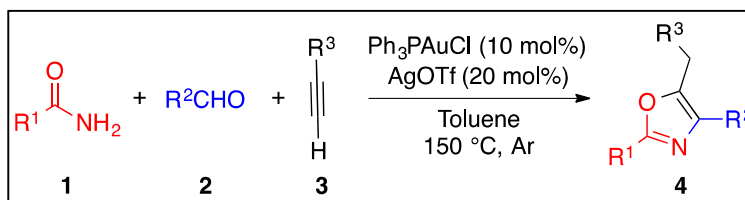


Gold-Catalyzed Tandem Reactions of Amide-Aldehyde-Alkyne Coupling and Cyclization - Synthesis of 2,4,5-Trisubstituted Oxazoles

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Supplementary Information

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1. General Information

Solvents and reagents were purchased from Sigma-Aldrich chemical company and were used without further purification unless otherwise specified. NMR spectra were recorded on a Bruker AV500 spectrometer operating respectively at 500 MHz and 126 MHz for ^1H and ^{13}C acquisitions.

Chemical shifts are reported in ppm with a solvent resonance as an internal standard (^1H -NMR; chloroform as internal standards, indicating 7.26ppm, ^{13}C -NMR; chloroform as internal standard, indicating 77.00ppm). Data are reported as following: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, br = broad signal) and integration. High-resolution mass spectrometry was conducted using atmospheric pressure chemical ionization (APCI) or electro-spraying ionization (ESI), and was performed by McGill University on a Thermo-Scientific Exactive Orbitrap. Protonated molecular ions (M+H)⁺ or sodium adducts (M+Na)⁺, were used for empirical formula confirmation. All preparative chromatography were performed using gradient elution (hexanes and ethyl acetate) on a Biotage Isolera™ One automated chromatography system with SNAP ultra silica gel cartridges and sample cartridges.

2 Experimental details and characterization data for all compounds

General Procedure for optimization of reactions conditions

A V-shaped 10 mL Biotage reaction vial was charged with Ph_3PAuCl (10 mol%, 5.0 mg), AgOTf (20 mol%, 5.0 mg), and the corresponding benzamide (0.1 mmol), evacuated and refilled with argon three times. Freshly distilled toluene (0.25 mL) was added followed by subsequent addition of cyclohexane carboxaldehyde (0.15 mmol) and phenylacetylene (0.15 mmol). The reaction vessel was sealed, placed in an oil bath pre-heated at 150 °C under vigorous stirring (approx. 1400 rpm) and hold for 6 hours. The mixture was cooled to room temperature, diluted with ethyl acetate, filtered through a pad of silica, and rinsed with additional ethyl acetate. The combined rinsing were concentrated and purified by column chromatography or preparative thin layer chromatography to yield the corresponding oxazoles **4**.

Dibromomethane was used as internal standard for ^1H -NMR analysis.

Selected reaction conditions

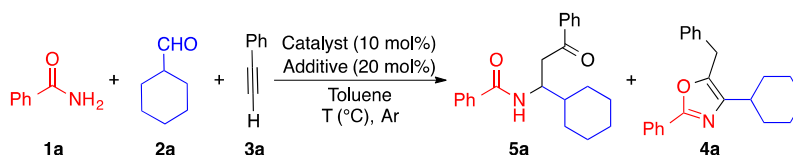


Table S1: Screening and optimization of reaction conditions¹

Entry	Catalyst (10 mol%)	Additive (20 mol%)	T (°C)	Yield (NMR %)	
				5a	4a
1	Cu(OTf) ₂	-	100	35	0
2	Cu(OTf) ₂	PTSA (1 eq)	100	0	0
3	Cu(OTf) ₂	KOAc (1eq)	100	10	0
4	(Cu(OTf) ₂) ₂	-	100	10	0
5	CuCN	-	100	3	0
6	CuCl ₂	-	100	12	0
7	CuBr	-	100	0	0
8	CuBr	RuCl ₃	100	0	0
9	AgOTf	-	100	58	0
10	AgOTf	H ₂ O (1 eq)	100	40	0
11	AgCl	-	100	0	0
12	AuCl(SMe) ₂	-	100	10	0
13	AuBr ₃	-	100	15	0

We started the optimization based on our previous work,² on Copper(II) Triflate-Catalyzed Three-Component Coupling of Aldehydes, Alkynes and Carbamates. Following the optimal conditions developed previously, copper(II) triflate as the catalyst in toluene under 100°C, we were pleased to see the formation of **5a** in 35% yield (entry 1). In order to develop our designed reaction, we looked at the metal acetylide formation, which is a crucial step. Thus the use of organic or inorganic bases in order to help the metal acetylide formation via deprotonation of the terminal alkyne was evaluated. Unfortunately, the use of acid or base (entries 2 and 3) was not beneficial for the formation of **4a**. Copper salt were screened and evaluated in table S1, however **4a** was never detected.

Coinage transition-metal catalysts, such as gold, have shown excellent activity for the A³-coupling, and have been highly effective for the cyclization of acetylenic compounds. Thus, we envisioned that a judicious choice of gold catalyst might effectively catalyze both the A³-coupling and the tandem cyclization steps. Formation of metal-acetylide with silver or gold has been shown in many examples.³ However, gold(I), gold(III) and silver metal catalysts were not efficient to conduct the formation of **4a**. Nevertheless, we were pleased to see that 60% of **5a** was produced in the presence of silver triflate (entry 9). We hypothesized that **5a** was formed via hydration by water, which was delivered during the process. Addition of 1 equivalent of water was not beneficial for the reaction, since the yield dropped to 40% (entry 10).

