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

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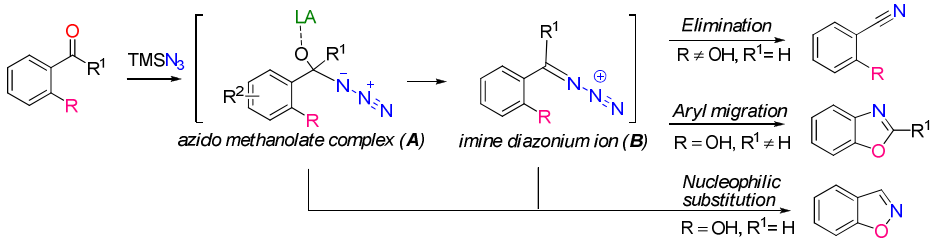


ABSTRACT

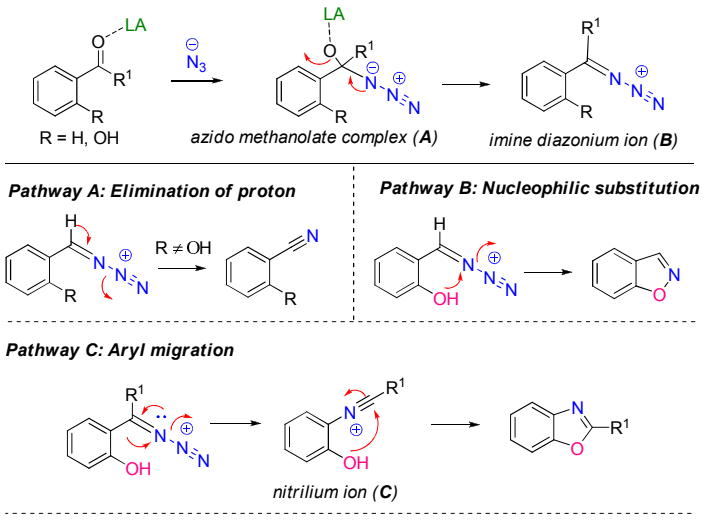
The utilities of the nitrogen extrusion reaction of azido complexes, generated *in situ* from the corresponding aldehydes or ketones with $TMSN_3$ under the presence of $ZrCl_4$ or TfOH, have been described. These azido complexes could undergo three different pathways, depending on the substrates. First, azido methanolate complexs 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 the 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 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 could lead to one remaining nitrogen atom attached to the desired products. Schmidt reaction and Curtius rearrangement are the well-known classical reactions which also involve with the 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 to replace this hazardous combination with the safer alternative of Lewis acid and $TMSN_3$.[11] In this work, we aim to develop the new synthetic methods for the synthesis of nitriles, benzoxazoles and benzisoxazoles using arylaldehyde and arylketone substrates as proposed in Scheme 1. In our proposed strategy, the aldehyde or ketone will be activated by Lewis acid and will then undergo the 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 the 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 the nucleophilic substitution in case of substrates containing *o*-hydroxyl group (pathway **B**). Lastly, when $R^1 \neq H$, we anticipated the elimination could not occur, and the aryl migration will 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.

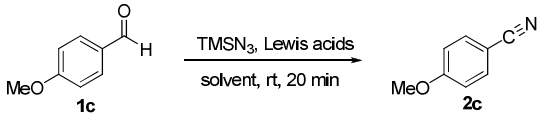


■ RESULTS AND DISCUSSION

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 trace amount of the desired product (**2c**) (entries 1-2), 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 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 eq 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, and found the highest yield was obtained when the reaction was carried out in CH_3CN (entry 9). Increasing the equivalent of $ZrCl_4$ could not significantly improve the yield of the product (entry 10), whereas reducing $ZrCl_4$ to 0.5 equiv. lowered the yield of the product (entry 11). The results showed that the 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]

Table 1. Optimization for the synthesis of benzonitrile **2c**.[a]



