JOC The Journal of Organic Chemistry

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Iodine(III)-Mediated [3 + 2] Cyclization for One-Pot Synthesis of Benzo[*d*]isoxazole-4,7-diols in Aqueous Medium

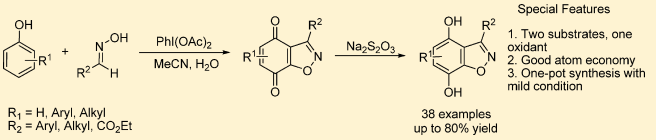
Yingwei Hou,[†] Shichao Lu,[†] and Gang Liu*[,†,‡,§]

[†]Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, 2 Nanwei Road, Xicheng District, Beijing 100050, P. R. China

[‡]Tsinghua-Peking Center for Life Sciences and [§]Department of Pharmacology and Pharmaceutical Sciences, School of Medicine, Tsinghua University, Haidian District, Beijing 100084, P. R. China.

Supporting Information

ABSTRACT: A one-pot [3 + 2] cycloadditive synthesis of benzo[*d*]isoxazole-4,7-diols in aqueous medium was carried out via nitrile oxides and benzoquinone intermediates by taking advantage of iodobenzene diacetate as an oxidant. This method can also be used to synthesize benzodiisoxazole-4,8-diols, isoxazolo[5,4-*a*]phenazines, and indazole-4,7-diols, which are difficult to obtain by classical methods.



INTRODUCTION

Benzisoxazole is an important heterocyclic scaffold of privileged structures with its various biological activities in drug discovery and development. In particular, certain benzisoxazole units are known to possess druggable properties with antidepressant, antipsychotic, and neuroleptic activities (Figure 1).[1] Methods reported in the literature for the synthesis of benzisoxazoles are depicted in Scheme 1. The methods using intramolecular cyclization (Scheme 1, routes 1 and 2) include three-to-four-step reactions with intermediates under harsh conditions,[2] as well as the use of toxic solvents such as tetrahydrofuran, toluene, dioxane, carbon tetrachloride, or nitrobenzene. Recently, Larock reported[3] the synthesis of benzisoxazoles by the [3 + 2] cycloaddition of in situ generated nitrile oxides and arynes (Scheme 1, route 3). In this paper, we report a facile one-pot synthesis of benzo[*d*]isoxazole-4,7-diol via iodine(III)-mediated [3 + 2] cycloaddition from phenol and nitrile oxides in aqueous medium. Such a strategy is alternatively used to synthesize benzodiisoxazole-4,8-diols, isoxazolo[5,4-*a*]-phenazines, and indazole-4,7-diols, which are difficult to obtain by classical methods.

Iodobenzene diacetate [$PhI(OAc)_2$, DIB], one of the most important and commercially available representatives of aryliodine(III) carboxylates, is a mild oxidizing agent used for various selective oxidative transformations of complex molecules.[4] For example, nitrile oxides were efficiently prepared via oxidation of aldoximes by DIB and further trapped by bimolecular and intramolecular modes.[5] Meanwhile, phenol is also oxidized by DIB forming *p*-benzoquinone. Being able to gain both nitrile oxides and *p*-benzoquinones by DIB oxidation creates a good condition for one-pot synthesis of organic products via a [3 + 2] cycloaddition.