¹ All reported yields were determined by ¹H NMR spectroscopy using dibromomethane as internal standard.

² X.-Y. Dou, Q. Shuai, L.-N. He and C.-J. Li, *Adv. Synth. Catal.*, 2010, **352**, 2437

³ (a) J. Bucher, T. Wurm, K. S. Nalivela, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Angew. Chem. Int. Ed.*, 2014, **53**, 3854; (b) D. J. Gorin and F. D. Toste, *Nature*, 2007, **446**, 395.

Table S2: Screening and optimization of reaction conditions⁴

Entry	Catalyst (10 mol%)	Additive (20 mol%)	T (°C)	Yield (NMR %)	
				5a	4a
1	AgOTf	DCE	100	44	0
2	AgOTf	MeCN	100	<i>nd</i>	0
3	AgOTf	THF	100	8	0
4	AgOTf	Dioxane	100	14	0
5	AgOTf	H ₂ O	100	0	0
6	AgOTf	MeOH	100	<i>nd</i>	0
7	AgOTf	DMSO	100	<i>nd</i>	0

After a screening of a broad range of different solvent in term of polarity and proticity, toluene demonstrated the best properties for the formation of **5a** (entry 9). In acetonitrile, MeOH and DMSO, we were not able to determine the yield of **5a** due to signals overlap.

After extensive screening of conditions using copper and silver transition metal catalyst, without significant results, we focused our attention on gold catalysis.

Table S3: Screening and optimization of reaction conditions

Entry	Catalyst (10 mol%)	Additive (20 mol%)	T (°C)	Yield (NMR %)	
				5a	4a
1	AuCl	iPr.Cl	100	5	0
2	Ph ₃ PAuCl	AgOTf	100	45	30
3	Et ₃ PAuCl	AgOTf	100	44	14
4	iMesAuCl	AgOTf	100	38	1
5	Ph ₃ PAuCl	AgOTf + acetic anhydride (1 eq)	100	2	2
6	Ph ₃ PAuCl	AgOTf + 4A or 5A Molecular sieves	100	0	0
7	Ph ₃ PAuCl	AgOTf + MgSO ₄	100	0	0
8	Ph ₃ PAuCl	AgOTf + Na ₂ SO ₄	100	33	0
9	AuCl ₃	AgOTf	100	46	0

We were extremely please to see the formation of compound **4a** when gold(I) cationic catalyst was used (entry 2). Evaluating other electronic properties of the phosphine ligands, we did not managed to improve the yield above 30% (entry 3). Other types of ligands, such as N-heterocyclic carbene, were not efficient for

⁴ "nd" : not determined. NMR signals of related product could not clearly be analyzed due to overlapping signals.

the reaction (entry 4). Seeing the overall yield of the reaction reaching the 75%, we wanted to be able to control the selectivity towards the formation of **4a**. Our hypothesis was to trap the water released during the condensation via different methods. Acetic anhydride was used as a water trap, but it resulted in a decrease in yield (entry 5). Dehydrating agents (molecular sieves, MgSO₄) have shown strong impact on the reaction yield (entries 6-7) but none of them have shown any improvement and even completely killed the reaction.

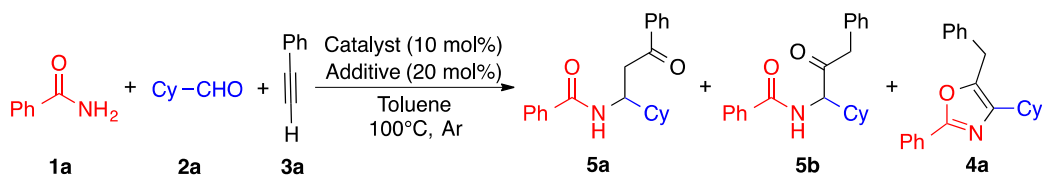


Table S4: Study of reaction time

Entry	Catalyst / Additive	Time	Yield (NMR %)		
			5a	5b	4a
1	Ph ₃ PAuCl / AgOTf	3h	18	11	7
2	Ph ₃ PAuCl / AgOTf	6h	45	10	30
3	Ph ₃ PAuCl / AgOTf	18h	43	12	26
4	Ph ₃ PAuCl / AgOTf	64h	50	10	25

Evaluating the reaction time of our system, no big difference in term of NMR yield was observed. Nevertheless, those results allowed us to get more information about the mechanism of the reaction. Once the hydrated side products **5a** or **5b** were formed, their transformation to the corresponding oxazole moiety was not detected after prolonged reaction time under our reaction condition suggesting that the Robinson-Gabriel pathway is unlikely.

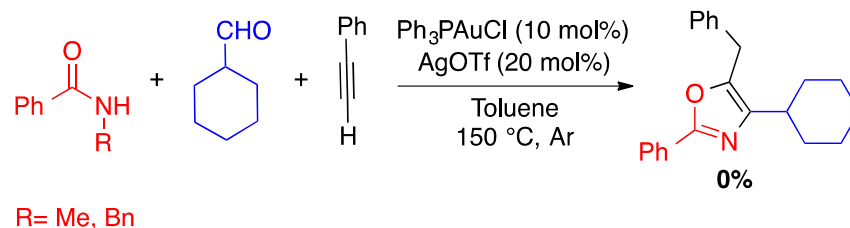
Table S5: Study of reaction temperature.