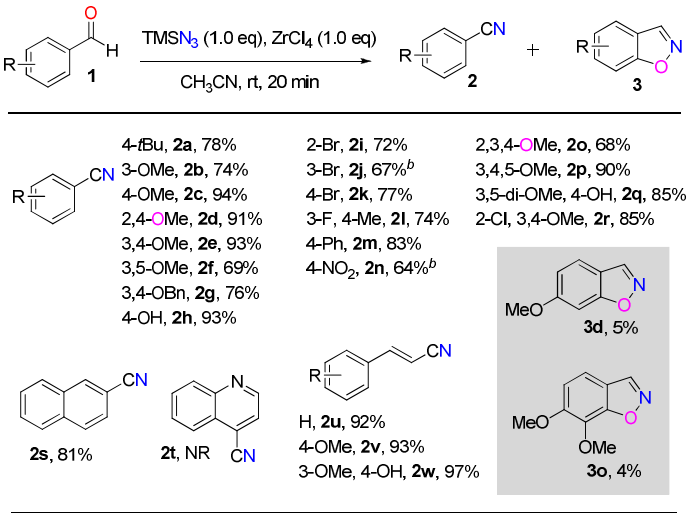
Entry	**1** (eq)	$TMSN_3$ (eq)	Lewis acids (eq)	Solvent	Yield (%)
1	1.0	1.0	$Sc(OTf)_3$ (10 % mol)[b]	DCM	trace
2	1.0	1.0	$Bi(OTf)_3$ (10 % mol)[b]	DCM	trace
3	1.0	1.0	$BF_3{\cdot}OEt_2$ (10 % mol)[b]	DCM	NR
4	1.0	1.0	$ZrCl_4$ (1.0 eq)	DCM	81
5	1.0	1.0	$ZrCl_4$ (1.0 eq)	DCE	89
6	1.0	1.0	$ZrCl_4$ (1.0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

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

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 *meta*-methoxy substituent of benzaldehyde derivatives decreased the yields of the desired products (**2b,** 74% and **2f**, 69%). Similarly, benzaldehydes substituted with *meta*-bromine provided the corresponding product in lower yield (**2j**, 67%), as compared to the *ortho*- and *para*-positions (**2i**, 72% and **2k**, 77%,

respectively). In addition, benzaldehyde possessing a strong electron-withdrawing *para*-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 could tolerate well under these optimal conditions. Conversely, benzyl group could be partially deprotected to give the corresponding product in lower yield such as 3,4-dibenzyloxybenzonitrile (**2g**, 76%), as compared to 3,4-dimethoxybenzonitrile (**2e**, 93%). However, 4-formylquinoline (**2t**) did not react under these conditions. The current procedure could also be applied to synthesize the cinnamonitrile derivatives in excellent yields (**2u**-**2w**). 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.

Scheme 2. The synthesis of nitriles from aldehydes.[a]



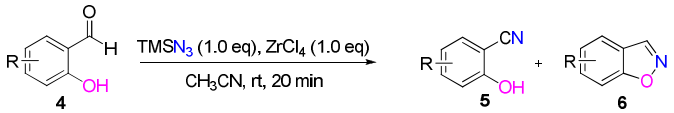
[a]Isolated yields. [b]The reaction was carried out using 1.5 eq of $TMSN_3$ and $ZrCl_4$ and stirred at room temperature for overnight.

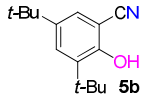
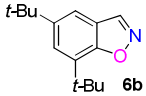
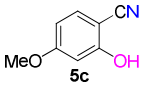
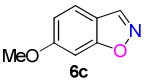
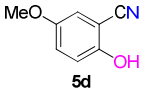
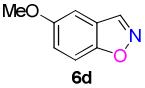
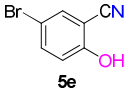
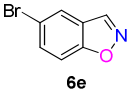
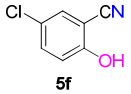
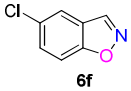
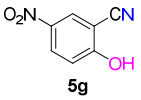
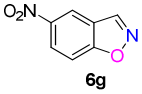
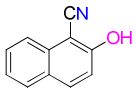
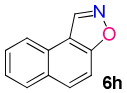
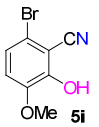
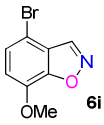
We attempted to optimize the reaction conditions to maximize yields of benzisoxazoles **6**.[14] However, we were not able to selectively control the formation of the desired products. We rationalized that the