RESULTS AND DISCUSSION

2,3-Dimethylphenol (**1a**) and pyridyl nitrile oxide (**A**) from oxidated picolinaldehyde oxime (**2a**) were chosen as the reactants to investigate the optimal reaction conditions (Table 1, Scheme 2). Methanol (Table 1, entry 1) and acetonitrile (Table 1, entry 3) were initially used as alternative solvents for testing in the reaction. The reaction did not proceed in acetonitrile. However, the anticipated product of **4a** was obtained in 59% yield, while an intermediate **3a** was isolated in 36% yield[6] (Scheme 2). The reaction mechanism is depicted in Scheme 2. The methanol, as a nucleophile, first attacked **1a**, aided by 1.0 equiv DIB oxidation, to afford 4-methoxylphenol (**B**). DIB was continuously added in methanol to afford **3a**,[7] which could be isolated in 85% yield. Product **3a** reacted with nitrile oxide (**A**) to afford the product **4a**[8] (Scheme 2, route 1). The byproduct of a dimer of nitrile oxide, 3,5-di(pyridin-2-yl)-1,2,4-oxadiazole 4-oxide (**C**) was observed[3] in 13% yield (Scheme 2, route 3). It is believed that a dimerization of nitrile oxide (**A**) competitively occurred as a [3 + 2] cycloaddition of nitrile oxide.[3] We assumed that the electrophilicity of **3a** was effectively weakened by the methoxyl groups, so that the **A**'s competitive [3 + 2] cycloaddition between **3a** and additional **A** occurred. A lower reaction temperature (0 °C) increased the yield of anticipated **4a** (Table 1, entry 2), suggesting that the dimerization is temperature dependent. Water, as a nucleophile, was then considered as an alternative solvent, avoiding the formation of **3a**, because the formed hydroquinone (**D**) can be further oxidized to be **3b** by the excess DIB in situ (Scheme 2, route 2).

Considering the solubility of various reactants, we screened reaction conditions for the use of water mixed with acetonitrile (Table 1, entries 4−10). By using the above procedure (Table

Received: May 16, 2013

   dx.doi.org/10.1021/jo401077q | *J. Org. Chem.* XXXX, XXX, XXX−XXX

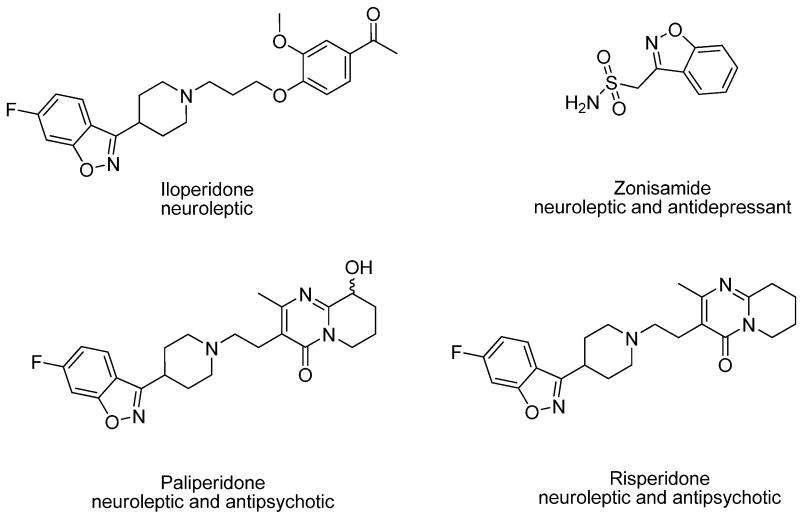
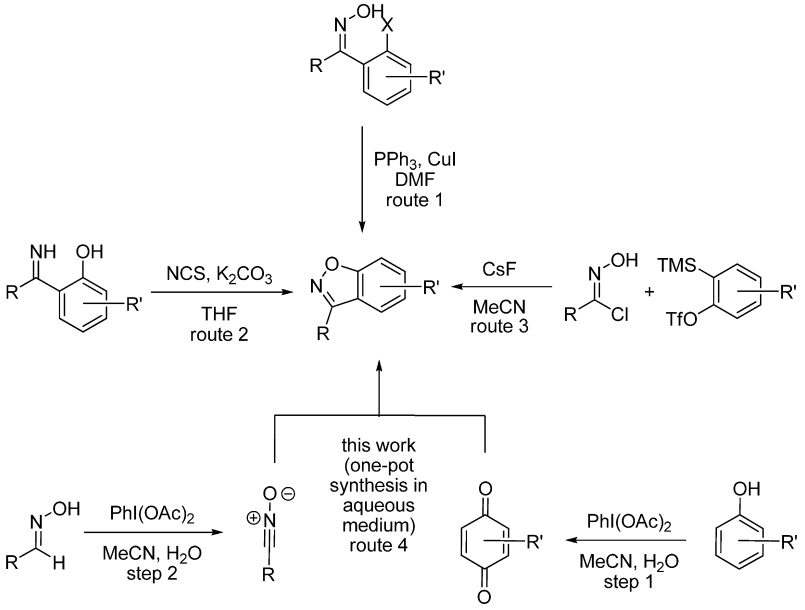


