux for 6 h, and then EtOAc (5.0 mL) and $Cu(OAc)_2$ (0.01 mmol) were added. After stirring at the indicated temperature for the indicated time, the resulting mixture was cooled to room temperature and then diluted with EtOAc (20 mL). The organic phase was washed with water (10 mL) and then dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, followed by purification by column chromatography, the desired triazolopyridine derivatives were isolated.

(B) Synthesis of Methyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}phenyl)acrylate (3a)

To a reaction tube equipped with a magnetic stir bar, 3-phenyl[1,2,3]triazolo[1,5-*a*]pyridine (**1a**, 48.8 mg, 0.25 mmol), methyl acrylate (**2a**, 43.1 mg, 0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (6.75 mg, 5 mol%), $FeCl_3$ (81.1 mg, 0.5 mmol), and base KOAc (24.5 mg, 0.25 mmol) were added, followed by dry 1,4-dioxane (1 mL). The mixture was heated in a carousel reaction station at 140 °C in a closed tube for 48 h, and progress was monitored by TLC. After completion of reaction, it was allowed to cool to room temperature. Then the mixture was poured into brine (30 mL). The product was extracted with EtOAc (3 × 15 mL) and dried with anhydrous Na_2SO_4. After filtration and removal of solvent under reduced pressure the residue was purified by column chromatography using silica gel (20% EtOAc/hexane) to afford **3a** (62.8 mg, 90% yield).

Characterization DataMethyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}phenyl)acrylate (3a)

Yield (62.8 mg, 90% yield, semisolid), eluent 25% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 7.2 Hz, 1 H), 7.89 (d, *J* = 16.0 Hz, 1 H), 7.81 (d, *J* = 7.7 Hz, 1 H), 7.66–7.64 (m, 2 H), 7.53 (t, *J* = 7.4 Hz, 1 H), 7.49 (d, *J* = 7.2 Hz, 1 H), 7.31–7.27 (m, 1 H), 7.06 (t, *J* = 6.8 Hz, 1 H), 6.51 (d, *J* = 16.0 Hz, 1 H), 3.73 (s, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.1, 143.2, 136.6, 133.4, 132.0, 131.2, 130.8, 130.1, 128.7, 127.1, 125.8, 125.5, 119.3, 118.1, 115.5, 51.6. ESI-HRMS: *m/z* [M + Na]$^+$ calcd for $C_{19}H_{15}NONa$: 302.0900; found: 302.0898.

Ethyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}phenyl)acrylate (3b)

Yield (52.8 mg, 72% yield, semisolid), eluent 20% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.79 (dd, *J* = 6.9, 2.7 Hz, 1 H), 7.85 (d, *J* = 16.0 Hz, 1 H), 7.80 (d, *J* = 7.7 Hz, 1 H), 7.66 (dd, *J* = 15.4, 8.1 Hz, 2 H), 7.52–7.49 (m, 1 H), 7.47 (t, *J* = 7.4 Hz, 1 H), 7.28 (d, *J* = 6.9 Hz, 1 H), 7.03 (t, *J* = 6.9 Hz, 1 H), 6.49 (d, *J* = 15.4 Hz, 1 H), 4.19–4.15 (m, 2 H), 1.25 (td, *J* = 6.9, 1.9 Hz, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.6, 143.0, 136.6, 133.4, 132.0, 131.2, 130.8, 130.1, 128.7, 127.1, 125.8, 125.5, 119.8, 118.1, 115.4, 60.4, 14.2. ESI-HRMS: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}N_3O_2Na$: 316.1056; found: 316.1056.

Butyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}phenyl)acrylate (3c)

Yield (69.1 mg, 86% yield, semisolid), eluent 20% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.79 (d, *J* = 7.1 Hz, 1 H), 7.83–7.79 (m, 2 H), 7.67 (d, *J* = 7.3 Hz, 1 H), 7.63 (d, *J* = 8.9 Hz, 1 H), 7.53–7.450 (m, 1 H), 7.48 (t, *J* = 7.5 Hz, 1 H), 7.29–7.26 (m, 1 H), 7.04 (q, *J* = 7.1 Hz, 1 H), 6.50 (d, *J* = 15.9 Hz, 1 H), 4.13 (t, *J* = 6.5 Hz, 2 H), 1.61–1.55 (m, 2 H), 1.34–1.24 (m, 2 H), 0.91–0.86 (m, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.7, 142.9, 142.2, 136.6, 133.4, 132.0, 131.2, 130.9, 130.1, 128.7, 128.1, 127.0, 125.8, 125.5, 120.7, 119.8, 118.1, 115.4, 64.3, 30.6, 19.1, 19.0, 13.7. GC–MS: *m/z* [M] calcd for $C_{19}H_{19}N_3O_2$: 321.1477; found: 321.00.

Methyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}phenyl)-2-methylacrylate (3d)

Yield (63.8 mg, 87% yield, semisolid), eluent 25% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.76 (d, *J* = 7.1 Hz, 1 H), 7.71–7.70 (m, 1 H), 7.63 (s, 1 H), 7.55 (d, *J* = 8.7 Hz, 1 H), 7.50–7.46 (m, 3 H), 7.25–7.22 (m, 1 H), 7.01 (t, *J* = 6.7 Hz, 1 H), 3.68 (s, 3 H), 2.06 (s, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.1, 166.7, 143.7, 143.6, 141.0, 134.8, 133.9, 130.8, 130.7, 130.5, 129.8, 129.2, 129.1, 128.4, 127.9, 124.0, 122.9, 120.4, 112.8, 52.5, 29.8. GC–MS: *m/z* [M] calcd for $C_{17}H_{15}N_3O_2$: 293.1164; found: 293.10.

2-Methoxyethyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}-phenyl)acrylate (3e)

Yield (65.5 mg, 81% yield, semisolid), eluent 25% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.83 (d, *J* = 7.0 Hz, 1 H), 7.84 (s, 1 H), 7.82–7.80 (m, 2 H), 7.65 (d, *J* = 8.5 Hz, 2 H), 7.53 (dd, *J* = 8.2, 1.8 Hz, 1 H), 7.36–7.32 (m, 1 H), 7.10 (t, *J* = 6.7 Hz, 1 H), 6.60 (d, *J* = 15.9 Hz, 1 H), 4.34–4.32 (m, 2 H), 3.65–3.63 (m, 2 H), 3.41 (s, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.4, 142.4,

135.7, 135.1, 135.0, 132.2, 130.3, 129.8, 127.2, 126.3, 125.7, 120.7, 118.0, 115.7, 70.5, 63.8, 59.1. GC–MS: *m/z* [M] calcd for $C_{18}H_{17}N_3O_3$: 323.1270; found: 323.00.

2-Hydroxyethyl (*E*)-3-(2-{[1,2,3]triazolo[1,5-*a*]pyridin-3-yl}phenyl)but-2-enoate (3f)

Yield (56.6 mg, 70% yield, semisolid), eluent 50% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.76 (s, 1 H), 7.76 (d, *J* = 41.3 Hz, 2 H), 7.60 (s, 1 H), 7.51–7.48 (m, 3 H), 7.26 (s, 2 H), 7.01 (s, 1 H), 4.24 (s, 2 H), 3.78 (s, 2 H), 2.07 (s, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.7, 139.2, 137.2, 134.7, 131.8, 130.8, 130.2, 128.8, 128.5, 128.1, 125.6, 118.4, 115.5, 66.6, 61.4, 14.2. GC–MS: *m/z* [M] calcd for $C_{18}H_{17}N_3O_3$: 323.1270; found: 323.00.