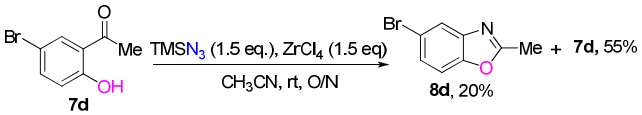
electronic property of the aryl ring may impose effects on the product distribution and therefore the titled conditions were applied to several salicylaldehyde derivatives to evaluate our hypothesis. The reaction of salicylaldehyde (**4a**) provided the *o*-hydroxybenzonitrile (**5a**, 43%) and benzisoxazole (**6a**, 29%) in almost 1.5:1 ratio and a similar result could be observed in case of compound **4b**. Using electron-rich substrates, aldehydes **4c** and **4d**, benzonitriles (**5c** and **5d**) could be obtained as major products and benzisoxazoles (**6c** and **6d**) as minor products in 3.5:1 and 2:1 ratios, respectively. The ratio of two products was reversed when using the substrates containing electron-deficient substituents. For examples, 5-bromosalicylaldehyde (**4e**) and 5-chlorosalicylaldehyde (**4f**) provided benzonitriles as minor products (**5e**, 35% and **5f**, 32%) whereas the major products (**6e** and **6f**) were obtained in 52% and 49%, respectively. The effect of a strong 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% and benzonitrile **5h** in 15%. 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 aryl ring have a substantial influence on the reaction mechanism and products 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 making the competing nucleophilic substitution of azido methanolate complex **A** 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 the 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 the increased equivalents of both $TMSN_3$ and $ZrCl_4$ (1.5 eq) 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 the intramolecular nucleophile (*ortho*-OH) to provide the desired benzoxazole **8**.

Table 2. The synthesis of benzisoxazoles.[a]

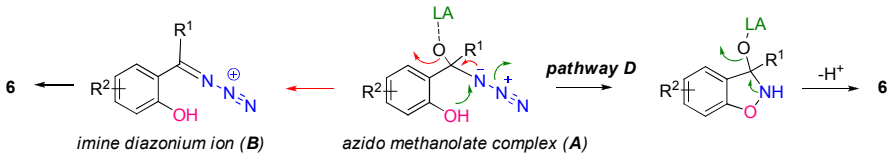


Entry	Product (**5**)	Product (**6**)	Yield of **5**	Yield of **6**
1	 **5a**	 **6a**	43%	29%
2[b]	 *t*-Bu **5b**	 *t*-Bu **6b**	28%	21%
3[b]	 **5c**	 **6c**	77%	22%
4[b]	 **5d**	 **6d**	65%	28%
5	 **5e**	 **6e**	35%	52%
6	 **5f**	 **6f**	33%	49%
7[b]	 **5g**	 **6g**	11%	62%
8[b]	 **5h**	 **6h**	15%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



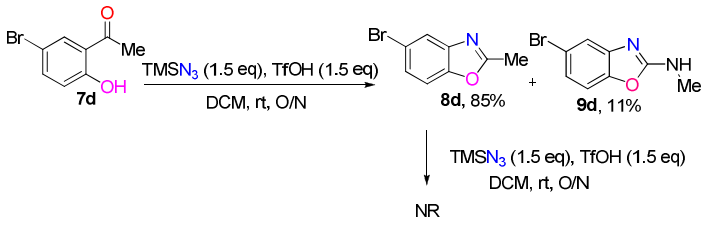
[a]Isolated yields. [b]The reaction was carried out using 1.5 eq of $TMSN_3$ and $ZrCl_4$ and stirred at room temperature for overnight.

Scheme 3. Proposed mechanism for the formation of benzisoxazoles.