Figure 1. Launched drugs with benzisoxazole scaffold.

Scheme 1. Method Utilized To Synthesize Benzo[*d*]isoxazoles



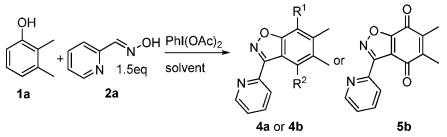
1, entry 4), **4b** was obtained in 78% yield. This was still not considered satisfactory because another byproduct **5b**, an overoxidized product of **4b**, was observed in 10% yield. Assuming that the formation of **5b** consumes the oxidant in a one-pot procedure, a larger amount of oxidant was added to ensure that phenol and oxime reacted completely (Table 1, entries 5 and 6). It was finally observed that 4.0 equiv of DIB is sufficient for complete transformation into **5b**. After addition of an aqueous solution of sodium thiosulfate as reductant after the reaction[6] (Table 1, entry 7), **4b** was achieved in good yield (Table 1, entry 7). Thermodynamically decreasing the nitrile oxide dimerization at lower temperature (0 °C) with an optimal ratio of solvents gave an excellent yield of 93% (Table 1, entry 8). Optimal conditions were found to be MeCN/H_2O (v/v = 2:1), 4.0 equiv of DIB, 0 °C. The total 4.0 equiv of DIB is used for phenol oxidation by 2.0 equiv of DIB, in situ generation of oxime, and **4b** overoxidation by an additional 2.0 equiv of DIB, respectively.

Once we had a full understanding of the reaction mechanism, an optimal one-pot experimental procedure was carried out. Compound **1a** (1.0 mmol) in 4 mL of MeCN and 2 mL of H_2O was first treated with DIB (2.0 mmol) for 2 h at 0 °C to form **3b**, and then 1.5 mmol of **2a**, another 2.0 mmol of DIB in 8 mL MeCN, and 4 mL of H_2O was added dropwise, at 0 °C. The reaction was continued for 6 h at 0 °C, and **5b** was completely reduced to gain the desired product **4b** by addition of 2.0 mmol of $Na_2S_2O_3$ in 8 mL of water for overnight at rt.

The scope of the reaction was systematically investigated. When the oxime was varied (Table 2), the results indicated that the target products were obtainable in good to excellent yields. The benzaldehyde oxime underwent smooth cycloaddition with high yield (Table 2, **4c**). The substituents of benzaldehyde oximes contributed their effects of yields (Table 2, entries 2–16). All alkoxy substitutions were >80% in yield, except **4i** (Table 2, compounds **4d–j**). Single or multiple chloro or fluoro substitutions slightly or significantly decreased the yield (Table 2, **4k–m** or **4n–o**). Electron-donating groups, such as

