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NICKEL-CATALYZED LIGAND-FREE SYNTHESIS OF BENZOXAZOLES AND OXAZOLINES VIA ISOCYANIDE INSERTION

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Abstract – A novel and efficient route to benzoxazoles and oxazolines involving a nickel-catalyzed three-component coupling reaction of iodobenzene, an amino alcohol and *tert*-butyl isocyanide has been developed. A wide array of products have been prepared in good to excellent yields in the absence of ligand.

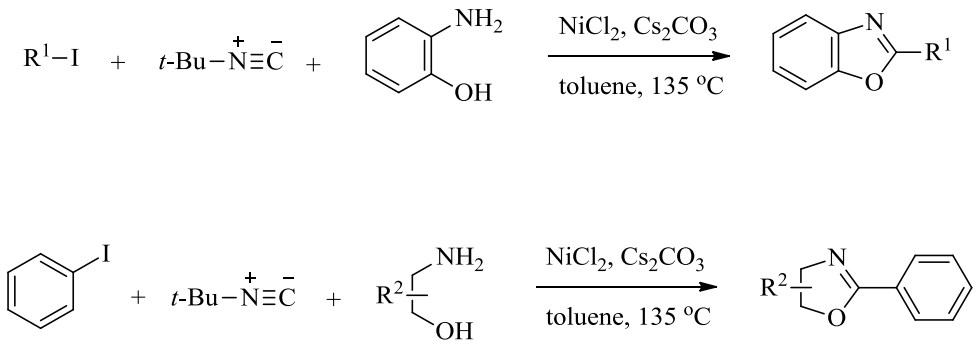
INTRODUCTION

Benzoxazoles and oxazolines exist widely in natural products[1] and some of them have been shown to exhibit excellent bioactivities.[2] They are also a subunit of many compounds from different areas of chemistry, such as fluorescent probes,[3] heat-resistant polymers[4] and other functional synthetics. Consequently, some synthetic routes to benzoxazoles have been reported involving transition metal catalyzed direct arylation of oxazoles,[5,6] cyclization of *o*-haloanilides,[7] and C-H activation of anilides.[8] Oxazolines are generally prepared from the corresponding carboxylic acids, carboxylic esters, nitriles, or aldehydes.[9] Nevertheless, many of their synthesis methods require the high catalyst loading or additives such as ligands and CuI.[10] Recently, an alternative approach employing CO as a one-carbon unit has been reported,[11] however, toxicity and poor maneuverability of CO remains a major drawback. Thus, the development of new and improved methods for the efficient synthesis of this type of skeleton is highly desired.

Since the pioneering work of Passerini[12] and Ugi,[13] isocyanides are considered as isoelectronic[14] with carbon monoxide, therefore, they can be used as an alternative to carbon monoxide in the construction of many molecules. Many seminal papers describing two-component reactions[15] and multicomponent reactions (MCRs)[16] have been reported. Recently, reactions involving isocyanide insertion to form

C-N,[17-19] C-O[20] and C-C[21] bonds have become increasingly important. Nevertheless, most of the reactions via isocyanide insertion are catalyzed by palladium species. For example, Lang's group describes a convenient palladium-catalyzed cascade process to give benzoxazoles and benzothiazoles in one step.[18] Also, Suckling et al. demonstrate a powerful one-pot palladium-catalyzed multicomponent process for the preparation of oxazolines and benzoxazoles.[19] In a continuation of our interest in the synthesis of heterocyclic compounds utilizing isocyanides, we are trying to explore more efficient and novel catalyst systems. To our delight, nickel catalysts might be considered because they have many characteristics similar to palladium catalysts as a kind of inexpensive transition metal.

Based on these findings, we envisage that a nickel-catalyzed coupling reaction of aryl iodides, amino alcohols, and *tert*-butyl isocyanide would allow an efficient access to benzoxazoles and oxazolines (Scheme 1). To the best of our knowledge, this methodology has not yet been reported. Herein, we disclose a nickel-catalytic system to construct intermolecular C-N bonds to give benzoxazoles and oxazolines in excellent yields.