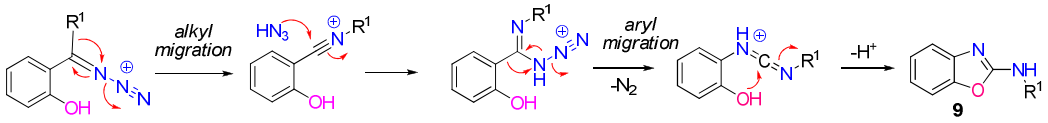


In order to achieve a complete conversion, we decided to screen for new optimal conditions using compound **7d** as the substrate. We found that the desired product (**8d**) was obtained in highest yield (85%) when using 1.5 eq each of TfOH and $TMSN_3$ in DCM after stirring the reaction overnight (Scheme 4) along with 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 the 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 proposed 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 compared 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 by-product **9** as demonstrated in Scheme 5. In fact, the rate of the aryl is much faster than the alkyl migration, resulting in benzoxazole **8d** as the major product. In the current strategy for the synthesis of benzoxazoles from arylketones, 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 arylketones under these conditions was not as exothermic as the reaction of arylaldehydes. Additonally, benzoxazole products could be conveniently generated directly from the corresponding ketones.

Scheme 4. Synthesis of benzoxazole.



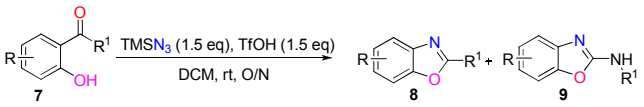
Scheme 5. Proposed mechanism for the formation of **9**.

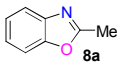
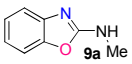
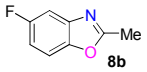
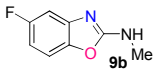
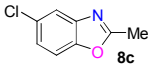
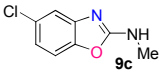
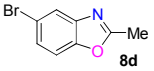
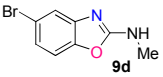
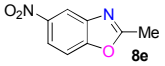
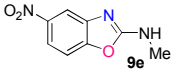
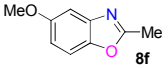
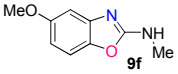
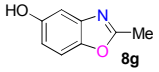
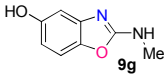
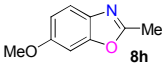
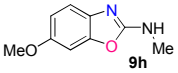
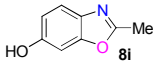
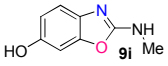
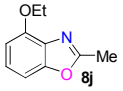
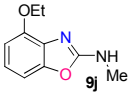
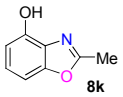
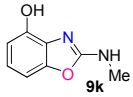
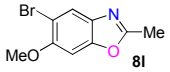
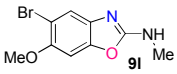
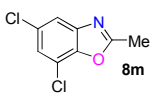
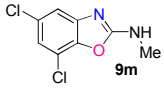
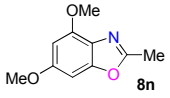
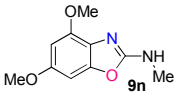
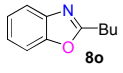
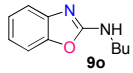


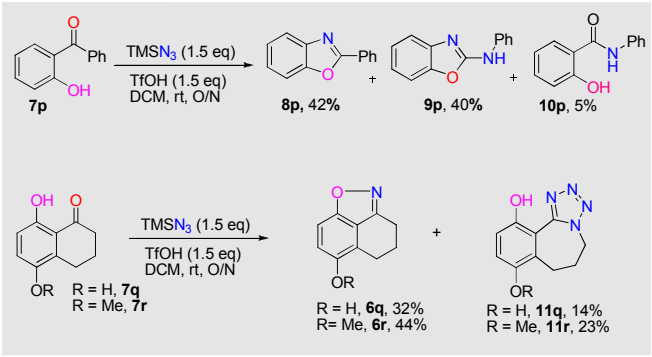
To evaluate the generality of the current procedure, we examined a variety of *o*-hydroxyacetophenone derivatives (**7**) as shown in Table 3. Substrates containing electron-donating groups or electron-withdrawing groups such as H, F, Cl, Br, NO_2, OMe, and OH at position 5 of *o*-hydroxyacetophenone were smoothly converted to benzoxazole products in good yields (**8a-8g**) with only small amounts of by-products (**9a-9f**) obtained. Similarly, the reaction of *o*-hydroxyacetophenones **7h** and **7i** also proceeded well under these conditions, providing the corresponding products in excellent yields (**8h** and **8i**). Surprisingly, the proportions of by-products **9** increased when the substituent was located at position 6 (**7j** and **7k**). These results might be possibly 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 aryl migration process could not be achieved and the competing methyl migration became more viable, resulting in the increase of by-product. Further investigations were attempted with *o*-hydroxyacetophenones **7l** and **7m** to furnish the corresponding products in good yields. For 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*-