dx.doi.org/10.1021/jo401077q | *J. Org. Chem.* XXXX, XXX, XXX–XXX

Table 1. Formulation of the Reaction Conditions and Results of Reactions



entry	solvent	temp (°C)	DIB quantity (equiv)	product	yield (%)
1	MeOH	25	3.5	**4a** (R^1 = OMe, R^2 = OH)	59
2	MeOH	0	3.5	**4a** (R^1 = OMe, R^2 = OH)	82
3	MeCN	25	3.5		0
4	MeCN/H_2O (2:1)	25	3.5	**4b** (R^1 = R^2 = OH)	78
5	MeCN/H_2O (2:1)	25	4.5	**5b**	85
6	MeCN/H_2O (2:1)	25	4	**5b**	85
7[a]	MeCN/H_2O (2:1)	25	4	**4b** (R^1 = R^2 = OH)	88
8[a]	MeCN/H_2O (2:1)	0	4	**4b** (R^1 = R^2 = OH)	93
9[a]	MeCN/H_2O (3:1)	0	4	**4b** (R^1 = R^2 = OH)	80
10[a]	MeCN/H_2O (1:1)	0	4	**4b** (R^1 = R^2 = OH)	86

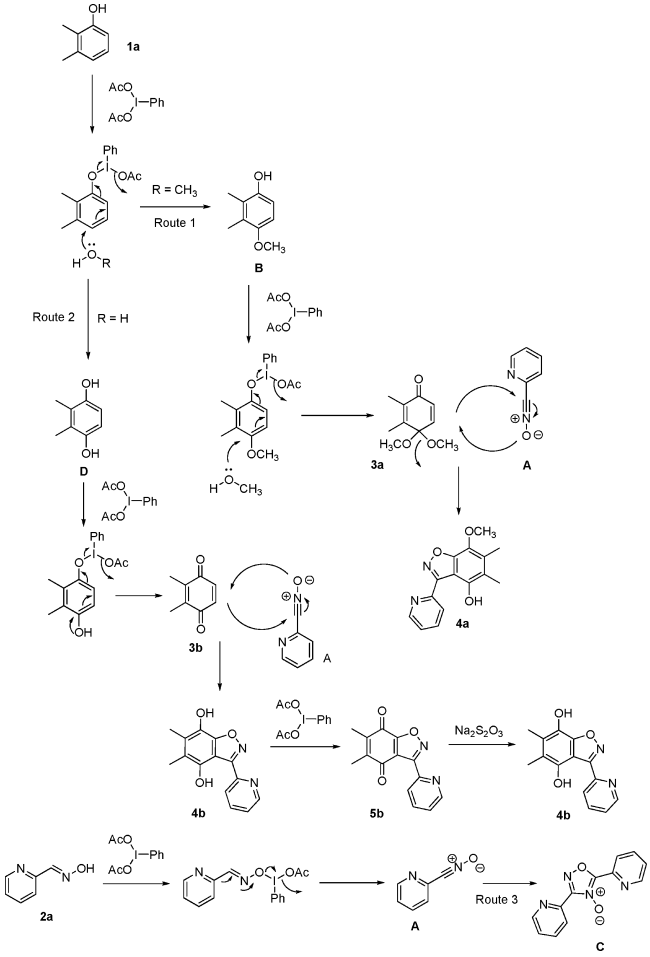
[a]Treated with saturated solution of $Na_2S_2O_3$.

isopropyl, acetamido, and hydroxyl gave good yields (Table 2, **4p**−**r**). The naphthyl oxime significantly decreased the **4s** yield that is believed the steric effect of naphthyl group slowed the cycloaddition. Heteroaromatic oximes, such as pyridine and imidazole oximes, yielded the anticipated compounds in excellent yields (Table 1, **4b**, Table 2, **4t** and **4u**). However, the furan, thiophene, pyrrole, and *N*-methylpyrrole oximes did not produce any desired products. Alkyl oxime yielded the anticipated compound in a good yield as well (Table 2, **4v**). Ethyl 2-(hydroxyimino)-3-oxobutanonate (**2w**, Scheme 3) was also used as an alternative oxime. When treated with DIB under weak acid conditions, the oxidative attack of **2w** by DIB in MeOH or H_2O led to the formation of nitrile oxides (**E**) via a solvolytic fragmentation of the carbonyl-imino C−C bond (Scheme 3),[9] which underwent an addition with benzoquinone to afford compound **4w** (Table 2, entry 21).