Entry	Catalyst (10 mol%)	Additive (20 mol%)	T (°C)	Yield % (NMR)	
				5a	4a
1	Ph ₃ PAuCl	-	100	5	0
2	Ph ₃ PAuCl	AgOTf	100	45	30
3	Ph ₃ PAuCl	AgOTf	130	5	45
4	Ph ₃ PAuCl	AgOTf	150	0	99 (95)
5	-	-	150	0	0
6	-	AgOTf	150	10	0

While triphenylphosphinegold(I) chloride on its own did not generate any desired product, the addition of silver(I) triflate furnished product **4a** in 30% yield (entry 2). The counter-anion of silver salt dramatically influenced the yields of the reaction, with triflate giving the best result. When Ph₃PAuCl/AgOTf was

used in toluene at 100 °C, a significant amount of 3-acylamidoketone **5a** was detected, as well as its regioisomer **5b** in a trace amount (< 10%, see Scheme 2). Although a slight improvement of the reaction yield was observed at 130 °C, increasing the reaction temperature to 150 °C drastically accelerated the reaction, leading to complete conversion and excellent yield of the desired product (entries 3-4). In the absence of metal catalyst or additive, no desired product was observed (entry 5-6).

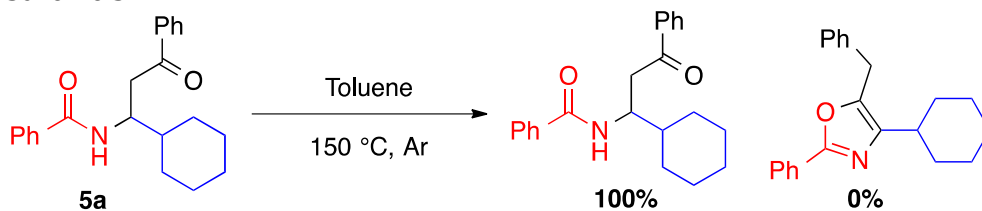
Study of protected amide

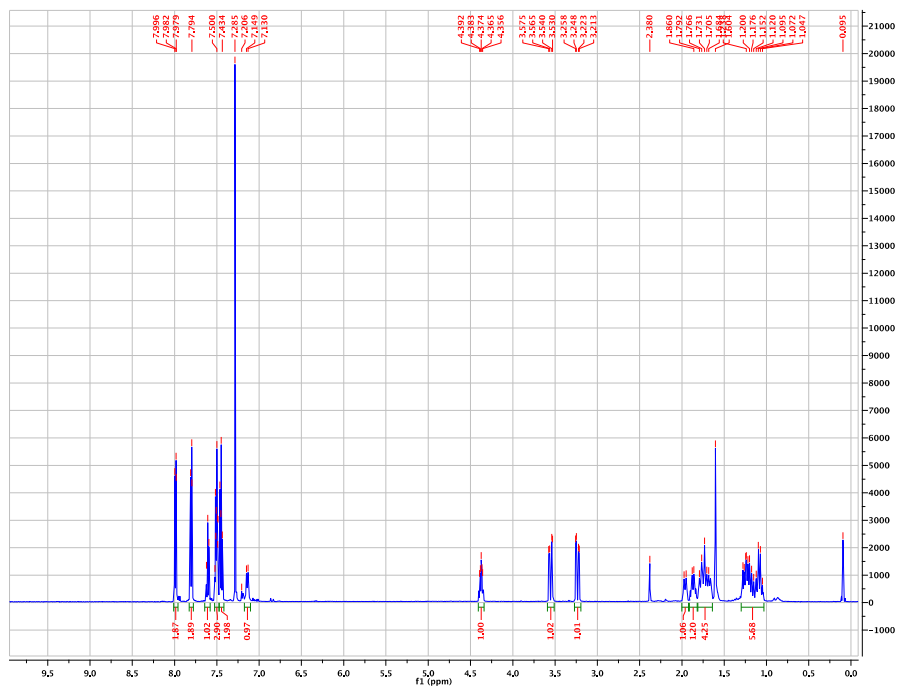


N-protected benzamide were studied in our reaction condition. However the reactions were not successful in forming the corresponding oxazoles. The starting materials were recovered.

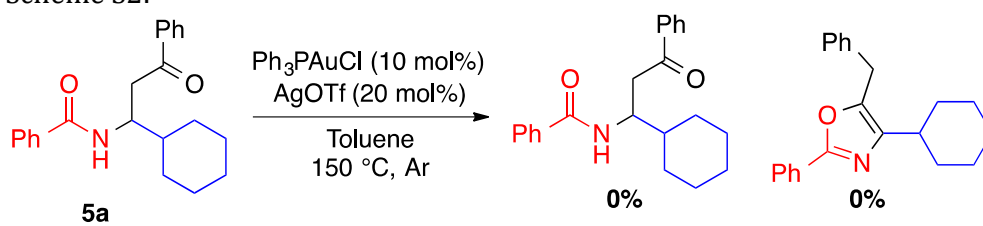
Control experiments concerning 5a (side-product)