hydroxyarylketones were examined. Therefore, *o*-hydroxyphenylbutylketone (**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 A) and the phenyl ring (ring B) were comparable, resulting in the formation of the nitrilium intermediates **7p-A** and **7p-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 products **9p** and **10p** in 45% combined yields.

Table 3. The scope of benzoxazole synthesis.[a]

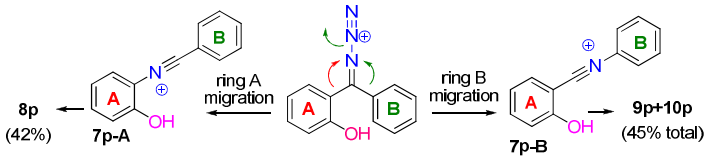


Entry	Product (8)	Product (9)	Yield of 5[a]	Yield of 6[a]
1	 8a	 9a	77%	8%
2	 8b	 9b	83%	13%
3	 8c	 9c	87%	12%
4	 8d	 9d	85%	11%
5	 8e	 9e	83%	12%
6	 8f	 9f	78%	10%
7	 8g	 9g	77%	-[b]
8	 8h	 9h	90%	8%
9	 8i	 9i	89%	-[b]
10	 8j	 9j	49%	48%
11	 8k	 9k	50%	25%
12	 8l	 9l	88%	7%
13	 8m	 9m	89%	7%
14	 8n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



[a]Isolated yields. [b]By-product could not be detected.

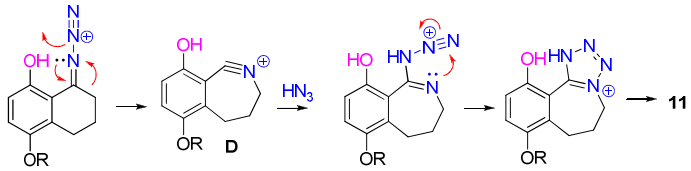
Scheme 6. The nitrilium ion formation from compound **7p**



The results of all cases revealed that the migration of an aryl group is more favorable than 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** and **7r**) were performed under the current optimal conditions. Surprisingly in both entries, the intramolecular nucleophilic substitution (pathway **B**) was preferred to the aryl migration (pathway **C**), providing benzisoxazoles **6q** and **6r** 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** and **11r** were obtained as minor products.[15] The proposed mechanism is illustrated in Scheme 7.

Scheme 7. The proposed formation of products **11q** and **11**r.



■ CONCLUSIONS

We have demonstrated the utilities of nitrogen-extrusion of azido complexes, generated from aldehydes or ketones with appropriate substituents in 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 when they contain *o*-hydroxyl group, both nitriles and benzisoxazoles are obtained with varying ratios, depending on the nature of other substituents. When *o*-hydroxyarylketones are employed, the rearrangement of the initial azido intermediates leads to an aryl migration to form the nitrilium ion which could cyclize to form benzoxazoles in good yields.

■ EXPERIMENTAL SECTION

General Procedure. The commercial grade chemicals were used without further purification, unless otherwise specified. All solvents used were purified by the solvent purification system. The oven-dried

glassware (110 ºC at least for two hours) was used for all reactions. Crude reaction mixtures were concentrated under reduced pressure by removing organic solvent with the 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. The nuclear magnetic resonance (NMR) spectra were recorded in deuterochloroform ($CDCl_3$) 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 were reported in part per million (ppm, δ), relative to tetramethylsilane (TMS) as the internal reference. Coupling constants (*J*) were reported in Hertz (Hz). Infrared spectra were measured using FT-IR spectrometer and were reported in cm^{-1}. High resolution mass spectra (HRMS) were obtained using time-of-flight (TOF).

