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Utility of Nitrogen Extrusion of Azido Complexes for the Synthesis of Nitriles, Benzoxazoles, and Benzisoxazoles

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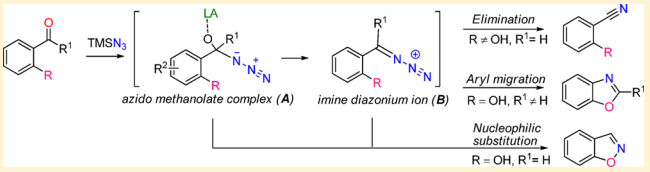
Supporting Information

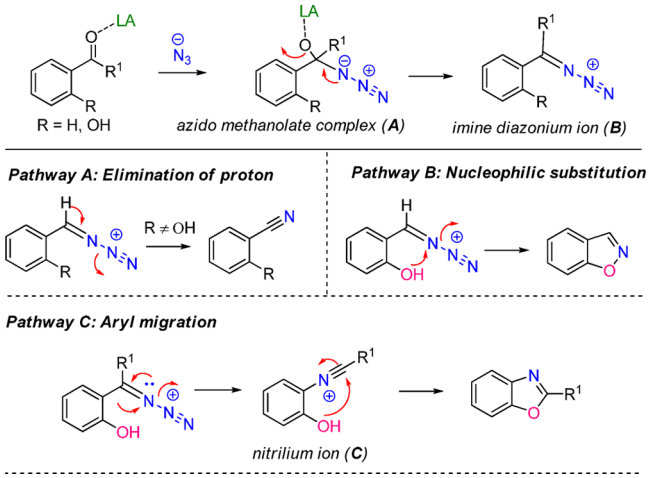
ABSTRACT: The utility of the nitrogen extrusion reaction of azido complexes, generated in situ from the corresponding aldehydes or ketones with $TMSN_3$ in the presence of $ZrCl_4$ or TfOH, has been described. These azido complexes could undergo three different pathways, depending on the substrates. First, azido methanolate complexes or imine diazonium ions could lead to benzisoxazole products via an intramolecular nucleophilic substitution. Second, imine diazonium ions could also undergo either the elimination of proton to provide nitrile products in good to excellent yields or an aryl migration, followed by an intramolecular nucleophilic addition, to give benzoxazole products in good yields.



INTRODUCTION

Nitriles,[1] benzisoxazoles,[2] and benzoxazoles[3] are important precursors for the synthesis of more complex chemical structures,[4] including natural products and pharmaceutical agents.[5] Currently, several synthetic approaches for the synthesis of such compounds use different nitrogen sources. One of the most powerful nitrogen sources for the preparation of several classes of N-containing compounds is azide.[6] The N_2 extrusion of azides can be induced by both Lewis and Brønsted acids,[7] which can lead to one remaining nitrogen atom attached to the desired products. The Schmidt reaction and Curtius rearrangement are well-known classical reactions which also involve N_2 extrusion chemistry.[8] Therefore, several synthetic methods pertaining to this chemistry have been developed for the synthesis of N-containing molecules. Recently, the conversion of aldehydes to nitriles by HN_3 generated from NaN_3 and TfOH has been reported.[9] However, the reaction between HN_3 and strongly electrophilic aldehyde under these conditions is highly exothermic, presenting a great explosion risk.[10] Due to the explosion hazard of sodium azide and Brønsted acids, we envision replacing this hazardous combination with the safer alternative of a Lewis acid and $TMSN_3$.[11] In this work, we aim to develop new synthetic methods for the synthesis of nitriles, benzoxazoles, and benzisoxazoles using aryl aldehyde and aryl ketone substrates, as proposed in Scheme 1. In our proposed strategy, the aldehyde or ketone will be activated by a Lewis acid and will then undergo nucleophilic addition with azide to provide the azido methanolate complex **A**, followed by an elimination to generate the imine diazonium ion intermediate **B**. We proposed that this imine diazonium ion could undergo nitrogen extrusion by three different pathways, depending on the substrates. First, it could undergo the elimination of proton to provide the benzonitrile product as shown in pathway A. Alternatively, the O−N bond formation may take place through nucleophilic substitution in the case of substrates containing an *o*-hydroxyl group (pathway B). Finally, when $R^1 \neq H$, we anticipated that the elimination could not occur and aryl migration would ensue to generate the nitrilium ion **C**, which could cyclize via nucleophilic addition of the *o*-hydroxyl group to provide the benzoxazole product, as shown in pathway C.

Scheme 1. Our Proposed Synthetic Methodology



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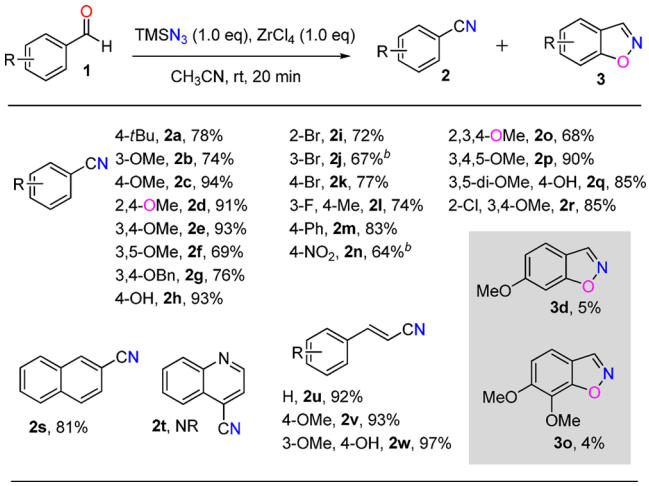
Scheme 2. Synthesis of Nitriles from Aldehydes[a]



[a]Isolated yields. [b]The reaction was carried out using 1.5 equiv of $TMSN_3$ and $ZrCl_4$, and the mixture was stirred at room temperature overnight.

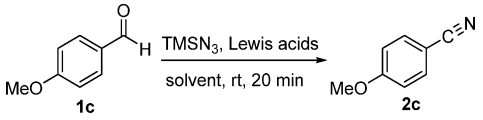
RESULTS AND DISCUSSION

To demonstrate the plausibility of our proposed methodology, we chose *p*-methoxybenzaldehyde (**1c**) as the initial substrate for our screening of conditions. Treatment of compound **1c** with either $Sc(OTf)_3$ or $Bi(OTf)_3$ in DCM resulted in a trace amount of the desired product (**2c**) (Table 1, entries 1 and 2), whereas no product was obtained when the reaction was performed using $BF_3{\cdot}OEt_2$ (entry 3). We have previously reported that $ZrCl_4$ was an effective activator for the nitrogen extrusion of azides;[12] therefore, we directed our attention to this reagent for our experiments. The results showed that 1.0 equiv of $ZrCl_4$ in DCM could provide the desired product in 81% yield (entry 4). Next, the effects of solvents were examined, employing $ZrCl_4$ in several solvents such as DCE, THF, $PhCH_3$, EtOH, and CH_3CN; the highest yield was obtained when the reaction was carried out in CH_3CN (entry 9). Increasing the amount of $ZrCl_4$ did not significantly improve the yield of the product (entry 10), whereas reducing the amount of $ZrCl_4$ to 0.5 equiv lowered the yield of the product (entry 11). The results showed that a combination of $ZrCl_4$ and $TMSN_3$ in CH_3CN could be used to convert aldehydes to nitriles, while providing advantages of safer handling of reagents, room-temperature reaction, and short reaction time.[13]

To explore the scope of substrates, a variety of aldehydes were studied using the optimal conditions established above (Table 1, entry 9). Most of the benzaldehyde derivatives were converted to the corresponding products in good to excellent yields. However, it was found that the inductive effect of a *m*-methoxy substituent of benzaldehyde derivatives decreased the yields of the desired products (**2b**, 74%; **2f**, 69%). Similarly, benzaldehydes substituted with bromine at the meta position provided the corresponding product in lower yield (**2j**, 67%), in comparison to yields for subsitution at the ortho (**2i**, 72%) and para positions (**2k**, 77%). In addition, benzaldehyde possessing a strongly electron withdrawing *p*-NO_2 group also afforded the benzonitrile **2n** in moderate yield. The results also showed that several functional groups such as methoxy, hydroxyl, alkyl, aryl, halogen, and nitro groups were tolerated well under these optimal conditions. Conversely, the benzyl group could be partially deprotected to give the corresponding product in lower yield such as 3,4-dibenzyloxybenzonitrile (**2g**, 76%), in comparison to 3,4-dimethoxybenzonitrile (**2e**, 93%). However, 4-formylquinoline (**1t**) did not react under these conditions. The current procedure could also be applied to synthesize the cinnamonitrile derivatives in excellent yields (**2u**–**w**). It is important to note that the reaction provided benzisoxazoles as the side products when benzaldehyde substrates contained an *o*-methoxy group, such as 2,4-dimethoxybenzaldehyde (**1d**) and 2,3,4-trimethoxybenzaldehyde (**1o**). These results provided a strong support that our proposed reaction for the synthesis of benzisoxazole would occur through pathway B. Therefore, we decided to use *o*-hydroxybenzaldehyde derivatives to investigate the proposed methodology as shown in Table 2.

We attempted to optimize the reaction conditions to maximize yields of benzisoxazoles **6**.[14] However, we were not able to selectively control the formation of the desired products. We rationalized that the electronic property of the aryl ring may have an effect on the product distribution and therefore the title conditions were applied to several salicylaldehyde derivatives to evaluate our hypothesis. The

Table 1. Optimization for the Synthesis of Benzonitrile 2c[a]



entry	1 (equiv)	$TMSN_3$ (equiv)	Lewis acid (amt)	solvent	yield (%)
1	1.0	1.0	$Sc(OTf)_3$ (10 mol %)[b]	DCM	trace
2	1.0	1.0	$Bi(OTf)_3$ (10 mol %)[b]	DCM	trace
3	1.0	1.0	$BF_3{\cdot}OEt_2$ (10 mol %)[b]	DCM	NR
4	1.0	1.0	$ZrCl_4$ (1.0 equiv)	DCM	81
5	1.0	1.0	$ZrCl_4$ (1.0 equiv)	DCE	89
6	1.0	1.0	$ZrCl_4$ (1.0 equiv)	THF	84
7	1.0	1.0	$ZrCl_4$ (1.0 equiv)	$PhCH_3$	43
8	1.0	1.0	$ZrCl_4$ (1.0 equiv)	EtOH	NR
9	1.0	1.0	$ZrCl_4$ (1.0 equiv)	CH_3CN	94
10	1.0	1.0	$ZrCl_4$ (1.5 equiv)	CH_3CN	95
11	1.0	1.5	$ZrCl_4$ (0.5 equiv)	CH_3CN	81

[a]Isolated yields. [b]The reaction mixture was stirred overnight.