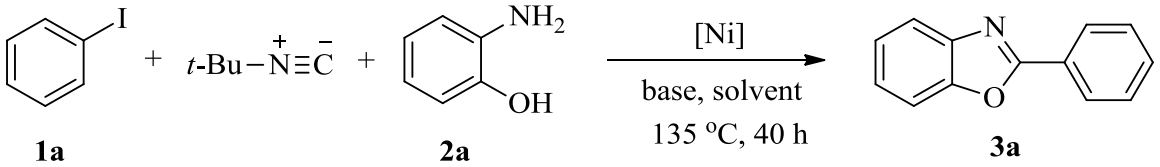
Scheme 1

RESULTS AND DISCUSSION

We commenced our investigation by screening different combinations of ligands, bases, solvents, and catalysts; selected results are summarized in Table 1. In our initial attempt, the product 2-phenylbenzo[*d*]oxazole (**3a**) was formed in 54% yield with $NiCl_2$ as catalyst in the presence of 1,1'-bis(diphenylphosphino)ferrocene (**La**) and Cs_2CO_3 in anhydrous toluene (entry 1). Then, several ligands and ligand-free conditions were tested in the reaction. **3a** was obtained in 91% yield in the absence of ligand, indicating that a ligand was not essential to the reaction (entries 2-4). Different bases were also examined, and Cs_2CO_3 was found to be superior to the others (entries 5-7). Solvent screening revealed that toluene appeared to be the best solvent (entries 8-10). Other catalysts, such as $Ni(OAc)_2$ or $Ni(acac)_2$, proved to be less effective (entries 11 and 12). Furthermore, lowering the quantity of 2-aminophenol (**2a**) from 5 equiv. to 3 equiv. led to a diminished yield (entry 13). Thus, the best result for

the reaction was obtained with $NiCl_2$ (10 mol%) and 2-aminophenol (5 equiv.) in anhydrous toluene (3.0 ml) with Cs_2CO_3 (1.3 equiv.) as base at 135 °C for 40 h.

Table 1. Optimization of the reaction conditions[a]



1a **2a** **3a**

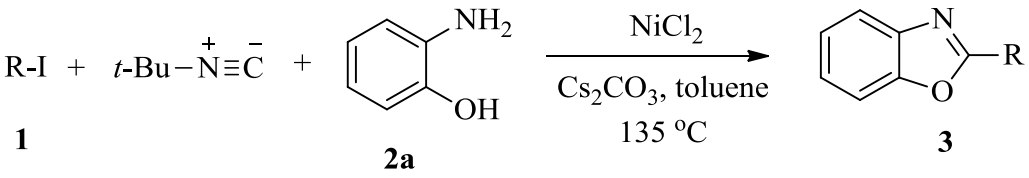
Entry	Catalyst	Ligand[b]	Base	Solvent	Yield (%)[c]
1	$NiCl_2$	**La**	Cs_2CO_3	toluene	54
2	$NiCl_2$	**Lb**	Cs_2CO_3	toluene	82
3	$NiCl_2$	**Lc**	Cs_2CO_3	toluene	90
4	$NiCl_2$	_	Cs_2CO_3	toluene	91
5	$NiCl_2$	_	K_2CO_3	toluene	28
6	$NiCl_2$	_	CsF	toluene	trace
7	$NiCl_2$	_	K_3PO_4	toluene	trace
8	$NiCl_2$	_	Cs_2CO_3	dioxane	90
9	$NiCl_2$	_	Cs_2CO_3	DMF	89
10	$NiCl_2$	_	Cs_2CO_3	DMSO	87
11	$Ni(OAc)_2$	_	Cs_2CO_3	toluene	11
12	$Ni(acac)_2$	_	Cs_2CO_3	toluene	trace
13	$NiCl_2$	_	Cs_2CO_3	toluene	84[d]

[a] Conditions: **1a** (0.5 mmol), **2a** (2.5 mmol), catalyst (10 mol%), ligand (10 mol%), *tert*-butyl isocyanide (0.75 mmol), base (1.3 mmol), and solvent (3.0 mL), under Ar. [b] **La** 1,1'-bis(diphenylphosphino)ferrocene. **Lb** tricyclohexylphosphine. **Lc** butyldi-1-adamantylphosphine.
[c] Isolated yield. [d] As before except **2a** (1.5 mmol).