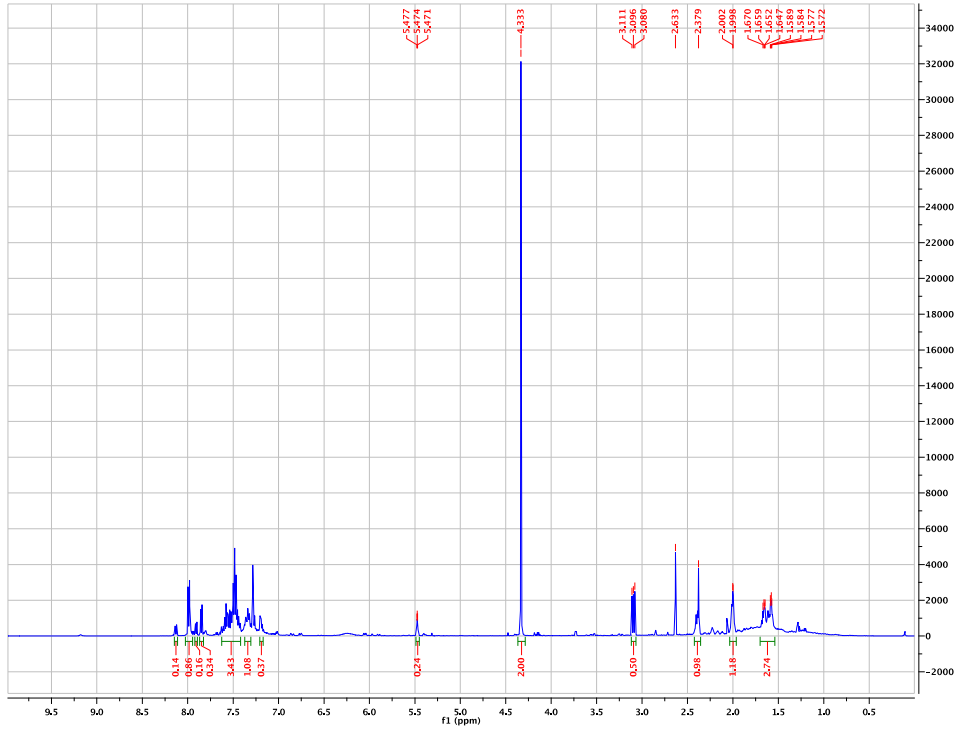
Scheme S1:



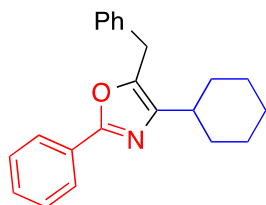


Scheme S2:





3 ^1H NMR and ^{13}C NMR spectra for new compounds



4a

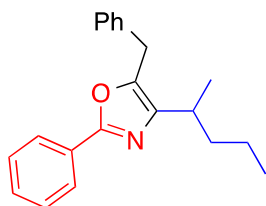
Use the general procedure described above, compound **4a** was obtained from benzamide (0.2 mmol, 24.2 mg), cyclohexane carboxaldehyde (0.3 mmol, 36.3 μL) and phenylacetylene (0.3 mmol, 34 μL) as a white solid (62.7 mg) in 95% yield.

^1H NMR (CDCl₃, 500 MHz): δ = 8.00-7.98 (m, 2H), 7.43-7.39 (m, 3H), 7.33-7.32 (m, 2H), 7.27-7.25 (m, 3H), 4.08 (s, 2H), 2.61-2.55 (tt, J = 11.7, 3.5 Hz, 1H), 1.87-1.80 (m, 4H), 1.74-1.69 (m, 3H), 1.38-1.34 (m, 3H).

^{13}C NMR (CDCl₃, 126 MHz): δ = 159.75, 143.95, 142.13, 138.00, 129.62, 128.60, 128.52, 128.32, 128.02, 126.56, 126.12, 35.67, 32.41, 31.14, 26.55, 25.87.

HRMS (ESI) m/z : $[M + H]^+$ calculated for C₂₂H₂₄NO 318.1858, found 318.18585.

R_f (hexane/EtOAc 4:1): 0.5.



4b

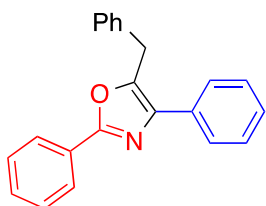
Use the general procedure described above, compound **4b** was obtained from benzamide (0.2 mmol, 24.2 mg), 2-methylpentanal (0.3 mmol, 37 μL) and phenylacetylene (0.3 mmol, 34 μL) as a white solid (30.5 mg) in 50% yield.

^1H NMR (CDCl₃, 500 MHz): δ = 8.01-7.99 (m, 2H), 7.42-7.39 (m, 3H), 7.35-7.32 (m, 2H), 7.27-7.25 (m, 3H), 4.05 (s, 2H), 2.73-2.80 (sext, J = 6.8 Hz, 1H), 1.76-1.70 (m, 1H), 1.61-1.54 (m, 1H), 1.29-1.28 (d, J = 6.9 Hz, 3H), 1.28-1.24 (m, 1H), 0.99-0.92 (m, 1H), 0.87-0.90 (t, J = 7.4 Hz, 3H).

^{13}C NMR (CDCl₃, 126 MHz): δ = 159.89, 144.46, 141.62, 137.95, 129.63, 128.52, 128.48, 128.36, 128.06, 126.56, 126.15, 38.44, 31.02, 30.60, 20.87, 20.58, 14.07.

HRMS (ESI) m/z : $[M + H]^+$ calculated for C₂₁H₂₄NO 306.1858, found 306.18542.

R_f (hexane/EtOAc 4:1): 0.5.