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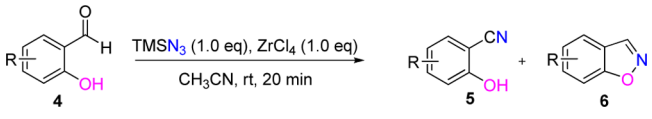
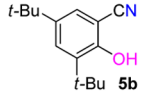
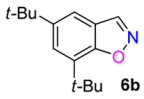
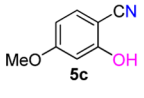
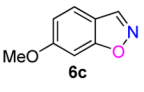
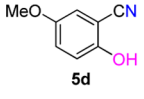
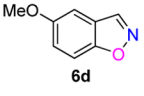
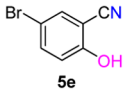
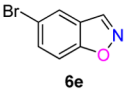
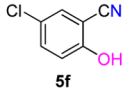
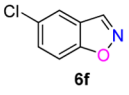
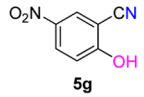
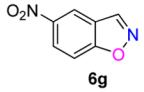
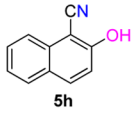
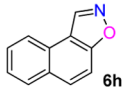
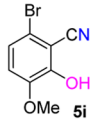
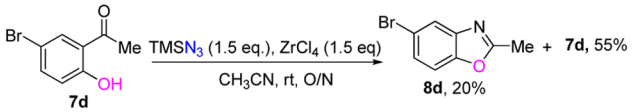
Table 2. Synthesis of Benzisoxazoles[a]



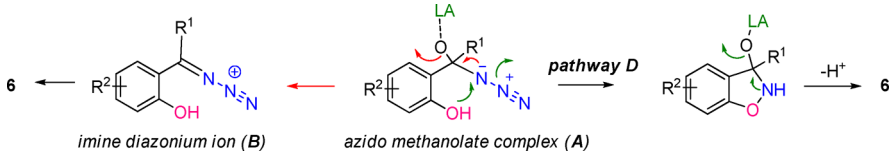
Entry	Product (**5**)	Product (**6**)	Yield of **5**	Yield of **6**
1	 **5a**	 **6a**	43%	29%
2[b]	 *t*-Bu **5b**	 *t*-Bu **6b**	28%	21%
3[b]	 **5c**	 **6c**	77%	22%
4[b]	 **5d**	 **6d**	65%	28%
5	 **5e**	 **6e**	35%	52%
6	 **5f**	 **6f**	33%	49%
7[b]	 **5g**	 **6g**	11%	62%
8[b]	 **5h**	 **6h**	15%	65%
9[b]	 OMe **5i**	 OMe **6i**	49%	35%



[a]Isolated yields. [b]The reaction was carried out using 1.5 equiv of $TMSN_3$ and $ZrCl_4$, and the mixture was stirred at room temperature overnight.

reaction of salicylaldehyde (**4a**) provided the *o*-hydroxybenzonitrile (**5a**, 43%) and benzisoxazole (**6a**, 29%) in an almost 1.5:1 ratio, and a similar result could be observed in the case of compound **4b**. Using the electron-rich substrates aldehydes **4c,d**, benzonitriles **5c,d** could be obtained as major products and benzisoxazoles **6c,d** as minor products in 3.5:1 and 2:1 ratios, respectively. The ratio of the two products was reversed when substrates containing electron-deficient substituents were used. For examples, 5-bromosalicylaldehyde (**4e**) and 5-chlorosalicylaldehyde (**4f**) provided benzonitriles as minor products (**5e**, 35%; **5f**, 33%), whereas the major products **6e,f** were obtained in 52% and 49% yields, respectively. The effect of a strongly electron withdrawing substituent was even more pronounced in 5-nitrosalicylaldehyde (**4g**), which dramatically increased the yield of benzisoxazole **6g** to 62% together with only 11% of benzonitrile **5g**. 2-Hydroxynaphthaldehyde (**4h**) also followed the same trend as **4g**, furnishing benzisoxazole **6h** in 65% yield and benzonitrile **5h** in 15% yield. In the case of 3-methoxy-6-bromosalicylaldehyde (**4i**), the corresponding nitrile **5i** was obtained as the major product (49%) together with the minor product **6i** in 35% yield. The results from all cases revealed that the substituents on the aryl ring have a substantial influence on the reaction mechanism and product distribution. The electron-donating group on the aryl aldehyde substrates could accelerate the C−O bond cleavage to give the imine diazonium intermediate, which readily eliminates the proton to form benzonitriles as the major products (pathway A, Scheme 1). In contrast, the ability of C−O bond cleavage was diminished when the electron-withdrawing group was present on the aryl ring, causing the competing nucleophilic substitution of azido methanolate complex **A** to prevail (pathway D, Scheme 3). Our current method for the synthesis of benzisoxazoles is comparable to the previously reported methods[2] in that the N−O bond formation occurred by displacement of the leaving group (N_2^+ in our case) on the imine nitrogen. However, the current method still differs significantly from those in the literature, in which the formation of the imine functional group and the installation of a leaving group occurred in sequential steps, while the entire process took place directly from the corresponding aldehyde in a single step using our method. According to our proposed mechanisms, the elimination pathway may be inhibited when using the *o*-hydroxyarylalkylketone substrates and only benzoxazoles and benzisoxazoles might be formed, as shown in pathways B and C. We therefore used 5-bromo-2-hydroxyacetophenone (**7d**) to investigate the reaction under the current optimal conditions. The result showed that substrate **7d** could only be slightly converted even with increased amounts of both $TMSN_3$ and $ZrCl_4$ (1.5 equiv) to afford benzoxazole **8d** in only 20% yield along with 55% of recovered starting material (**7d**). This result revealed that the reaction mechanism of aryl ketone substrates (**7**) favored the aryl migration (pathway C) to form the nitrilium ion intermediate **C** (Scheme 1), which could further react with

Scheme 3. Proposed Mechanism for the Formation of Benzisoxazoles



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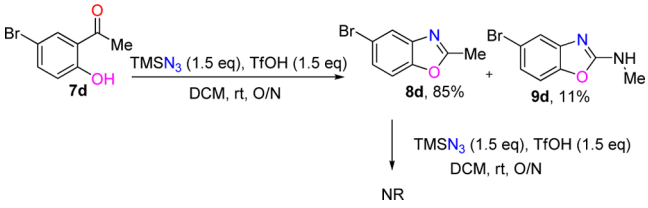
the intramolecular nucleophile (*o*-OH) to provide the desired benzoxazole **8**.

In order to achieve a complete conversion, we decided to screen for new optimal conditions using compound **7d** as the substrate. We found that the desired product **8d** was obtained in highest yield (85%) when using 1.5 equiv each of TfOH and $TMSN_3$ in DCM after the reaction mixture was stirred overnight (Scheme 4), along with the side product 2-*N*-methylaminobenzoxazole **9d**, which was obtained in 11% yield. Unfortunately, we could not avoid the formation of **9d** under these optimal conditions. To understand the formation of the side product, compound **8d** was subjected to identical reaction conditions, which resulted in no reaction. This experiment indicated that the side product **9d** did not form from the decomposition of benzoxazole **8d**. Therefore, we propose that the competing reaction proceeded through the double-migration mechanism. Initially, the imine diazonium ion intermediate underwent an alkyl migration, which is a less favored pathway in comparison to an aryl migration, providing *o*-hydroxyarylnitrilium ion. This intermediate could not react intramolecularly with the adjacent OH but could further react with HN_3 via an intermolecular nucleophilic addition, followed by an aryl migration to give the carbodiimide intermediate, which cyclized intramolecularly to furnish byproduct **9**, as demonstrated in Scheme 5. In fact, the rate of the aryl migration is much faster than that of the alkyl migration, resulting in benzoxazole **8d** as the major product. In the current strategy for the synthesis of benzoxazoles from aryl ketones, we could not avoid the use of $TMSN_3$ and TfOH, which generated HN_3 in situ, under the optimal conditions. It is important to note that the reaction of aryl ketones under these conditions was not as exothermic as the reaction of arylaldehydes. Additionally, benzoxazole products could be conveniently generated directly from the corresponding ketones.

Scheme 4. Synthesis of Benzoxazole



To evaluate the generality of the current procedure, we examined a variety of *o*-hydroxyacetophenone derivatives **7**, as shown in Table 3. Substrates containing electron-donating groups or electron-withdrawing groups such as H, F, Cl, Br, NO_2, OMe, and OH at position 5 of *o*-hydroxyacetophenone were smoothly converted to benzoxazole products **8a**–**g** in good yields with only small amounts of byproducts **9a**–**f** obtained. Similarly, the reaction of *o*-hydroxyacetophenones **7h,i** also proceeded well under these conditions, providing the corresponding products **8h,i** in excellent yields. Surprisingly, the proportions of byproducts **9** increased when the substituent was located at position 6 (**7j,k**). These results might be caused by the steric hindrance of the 2,6-disubstituted arylimine diazonium ion making the coplanarity of the aromatic ring difficult to attain. Thus, the optimal overlap for the aryl migration process could not be achieved and the competing methyl migration became more viable, resulting in an increase of byproduct. Further investigations were attempted with *o*-hydroxyacetophenones **7l,m** to furnish the corresponding products in good yields. For the less electrophilic ketone **7n**, the substrate was not completely consumed under these conditions, providing 37% of the recovered starting material along with 49% of the desired product **8n** and 7% of minor product **9n**. To see the substituent effects on the migration–nitrogen extrusion step, other *o*-hydroxyaryl ketones were examined. Therefore, *o*-hydroxyphenyl butyl ketone (**7o**) was chosen as the substrate, which furnished benzoxazole **8o** in good yield (79%) together with compound **9o** in 16% yield. Moreover, *o*-hydroxybenzophenone **7p** was subjected to the same conditions. In this case, the results indicated that the rates of migration of both the electron-rich *o*-hydroxyphenyl ring (ring A) and the phenyl ring (ring B) were comparable, resulting in the formation of the nitrilium intermediates **7p-A**,**p-B**, respectively, as shown in Scheme 6. The subsequent reaction of the nitrilium ion **7p-A** led to the desired product **8p** in 42% yield, whereas the reactions of the nitrilium ion **7p-B** yielded the products **9p** and **10p** in 45% combined yield.