With the optimized conditions in hand, a diverse set of iodobenzenes **1** were utilized to test the scope of the reaction. The results are summarized in Table 2. **2a** was efficiently reacted with different iodobenzenes bearing *ortho*, *meta*, and *para* substituents on the phenyl ring to afford the desired products **3a-3l** in moderate to high yields (entries 1-12). In most cases, iodobenzenes bearing electron-withdrawing groups (entries 2-6) gave higher yields than those bearing electron-donating groups (entries 7-12). Furthermore, in accordance with steric hindrance effects, the yield for the reaction was lower when a methyl group was in the *ortho* position compared to the *meta* and *para* positions (entries 8-10). This

reaction was not limited to an aryl moiety; the heterocycle-containing substrates such as 2-iodothiophene (**1m**) and 2-iodopyridine (**1n**) also underwent smooth reactions to afford the corresponding products 2-(thiophen-2-yl)benzo[*d*]oxazole (**3m**) and 2-(pyridin-2-yl)benzo[*d*]oxazole (**3n**) in good yields (entries 13 and 14).

Table 2. Nickel-catalyzed synthesis of benzoxazoles[a]



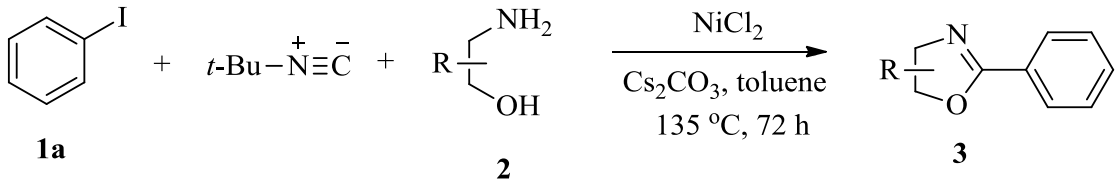
1 **2a** **3**

Entry	Substrate	R	Product	Time (h)	Yield (%)[b]
1	**1a**	Ph	**3a**	40	91
2	**1b**	4-Cl-C_6H_4	**3b**	36	99
3	**1c**	4-F-C_6H_4	**3c**	36	92
4	**1d**	3,5-F,F-C_6H_3	**3d**	36	98
5	**1e**	4-CF_3-C_6H_4	**3e**	36	88
6	**1f**	4-CN-C_6H_4	**3f**	36	80
7	**1g**	4-MeO-C_6H_4	**3g**	48	88
8	**1h**	4-Me-C_6H_4	**3h**	48	85
9	**1i**	3-Me-C_6H_4	**3i**	48	64
10	**1j**	2-Me-C_6H_4	**3j**	72	45
11	**1k**	4-Ph-C_6H_4	**3k**	48	81
12	**1l**	1-naphthalene	**3l**	48	80
13	**1m**	2-thiophene	**3m**	48	99
14	**1n**	2-pyridine	**3n**	48	42

[a] All reactions were performed under an atmosphere of argon on a 0.5 mmol scale, using *tert*-butyl isocyanide (1.5 equiv.), 2-aminophenol (5 equiv.), $NiCl_2$ (10 mol%) and Cs_2CO_3 (1.3 equiv.) in anhydrous toluene (3.0 mL). [b] Isolated yield after column chromatography.

Next, 2-aminoethanol derivatives **2b-2f** were used as substrates to afford oxazolines (Table 3). As established in Table 3, oxazoline products were formed in moderate yields (entries 1-5). Compared to aryl substituted substrates, aliphatic ones led to the desired product in lower yields and generally required a longer reaction time.