4c

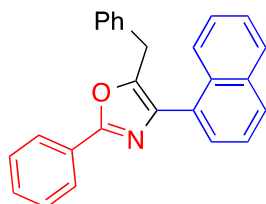
Use the general procedure described above, compound **4c** was obtained from benzamide (0.2 mmol, 24.2 mg), benzaldehyde (0.3 mmol, 32 uL) and phenylacetylene (0.3 mmol, 34 uL) as a white solid (49.7 mg) in 80% yield.

¹H NMR (CDCl₃, 500 MHz): δ = 8.11-8.10 (m, 2H), 7.78-7.76 (m, 2H), 7.49-7.44 (m, 5H), 7.38-7.32 (m, 5H), 7.30-7.28 (m, 1H), 4.34 (s, 2H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.18, 145.62, 137.26, 137.23, 132.06, 130.15, 128.80, 128.69, 128.29, 127.72, 127.54, 127.05, 126.81, 126.34, 31.96.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₂H₁₈NO 312.1388, found 312.13873.

R_f (hexane/EtOAc 4:1): 0.4.



4d

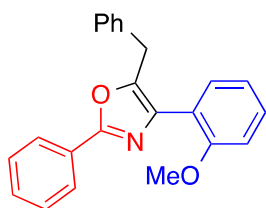
Use the general procedure described above, compound **4d** was obtained from benzamide (0.2 mmol, 24.2 mg), 1-naphthaldehyde (0.3 mmol, 40.8 uL) and phenylacetylene (0.3 mmol, 34 uL) as a white solid (46.9 mg) in 65% yield.

¹H NMR (CDCl₃, 500 MHz): δ = 8.16-8.12 (m, 3H), 7.94-7.92 (m, 2H), 7.57-7.51 (m, 5H), 7.50-7.46 (m, 3H), 7.33-7.30 (m, 2H), 7.26-7.24 (m, 3H), 4.11 (s, 2H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.30, 147.57, 137.37, 136.66, 133.95, 132.25, 130.17, 129.17, 129.00, 128.17, 128.64, 128.49, 128.27, 127.86, 127.63, 126.69, 126.41, 126.36, 126.07, 126.03, 125.21, 31.47.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₆H₂₀NO 362.1545, found 362.15439.

R_f (hexane/EtOAc 4:1): 0.6.



4e

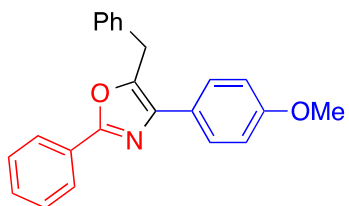
Use the general procedure described above, compound **4e** was obtained from benzamide (0.2 mmol, 24.2 mg), 2-methoxybenzaldehyde (0.3 mmol, 36.3 uL) and phenylacetylene (0.3 mmol, 34 uL) as a white solid (41.5 mg) in 61% yield.

¹H NMR (CDCl₃, 500 MHz): δ = 8.09-8.07 (m, 2H), 7.63-7.61 (m, 1H), 7.46-7.43 (m, 3H), 7.39-7.36 (m, 1H), 7.33-7.27 (m, 4H), 7.27-7.24 (m, 1H), 4.15 (s, 2H), 3.75 (s, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.26, 156.72, 147.35, 137.87, 133.91, 131.31, 129.78, 129.58, 128.60, 128.51, 128.41, 127.64, 126.40, 126.30, 121.06, 120.84, 111.08, 55.32, 32.15.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₃H₂₀NO₂ 342.1494, found 342.14942.

Rf (hexane/EtOAc 4:1): 0.6.



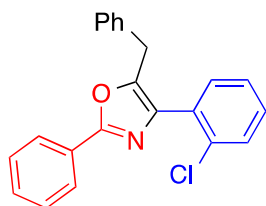
4f

Use the general procedure described above, compound **4f** was obtained from benzamide (0.2 mmol, 24.2 mg), 4-methoxybenzaldehyde (0.3 mmol, 36.6 uL) and phenylacetylene (0.3 mmol, 34 uL) as a white solid (32.0 mg) in 47% yield.

¹H NMR (CDCl₃, 500 MHz): δ = 8.10-8.08 (m, 2H), 7.70-7.67 (m, 2H), 7.48-7.43 (m, 3H), 7.37-7.28 (m, 4H), 7.00-6.97 (m, 2H), 4.31 (s, 2H), 3.86 (s, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.00, 159.23, 144.70, 137.40, 137.05, 130.04, 128.77, 128.65, 128.31, 128.26, 127.63, 126.75, 126.26, 124.69, 114.13, 55.32, 31.91.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₃H₂₀NO₂ 342.1494, found 342.14943.
Rf (hexane/EtOAc 4:1): 0.6.



4g

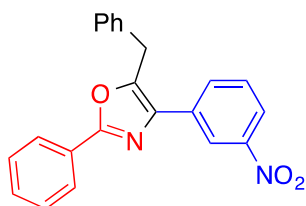
Use the general procedure described above, compound **4g** was obtained from benzamide (0.2 mmol, 24.2 mg), 2-chlorobenzaldehyde (0.3 mmol, 33.6 uL) and phenylacetylene (0.3 mmol, 34 uL) as a white solid (65.7 mg) in 95% yield.