The results of all cases revealed that the migration of an aryl group is more favorable than that of an alkyl group of acyclic ketone substrates to afford the desired benzoxazole products. Furthermore, cyclic ketones were next explored. The reactions of tetralone derivatives **7q,r** were performed under the current optimal conditions. Surprisingly in both entries, intramolecular nucleophilic substitution (pathway B) was preferred to aryl migration (pathway C), providing benzisoxazoles **6q,r** as the major products in 32% and 44% yields, respectively. Additionally, the alkyl migration was also more favored than the aryl migration to form the cyclic nitrilium ion intermediate **D**, which was subsequently added by HN_3; following an intramolecular cyclization, compounds **11q,r** were obtained as minor products.[15] The proposed mechanism is illustrated in Scheme 7.

■ CONCLUSIONS

We have demonstrated the utility of nitrogen extrusion of azido complexes, generated from aldehydes or ketones with appropriate substituents in the presence of $TMSN_3$ and $ZrCl_4$ or TfOH, to deliver a variety of N-containing compounds. With aldehydes, the products obtained are nitriles, whereas in the presence of an *o*-hydroxyl group, both nitriles and benzisoxazoles are obtained with varying ratios, depending on the nature of other substituents. When *o*-hydroxyaryl ketones were employed, the rearrangement of the initial azido intermediates led to an aryl migration to form the nitrilium ion, which could cyclize to form benzoxazoles in good yields.

Scheme 5. Proposed Mechanism for the Formation of 9

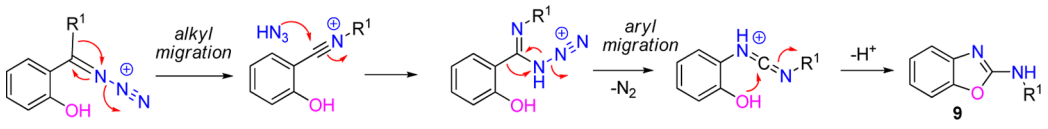


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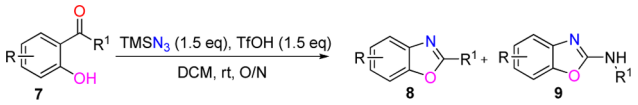
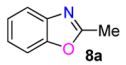
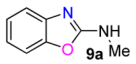
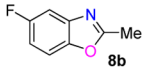
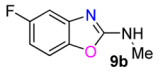
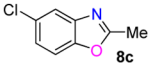
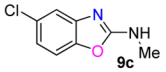
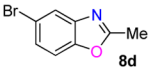
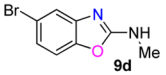
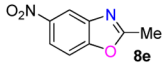
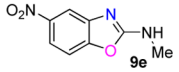
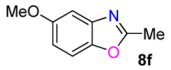
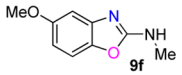
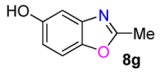
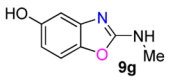
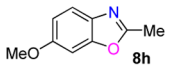
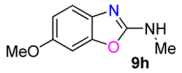
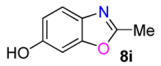
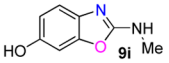
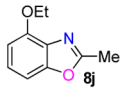
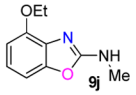
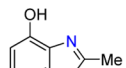
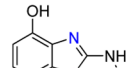
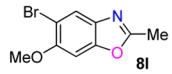
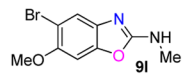
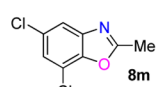
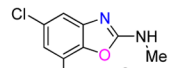
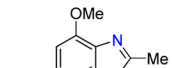
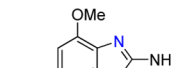
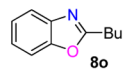
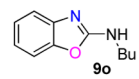
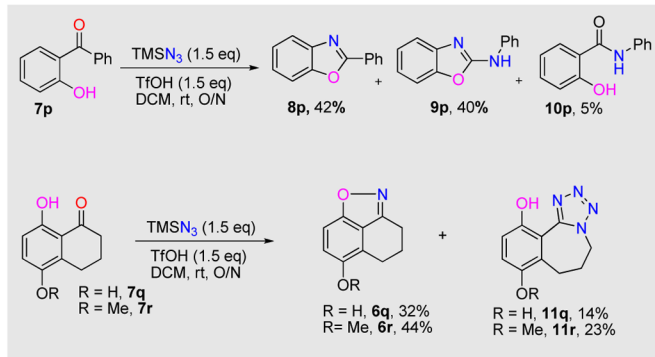
Table 3. Scope of Benzoxazole Synthesis[a]

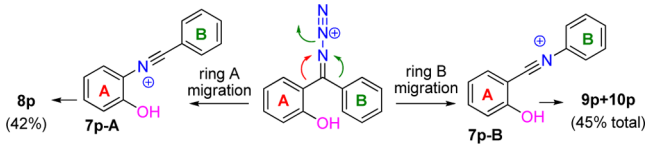


Entry	Product (8)	Product (9)	Yield of 8[a]	Yield of 9[a]
1	 8a	 9a	77%	8%
2	 8b	 9b	83%	13%
3	 8c	 9c	87%	12%
4	 8d	 9d	85%	11%
5	 8e	 9e	83%	12%
6	 8f	 9f	78%	10%
7	 8g	 9g	77%	[b]
8	 8h	 9h	90%	8%
9	 8i	 9i	89%	[b]
10	 8j	 9j	49%	48%
11	 8k	 9k	50%	25%
12	 8l	 9l	88%	7%
13	 8m	 9m	89%	7%
14	 8n	 9n	49%	7%
15	 8o	 9o	79%	16%

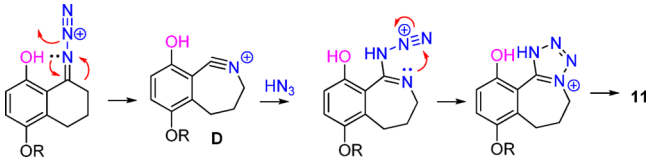


[a]Isolated yields. [b]Byproduct could not be detected.

Scheme 6. Nitrilium Ion Formation from Compound 7p



Scheme 7. Proposed Formation of Products 11q,r



EXPERIMENTAL SECTION

General Procedure. Commercial grade chemicals were used without further purification, unless otherwise specified. All solvents used were purified by the solvent purification system. Oven-dried glassware (110 °C at least for 2 h) was used for all reactions. Crude reaction mixtures were concentrated under reduced pressure by removing the organic solvent with a rotary evaporator. Column chromatography was performed using silica gel 60 (particle size 0.06–0.2 mm; 70–230 mesh ASTM). Analytical thin-layer chromatography (TLC) was performed with silica gel 60 F_{254} aluminum sheets. Nuclear magnetic resonance (NMR) spectra were recorded in deuteriochloroform ($CDCl_3$) or dimethyl sulfoxide-d_6 (DMSO-d_6) with 300 and 600 MHz spectrometers. Chemical shifts for ^{1}H NMR and ^{13}C NMR spectra are reported in parts per million (ppm, δ), relative to tetramethylsilane (TMS) as the internal reference. Coupling constants (J) are reported in hertz (Hz). Infrared spectra were measured using an FT-IR spectrometer and are reported in cm^{-1}. High-resolution mass spectra (HRMS) were obtained using a time-of-flight (TOF) instrument.

General Procedure for the Synthesis of Benzonitriles 2a–w (Scheme 2). A solution of aldehyde **1c** (134.6 mg, 0.9886 mmol, 1.0 equiv) in CH_3CN (2.0 mL/mmol) was added to $TMSN_3$ (131 μL, 0.9886 mmol, 1.0 equiv) and $ZrCl_4$ (130.4 mg, 0.9886 mmol, 1.0 equiv) at room temperature. The reaction mixture was stirred for 20 min and then quenched with saturated sodium bicarbonate

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($NaHCO_3$). The resulting solution was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to provide the crude product, which was purified on silica gel (1/4 EtOAc/hexane) to yield the corresponding nitrile product **2c** (123.6 mg, 94%). The reaction mixtures of substrates **1j,n** were stirred at room temperature overnight, and the reaction mixtures of substrates **1h,w** were quenched with water.

*4-tert-Butylbenzonitrile (**2a**):*[1f] yield 127.0 mg (78%, yellow oil); (1/4 EtOAc/hexane); IR (neat) ν_{max} 2965, 2228, 1606, 1505, 1465, 1365, 1270, 1106, 1018, 837 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, 2H, J = 8.4 Hz), 7.48 (d, 2H, J = 8.4 Hz), 1.33 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 131.9, 126.1, 119.2, 109.2, 35.2, 30.9; LRMS (EI) m/z (rel intensity) 159 (M^+, 20), 144 (100), 116 (54), 57 (10).

*3-Methoxybenzonitrile (**2b**):* yield 96.5 mg (74%, brown oil) (1/9 EtOAc/hexane); IR (neat) ν_{max} 3078, 2943, 2230, 1595, 1578, 1483, 1289, 1263, 1035, 784, 680 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.34 (m, 1H), 7.27−7.22 (m, 1H), 7.14−7.13 (m, 2H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 130.2, 124.4, 119.2, 118.6, 116.8, 113.1, 55.4; HRMS (ESI-TOF) calcd for C_8H_7NNaO $(M + Na)^+$ 156.0420 found 156.0413.

*4-Methoxybenzonitrile (**2c**):* yield 123.6 mg (94%, brown solid); mp 58−59 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3010, 2925, 2224, 1604, 1507, 1464, 1255, 1022, 833, 682 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62−7.57 (m, 2H), 6.98−6.93 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 133.8, 119.1, 114.6, 103.8, 55.4; HRMS (ESI-TOF) calcd for C_8H_7NNaO $(M + Na)^+$ 156.0420, found 156.0414.