Table 3. Nickel-catalyzed synthesis of oxazolines[a]



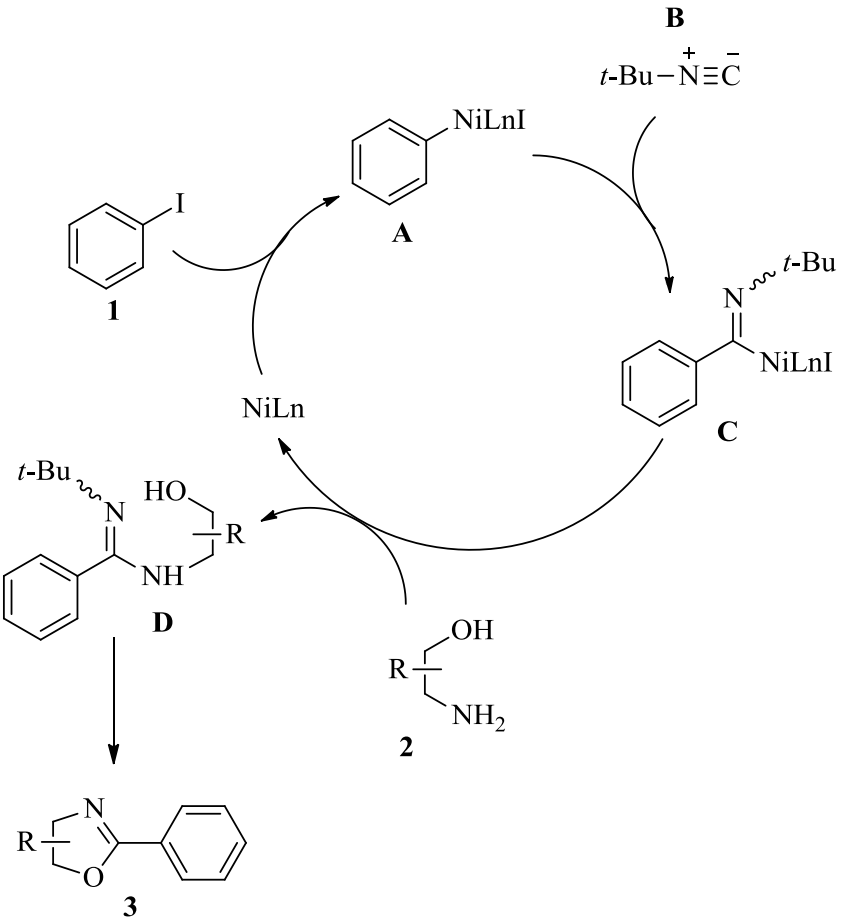
1a **2** **3**

Entry	Substrate	R	Product	Yield (%)[b]
1	**2b**	H	**3o**	63
2	**2c**	2-Me	**3p**	50
3	**2d**	2-*i*Pr	**3q**	56
4	**2e**	2-Ph	**3r**	85
5	**2f**	1,2-(2,3-dihydro-1*H*-inden)	**3s**	66

[a] All reactions were performed under an atmosphere of argon on a 0.5 mmol scale, using *tert*-butyl isocyanide (1.5 equiv.), 2-aminoethanols (5 equiv.) $NiCl_2$ (10 mol%), and Cs_2CO_3 (1.3 equiv.) in anhydrous toluene (3.0 mL). [b] Isolated yield after column chromatography.

A proposed reaction mechanism is outlined in Scheme 2. Oxidative addition of **1** leads to nickel complex **A**. Then it undergoes an insertion process with *tert*-butyl isocyanide **B** to afford **C**, followed by addition of **2** to give amidine intermediate **D** and regeneration of NiLn. Then, the intermediate **D** allows the formation of desired product **3** via cyclization.

In conclusion, we have developed an efficient coupling method for the synthesis of benzoxazoles and oxazolines from easily accessible substrates via *tert*-butyl isocyanide insertion. The process reported here was characterized by a ligand-free nickel catalyzed reaction demonstrating that nickel is also a highly efficient transition-metal catalyst for isocyanide insertion. This approach was tolerant of a wide range of substrates and applicable to library synthesis. Further studies on nickel-catalyzed reactions are currently underway in our laboratory.