¹H NMR (CDCl₃, 500 MHz): δ = 8.08-8.06 (m, 2H), 7.52-7.49 (m, 2H), 7.46-7.45 (m, 3H), 7.36-7.34 (m, 2H), 7.32-7.29 (m, 2H), 7.25-7.24 (m, 3H), 4.11 (s, 2H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.31, 147.51, 136.98, 135.12, 133.96, 132.04, 131.07, 130.21, 129.94, 129.79, 128.69, 128.57, 128.56, 127.44, 126.81, 126.70, 126.31, 55.32, 31.90.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₂H₁₇ClNO 346.0999, found 346.09961.

Rf (hexane/EtOAc 4:1): 0.6.



4h

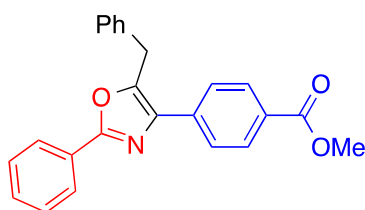
Use the general procedure described above, compound **4h** was obtained from benzamide (0.2 mmol, 24.2 mg), 3-nitrobenzaldehyde (0.3 mmol, 45.3 mg), and phenylacetylene (0.3 mmol, 34 μ L) as a white solid (65.7 mg) in 55% yield.

$^1\text{H NMR}$ (CDCl_3 , 500 MHz): δ = 8.64 (s, 1H), 8.18-8.19 (m, 1H), 8.12-8.08 (m, 3H), 7.62-7.58 (m, 1H), 7.50-7.49 (m, 3H), 7.39-7.33 (m, 4H), 7.31-7.29 (m, 1H), 4.38 (s, 2H).

$^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): δ = 160.51, 148.57, 147.12, 136.28, 135.04, 133.86, 132.55, 130.56, 129.62, 128.99, 128.82, 128.63, 128.30, 127.14, 126.41, 122.25, 121.76, 32.19.

HRMS (ESI) m/z: $[\text{M} + \text{H}]^+$ calculated for $\text{C}_{22}\text{H}_{17}\text{N}_2\text{O}_3$ 357.1239, found 357.12347.

R_f (hexane/EtOAc 4:1): 0.6.



4i

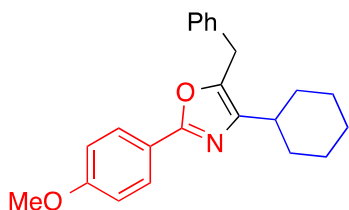
Use the general procedure described above, compound **4i** was obtained from benzamide (0.2 mmol, 24.2 mg), methyl 4-formylbenzoate (0.3 mmol, 49.2 mg) and phenylacetylene (0.3 mmol, 34 μ L) as a white solid (83.1 mg) in 75% yield.

$^1\text{H NMR}$ (CDCl_3 , 500 MHz): δ = 8.13-8.09 (m, 4H), 7.86-7.84 (m, 2H), 7.49-7.47 (m, 3H), 7.36-7.35 (m, 2H), 7.32-7.29 (m, 3H), 4.37 (s, 2H), 3.95 (s, 3H).

$^{13}\text{C NMR}$ (CDCl_3 , 126 MHz): δ = 166.86, 160.41, 146.91, 136.72, 136.54, 136.34, 130.38, 130.00, 129.10, 128.89, 128.75, 128.24, 127.27, 126.98, 126.71, 126.39, 52.13, 32.17.

HRMS (ESI) m/z: $[\text{M} + \text{H}]^+$ calculated for $\text{C}_{24}\text{H}_{20}\text{NO}_3$ 370.1443, found 370.14462.

R_f (hexane/EtOAc 4:1): 0.5.

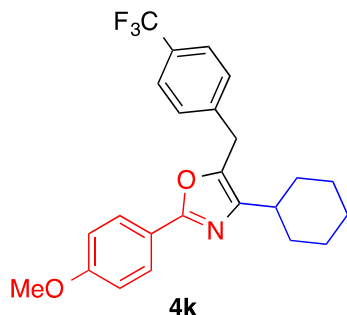


4j

Use the general procedure described above, compound **4j** was obtained from 4-methoxybenzamide (0.2 mmol, 30.24 mg), cyclohexane carboxaldehyde (0.3 mmol, 36.3 μ L) and phenylacetylene (0.3 mmol, 34 μ L) as a white solid (90.6 mg) in 87% yield.

$^1\text{H NMR}$ (CDCl_3 , 500 MHz): δ = 7.93-7.91 (m, 2H), 7.35-7.32 (m, 2H), 7.28-7.25 (m, 3H), 6.94-6.92 (m, 2H), 4.06 (s, 2H), 3.85 (s, 3H), 2.59-2.54 (tt, J = 11.7, 3.5 Hz, 1H), 1.86-1.80 (m, 4H), 1.73-1.67 (m, 3H), 1.38-1.28 (m, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.81, 159.83, 143.29, 141.82, 138.16, 128.58, 128.31, 127.75, 126.51, 120.96, 113.92, 55.32, 35.70, 32.42, 31.12, 26.57, 25.88.
HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₃H₂₆NO₂ 348.1964, found 348.19570.
R_f (hexane/EtOAc 4:1): 0.5.



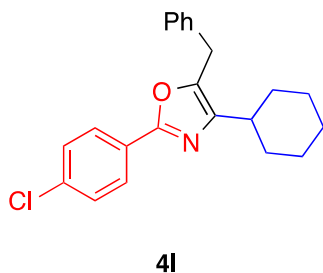
Use the general procedure described above, compound **4k** was obtained from 4-methoxybenzamide (0.2 mmol, 30.24 mg), cyclohexane carboxaldehyde (0.3 mmol, 36.3 uL) and 1-ethynyl-4-(trifluoromethyl) benzene (0.3 mmol, 32.6 uL) as a white solid (59.8 mg) in 72% yield.