*2,4-Dimethoxybenzonitrile (**2d**):* yield 146.7 mg (91%, yellow solid); mp 91−92 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3097, 2919, 2229, 1598, 1455, 1211, 1163, 1051, 827, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45 (dd, 1H, J = 8.7, 0.9 Hz), 6.52 (dd, 1H, J = 8.7, 2.1 Hz), 6.46 (d, 1H, J = 2.1 Hz), 3.90 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 162.6, 134.7, 116.9, 105.7, 98.2, 93.6, 55.8, 55.6; HRMS (ESI-TOF) calcd for $C_9H_9NNaO_2$ $(M + Na)^+$ 186.0526, found 186.0533.

*3,4-Dimethoxybenzonitrile (**2e**):*[9] yield 159.5 mg (93%, white solid); mp 50−51 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3086, 2939, 2224, 1598, 1512, 1461, 1266, 1244, 1136, 1018, 927, 852, 812, 765 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29 (dd, 1H, J = 8.4, 1.8 Hz), 7.08 (d, 1H, J = 1.8 Hz), 6.91 (d, 1H, J = 8.4 Hz), 3.94 (s, 3H), 3.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.4, 148.7, 126.0, 118.8, 113.5, 110.9, 103.3, 55.7, 55.67; LRMS (EI) m/z (rel intensity) 163 (M^+, 100), 148 (34), 120 (20), 92 (27), 77 (20).

*3,5-Dimethoxybenzonitrile (**2f**):* yield 116.3 mg (69%, light yellow solid); mp 85−86 °C (1/19 to 1/9 EtOAc/hexane); IR (neat) ν_{max} 3097, 2919, 2229, 1598, 1455, 1211, 1163, 1051, 827, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.76−6.75 (m, 2H), 6.66−6.64 (m, 1H), 3.81 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 118.7, 113.3, 109.8, 105.6, 55.6; HRMS (ESI-TOF) calcd for $C_9H_9NNaO_2$ $(M + Na)^+$ 186.0526, found 186.0526.

*3,4-Bis(benzyloxy)benzonitrile (**2g**):* yield 237.1 mg (76%, white solid); mp 61−62 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3033, 2871, 2224, 1597, 1509, 1454, 1266, 1135, 1003, 851, 809, 734 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42−7.28 (m, 10H), 7.22−7.17 (m, 1H), 7.11 (d, 1H, J = 1.5 Hz), 6.91 (d, 1H, J = 8.4 Hz), 5.18 (s, 2H), 5.12 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 148.6, 136.0, 135.8, 128.6, 128.1, 127.1, 127.0, 126.7, 119.0, 117.2, 113.8, 104.0, 71.2, 70.7; HRMS (ESI-TOF) calcd for $C_{21}H_{17}NNaO_2$ $(M + Na)^+$ 338.1152, found 338.1155.

*4-Hydroxybenzonitrile (**2h**):* yield 108.7 mg (93%, yellow solid); mp 108−109 °C (1/1 EtOAc/hexane); IR (neat) ν_{max} 3274, 2230, 1608, 1510, 1438, 1282, 1168, 836, 735, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, 2H, J = 8.7 Hz), 6.95 (d, 2H, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 134.3, 119.4, 116.4, 102.8; HRMS (ESI-TOF) calcd for C_7H_5NNaO $(M + Na)^+$ 142.0263, found 142.0269.

*2-Bromobenzonitrile (**2i**):* yield 126.6 mg (72%, white solid); mp 50−51 °C (1/19 EtOAc/hexane); IR (neat) ν_{max} 3748, 3088, 2922, 2225, 1821, 1701, 1584, 1466, 1435, 1264, 1044, 755, 658 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71−7.65 (m, 2H), 7.51−7.41 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.2, 133.8, 133.1, 127.6, 125.2, 117.0, 115.8; HRMS (ESI-TOF) calcd for C_7H_4BrNNa (Br-79) $(M + Na)^+$ 203.9419, found 203.9410.

*3-Bromobenzonitrile (**2j**):* yield 120.2 mg (67%, white solid); mp 38−39 °C (1/9 EtOAc/hexane); IR (neat) ν_{max} 3069, 2233, 1759, 1561, 1472, 1409, 1191, 1076, 882, 786, 675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.75 (d, 1H, J = 8.1 Hz), 7.61 (d, 1H, J = 7.8 Hz), 7.37 (t, 1H, J = 7.8); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.0, 134.7, 130.64, 130.55, 122.8, 117.2, 114.1; HRMS (ESI-TOF) calcd for C_7H_5BrN (Br-79) $(M + H)^+$ 181.9600, found 181.9608.

*4-Bromobenzonitrile (**2k**):* yield 140.6 mg (77%, light yellow solid); mp 109−110 °C (1/9 EtOAc/hexane); IR (neat) ν_{max} 3559, 2925, 2369, 2154, 1961, 1678, 1489, 1249, 1071, 1011, 822 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.66−7.62 (m, 2H), 7.55−7.51 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.4, 132.6, 128.0, 118.0, 111.2; HRMS (ESI-TOF) calcd for C_7H_5BrN (Br-79) $(M + H)^+$ 181.9600, found 181.9603.

*3-Fluoro-4-methylbenzonitrile (**2l**):*[16] yield 109.1 mg (74%, white solid); mp 41−42 °C (1/9 EtOAc/hexane); IR (neat) ν_{max} 2925, 2854, 2368, 2110, 1971, 1725, 1509, 1460, 1379, 1262, 1118, 803 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.28 (m, 3H), 2.35 (d, 3H, J = 1.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5 (d, J_{CF} = 247 Hz), 132.3 (d, J_{CF} = 6 Hz), 131.3 (d, J_{CF} = 17 Hz), 127.8 (d, J_{CF} = 4 Hz), 118.4 (d, J_{CF} = 26 Hz), 17.7 (d, J_{CF} = 3 Hz), 110.7 (d, J_{CF} = 9 Hz), 14.7 (d, J_{CF} = 3 Hz); LRMS (EI) m/z (rel intensity) 135 (M^+, 23), 123 (29), 111 (52), 97 (63), 57 (100).

*Biphenyl-4-carbonitrile (**2m**):* yield 148.9 mg (83%, white solid); mp 83−84 °C (1/19 EtOAc/hexane); IR (neat) ν_{max} 3404, 3061, 2226, 1931, 1605, 1484, 1396, 769, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74−7.66 (m, 4H), 7.61−7.57 (m, 2H), 7.52−7.39 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.6, 139.1, 132.6, 129.1, 128.6, 127.7, 127.2, 118.9, 110.8; HRMS (ESI-TOF) calcd for $C_{13}H_{10}N$ $(M + H)^+$ 180.0808, found 180.0802.

*4-Nitrobenzonitrile (**2n**):*[9] yield 95.2 mg (64%, white solid); mp 145−146 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3107, 3053, 2233, 1601, 1524, 1489, 1347, 1294, 859, 682 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.40−8.36 (m, 2H), 7.94−7.89 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 133.4, 124.2, 118.3, 116.8; LRMS (EI) m/z (rel intensity) 148 (M^+, 54), 118 (12), 102 (100), 90 (27).

*2,3,4-Trimethoxybenzonitrile (**2o**):* yield 131.1 mg (68%, white solid); mp 51−52 °C (1/49 to 1/9 EtOAc/hexane); IR (neat) ν_{max} 2945, 2226, 1592, 1491, 1471, 1415, 1298, 1095, 1033, 803, 708 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, 1H, J = 9.0 Hz), 6.69 (d, 1H, J = 8.7 Hz), 4.06 (s. 3H), 3.92 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 155.6, 141.6, 128.5, 116.3, 107.4, 98.8, 61.5, 60.9, 56.1; HRMS (ESI-TOF) calcd for $C_{10}H_{12}NO_3$ $(M + H)^+$ 194.0812, found 194.0814.

*3,4,5-Trimethoxybenzonitrile (**2p**):* yield 171.2 mg (90%, white solid); mp 90−91 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3071, 2940, 2225, 1716, 1581, 1501, 1335, 1239, 1128, 996, 736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.79 (s, 2H), 3.82 (s, 3H), 3.80 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4, 142.2, 118.8, 109.3, 106.5, 60.8, 56.2; HRMS (ESI-TOF) calcd for $C_{10}H_{11}NNaO_3$ $(M + Na)^+$ 216.0631, found 216.0636.

*4-Hydroxy-3,5-dimethoxybenzonitrile (**2q**):* yield 151.1 mg (85%, orange solid); mp 118−119 °C (1/1 EtOAc/hexane); IR (neat) ν_{max} 3361, 2941, 2224, 1606, 1512, 1455, 1334, 1207, 1109, 852, 736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.88 (s, 2H), 6.12 (br s, 1H), 3.92 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1, 139.2, 119.2, 109.0, 102.1, 56.5; HRMS (ESI-TOF) calcd for $C_9H_{10}NO_3$ $(M + H)^+$ 180.0655, found 180.0660.

*2-Chloro-3,4-dimethoxybenzonitrile (**2r**):* yield 168.9 mg (85%, white solid); mp 93−94 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3015, 2943, 2580, 2227, 1872, 1585, 1484, 1301, 1272, 1039, 1026, 927, 807, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, 1H, J = 8.7 Hz), 6.93 (d, 1H, J = 8.7 Hz), 3.97 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 146.0, 130.7, 129.6, 116.0, 110.8, 105.3, 60.6,

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56.2; HRMS (ESI-TOF) calcd for $C_9H_8ClNNaO_2$ (Cl-35) $(M + Na)^+$ 220.0136, found 220.0142.

*2-Naphthonitrile (**2s**):* yield 120.4 mg (81%, yellow solid); mp 60−61 °C (1/9 EtOAc/hexane); IR (neat) ν_{max} 3059, 2226, 1694, 1627, 1597, 1502, 1366, 1271, 1160, 899, 861, 814, 746 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.94−7.88 (m, 3H), 7.68−7.88 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.4, 133.9, 132.0, 129.0, 128.9, 128.2, 127.9, 127.5, 126.1, 119.1, 109.1; HRMS (ESI-TOF) calcd for $C_{11}H_8N$ $(M + H)^+$ 154.0651, found 154.0658.