Scheme 2. Plausible mechanism

EXPERIMENTAL

General

Reagents and chemicals were purchased from commercial suppliers and used without further purification. Flash chromatography (FC): silica gel (SiO_2; 200-300 mesh) from Qingdao Ocean Chemicals, P. R. China. TLC: Silica-gel GF254 plates. Melting points were determined with a XT5 digital melting-point apparatus from Beijing Keyi Elec-opti Instrument Factory. ^{1}H NMR and ^{13}C NMR spectra were obtained from a solution in $CDCl_3$ with TMS as internal standard using a 400/101 MHz (^{1}H/^{13}C) spectrometer, δ in parts per million (ppm), and J in hertz (Hz). IR measurements were recorded in KBr pellets, and wavenumbers are reported as cm^{-1}. LRMS or HRMS were measured with an electrospray ionization (ESI) mass spectrometry.

General procedure for the synthesis of Benzoxazoles and Oxazolines (3):

Reactions were carried out under Ar. To an oven-dried, sealed tube (15 mL) containing **1** (0.5 mmol) in anhydrous toluene (3.0 mL), **2** (2.5 mmol), *tert*-butyl isocyanide (0.75 mmol, 85μL), $NiCl_2$ (6.5 mg, 0.05 mmol), Cs_2CO_3 (212 mg, 1.3 mmol) were added, and the contents were stirred at 135 °C. After

completion of the reaction, the mixture was filtered, and the residue was purified by column chromatography on silica gel using petroleum ether/EtOAc as eluent to afford pure target products **3**.

2-Phenylbenzo[*d*]oxazole (3a):[22] white solid (petroleum ether/EtOAc), mp 102-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, *J* = 3.6 Hz, 2H), 7.78 (d, *J* = 4.5 Hz, 1H), 7.57 (d, *J* = 5.2 Hz, 1H), 7.52 (s, 3H), 7.35 (d, *J* = 3.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.9, 150.7, 142.0, 131.4, 128.8, 127.5, 127.1, 125.0, 124.5, 119.9, 110.5. IR (KBr): 3060, 1617, 1552, 1455, 1447, 1242, 1197, 1053, 1022, 808, 745, 703, 687. LRMS (ESI): calcd. for $C_{13}H_9NO$ $[M+H]^+$ 196.1, found: 196.0.

2-(4-Chlorophenyl)benzo[*d*]oxazole (3b):[23] white solid (petroleum ether/EtOAc), mp 147-149 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.1 Hz, 2H), 7.75 (s, 1H), 7.53 (s, 1H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 2.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.1, 150.8, 142.1, 137.8, 129.3, 128.9, 125.7, 125.4, 124.8, 120.2, 110.7. IR (KBr): 3060, 1618, 1578, 1484, 1453, 1405, 1092, 1056, 739. LRMS (ESI): calcd. for $C_{13}H_8ClNO$ $[M+H]^+$ 230.0, found: 230.0.

2-(4-Fluorophenyl)benzo[*d*]oxazole (3c):[22] white solid (petroleum ether/EtOAc), mp 104-105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 – 8.17 (m, 2H), 7.75 (d, *J* = 4.6 Hz, 1H), 7.56 (d, *J* = 4.2 Hz, 1H), 7.42 – 7.29 (m, 2H), 7.19 (t, *J* = 8.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.0 (d, *J* = 252.6 Hz), 162.3, 150.9, 142.1, 130.0 (d, *J* = 9.0 Hz), 125.2, 124.8, 123.6, 120.1, 116.3 (d, *J* = 22.4 Hz), 110.7. IR (KBr): 3060, 1622, 1499, 1453, 1414, 1246, 1232, 1156, 1055, 835, 743, 628. LRMS (ESI): calcd. for $C_{13}H_8FNO$ $[M+H]^+$ 214.1, found: 214.0.

2-(3,5-Difluorophenyl)benzo[*d*]oxazole (3d):[24] white solid (petroleum ether/EtOAc), mp149-151 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, *J* = 10.9, 6.1 Hz, 3H), 7.60 – 7.50 (m, 1H), 7.42 – 7.29 (m, 2H), 6.94 (t, *J* = 8.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163,3 (dd, *J* = 12.4, 250.0 Hz), 160.7 (t, *J* = 3.9 Hz), 150.8, 141.8, 130.1 (t, *J* = 10.5 Hz), 126.0, 125.1, 120.5, 110.9, 110.5 – 110.8 (m), 106.9 (t, *J* = 25.2 Hz). IR (KBr): 3074, 1632, 1601, 1558, 1471, 1441, 1350, 1244, 1130, 1074, 993, 948, 876, 864, 760, 740, 665. LRMS (ESI): calcd. for $C_{13}H_7F_2NO$ $[M+H]^+$ 232.1, found: 232.1.