Phenol variabilities were next studied (Table 3). It was found that less alkyl substitution on phenol resulted in low yield (Table 3, entries 1−4). When there was only one substituent at the 2- or 3-position of phenol, two isomers of the 5- or 6-substituted benzo[*d*]isoxazoles were simutaneously produced, i.e., **6a** and **6b** (Table 3). When substituted by propionate, the corresponding mixed products of 3-(3-hydroxyphenyl)-propanoic acids (**6d** and **6e**, **6f** and **6g**) were obtained in low yields (Table 3, entries 3 and 4).

Tetrahydronaphthol (**1e**) was found to give good yields of anticipated products whatever oximedes were employed (Table 3, entries 5−8). Interestingly, *tert*-butyl substitution (**1f** and **1g**) provided excellent yields of all desired products (Table 3, entries 9−16), although there is no reactive selectivity whether 2- or 3-*tert*-butylphenol (**1f** and **1g**) was used. All observations of gained 5- and 6-substituted benzo[*d*]isoxazolesin good to excellent yields implied that there is an opportunity for oxime (**A**) occurring a nucleophilic addition of **3b** (Scheme 2).

Scheme 2. Reaction Mechanism of One-Pot Synthesis of Benzo[*d*]isoxazole



As discussed above, compound **5** can be completely obtained by DIB when a longer oxidation time is used (Scheme 4). Isoxazolo[5,4-*a*]phenazines (Table 4, **7a**−**d**) were then synthesized in one pot via intermediate **5h**. Phenazines are produced by bacteria such as *Pseudomonas* spp., *Streptomyces* spp., and *Pantoea agglomerans*.[10] These natural phenazine products have been implicated in the virulence and competitive fitness of producing organisms. For example, the phenazine pyocyanin produced by *Pseudomonas aeruginosa* contributes to its ability to colonize the lungs of cystic fibrosis patients.[11] Using our method described above (Scheme 4, route 1), analogues of phenazine, compounds **7a**−**d**, were prepared in one pot via **5h**. This is different from the synthesis described by Brahmeshwari et al., which uses acetic acid as solvent and involves multiple steps.[12]

A [3 + 2] cycloaddition also occurred on the benzo[*d*]-isoxazole-4,7-dione intermediate (**5f**), affording benzodiisox-azole-4,8-diols **8a**−**d** in one pot (Table 4, Scheme 4, route 2).

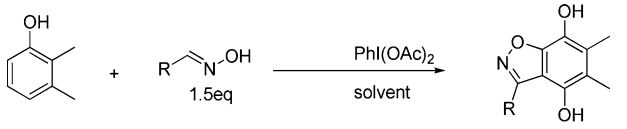
Similarly, 1*H*-indazole compounds **10a**−**f** (Table 4) were synthesized in one pot when intermediate benzoquinone (**3**) was treated with base and tosylhydrazone (**9**) at 60 °C (Scheme 4, route 3).

CONCLUSION

We have presented an efficient and practical protocol for the synthesis of benzo[*d*]isoxazole-4,7-diols by iodine(III)-mediated cycloaddition in one pot. In this reaction, various

dx.doi.org/10.1021/jo401077q | J. Org. Chem. XXXX, XXX, XXX−XXX

Table 2. Synthesis of 3-Substituted 5,6-Dimethylbenzo[*d*]isoxazole-4,7-diols with Different Oximes