*Cinnamonitrile (**2u**):* yield 122.6 mg (92%, yellow oil) (1/9 EtOAc/hexane); IR (neat) ν_{max} 3054, 2217, 1617, 1448, 964, 746, 688 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.34 (m, 6H), 5.85 (d, 1H, J = 16.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 133.3, 131.0, 128.9, 127.2, 118.0, 96.2; HRMS (ESI-TOF) calcd for C_9H_7NNa $(M + Na)^+$ 152.0471, found 152.0475.

*(E)-3-(4-Methoxyphenyl)acrylonitrile (**2v**):* yield 156.7 mg (93%, white solid); mp 58−59 °C (1/9 EtOAc/hexane); IR (neat) ν_{max} 3057, 2936, 2214, 1782, 1615, 1599, 1508, 1250, 1174, 1022, 985, 806 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.35 (m, 2H), 7.29 (d, 1H, J = 16.5 Hz), 6.93−6.88 (m, 2H), 5.69 (d, 1H, J = 16.5 Hz), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 149.8 128.9, 126.1, 118.5, 114.3, 93.1, 55.2; HRMS (ESI-TOF) calcd for $C_{10}H_9NNaO$ $(M + Na)^+$ 182.0576, found 182.0583.

*(E)-3-(4-Hydroxy-3-methoxyphenyl)acrylonitrile (**2w**):* yield 172.1 mg (97%, yellow solid); mp 107−108 °C (3/7 EtOAc/hexane); IR (neat) ν_{max} 3386, 3017, 2212, 1775, 1598, 1508, 1457, 1272, 1185, 970, 807 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, 1H, J = 16.5 Hz), 7.01−6.90 (m, 3H), 5.70 (d, 1H, J = 16.5 Hz), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 148.6, 146.8, 126.0, 122.3, 118.6, 114.8, 108.6, 93.0, 55.9; HRMS (ESI-TOF) calcd for $C_{10}H_{10}NO_2$ $(M + H)^+$ 176.0706, found 176.0707.

*6,7-Dimethoxybenzo[d]isoxazole (**3o**):* yield 7.2 mg (4%, yellow solid); mp 52−53 °C (1/49 to 1/9 EtOAc/hexane); IR (neat) ν_{max} 2942, 1619, 1489, 1311, 1281, 1240, 1098, 979, 796 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.32 (d, 1H, J = 8.4 Hz), 7.01 (d, 1H, J = 8.7 Hz), 4.24 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4, 151.9, 146.0, 132.9, 117.8, 114.8, 111.2, 60.7, 57.2; HRMS (ESI-TOF) calcd for $C_9H_{10}NO_3$ $(M + H)^+$ 180.0655, found 180.0660.

General Procedure for the Synthesis of Benzisoxazoles (Table 2). A solution of aldehyde **4f** (152.6 mg, 0.9746, 1.0 equiv) in CH_3CN (2.0 mL/mmol) was added to $TMSN_3$ (130 μL, 0.9746 mmol, 1.0 equiv) and $ZrCl_4$ (227.1 mg, 0.9746 mmol, 1.0 equiv) at room temperature. The reaction mixture was stirred for 20 min and then quenched with saturated sodium bicarbonate ($NaHCO_3$). The resulting solution was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to provide the crude product, which was purified on silica gel (3/7 EtOAc/hexane) to yield the corresponding nitrile product **5f** (49.9 mg, 33%) and benzisoxazole **6f** (72.8 mg, 49%) The reaction mixtures of substrates **4b**−**d**,**g**−**i** and **7d** were stirred at room temperature overnight, and the reaction mixtures of substrates **4a**−**i** and **7d** were quenched with water.

*2-Hydroxybenzonitrile (**5a**):*[1g] yield 59.3 mg (43%, light yellow solid); mp 90−91 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3282, 2953, 2230, 1604, 1455, 1352, 1305, 1233, 1099, 846, 748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−7.39 (m, 2H), 7.05 (d, 1H, J = 8.4 Hz), 6.96 (t, 1H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 134.9, 133.0, 120.5, 116.6, 116.5, 98.9; LRMS (EI) m/z (rel intensity) 119 (M^+, 92), 97 (33), 91 (100), 81 (43), 69 (58), 57 (46).

*Benzo[d]isoxazole (**6a**):*[2c] yield 39.7 mg (29%, light yellow oil) (1/4 EtOAc/hexane); IR (neat) ν_{max} 3098, 1611, 1512, 1430, 1228, 1175, 934, 839, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.73 (d, 1H, J = 7.8 Hz), 7.63−7.53 (m, 2H), 7.32 (t, 1H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 146.1, 130.0, 123.6, 121.9, 121.2, 109.6.

*3,5-Di-tert-Butyl-2-hydroxybenzonitrile (**5b**):* yield 66.0 mg (28%, light yellow solid); mp 113−114 °C (1/49 to 1/19 EtOAc/hexane); IR (neat) ν_{max} 3300, 2961, 2232, 1603, 1479, 1363, 1218, 1201, 878 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45 (d, 1H, J = 2.4 Hz), 7.23 (d, 1H, J = 2.4 Hz), 5.94 (br s, 3H), 1.34 (s, 9H), 1.21 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.8, 143.6, 137.1, 129.8, 126.0, 117.3, 99.5, 35.1, 34.4, 31.2, 29.4; HRMS (ESI-TOF) calcd for $C_{15}H_{22}NO$ $(M + H)^+$ 232.1696, found 232.1693.

*5,7-Di-tert-butylbenzo[d]isoxazole (**6b**):* yield 48.7 mg (21%, yellow oil) (1/49 to 1/19 EtOAc/hexane); IR (neat) ν_{max} 2959, 2871, 1616, 1465, 1364, 1168, 883, 854, 765 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.45 (d, 1H, J = 1.8 Hz), 7.42 (d, 1H, J = 1.5 Hz), 1.45 (s, 9H), 1.30 (s. 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 147.0, 146.3, 133.5, 124.5, 121.8, 115.0, 34.9, 34.6, 31.6, 29.7; HRMS (ESI-TOF) calcd for $C_{15}H_{22}NO$ $(M + H)^+$ 232.1696, found 232.1696.

*2-Hydroxy-4-methoxybenzonitrile (**5c**):*[1d] yield 123.4 mg (77%, white solid); mp 171−172 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3218, 2227, 1595, 1435, 1276, 1212, 1104, 830, 673 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 7.49 (d, 1H, J = 9.0 Hz), 6.53−6.50 (m, 2H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.0, 161.8, 134.3, 117.4, 106.6, 101.1, 91.3, 55.5. LRMS (EI) m/z (rel intensity) 149 (M^+, 100), 119 (12), 106 (38), 91 (30).

*6-Methoxybenzo[d]isoxazole (**6c**):*[2d] yield 36.0 mg (22%, colorless oil) (1/4 EtOAc/hexane); IR (neat) ν_{max} 3091, 2942, 1615, 1491, 1300, 1273, 1114, 946, 822 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.58 (s, 1H), 7.56 (d, 1H, J = 8.7 Hz), 7.04 (s, 1H), 6.93 (dd, 1H, J = 8.7, 2.1 Hz), 3.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1, 162.2, 145.8, 122.0, 114.7, 114.6, 92.3, 55.7. LRMS (EI) m/z (rel intensity) 149 (M^+, 100), 134 (17), 111 (14), 106 (36), 91 (20).

*2-Hydroxy-5-methoxybenzonitrile (**5d**):*[2d] yield 68.0 mg (65%, orange solid); mp 129−130 °C (3/7 EtOAc/hexane); IR (neat) ν_{max} 3292, 2965, 2232, 1599, 1508, 1424, 1202, 1156, 1032, 820 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 10.53 (s, 1H), 7.16−7.09 (m, 2H), 6.94 (d, 1H, J = 9.0 Hz), 3.71 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 154.4, 151.8, 122.2, 117.3, 116.9, 115.9, 98.5, 55.8. LRMS (EI) m/z (rel intensity) 149 (M^+, 100), 134 (93), 106 (33).

*5-Methoxybenzo[d]isoxazole (**6d**):* yield 29.1 mg (28%, yellow oil) (3/7 EtOAc/hexane); IR (neat) ν_{max} 3100, 2939, 1621, 1515, 1448, 1290, 1209, 1145, 1026, 850, 801, 749 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.52 (d, 1H, J = 9.3 Hz), 7.19 (dd, 1H, J = 9.0, 2.1 Hz), 7.08 (d, 1H, J = 1.9 Hz), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 156.4, 146.1, 121.6, 120.7, 110.4, 101.8, 55.8; HRMS (ESI-TOF) calcd for $C_8H_7NO_2$ $(M + H)^+$ 150.0550, found 150.0554.

*5-Bromo-2-hydroxybenzonitrile (**5e**):* yield 70.1 mg (35%, yellow solid); mp 156−157 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3276, 2926, 2236, 1602, 1491, 1409, 1299, 1121, 822, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.42 (br s, 1H), 7.84 (d, 1H, J = 2.7 Hz), 7.64 (dd, 1H, J = 8.7, 2.4 Hz), 6.96 (d, 1H, J = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 137.5, 135.0, 118.3, 115.6, 109.7, 100.9; HRMS (ESI-TOF) calcd for C_7H_3BrNO (Br-79) $(M - H)^-$ 195.9404, found 195.9404.

*5-Bromobenzo[d]isoxazole (**6e**):*[2g] yield 106.4 mg (52%, white solid); mp 76−77 °C (1/4 EtOAc/hexane); IR (neat) ν_{max} 3095, 2238, 1901, 1604, 1507, 1420, 1226, 1170, 892, 808, 778, 679 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.89 (d, 1H, J = 1.2 Hz), 7.67 (dd, 1H, J = 8.7, 1.8 Hz), 7.52 (d, 1H, J = 9.0); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 145.4, 133.1, 124.4, 123.2, 116.6, 111.2; LRMS (EI) m/z (rel intensity) 198 (M^+, 96), 196 (100), 171 (61), 169 (64), 69 (62), 57 (45).

*5-Chloro-2-hydroxybenzonitrile (**5f**):* yield 49.2 mg (33%, brown solid); mp 162−163 °C (3/7 EtOAc/hexane); IR (neat) ν_{max} 3240, 2240, 1606, 1498, 1412, 1303, 824 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.42 (br s, 1H), 7.76 (d, 1H, J = 2.7 Hz), 7.54 (dd, 1H, J = 9.0, 2.7 Hz), 7.02 (d, 1H, J = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 134.7, 132.2, 122.7, 117.9, 115.7, 100.3; HRMS (ESI-TOF) calcd for C_7H_3ClNO (Cl-35) $(M - H)^-$ 151.9909, found 151.9907.