2-(4-(Trifluoromethyl)phenyl)benzo[*d*]oxazole (3e):[6] white solid (petroleum ether/EtOAc), mp 141-143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.2 Hz, 2H), 7.76 (dd, *J* = 14.1, 6.4 Hz, 3H), 7.60 – 7.53 (m, 1H), 7.41 – 7.32 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.5, 150.9, 142.0, 133.0 (q, *J* = 33.5 Hz), 130.5, 127.9, 126.0 (d, *J* = 3.8 Hz), 125.9, 125.0, 123.9 (d, *J* = 274.0 Hz), 120.5, 110.9. IR (KBr): 3243, 1618, 1559, 1454, 1415, 1322, 1169, 1118, 1070, 1014, 847, 751, 744, 697. LRMS (ESI): calcd. for $C_{14}H_8F_3NO$ $[M+H]^+$ 264.1, found: 264.0.

4-(Benzo[*d*]oxazol-2-yl)benzonitrile (3f):[23] white solid (petroleum ether/EtOAc), mp 206-207 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 7.8 Hz, 2H), 7.76 (d, *J* = 7.1 Hz, 3H), 7.57 (d, *J* = 5.4 Hz, 1H), 7.38 (d, *J* = 3.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.9, 150.9, 141.9, 132.7, 131.1, 127.9, 126.2, 125.2, 120.6, 118.2, 114.7, 110.9. IR (KBr): 3097, 2229, 1615, 1548, 1494, 1452, 1411, 1242, 1056, 1013,

843, 762, 752, 548. LRMS (ESI): calcd. for $C_{14}H_8N_2O$ $[M+H]^+$ 221.1, found: 221.0.

2-(4-Methoxyphenyl)benzo[*d*]oxazole (3g):[22] white solid (petroleum ether/EtOAc), mp 97-98 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 6.7 Hz, 1H), 7.52 (d, *J* = 6.9 Hz, 1H), 7.30 (d, *J* = 3.2 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.2, 162.4, 150.7, 142.3, 129.4, 124.6, 124.5, 119.7, 114.4, 110.4, 109.9, 55.5. IR (KBr): 3049, 2922, 1618, 1605, 1504, 1454, 1256, 1244, 1170, 1019, 832, 742, 730. LRMS (ESI): calcd. for $C_{14}H_{11}NO_2$ $[M+H]^+$ 226.1, found: 226.0.

2-*p*-Tolylbenzo[*d*]oxazole (3h):[25] white solid (petroleum ether/EtOAc), mp 115-116 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 7.7 Hz, 2H), 7.81 – 7.72 (m, 1H), 7.59 – 7.52 (m, 1H), 7.33 (t, *J* = 6.6 Hz, 4H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.4, 150.8, 142.3, 142.2, 129.8, 127.7, 125.0, 124.6, 124.5, 119.9, 110.6, 21.8. IR (KBr): 3057, 2919, 2851, 1622, 1502, 1451, 1409, 1244, 1173, 1055, 821, 746, 727. LRMS (ESI): calcd. for $C_{14}H_{11}NO$ $[M+H]^+$ 210.1, found: 210.0.

2-*m*-Tolylbenzo[*d*]oxazole (3i):[6] white solid (petroleum ether/EtOAc), mp 82-84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 8.05 (d, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 4.6 Hz, 1H), 7.57 (d, *J* = 4.9 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.34 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.3, 150.8, 142.2, 138.8, 132.4, 128.9, 128.3, 127.1, 125.1, 124.8, 124.6, 120.0, 110.6, 29.8. IR (KBr): 3070, 2921, 1637, 1552, 1454, 1246, 1058, 761, 745, 687. LRMS (ESI): calcd. for $C_{14}H_{11}NO$ $[M+H]^+$ 210.1, found: 210.0.