2,2,2-Trifluoroethyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}phenyl)acrylate (3g)

Yield (78.0 mg, 90% yield, semisolid), eluent 10% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 7.1 Hz, 1 H), 8.02 (d, *J* = 15.9 Hz, 1 H), 7.83 (d, *J* = 7.9 Hz, 1 H), 7.69 (d, *J* = 7.8 Hz, 1 H), 7.65 (d, *J* = 8.9 Hz, 1 H), 7.55 (t, *J* = 7.7 Hz, 1 H), 7.49 (d, *J* = 7.6 Hz, 1 H), 7.31–7.28 (m, 1 H), 7.06 (t, *J* = 6.8 Hz, 1 H), 6.56 (d, *J* = 16.0 Hz, 1 H), 4.55 (q, *J* = 8.2 Hz, 2 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.0, 164.2, 146.9, 145.8, 136.4, 132.9, 132.1, 131.7, 130.8, 130.3, 129.6, 129.4, 129.1, 128.9, 128.0, 127.4, 126.7, 126.2, 125.7, 125.7, 125.6, 125.5, 124.0, 122.2, 118.5, 118.2, 118.0, 117.4, 115.6, 115.6, 60.7, 60.4, 60.2, 60.0. GC–MS: *m/z* [M] calcd for $C_{17}H_{12}F_3N_3O_2$: 347.0882; found: 347.00.

(*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}phenyl)acrylonitrile (3h)

Yield (56.0 mg, 91% yield, semisolid), eluent 30% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 7.0 Hz, 1 H), 7.77 (d, *J* = 16.8 Hz, 1 H), 7.72 (d, *J* = 7.8 Hz, 1 H), 7.69 (d, *J* = 8.7 Hz, 1 H), 7.64 (d, *J* = 7.6 Hz, 1 H), 7.57 (t, *J* = 7.5 Hz, 1 H), 7.50 (t, *J* = 7.5 Hz, 1 H), 7.36–7.33 (m, 1 H), 7.09 (t, *J* = 6.9 Hz, 1 H), 5.94 (d, *J* = 17.0 Hz, 1 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.3, 136.1, 132.7, 132.0, 131.0, 130.8, 130.6, 130.6, 128.8, 126.5, 126.3, 125.6, 118.1, 117.7, 115.7, 97.5. GC–MS: *m/z* [M] calcd for $C_{15}H_{10}N_4$: 246.0905; found: 246.20.

2-Ethylhexyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}phenyl)acrylate (3i)

Yield (60.6 mg, 67% yield, yellow liquid), eluent 15% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.80–8.79 (m, 1 H), 7.78–7.72 (m, 2 H), 7.62 (t, *J* = 8.7 Hz, 2 H), 7.49 (dd, *J* = 8.1, 2.3 Hz, 1 H), 7.31–7.29 (m, 1 H), 7.06 (t, *J* = 6.5 Hz, 1 H), 6.51 (d, *J* = 16.1 Hz, 1 H), 4.07 (qd, *J* = 10.9, 5.7 Hz, 2 H), 1.56 (t, *J* = 6.0 Hz, 1 H), 1.31–1.24 (m, 11 H), 0.88–0.83 (m, 8 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.6, 141.6, 135.7, 135.1, 134.9, 132.2, 132.1, 130.2, 129.8, 127.1, 126.2, 125.7, 121.1, 118.0, 115.6, 67.1, 38.8, 30.4, 29.0, 23.8, 23.0, 14.1, 11.1. GC–MS: *m/z* [M] calcd for $C_{23}H_{27}N_3O_2$: 377.2103; found: 377.30.

Methyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}-5-chlorophenyl)acrylate (4a)

Yield (65.1 mg, 83% yield, semisolid), eluent 25% ethyl acetate/hexane). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 7.0 Hz, 1 H), 7.81–7.76 (m, 2 H), 7.61–7.58 (m, 2 H), 7.49 (d, *J* = 8.1 Hz, 1 H), 7.32–7.30 (t, *J* = 6.0 Hz, 1 H), 7.06 (d, *J* = 6.8 Hz, 1 H), 6.50 (d, *J* = 16.1 Hz, 1 H), 3.73 (s, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.7, 141.9, 135.5, 135.0, 134.8, 132.0, 130.1, 129.6, 127.1, 126.2, 125.6, 120.5, 117.8, 115.6, 51.8. GC–MS: *m/z* [M] calcd for $C_{16}H_{12}ClN_3O_2$: 313.0618; found: 313.00.

Ethyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}-5-chlorophenyl)acrylate (4b)

Yield (61.3 mg, 75% yield, semisolid), eluent 20% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.77 (s, 1 H), 7.84–7.79 (m, 2 H), 7.65 (s, 2 H), 7.50–7.46 (m, 2 H), 7.27 (s, 1 H), 7.02 (s, 1 H), 6.49 (d, *J* = 15.7 Hz, 1 H), 4.17 (s, 2 H), 1.24 (s, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.8, 143.1, 136.7, 133.6, 132.2, 131.4, 131.0, 130.2, 128.9, 127.2, 125.9, 125.6, 120.0, 118.3, 115.6, 60.5, 14.4. ESI-HRMS: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{14}ClN_3O_2Na$: 350.0667; found: 350.0632.

Butyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}-5-chlorophenyl)acrylate (4c)

Yield (76.5 mg, 86% yield, semisolid), eluent 20% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 7.1 Hz, 1 H), 7.82 (d, *J* = 7.8 Hz, 1 H), 7.68 (d, *J* = 7.3 Hz, 1 H), 7.64 (d, *J* = 8.9 Hz, 1 H), 7.54 (t, *J* = 7.4 Hz, 1 H), 7.49 (t, *J* = 7.5 Hz, 1 H), 7.30–7.27 (m, 1 H), 7.05 (t, *J* = 6.8 Hz, 1 H), 6.51 (d, *J* = 15.9 Hz, 1 H), 4.14 (t, *J* = 6.5 Hz, 2 H), 1.62–1.58 (m, 2 H), 1.36–1.33 (m, 2 H), 0.92–0.88 (m, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.0, 159.3, 156.9, 143.9, 138.1, 136.8, 136.2, 130.2, 129.1, 127.6, 122.3, 120.9, 120.5, 114.9, 114.4, 114.3, 113.9, 112.1, 105.4, 55.3, 32.4, 31.2, 30.3. GC–MS: *m/z* [M] calcd for $C_{19}H_{18}ClN_3O_2$: 355.1058; found: 355.10.

Methyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}-5-chlorophenyl)-2-methylacrylate (4d)

Yield (67.2 mg, 82% yield, semisolid), eluent 25% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.77 (d, *J* = 7.1 Hz, 1 H), 7.72–7.70 (m, 1 H), 7.64 (s, 1 H), 7.56 (d, *J* = 8.7 Hz, 1 H), 7.51–7.49 (m, 1 H), 7.48 (d, *J* = 3.3 Hz, 1 H), 7.25 (t, *J* = 7.32 Hz, 1 H), 7.02 (t, *J* = 6.7 Hz, 1 H), 3.69 (s, 3 H), 2.07 (s, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.0, 134.8, 131.2, 129.9, 129.0, 128.5, 126.5, 124.8, 124.2, 123.0, 121.7, 121.0, 115.0, 114.3, 109.2, 55.5, 29.7. GCMS: *m/z* [M] calcd for $C_{17}H_{14}ClN_3O_2$: 327.0775; found: 327.05.

2-Methoxyethyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}-5-chlorophenyl)acrylate (4e)

Yield (69.8 mg, 78% yield, semisolid), eluent 25% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.79 (d, *J* = 7.0 Hz, 1 H), 7.80–7.76 (m, 2 H), 7.60 (d, *J* = 8.5 Hz, 2 H), 7.49 (dd, *J* = 8.2, 1.8 Hz, 1 H), 7.32–7.28 (m, 1 H), 7.06 (t, *J* = 6.7 Hz, 1 H), 6.56 (d, *J* = 15.9 Hz, 1 H), 4.30–4.28 (m, 2 H), 3.61–3.59 (m, 2 H), 3.37 (s, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.2, 142.2, 135.5, 134.9, 134.8, 132.0, 130.2, 129.7, 127.1, 126.2, 125.6, 120.5, 117.8, 115.6, 70.4, 63.7, 59.0. GC–MS: *m/z* [M] calcd for $C_{18}H_{16}ClN_3O_3$: 357.0880; found: 357.10.