*5-Chlorobenzo[d]isoxazole (**6f**):* yield 72.3 mg (49%, light yellow solid); mp 59−60 °C (3/7 EtOAc/hexane); IR (neat) ν_{max} 3097, 1739, 1614, 1502, 1423, 1228, 1173, 1116, 807, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.71 (d, 1H, J = 0.9 Hz), 7.58−7.50 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 145.6, 130.5, 129.3, 122.5, 121.2, 110.8; HRMS (ESI-TOF) calcd for C_7H_5ClNO (Cl-35) $(M + H)^+$ 154.0054, found 154.0048.

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*2-Hydroxy-5-nitrobenzonitrile (**5g**):*[1d] yield 18.2 mg (11%, yellow solid); mp 171−172 °C (3/7 EtOAc/hexane); IR (neat) ν_{max} 3084, 2235, 1591, 1532, 1489, 1341, 1299, 1134, 1079, 910, 834, 748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, 1H, J = 3.0 Hz), 8.25 (dd, 1H, J = 9.6, 3.0 Hz), 6.96 (d, 1H, J = 9.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 137.1, 130.6, 130.0, 117.7, 116.0, 99.8; LRMS (EI) m/z (rel intensity) 164 (M^+, 24), 149 (100), 111 (34), 85 (48), 69 (57) 57 (76).

*5-Nitrobenzo[d]isoxazole (**6g**):*[17] yield 99.7 mg (62%, light yellow solid); mp 122−123 °C (3/7 EtOAc/hexane); IR (neat) ν_{max} 3108, 1619, 1520, 1350, 1267, 1073, 912, 827, 688 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.66 (d, 1H, J = 2.1 Hz), 8.42 (dd, 1H, J = 9.3, 2.4 Hz), 7.68 (d, 1H, J = 9.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.2, 147.0, 144.6, 125.5, 121.8, 119.2, 110.4; LRMS (EI) m/z (rel intensity) 164 (M^+, 32), 149 (100), 134 (24), 71 (47).

*2-Hydroxy-1-naphthonitrile (**5h**):* yield 28.3 mg (15%, light yellow solid); mp 148−149 °C (1/9 to 1/4 EtOAc/hexane); IR (neat) ν_{max} 3245, 2925, 2224, 1626, 1515, 1438, 1286, 817, 748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, 1H, J = 8.4 Hz), 7.95 (d, 1H, J = 9.0 Hz), 7.82 (d, 1H, J = 8.1 Hz), 7.64 (ddd, 1H, J = 8.4, 7.2, 1.2 Hz), 7.46 (ddd, 1H, J = 8.1, 7.2, 1.2 Hz), 7.18 (d, 1H, J = 9.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.4, 135.3, 132.8, 129.1, 128.6, 128.1, 125.2, 124.0, 117.3, 115.6, 92.8; HRMS (ESI-TOF) calcd for $C_{11}H_7NNaO$ $(M + Na)^+$ 192.0420, found 192.0415.

*Naphtho[1,2-d]isoxazole (**6h**):* yield 119.3 mg (65%, light yellow solid); mp 74−75 °C (1/9 to 1/4 EtOAc/hexane); IR (neat) ν_{max} 3098, 3068, 1632, 1581, 1532, 1486, 1254, 1170, 930, 812, 753 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.16 (d, 1H, J = 8.4 Hz), 8.01−7.96 (m, 2H), 7.75−7.67 (m, 2H), 7.60−7.55 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 144.8, 131.6, 130.3, 128.9, 128.1, 126.6, 125.5, 123.1, 116.3, 110.1; HRMS (ESI-TOF) calcd for $C_{11}H_8NO$ $(M + H)^+$ 170.0600, found 170.0605.

*6-Bromo-2-hydroxy-3-methoxybenzonitrile (**5i**):* yield 116.1 mg (49%, brown solid); mp 123−124 °C (1/19 EtOAc/hexane); IR (neat) ν_{max} 3276, 2938, 2240, 1595, 1488, 1438, 1279, 1257, 1068, 881, 804 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, 1H, J = 8.7 Hz), 6.90 (d, 1H, J = 8.7 Hz), 3.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 145.9, 123.7, 115.2, 114.6, 114.2, 102.4, 56.5; HRMS (ESI-TOF) calcd for $C_8H_6BrNNaO_2$ (Br-79) $(M + Na)^+$ 249.9474, found 249.9482.

*4-Bromo-7-methoxybenzo[d]isoxazole (**6i**):* yield 82.5 mg (35%, brown solid); mp 123−124 °C (1/19 EtOAc/hexane); IR (neat) ν_{max} 3094, 3004, 2848, 2324, 1860, 1719, 1606, 1460, 1260, 1177, 981, 816. 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.28−7.26 (d, 1H, J = 8.4 Hz), 6.79 (d, 1H, J = 8.1 Hz), 3.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 146.3, 143.9, 127.2, 124.2, 112.2, 103.7, 56.5; HRMS (ESI-TOF) calcd for $C_8H_7BrNO_2$ (Br-79) $(M + H)^+$ 227.9655, found 227.9661.

General Procedure for the Synthesis of Benzoxazoles 8a−p and Benzisoxazoles 6q,r (Table 3). A solution of ketone **7d** (133.4 mg, 0.6203 mmol, 1.0 equiv) in dry DCM (2 mL, 3.0 mL/mmol) was added to $TMSN_3$ (130 μL, 0.9305 mmol, 1.5 equiv) and TfOH (80 μL, 0.9305 mmol, 1.5 equiv) at room temperature, and the mixture was stirred overnight. Then, the reaction mixture was quenched with saturated sodium bicarbonate ($NaHCO_3$). The resulting solution was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to provide the crude product, which was purified on silica gel (1/9 to 1/1 EtOAc/hexane) to yield the corresponding products **8d** (111.6 mg, 85%) and **9d** (14.9 mg, 11%). The reaction mixtures of substrates **7g,i,k,q** were quenched with water.

*2-Methylbenzo[d]oxazole (**8a**):* yield 102.0 mg (77%%, colorless oil) (1/9 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 2919, 1241, 1059 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68−7.62 (m, 1H), 7.48−7.43 (m, 1H), 7.30−7.24 (m, 2H), 2.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 150.9, 141.3, 124.4, 124.0, 119.3, 110.1, 14.4; ESI-HRMS calcd for C_8H_8NO $(M + H)^+$ 136.0600, found 134.0605.

*N-Methylbenzo[d]oxazol-2-amine (**9a**):* yield 11.1 mg (8%, colorless crystal); mp 96−97 °C (1/9 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3223, 1646, 1584, 1459, 1241, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37 (dd, 1H, J = 7.8, 0.6 Hz), 7.24 (d, 1H, J = 7.8 Hz), 7.16 (td, 1H, J = 7.8, 1.2 Hz), 7.03 (td, 1H, J = 7.8, 1.2 Hz), 3.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 148.5, 142.8, 123.9, 120.8, 116.2, 108.7, 29.4; ESI-HRMS calcd for $C_8H_9N_2O$ $(M + H)^+$ 149.0709, found 149.0712.

*5-Fluoro-2-methylbenzo[d]oxazole (**8b**):* yield 120.8 mg (83%, colorless oil); (1/9 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 2920, 1457, 1261, 1028, 801 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39−7.30 (m, 2H), 7.00 (td, 1H, J = 9.3, 2.7 Hz), 2.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 159.7 (d, J_{CF} = 238 Hz), 147.1 (d, J_{CF} = 1.0 Hz), 142.1 (d, J_{CF} = 13 Hz), 111.8 (d, J_{CF} = 26 Hz), 110.3 (d, J_{CF} = 10 Hz), 105.8 (d, J_{CF} = 26 Hz), 14.5; ESI-HRMS calcd for C_8H_7FNO $(M + H)^+$ 152.0506, found 152.0508.

*5-Fluoro-N-methylbenzo[d]oxazol-2-amine (**9b**):* yield 20.4 mg (13%, white solid); mp 117−118 °C (1/9 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3174, 2924, 1682, 1587, 1416, 1130, 833 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.15 (dd, 1H, J = 8.7, 4.5 Hz), 7.05 (dd, 1H, J = 8.7, 2.4 Hz), 6.73 (td, 1H, J = 9.6, 2.7 Hz), 3.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 160.1 (d, J_{CF} = 237 Hz), 144.7, 143.5 (d, J_{CF} = 13.0 Hz), 108.7 (d, J_{CF} = 10 Hz), 107.4 (d, J_{CF} = 26 Hz), 103.4 (d, J_{CF} = 27 Hz), 29.4; ESI-HRMS calcd for $C_8H_8FN_2O$ $(M + H)^+$ 167.0615, found 167.0622.

*5-Chloro-2-methylbenzo[d]oxazole (**8c**):* yield 129.5 mg (87%, white solid); mp 51−52 °C (1/9 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 2925, 1658, 1457, 1260, 1029 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, 1H, J = 2.1 Hz), 7.38 (d, 1H, J = 8.7 Hz), 7.26 (dd, 1H, J = 8.7, 2.1 Hz), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 149.5, 142.5, 129.6, 124.7, 119.4, 110.9, 14.5; ESI-HRMS calcd for C_8H_7ClNO (Cl-35) $(M + H)^+$ 168.0211, found 168.0208.

*5-Chloro-N-methylbenzo[d]oxazol-2-amine (**9c**):* yield 20.0 mg (12%, white solid); mp 132−133 °C (1/9 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3062, 2923, 1686, 1578, 1463, 1255, 799 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, 1H, J = 1.8 Hz), 7.14 (d, 1H, J = 8.4 Hz), 6.99 (dd, 1H, J = 8.4, 1.8 Hz), 3.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 147.1, 143.8, 129.4, 120.8, 116.2, 109.3, 29.4; ESI-HRMS calcd for $C_8H_8ClN_2O$ (Cl-35) $(M + H)^+$ 183.0320, found 183.0321.