2-(*o*-Tolyl)benzo[*d*]oxazole (3j):[25] white solid (petroleum ether/EtOAc), mp 62-64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 7.7 Hz, 1H), 7.86 – 7.76 (m, 1H), 7.60 (dd, *J* = 5.1, 3.3 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.36 (d, *J* = 5.7 Hz, 4H), 2.83 (s, 3H). ^{13}C NMR (101MHz, $CDCl_3$): δ 163.5, 150.4, 142.3, 139.0, 131.9, 131.0, 130.1, 126.4, 126.2, 125.1, 124.5, 120.3, 110.6, 22.4. IR (KBr): 2958, 2921, 1616, 1549, 1453, 1241, 1029, 748, 724. LRMS (ESI): calcd. for $C_{14}H_{11}NO$ $[M+H]^+$ 210.1, found: 210.0.

2-([1,1'-Biphenyl]-4-yl)benzo[*d*]oxazole (3k):[26] white solid (petroleum ether/EtOAc), mp 140-141 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 2H), 7.41 (d, *J* = 7.4 Hz, 1H), 7.35 (dd, *J* = 9.6, 5.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.9, 150.8, 144.1, 142.2, 139.9, 129.0, 128.1, 127.5, 127.2, 125.9, 125.1, 124.6, 120.0, 110.6. IR (KBr): 3239, 1618, 1571, 1485, 1453, 1407, 1298, 1246, 1060, 845, 738, 623. LRMS (ESI): calcd. for $C_{19}H_{13}NO$ $[M+H]^+$ 272.1, found: 272.0.

2-(Naphthalen-1-yl)benzo[*d*]oxazole (3l):[6] white solid (petroleum ether/EtOAc), mp 103-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (d, *J* = 8.5 Hz, 1H), 8.44 (d, *J* = 7.3 Hz, 1H), 8.03 (d, *J* = 8.1 Hz, 1H), 7.93 (t, *J* = 8.4 Hz, 2H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.60 (t, *J* = 7.7 Hz, 2H), 7.42 (dd, *J* = 6.4, 2.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.9, 150.2, 142.4, 134.0, 132.4, 130.8, 129.4, 128.8, 128.0, 126.5, 126.4, 125.4, 125.0, 124.6, 123.7, 120.4, 110.6. IR (KBr): 3050, 1576, 1539, 1509, 1452, 1395, 1243, 1178, 1121, 1003, 971, 805, 777, 734. LRMS (ESI): calcd. for $C_{17}H_{11}NO$ $[M+H]^+$ 246.1,

found: 246.1.

2-(Thiophen-2-yl)benzo[*d*]oxazole (3m):[23] white solid (petroleum ether/EtOAc), mp 103-104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 3.1 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.55 – 7.48 (m, 2H), 7.35 – 7.27 (m, 2H), 7.18 – 7.12 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.1, 150.4, 142.0, 130.3, 130.0, 129.7, 128.3, 125.1, 124.8, 119.8, 110.5. IR (KBr): 3085, 1616, 1570, 1494, 1451, 1419, 1245, 1227, 1049, 1007, 852, 743. LRMS (ESI): calcd. for $C_{11}H_7NOS$ $[M+H]^+$ 202.0, found: 201.9.

2-(Pyridin-2-yl)benzo[*d*]oxazole (3n):[27] white solid (petroleum ether/EtOAc), mp 108-109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.83 (s, 1H), 8.37 (d, *J* = 7.5 Hz, 1H), 7.91 (t, *J* = 7.1 Hz, 1H), 7.83 (d, *J* = 6.0 Hz, 1H), 7.67 (d, *J* = 6.4 Hz, 1H), 7.50 – 7.34 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.4, 151.2, 150.3, 146.1, 141.9, 137.4, 126.2, 125.8, 125.1, 123.6, 120.8, 111.4. IR (KBr): 3059, 2924, 1584, 1554, 1453, 1243, 1077, 741. LRMS (ESI): calcd. for $C_{12}H_8N_2O$ $[M+H]^+$ 197.1, found: 197.0.