General procedure for the synthesis of benzonitriles (2a-2w, 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 $TMSN_3$ (131µL, 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 ($NaHCO_3$). 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 reactions of substrates **1j** and **1n** were stirred at room temperature for overnight and the reactions of substrates **1h** and **1w** were quenched with water).

4-tert-Butylbenzonitrile (**2a**):[1f] Yield 127.0 mg (78%, yellow oil); (1:4 EtOAc/Hexane); IR (neat): υ_{max} 2965, 2228, 1606, 1505, 1465, 1365, 1270, 1106, 1018, 837 cm^{-1}; ^{1}H 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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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, 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): υ_{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): υ_{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): υ_{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): υ $_{max}$ 3386, 3017, 2212, 1775, 1598, 1508, 1457, 1272, 1185, 970, 807 cm^{-1}; ^{1}H 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): υ $_{max}$ 2942, 1619, 1489, 1311, 1281, 1240, 1098, 979, 796 cm^{-1}; ^{1}H 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 $TMSN_3$ (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 reactions of substrates **4b**-**4d**, **4g**-**4i**, and **7d** were stirred at room temperature for overnight and the reactions of substrates **4a**-**4i**, 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): υ max 3282, 2953, 2230, 1604, 1455, 1352, 1305, 1233, 1099, 846, 748 cm-1; 1H NMR (300 MHz, CDCl3) 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, CDCl3) 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): υ_{max} 3098, 1611, 1512, 1430, 1228, 1175, 934, 839, 744 cm^{-1}; ^{1}H 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): υ_{max} 3300, 2961, 2232, 1603, 1479, 1363, 1218, 1201, 878 cm^{-1}; ^{1}H 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): υ_{max} 2959, 2871, 1616, 1465, 1364, 1168, 883, 854, 765 cm^{-1}; ^{1}H 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): υ_{max} 3218, 2227, 1595, 1435, 1276, 1212, 1104, 830, 673 cm^{-1}; ^{1}H 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): υ_{max} 3091, 2942, 1615, 1491, 1300, 1273, 1114, 946, 822 cm^{-1}; ^{1}H 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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{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): υ_{max} 3097, 1739, 1614, 1502, 1423, 1228, 1173, 1116, 807, 700 cm^{-1}; ^{1}H 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.

2-Hydroxy-5-nitrobenzonitrile (**5g**):[1d] Yield 18.2 mg (11%, yellow solid); mp 171-172 °C. (3:7 EtOAc/Hexane); IR (neat): υ_{max} 3084, 2235, 1591, 1532, 1489, 1341, 1299, 1134, 1079, 910, 834, 748 cm^{-1}; ^{1}H 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): υ_{max} 3108, 1619, 1520, 1350, 1267, 1073, 912, 827, 688 cm^{-1}; ^{1}H 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): υ_{max} 3245, 2925, 2224, 1626, 1515, 1438, 1286, 817, 748 cm^{-1}; ^{1}H 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): υ_{max} 3098, 3068, 1632, 1581, 1532, 1486, 1254, 1170, 930, 812, 753 cm^{-1};