2-Hydroxyethyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}-5-chlorophenyl)but-2-enoate (4f)

Yield (58.1 mg, 65% yield, semisolid), eluent 45% ethyl acetate/hexane). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.83 (d, *J* = 7.1 Hz, 1 H), 7.84–7.80 (m, 2 H), 7.65 (d, *J* = 8.6 Hz, 2 H), 7.53 (d, *J* = 8.3 Hz, 1 H), 7.36–7.32 (m, 1 H), 7.10 (t, *J* = 6.8 Hz, 1 H), 6.60 (d, *J* = 15.8 Hz, 1 H), 4.33 (t, *J* = 4.7 Hz, 2 H), 3.65 (t, *J* = 4.7 Hz, 2 H), 3.41 (s, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.7, 139.2, 137.2, 134.6, 131.8, 130.8, 130.2, 128.7, 128.5, 128.1, 125.6, 118.4, 115.5, 66.6, 61.4, 14.2. GC–MS: *m/z* [M] calcd for $C_{18}H_{16}ClN_3O_3$: 357.0880; found: 357.10.

2,2,2-Trifluoroethyl (*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}-5-chlorophenyl)acrylate (4g)

Yield (84 mg, 88% yield, semisolid), eluent 25% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.71 (d, *J* = 7.2 Hz, 1 H), 7.93 (d, *J* = 16.0 Hz, 1 H), 7.75 (d, *J* = 8.0 Hz, 1 H), 7.60 (d, *J* = 8.0 Hz, 1 H), 7.57 (d, *J* = 9.0 Hz, 1 H), 7.48 (t, *J* = 7.6 Hz, 1 H), 7.42 (q, *J* = 7.8, 7.3 Hz, 1 H), 6.97 (t, *J* = 6.9 Hz, 1 H), 6.47 (d, *J* = 16.0 Hz, 1 H), 4.46 (q, *J* = 8.1 Hz, 2 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.0, 166.6, 143.6, 143.5, 140.9, 134.7, 133.8, 130.7, 130.6, 130.4, 129.7, 129.1, 129.0, 128.3, 127.8, 123.9, 122.8, 120.3, 112.7, 52.4, 29.7. GC–MS: *m/z* [M] calcd for $C_{17}H_{11}ClF_3N_3O_2$: 381.0492; found: 381.30.

(*E*)-3-(2-{[1,2,3]Triazolo[1,5-*a*]pyridin-3-yl}-5-chlorophenyl)acrylonitrile (4h).

Yield (60.4 mg, 86% yield, semisolid), eluent 25% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 7.8 Hz, 1 H), 8.02 (d, *J* = 6.7 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 9.2 Hz, 1 H), 7.48 (t, *J* = 7.5 Hz, 2 H), 7.39 (t, *J* = 7.5 Hz, 1 H), 7.20 (t, *J* = 7.9 Hz, 1 H), 6.81 (t, *J* = 6.7 Hz, 1 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 149.3, 145.7, 140.1, 128.9, 125.3, 125.2, 124.3, 124.1, 124.0, 122.4, 121.5, 118.2, 111.9. GC–MS: *m/z* [M] calcd for $C_{15}H_9ClN_4$: 280.0516; found: 280.0.

Phenyl(pyridin-2-yl)methanone (5)[11]

Yield (14.0 mg, 31% yield, white solid), mp 42–44 ℃), 5% ethyl acetate/hexane. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.71 (d, *J* = 4.3 Hz, 1 H), 8.07 (d, *J* = 7.7 Hz, 2 H), 8.03 (d, *J* = 7.8 Hz, 1 H), 7.88 (t, *J* = 7.7 Hz, 1 H), 7.58 (t, *J* = 7.3 Hz, 1 H), 7.47 (dd, *J* = 14.2, 6.9 Hz, 3 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.7, 154.9, 148.4, 136.9, 136.1, 132.7, 130.8, 128.0, 126.0, 124.4.

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