2-Phenyl-4,5-dihydrooxazole (3o):[28] colorless liquid (petroleum ether/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 7.5 Hz, 2H), 7.49 – 7.43 (m, 1H), 7.40 (t, *J* = 7.2 Hz, 2H), 4.42 (t, *J* = 9.4 Hz, 2H), 4.05 (t, *J* = 9.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.7, 131.4, 128.4, 128.2, 127.8, 67.7, 55.0. IR (KBr): 2961, 2925, 1639, 1541, 1490, 1451, 1364, 1270, 1177, 1069, 1026, 943, 711, 694, 616. LRMS (ESI): calcd. for C_9H_9NO $[M+H]^+$ 148.1, found: 148.0.

4-Methyl-2-phenyl-4,5-dihydrooxazole (3p):[29] colorless liquid (petroleum ether/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 7.7 Hz, 2H), 7.48 – 7.41 (m, 1H), 7.38 (t, *J* = 7.2 Hz, 2H), 4.50 (t, *J* = 8.6 Hz, 1H), 4.36 (dd, *J* = 15.0, 7.4 Hz, 1H), 3.93 (t, *J* = 7.8 Hz, 1H), 1.34 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.5, 131.3, 128.4, 128.3, 127.8, 74.1, 62.0, 21.5. IR (KBr): 2967, 2927, 1647, 1450, 1356, 1258, 1056, 969, 781, 693. LRMS (ESI): calcd. for $C_{10}H_{11}NO$ $[M+H]^+$ 162.1, found: 162.0.

4-Isopropyl-2-phenyl-4,5-dihydrooxazole (3q):[30] colorless liquid (petroleum ether/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.6 Hz, 2H), 7.48 – 7.42 (m, 1H), 7.39 (t, *J* = 7.4 Hz, 2H), 4.43 – 4.33 (m, 1H), 4.16 – 4.03 (m, 2H), 1.86 (dq, *J* = 12.8, 6.3 Hz, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.4, 131.3, 128.3, 128.3, 128.0, 72.6, 70.2, 32.9, 19.1, 18.2. IR (KBr): 2958, 2898, 1650, 1450, 1353, 1080, 1065, 965, 779, 693. LRMS (ESI): calcd. for $C_{12}H_{15}NO$ $[M+H]^+$ 190.1, found: 190.0.

2,4-Diphenyl-4,5-dihydrooxazole (3r):[31] colorless liquid (petroleum ether/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.1 Hz, 2H), 7.38 (d, *J* = 6.8 Hz, 1H), 7.33 (d, *J* = 7.0 Hz, 2H), 7.23 (d, *J* = 6.8 Hz, 2H), 7.20 (d, *J* = 4.8 Hz, 3H), 5.26 (t, *J* = 8.9 Hz, 1H), 4.67 (t, *J* = 9.1 Hz, 1H), 4.16 (t, *J* = 8.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.8, 142.4, 131.6, 128.8, 128.5, 128.4, 127.7, 127.5, 126.8, 74.9, 70.1. IR (KBr): 3030, 2899, 1644, 1533, 1450, 1317, 1273, 1066, 1025, 759, 693. LRMS (ESI): calcd. for $C_{15}H_{13}NO$ $[M+H]^+$ 224.1, found: 224.1.

2-Phenyl-4,8b-dihydro-3a*H*-indeno[2,1-*d*]oxazole (3s): yellow solid (petroleum ether/EtOAc), mp 104-106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 7.0 Hz, 2H), 7.58 (d, *J* = 4.3 Hz, 1H), 7.42 (d, *J* = 6.6 Hz, 1H), 7.37 (d, *J* = 6.9 Hz, 2H), 7.26 (s, 3H), 5.74 (d, *J* = 7.5 Hz, 1H), 5.48 (d, *J* = 6.9 Hz, 1H), 3.50 (dd, *J* = 17.9, 6.2 Hz, 1H), 3.36 (d, *J* = 17.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.1, 142.1, 139.8, 131.4, 128.5, 128.4, 128.3, 128.0, 127.6, 125.7, 125.4, 83.2, 76.8, 39.9. IR (KBr): 3032, 2964, 2928, 1641, 1494, 1450, 1300, 1249, 1082, 1065, 1024, 856, 753, 691. HRMS (ESI): calcd. for $C_{16}H_{13}NO$ [M+H]+ 236.1078, found: 236.1077.

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