¹H NMR (CDCl₃, 500 MHz): δ = 7.92-7.90 (m, 2H), 7.59-7.58 (m, 2H), 7.37-7.35 (m, 2H), 6.94-6.92 (m, 2H), 4.11 (s, 2H), 3.85 (s, 3H), 2.58-2.53 (tt, J = 11.7, 3.5 Hz, 1H), 1.87-1.79 (m, 4H), 1.73-1.66 (m, 3H), 1.38-1.31 (m, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.96, 160.14, 142.31, 142.21, 142.20, 142.16, 128.62, 127.79, 125.54 (q, J = 3 Hz), 120.69, 113.97, 55.33, 35.74, 32.42, 30.95, 26.52, 25.82.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₄H₂₅F₃NO₂ 416.1837, found 416.18309.

R_f (hexane/EtOAc 4:1): 0.5.



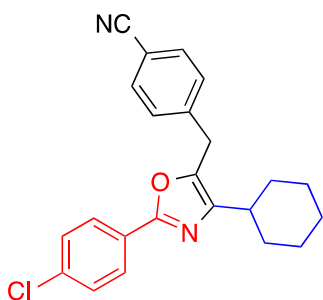
Use the general procedure described above, compound **4l** was obtained from 4-chlorobenzamide (0.2 mmol, 31.10 mg), cyclohexane carboxaldehyde (0.3 mmol, 36.3 uL) and phenylacetylene (0.3 mmol, 34 uL) as a white solid (49.2 mg) in 70% yield.

¹H NMR (CDCl₃, 500 MHz): δ = 7.93-7.91 (m, 2H), 7.40-7.37 (m, 2H), 7.35-7.30 (m, 2H), 7.28-7.24 (m, 3H), 4.07 (s, 2H), 2.60-2.54 (tt, J = 11.9, 3.6 Hz, 1H), 1.87-1.79 (m, 4H), 1.75-1.66 (m, 3H), 1.41-1.31 (m, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ = 158.85, 144.30, 142.31, 137.80, 135.63, 128.81, 128.65, 128.32, 127.41, 126.65, 126.49, 35.59, 32.40, 31.13, 26.52, 25.85.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₂H₂₃ClNO 352.1468, found 352.14639.

Rf (hexane/EtOAc 4:1): 0.5.



4m

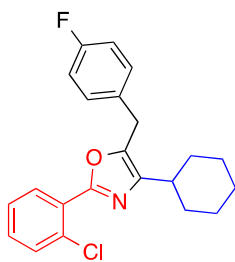
Use the general procedure described above, compound **4m** was obtained from 4-chlorobenzamide (0.2 mmol, 31.10 mg), 4-ethynylbenzonitrile (0.3 mmol, 38.2 mg) and cyclohexane carboxaldehyde (0.3 mmol, 36.3 uL) as a white solid (58.7 mg) in 78% yield.

¹H NMR (CDCl₃, 500 MHz): δ = 7.91-7.89 (m, 2H), 7.64-7.62 (m, 2H), 7.40-7.38 (m, 2H), 7.35-7.33 (m, 2H), 4.12 (s, 2H), 2.57-2.52 (tt, J = 11.8, 3.6 Hz, 1H), 1.87-1.74 (m, 4H), 1.71-1.67 (m, 3H), 1.38-1.33 (m, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ = 159.29, 143.30, 143.08, 142.56, 135.97, 132.51, 129.08, 128.91, 127.43, 126.19, 118.72, 110.77, 35.64, 32.37, 31.21, 26.44, 25.77.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₃H₂₂ClN₂O 377.1421, found 377.14175.

Rf (hexane/EtOAc 4:1): 0.3.



4n

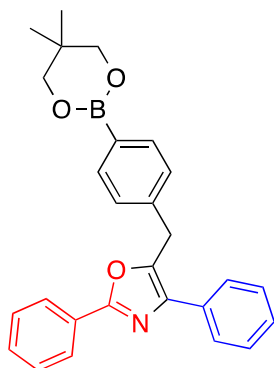
Use the general procedure described above, compound **4n** was obtained from 2-chlorobenzamide (0.2 mmol, 31.10 mg), cyclohexane carboxaldehyde (0.3 mmol, 36.3 uL) and 1-ethynyl-4-fluorobenzene (0.3 mmol, 34.4 uL) as a white solid (53.2 mg) in 72% yield.

¹H NMR (CDCl₃, 500 MHz): δ = 7.94-7.91 (m, 1H), 7.47-7.44 (m, 1H), 7.33-7.29 (m, 2H), 7.25-7.21 (m, 2H), 7.04-6.99 (m, 2H), 4.05 (s, 2H), 2.61-2.55 (tt, J = 11.7, 3.5 Hz, 1H), 1.85-1.80 (m, 4H), 1.76-1.66 (m, 3H), 1.42-1.30 (m, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ = 162.66, 160.72, 157.86, 144.50, 141.78, 133.49, 133.46, 132.33, 130.92, 130.53, 129.88, 129.81, 126.97, 126.65, 115.48, 115.31, 35.55, 32.41, 30.40, 26.50, 25.84.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₂H₂₂ClFNO 370.1374, found 370.13722.