*5-Bromo-2-methylbenzo[d]oxazole (**8d**):* yield 111.6 mg (85%, white solid); mp 57−58 °C (1/9 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 2921, 1567, 1449, 1258, 900, 800 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, 1H, J = 1.8 Hz), 7.39 (dd, 1H, J = 8.7, 2.1 Hz), 7.32 (d, 1H, J = 8.7 Hz), 2.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 149.8, 143.0, 127.4, 122.3, 116.7, 111.3, 14.4; ESI-HRMS calcd for C_8H_7BrNO (Br-79) $(M + H)^+$ 211.9706, found 211.9700.

*5-Bromo-N-methylbenzo[d]oxazol-2-amine (**9d**):* yield 14.9 mg (11%, yellow solid); mp 139−140 °C (1/9 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3149, 2948, 1684, 1651, 1581, 1299, 1246, 799 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, 1H, J = 1.8 Hz), 7.14 (dd, 1H, J = 8.7, 1.8 Hz), 7.10 (d, 1H, J = 8.4 Hz), 5.71 (br s, 1H), 3.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 147.5, 144.3, 123.5, 119.1, 116.7, 109.9, 29.4; ESI-HRMS calcd for $C_8H_8BrN_2O$ $(M + H)^+$ 226.9815, found 226.9819.

*2-Methyl-5-nitrobenzo[d]oxazole (**8e**):* yield 129.7 mg (83%, bright yellow solid); mp 154−155 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 1616, 1518, 1347, 829 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, 1H, J = 2.1 Hz), 8.26 (dd, 1H, J = 9.0, 2.4 Hz), 7.59 (d, 1H, J = 9.0 Hz), 2.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0, 154.4, 144.9, 141.8, 120.5, 115.6, 110.3, 14.5; ESI-HRMS calcd for $C_8H_7N_2O_3$ $(M + H)^+$ 179.0451, found 179.0455.

*N-Methyl-5-nitrobenzo[d]oxazol-2-amine (**9e**):* yield 18.9 mg (12%, yellow solid); mp 232−233 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 3086, 2921, 1700, 1517, 1343, 1261, 736 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 8.32 (br q, 1H, J = 4.5 Hz), 8.00 (s, 1H), 7.93 (dd, 1H, J = 8.7, 0.6 Hz), 7.55 (d, 1H, J = 8.7 Hz), 2.93 (d, 3H, J = 4.8 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.8, 152.5, 144.38, 144.35, 116.7, 110.1, 108.7, 28.8; ESI-HRMS calcd for $C_8H_8N_3O_3$ $(M + H)^+$ 194.0560, found 194.0561.

*5-Methoxy-2-methylbenzo[d]oxazole (**8f**):* yield 112.0 mg (78%, brown oil) (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 2932, 1577, 1482, 1172, 1151, 846 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (d,

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1H, J = 8.7 Hz), 7.14 (d, 1H, J = 2.4 Hz), 7.87 (dd, 1H, J = 9.0, 2.7 Hz), 3.82 (s, 3H), 2.59 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 156.9, 145.4, 142.1, 112.5, 110.1, 102.5, 55.7, 14.4; ESI-HRMS calcd for $C_9H_{10}NO_2$ $(M + H)^+$ 164.0706, found 164.0711.

*5-Methoxy-N-methylbenzo[d]oxazol-2-amine (**9f**):* yield 15.0 mg (10%, brown solid); mp 87−88 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3227, 2942, 1652, 1587, 1196, 1162, 1062 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (d, 1H, J = 8.7 Hz), 6.93 (d, 1H, J = 2.4 Hz), 6.59 (dd, 1H, J = 8.7, 2.7 Hz), 3.81 (s, 3H), 3.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 157.0, 143.5, 143.0, 108.6, 107.2, 101.4, 55.9, 29.4; ESI-HRMS calcd for $C_9H_{11}N_2O_2$ $(M + H)^+$ 179.0815, found 179.0814.

*2-Methylbenzo[d]oxazol-5-ol (**8g**):* yield 117.0 mg (77%, brown solid); mp 162−163 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 3136, 2926, 2344, 1612, 1577, 1474, 1282, 1153, 941, 844, 733 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, 1H, J = 8.7 Hz), 7.18 (d, 1H, J = 2.4 Hz), 6.86 (dd, 1H, J = 8.7, 2.4 Hz), 4.18 (br s, 1H), 2.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 153.6, 145.3, 141.2, 113.4, 110.5, 104.9, 14.5; HRMS (ESI-TOF) calcd for $C_8H_8NO_2$ $(M + H)^+$ 150.0550, found 150.0547.

*6-Methoxy-2-methylbenzo[d]oxazole (**8h**):* yield 141.4 mg (90%, brown oil); (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 2932, 1618, 1488, 1297, 1139, 822 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, 1H, J = 8.7 Hz), 6.99 (d, 1H, J = 2.4 Hz), 6.88 (dd, 1H, J = 8.7, 2.4 Hz), 3.83 (s, 3H), 2.59 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.7, 157.6, 151.6, 135.0, 119.1, 111.9, 95.2, 55.8, 14.3; ESI-HRMS calcd for $C_9H_{10}NO_2$ $(M + H)^+$ 164.0706, found 164.0707.

*6-Methoxy-N-methylbenzo[d]oxazol-2-amine (**9h**):* yield 14.5 mg (8%, reddish solid); mp 87−88 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3178, 1689, 1486, 1135, 1027, 815 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, 1H, J = 8.7 Hz), 6.87 (d, 1H, J = 2.4 Hz), 6.76 (dd, 1H, J = 8.4, 2.4 Hz), 5.14 (br s, 1H), 3.81 (s, 3H), 3.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 155.1, 149.1, 136.4, 115.9, 110.0, 95.9, 56.0, 29.5; ESI-HRMS calcd for $C_9H_{11}N_2O_2$ $(M + H)^+$ 179.0815, found 179.0815.

*2-Methylbenzo[d]oxazol-6-ol (**8i**):* yield 164.2 mg (89%, brown solid); mp 192−193 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 3092, 1625, 1486, 1299, 1232, 1138, 828 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, 1H, J = 8.7 Hz), 6.96 (d, 1H, J = 2.1 Hz), 6.77 (dd, 1H, J = 8.4, 2.1 Hz), 3.53 (br s, 1H), 2.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 155.7, 151.7, 134.0, 119.3, 112.9, 97.4, 14.3; ESI-HRMS calcd for $C_8H_8NO_2$ $(M + H)^+$ 150.0550, found 150.0547.

*4-Ethoxy-2-methylbenzo[d]oxazole (**8j**):* yield 58.9 mg (49%, white solid); mp 160−161 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) $\nu_{max\ 2931,}$ 1683, 1442, 1279, 1090 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (t, 1H, J = 8.1 Hz), 7.06 (d, 1H, J = 8.1 Hz), 7.74 (d, 1H, J = 8.1 Hz), 4.27 (q, 2H, J = 7.2 Hz), 2.62 (s, 3H), 1.51 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 152.3, 150.3, 130.8, 124.9, 106.6, 102.7, 64.4, 14.7; ESI-HRMS calcd for $C_{10}H_{12}NO_2$ $(M + H)^+$ 178.0863, found 178.0869.

*4-Ethoxy-N-methylbenzo[d]oxazol-2-amine (**9j**):* yield 61.7 mg (48%, colorless crystal); mp 161−163 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3043, 2967, 1679, 1070, 718 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96−6.88 (m, 2H), 6.70 (dd, 1H, J = 7.2, 1.8 Hz), 6.40 (br s, 1H), 4.22 (q, 2H, J = 6.9 Hz), 3.13 (s, 3H), 1.47 (t, 3H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 149.6, 148.1, 131.8, 120.7, 107.2, 102.0, 64.2, 29.3, 14.8, 14.2; ESI-HRMS calcd for $C_{10}H_{13}N_2O_2$ $(M + H)^+$ 193.0972, found 193.0967; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.62 (q, 1H, J = 4.8 Hz), 6.95 (dd, 1H, J = 7.8, 0.9 Hz), 6.88 (t, 1H, J = 7.8 Hz), 6.72 (dd, 1H, J = 8.1, 1.2 Hz), 4.19 (q, 2H, J = 6.9 Hz), 2.88 (d, 3H, J = 4.8 Hz), 1.35 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.3, 149.8, 147.9, 132.4, 120.9, 108.8, 102.3, 64.4, 29.3, 15.3.

*2-Methylbenzo[d]oxazol-4-ol (**8k**):* yield 77.5 mg (50%, white solid); mp 140−141 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 3104, 1610, 1243, 1186, 732 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (t, 1H, J = 8.1 Hz), 7.02 (dd, 1H, J = 8.1, 0.6 Hz), 6.89 (dd, 1H, J = 8.1, 0.9 Hz), 2.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 152.0, 148.2, 128.8, 125.8, 111.2, 101.7, 14.0; ESI-HRMS calcd for $C_8H_8NO_2$ $(M + H)^+$ 150.0550, found 150.0547.

*2-(Methylamino)benzo[d]oxazol-4-ol (**9k**):* yield 41.7 mg (25%, brown solid); mp 117−118 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 3387, 2945, 1644, 1247, 1034, 736 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (app t, 1H, J = 8.1 Hz), 6.83 (dd, 1H, J = 7.8, 0.9 Hz), 6.77 (dd, 1H, J = 8.1, 0.9 Hz), 3.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 149.3, 145.7, 129.4, 121.8, 111.6, 101.1, 29.2; ESI-HRMS calcd for $C_8H_9N_2O_2$ $(M + H)^+$ 165.0659, found 165.0659.

*5-Bromo-6-methoxy-2-methylbenzo[d]oxazole (**8l**):* yield 174.2 mg (88%, colorless crystal); mp 147−148 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 2951, 1610, 1469, 1297, 1037, 877 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.00 (s, 1H), 3.91 (s, 1H), 2.59 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 153.4, 150.7, 135.5, 122.9, 107.5, 94.4, 56.6, 14.3; ESI-HRMS calcd for $C_9H_9BrNO_2$ (Br-79) $(M + H)^+$ 241.9811, found 241.9810.

*5-Bromo-6-methoxy-N-methylbenzo[d]oxazol-2-amine (**9l**):* yield 15.7 mg (7%, reddish solid); mp 157−158 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 3151, 2961, 1646, 1469, 1297, 1130, 816 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (m, 1H), 6.94 (s, 1H), 5.19 (br s, 1H), 3.90 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6, 151.1, 148.2, 136.9, 120.0, 106.8, 95.1, 57.1, 29.6; ESI-HRMS calcd for $C_9H_{10}BrN_2O_2$ $(M + H)^+$ 256.9920, found 256.9925.