1a **2** **4**

entry	product	R	yield (%)
1	**4c**	C_6H_5	85
2	**4d**	4-$MeOC_6H_4$	82
3	**4e**	3-$MeOC_6H_4$	91
4	**4f**	2-$MeOC_6H_4$	80
5	**4g**	2,4,6-$(MeO)_3C_6H_2$	87
6	**4h**	3,4,5-$(MeO)_3C_6H_2$	85
7	**4i**	3-MeO-4-$EtOC_6H_3$	trace
8	**4j**	4-$BnOC_6H_4$	82
9	**4k**	4-ClC_6H_4	83
10	**4l**	3-ClC_6H_4	75
11	**4m**	2,4-$Cl_2C_6H_3$	81
12	**4n**	4-FC_6H_4	45
13	**4o**	3-FC_6H_4	65
14	**4p**	4-i-PrC_6H_4	82
15	**4q**	4-$AcNHC_6H_4$	79
16	**4r**	4-OHC_6H_4	66
17	**4s**	Naphthyl	32
18	**4t**	4-Pyr	89
19	**4u**	2-imidazole	85
20	**4v**	$C_6H_5C_2H_4$	85
21	**4w**[a]	EtOCO	47

[a]Ethyl 2-(hydroxyimino)-3-oxobutanoate was used as oxime.

substituted benzo[*d*]isoxazole-4,7-diol derivatives were efficiently synthesized. Such a strategy is alternatively used to synthesize benzodiisoxazole-4,8-diols, isoxazolo[5,4-*a*]-phenazines, and indazole-4,7-diols, which are difficult to obtain by classical methods. Some of the derivatives showed potential antituberculosis activity. Further investigations to increase the scope of this methodology and its application are underway in our research group.

EXPERIMENTAL SECTION

Unless otherwise noted, all reagents and starting materials were obtained from commercial suppliers and used without purification. All NMR experiments were carried out on a 300 or 400 MHz NMR spectrometer using DMSO-d_6 or acetone-d_6 as the solvent. Chemical shifts are reported in ppm (δ) relative to the solvent, and coupling constants (J) are reported in hertz. Melting points were determined without correction with a micromelting point apparatus. Automatic HPLC–MS analysis was performed on a mass spectrometer. The column was a Kromasil C18 column (4.6 μm, 4.6 mm ×50 mm) for analysis. The eluent was a mixture of acetonitrile and water containing 0.05% HCOOH with a linear gradient from 5:95 (v/v) to 95:5 (v/v) of acetonitrile–water within 5 min at a 1 mL/min flow rate for analysis. The UV detection was carried out at a UV wavelength of 254 nm. The 5% of the eluent was split into the MS system. Mass spectra were recorded in positive ion mode using electrospray ionization (ESI). High-resolution LC–MS was carried out by LC/MSD TOF using a column of C18 (rapid resolution, 3.5 μm, 2.1 mm ×30 mm) at a flow of 0.40 mL/min. The solvent is methanol/water = 75:25 (v/v) containing 5.0 mmol/L ammonium formate. The ion source is electrospray ionization (ESI). Flash column chromatography was performed with silica gel 60 (200–300 mesh). All tested compounds were purified until the purity was ≥95%, detected by HPLC under UV 254 nm wavelength, NMR, melting point, and HPLC–MS.

Preparation of Aldehyde Oxime Derivatives 2a–v. A mixture of aldehyde (10.0 mmol), potassium carbonate (11.0 mmol), hydroxylamino hydrochloride (11.0 mmol), and 50 mL of methanol was placed in a 100 mL round-bottomed flask, and the contents were stirred magnetically in room temperature until the reaction was complete. The progress of the reaction was monitored by TLC (ethyl acetate/hexane); after evaporation of the solvent under reduced pressure, the residue the reaction mixture was diluted with water (50 mL) and extracted with ethyl acetate (4 × 50 mL). The combined extract was washed with brine (2 × 50 mL) and dried over Na_2SO_4. After evaporation of the solvent, the crude product **2** was obtained, and the products were characterized by ^{1}H NMR and mass spectra after a proper purification procedure by chromatogram on silica gel.

*Picolinaldehyde oxime (**2a**):* white solid, 1.11 g, 91% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 10.78 (s, 1H), 8.62 (d, J = 4.6 Hz, 1H), 8.16 (s, 1H), 7.89–7.80 (m, 2H), 7.40–7.36 (m, 1H); ESI-MS m/z 123.1 $[M + H]^+$.