Rf (hexane/EtOAc 4:1): 0.8.



4o

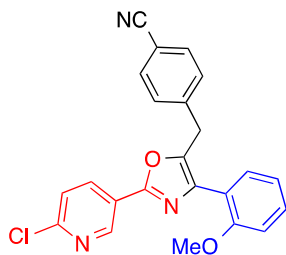
Use the general procedure described above, compound **4o** was obtained from benzamide (0.2 mmol, 24.2 mg), 2-(4-ethynylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (0.3 mmol, 32 mg) and benzaldehyde (0.3 mmol, 32 μ L) as a white solid (42.3 mg) in 50% yield.

^1H NMR (CDCl₃, 500 MHz): δ = 8.10-8.08 (m, 2H), 7.80-7.78 (m, 2H), 7.76-7.74 (m, 2H), 7.47-7.43 (m, 5H), 7.37-7.36 (m, 1H), 7.32-7.30 (m, 2H), 4.34 (s, 2H), 3.78 (s, 4H), 1.03 (s, 6H).

^{13}C NMR (CDCl₃, 126 MHz): δ = 160.17, 145.51, 143.90, 139.73, 137.73, 134.36, 132.07, 130.10, 128.66, 127.59, 127.05, 126.33, 72.31, 32.12, 31.89, 21.90.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₇H₂₇BNO₃ 423.2084, found 423.20742.

Rf (hexane/EtOAc 4:1): 0.5.



4p

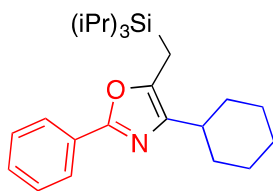
Use the general procedure described above, compound **4p** was obtained from 6-chloronicotinamide (0.2 mmol, 31.31 mg), 4-ethynylbenzonitrile (0.3 mmol, 38.2 mg) and 2-methoxybenzaldehyde (0.3 mmol, 36.3 μ L) as a white solid (49.8 mg) in 62% yield.

^1H NMR (CDCl₃, 500 MHz): δ = 9.04-9.03 (m, 1H), 8.28-8.25 (m, 1H), 7.62-7.59 (m, 3H), 7.43-7.39 (m, 2H), 7.37-7.35 (m, 1H), 7.11-7.08 (m, 1H), 6.99-6.97 (m, 1H), 4.22 (s, 2H), 3.71 (s, 3H).

^{13}C NMR (CDCl₃, 126 MHz): δ = 157.39, 156.43, 152.70, 147.44, 146.78, 142.98, 135.99, 135.24, 132.32, 131.11, 130.18, 129.27, 124.38, 122.65, 121.10, 120.06, 118.74, 111.18, 110.67, 55.32, 32.37.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₃H₁₇ClN₃O₂ 402.1009, found 401.10071.

Rf (hexane/EtOAc 4:1): 0.5.



4q

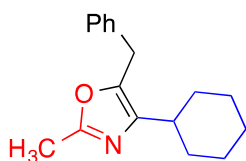
Use the general procedure described above, compound **4q** was obtained from benzamide (0.2 mmol, 24.2 mg), cyclohexane carboxaldehyde (0.3 mmol, 36.3 uL) and triisopropylsilyl acetylene (0.3 mmol, 67.3 uL) as a white solid (33.4 mg) in 42% yield.

¹H NMR (CDCl₃, 500 MHz): 7.97-7.95 (m, 2H), 7.44-7.41 (m, 2H), 7.39-7.38 (m, 1H), 2.51-2.46 (tt, J = 11.7, 3.5 Hz, 1H), 2.13 (s, 2H), 1.87-1.85 (m, 2H), 1.78-1.69 (m, 5H), 1.37-1.35 (m, 3H), 1.19-1.16 (m, 3H), 1.10-1.08 (d, J = 5.4 Hz, 18H).

¹³C NMR (CDCl₃, 126 MHz): δ = 158.29, 144.80, 129.19, 128.62, 128.59, 125.75, 125.70, 35.58, 32.26, 26.65, 25.90, 18.56, 11.30, 6.70.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₂₅H₄₀NOSi 398.2879, found 398.28751.

Rf (hexane/EtOAc 4:1): 0.8.



4r

Use the general procedure described above, compound **4r** was obtained from acetamide (0.2 mmol, 17.4 mg), cyclohexane carboxaldehyde (0.3 mmol, 36.3 uL) and phenylacetylene (0.3 mmol, 34 uL) as a white solid (26.5 mg) in 52% yield. to yield the corresponding oxazole **4r** as a yellowish solid (26.5 mg, 52%).

¹H NMR (CDCl₃, 500 MHz): 7.33-7.30 (m, 2H), 7.26-7.23 (m, 1H), 7.20-7.19 (m, 2H), 3.94 (s, 2H), 2.50-2.44 (tt, J = 11.9, 3.5 Hz, 1H), 2.37 (s, 3H), 1.84-1.82 (m, 2H), 1.75-1.71 (m, 3H), 1.65-1.58 (m, 2H), 1.37-1.27 (m, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ = 159.56, 143.34, 140.23, 138.08, 128.56, 128.29, 126.53, 35.24, 30.89, 26.55, 25.84, 14.01.

HRMS (ESI) m/z: [M + H]⁺ calculated for C₁₇H₂₂NO 255.1623, found 255.16241.

Rf (hexane/EtOAc 4:1): 0.7.

4 PDF file of ^1H NMR and ^{13}C NMR spectra for new compounds