*5,7-Dichloro-2-methylbenzo[d]oxazole (**8m**):* yield 131.1 mg (89%, white solid); mp 110−111 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 1609, 1574, 1399, 1162, 789 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, 1H, J = 1.8 Hz), 7.29 (d, 1H, J = 1.8 Hz), 2.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 146.3, 143.2, 129.9, 124.9, 118.1, 115.9, 14.5; ESI-HRMS calcd for $C_8H_6Cl_2NO$ $(M + H)^+$ 201.9821, found 201.9816.

*5,7-Dichloro-N-methylbenzo[d]oxazol-2-amine (**9m**):* yield 10.4 mg (7%, colorless crystal); mp 207−208 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3140, 2949, 1693, 1651, 1577, 1410, 998 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, 1H, J = 1.8 Hz), 7.07 (d, 1H, J = 1.8 Hz), 5.86 (br s, 1H), 3.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 143.5, 143.4, 130.1, 121.6, 114.8, 114.6, 29.6; ESI-HRMS calcd for $C_8H_7Cl_2N_2O$ $(M + H)^+$ 216.9930, found 216.9936.

*4,6-Dimethoxy-2-methylbenzo[d]oxazole (**8n**):* yield 73.1 mg (49%, colorless crystal); mp 72−73 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 1619, 1500, 1143, 1103, 848 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.59 (d, 1H, J = 2.1 Hz), 6.37 (d, 1H, J = 2.1 Hz), 3.96 (s, 3H), 3.81 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 158.4, 152.6, 150.7, 124.8, 95.5, 87.1, 55.9, 55.6, 14.0; ESI-HRMS calcd for $C_{10}H_{12}NO_3$ $(M + H)^+$ 194.0812, found 194.0814.

*4,6-Dimethoxy-N-methylbenzo[d]oxazol-2-amine (**9n**):* yield 11.5 mg (7%, white solid); mp 162−163 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 3170, 2923, 1683, 1101, 823 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.44 (br q, 1H, J = 4.5 Hz), 6.66 (d, 1H, J = 2.1 Hz), 6.35 (d, 1H, J = 2.1 Hz), 3.86 (s, 3H), 3.72 (s, 3H), 2.84 (d, 3H, J = 4.8 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.7, 155.4, 149.9, 148.6, 125.8, 95.9, 88.5, 56.3, 56.1, 29.3; ESI-HRMS calcd for $C_{10}H_{13}N_2O_3$ $(M + H)^+$ 209.0921, found 209.0914.

*2-Butylbenzo[d]oxazole (**8o**):* yield 122.8 mg (79%, brown oil); (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3749, 2960, 1615, 1572, 1456, 1242 1153, 762, 744 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70−7.64 (m, 1H), 7.50−7.44 (m, 1H), 7.32−7.25 (m, 2H), 2.93 (t, 2H, J = 7.8 Hz), 1.87 (quin, 2H, J = 7.5 Hz), 1.46 (sex, 2H, J = 7.5 Hz), 0.97 (t, 3H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 150.7, 141.3, 124.3, 124.0, 119.4, 110.2, 28.8, 28.3, 22.2, 13.6; HRMS (ESI-TOF) calcd for $C_{11}H_{14}NO$ $(M + H)^+$ 176.1070, found 176.1077.

*3-Butyl-4H-benzo[e][1,2,4]oxadiazine (**9o**):* yield 27.2 mg (16%, light yellow solid); mp 86−87 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3407, 3315, 3158, 3050, 2952, 2869, 1910, 1671, 1651, 1585, 1462, 1245, 1186, 1007, 943, 733 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (dd, 1H, J = 7.8, 0.6 Hz), 7.24 (d, 1H, J = 7.8 Hz), 7.15 (td, 1H, J = 7.5, 1.2 Hz), 7.01 (td, 1H, J = 7.5, 1.2 Hz), 5.65 (br s, 1H), 3.48 (t, 2H, J = 7.2 Hz), 1.67 (sep, 2H, J = 7.2 Hz), 1.42 (sep, 2H, J = 7.5 Hz), 0.96 (t, 3H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 148.4, 142.9, 123.8, 120.6, 116.0, 108.6, 42.8, 31.8, 19.9, 13.7; HRMS (ESI-TOF) calcd for $C_{11}H_{15}N_2O$ $(M + H)^+$ 191.1179, found 191.1181.

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*2-Phenylbenzo[d]oxazole (**8p**):* yield 64.3 mg (42%, white solid); mp 95−96 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3061, 1618, 1552, 1448, 1373, 1024, 924, 759, 744, 688 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.29−8.24 (m, 2H), 7.81−7.75 (m,1H), 7.59−7.50 (m, 4H), 7.38−7.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0, 150.7, 142.0, 131.5, 128.9, 127.6, 127.1, 125.1, 124.6, 120.0, 110.6; HRMS (ESI-TOF) calcd for $C_{13}H_{10}NO$ $(M + H)^+$ 196.0757, found 196.0753.

*3-Phenyl-4H-benzo[e][1,2,4]oxadiazine (**9p**):* yield 66.0 mg (40%, white solid); mp 170−171 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 3049, 1666, 1645, 1576, 1497, 1232, 751, 738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, 2H, J = 7.8 Hz), 7.49 (d, 1H, J = 7.8 Hz), 7.43−7.35 (m, 3H), 7.27−7.22 (m, 1H), 7.16−7.10 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 147.9, 141.8, 137.9, 129.3, 124.4, 123.4, 121.8, 118.7, 116.8, 109.2; HRMS (ESI-TOF) calcd for $C_{13}H_{11}N_2O$ $(M + H)^+$ 211.0866, found 211.0868.

*2-Hydroxy-N-phenylbenzamide (**10p**):* yield 8.8 mg (5%, light yellow solid); mp 118−119 °C (1/4 to 1/1 EtOAc/hexane); IR (neat) ν_{max} 2984, 2935, 1738, 1652 1446, 1373, 1235, 1044, 847, 757 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 11.96 (s, 1H), 7.92 (br s, 1H), 7.59−7.58 (m. 2H), 7.53 (dd, 1H, J = 8.0, 1.4 Hz), 7.46 (ddd, 1H, J = 8.5, 7.3, 1.4 Hz), 7.42−7.40 (m, 2H), 7.21 (t, 1H, J = 7.4 Hz), 7.04 (dd, 1H, J = 8.4, 0.9 Hz), 6.94−6.92 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 162.0, 136.7, 134.6, 129.2, 125.4, 125.3, 121.2, 119.0, 118.9, 114.6; HRMS (ESI-TOF) calcd for $C_{13}H_{12}NO_2$ $(M + H)^+$ 214.0862, found 214.0853.

*4,5-Dihydro-3H-naphtho[1,8-c,d]isoxazol-6-ol (**6q**):* yield 45.8 mg (32%, yellow crystal); mp 155−156 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 3219, 2956, 1622, 1535, 1282, 985, 788 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 9.36 (s, 1H), 7.22 (d, 1H, J = 8.4 Hz), 7.05 (d, 1H, J = 8.7 Hz), 2.94 (t, 2H, J = 6.3 Hz), 2.74 (t, 2H, J = 5.7 Hz), 2.01 (quin, 2H, J = 6.3 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 157.4, 154.6, 149.4, 123.0, 120.5, 118.6, 106.9, 23.5, 21.3, 21.2; HRMS (ESI-TOF) calcd for $C_{10}H_{10}NO_2$ $(M + H)^+$ 176.0706, found 176.0713.

*6,7-Dihydro-5H-benzo[c]tetrazolo[1,5-a]azepine-8,11-diol (**11q**):* yield 25.5 mg (14%, brown solid); mp 182−183 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 3263, 2957, 1717, 1620, 1503, 1470, 1263, 1236 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 9.79 (s, 1H), 9.18 (s, 1H), 6.93 (d, 1H, J = 9.0 Hz), 6.78 (d, 1H, J = 8.7 Hz), 4.68 (t, 2H, J = 6.6 Hz), 2.60 (t, 2H, J = 6.0 Hz), 2.22 (quin, 2H, J = 6.6 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 152.6, 149.5, 147.4, 126.2, 120.1, 115.8, 110.7, 46.7, 28.0, 22.7; HRMS (ESI-TOF) calcd for $C_{10}H_{11}N_4O_2$ $(M + H)^+$ 219.0876, found 219.0875.

*6-Methoxy-4,5-dihydro-3H-naphtho[1,8-c,d]isoxazole (**6r**):* yield 17.6 mg (44%, yellow crystal); mp 55−56 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 2924, 2854, 1617, 1524, 1499, 1451, 1377, 1248, 1067, 796, 771 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, 1H, J = 8.7 Hz), 7.11 (d, 1H, J = 8.7 Hz), 3.88 (s, 3H), 3.03 (t, 2H, J = 6.6 Hz), 2.86 (t, 2H, J = 6.0 Hz), 2.13 (quin, 2H, J = 6.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 155.7, 151.5, 123.2, 121.6, 115.9, 106.6, 57.1, 23.4, 21.7, 21.2; HRMS (ESI-TOF) calcd for $C_{11}H_{12}NO_2$ $(M + H)^+$ 190.0863, found 190.0871.

*8-Methoxy-6,7-dihydro-5H-benzo[c]tetrazolo[1,5-a]azepin-11-ol (**11r**):* yield 11.2 mg (23%, yellow solid); mp 146−147 °C (1/4 to 7/3 EtOAc/hexane); IR (neat) ν_{max} 2919, 2850, 1738, 1592, 1513, 1474, 1245, 1104, 1024, 731 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.06−6.98 (m, 2H), 4.69 (t, 2H, J = 6.3 Hz), 3.83 (s, 3H), 3.15−3.11 (m, 2H), 2.38−2.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 152.2, 149.7, 128.6, 116.9, 116.4, 108.5, 56.8, 50.4, 25.0, 24.5; HRMS (ESI-TOF) calcd for $C_{11}H_{13}N_4O_2$ $(M + H)^+$ 233.1033, found 233.1037.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01305.

^1H and ^{13}C NMR spectra of all prepared products (PDF)

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Notes

The authors declare no competing financial interest.

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