^{1}H 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): υ_{max} 3276, 2938, 2240, 1595, 1488, 1438, 1279, 1257, 1068, 881, 804 cm^{-1}; ^{1}H 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): υ_{max} 3094, 3004, 2848, 2324, 1860, 1719, 1606, 1460, 1260, 1177, 981, 816. 690 cm^{-1}; ^{1}H 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-8p) and benzisoxazoles (6q-6r, Table 3): A solution of ketones **7d** (133.4 mg, 0.6203 mmol, 1.0 equiv) in dry DCM (2 mL, 3.0 mL/mmol) was added $TMSN_3$ (130 μL, 0.9305 mmol, 1.5 equiv) and TfOH (80 μL, 0.9305 mmol, 1.5 equiv) at room temperature and stirred for 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 product **8d** (111.6 mg, 85%) and **9d** (14.9 mg, 11%). (The reactions of substrates **7g**, **7i**, **7k**, and **7q** 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}. ^{1}H 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 ºC. (1:9 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 3223, 1646, 1584, 1459, 1241, 740 cm^{-1}. ^{1}H 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}. ^{1}H 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 ºC. (1:9 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 3174, 2924, 1682, 1587, 1416, 1130, 833 cm^{-1}. ^{1}H 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 ºC. (1:9 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 2925, 1658, 1457, 1260, 1029 cm^{-1}. ^{1}H 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 ºC. (1:9 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 3062, 2923, 1686, 1578, 1463, 1255, 799 cm^{-1}. ^{1}H 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 ºC. (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 ºC. (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 ºC. (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 ºC. (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, 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 ºC. (1:4 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 3227, 2942, 1652, 1587, 1196, 1162, 1062 cm^{-1}. ^1H 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): υ_{max} 3136, 2926, 2344, 1612, 1577, 1474, 1282, 1153, 941, 844, 733 cm^{-1}; ^1H 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}. ^1H 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 ºC. (1:4 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 3178, 1689, 1486, 1135, 1027, 815 cm^{-1}. ^1H 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 ºC. (1:4 to 7:3 EtOAc/hexane); IR (neat): ν_{max} 3092, 1625, 1486, 1299, 1232, 1138, 828 cm^{-1}. ^1H 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 ºC. (1:4 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 2931, 1683, 1442, 1279, 1090 cm^{-1}. ^1H 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 ºC. (1:4 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 3043, 2967, 1679, 1070, 718 cm^{-1}. ^1H 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.

^1H 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 ºC. (1:4 to 7:3 EtOAc/hexane); IR (neat): ν_{max} 3104, 1610, 1243, 1186, 732 cm^{-1}. ^1H 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 ºC. (1:4 to 7:3 EtOAc/hexane); IR (neat): ν_{max} 3387, 2945, 1644, 1247, 1034, 736 cm^{-1}. ^1H 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 ºC. (1:4 to 7:3 EtOAc/hexane); IR (neat): ν_{max} 2951, 1610, 1469, 1297, 1037, 877 cm^{-1}. ^1H 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 ºC. (1:4 to 7:3 EtOAc/hexane); IR (neat): ν_{max} 3151, 2961, 1646, 1469, 1297, 1130, 816 cm^{-1}. ^1H 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 ºC. (1:4 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 1609, 1574, 1399, 1162, 789 cm^{-1}. ^1H 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 ºC. (1:4 to 1:1 EtOAc/hexane); IR (neat): ν_{max} 3140, 2949, 1693, 1651, 1577, 1410, 998 cm^{-1}. ^1H 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 ºC. (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 ºC. (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): υ_{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): υ_{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.

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): υ_{max} 3061, 1618, 1552, 1448, 1373, 1024, 924, 759, 744, 688 cm^{-1}; ^{1}H 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): υ_{max} 3049, 1666, 1645, 1576, 1497, 1232, 751, 738 cm^{-1}; ^{1}H 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): υ_{max} 2984, 2935, 1738, 1652 1446, 1373, 1235, 1044, 847, 757 cm^{-1}; ^{1}H 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-cd]isoxazol-6-ol (**6q**): Yield 45.8 mg (32%, yellow crystal); mp 155-156°C. (1:4 to 7:3 EtOAc/hexane); IR (neat): υ_{max} 3219, 2956, 1622, 1535, 1282, 985, 788 cm^{-1}; ^{1}H 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): υ_{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-cd]isoxazole (**6r**): Yield 17.6 mg (44%, yellow crystal); mp 55-56°C. (1:4 to 7:3 EtOAc/hexane); IR (neat): υ_{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): υ_{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.

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■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of all prepared products. This material is available free of charge via the Internet at http://pubs.acs.org/.

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Notes

The authors declare no competing financial interest.

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