*Benzaldehyde oxime (**2c**):* white solid, 1.06 g, 95% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 10.31 (s, 1H), 8.14 (s, 1H), 7.66–7.58 (m, 2H), 7.40–7.37 (m, 3H); ESI-MS m/z 122.1 $[M + H]^+$.

*4-Methoxybenzaldehyde oxime (**2d**).* White solid, 1.39 g, 92% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.93 (s, 1H), 8.05 (s, 1H), 7.50 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 3.75 (s, 3H); ESI-MS m/z 152.2 $[M + H]^+$.

*3-Methoxybenzaldehyde oxime (**2e**):* white solid, 1.33 g, 88% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.16 (s, 1H), 8.10 (s, 1H), 7.25 (t, J = 7.5 Hz, 1H), 7.13 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 7.5 Hz, 1H), 3.73 (s, 3H); ESI-MS m/z 152.3 $[M + H]^+$.

*2-Methoxybenzaldehyde oxime (**2f**):* white solid, 1.39 g, 92% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.19 (s, 1H), 8.29 (s, 1H), 7.65 (dd, J = 7.7 Hz, 1.4 Hz, 1H), 7.41–7.31 (m, 1H), 7.06 (d, J = 8.4 Hz, 1H), 6.95 (t, J = 7.5 Hz, 1H), 3.82 (s, 3H); ESI-MS m/z 152.1 $[M + H]^+$.

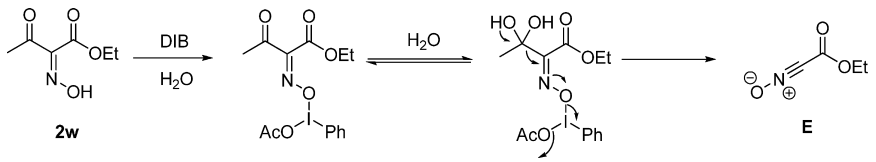
*2,4,6-Trimethoxybenzaldehyde oxime (**2g**):* white solid, 1.98 g, 94% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.78 (s, 1H), 8.12 (s, 1H), 6.26 (s, 2H), 3.81 (s, 3H), 3.77 (s, 6H); ESI-MS m/z 212.1 $[M + H]^+$.

*3,4,5-Trimethoxybenzaldehyde oxime (**2h**):* white solid, 2.02 g, 96% yield; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.19 (s, 1H), 8.06 (s, 1H), 6.94 (s, 1H), 3.84 (s, 6H), 3.74 (s, 3H); ESI-MS m/z 212.1 $[M + H]^+$.

*4-Ethoxy-3-methoxybenzaldehyde oxime (**2i**):* white solid, 1.79 g, 92% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 10.04 (s, 1H), 8.06 (s, 1H), 7.28 (d, J = 1.9 Hz, 1H), 7.09 (dd, J = 8.3 Hz, J = 1.9 Hz, 1H), 6.95 (d, J = 8.2 Hz, 1H), 4.07 (q, J = 7.0 Hz, 2H), 3.84 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H); ESI-MS m/z 196.3 $[M + H]^+$.

*4-Benzyloxybenzaldehyde oxime (**2j**):* white solid, 2.22 g, 98% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.95 (s, 1H), 8.04 (s, 1H), 7.60–7.23 (m, 7H), 7.02 (d, J = 8.6 Hz, 2H), 5.11 (s, 2H); ESI-MS m/z 228.3 $[M + H]^+$.

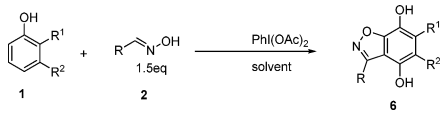
Scheme 3. Predicted Course of the DIB Oxidation of α-Oxo-oximes



2w **E**

dx.doi.org/10.1021/jo401077q | J. Org. Chem. XXXX, XXX, XXX–XXX

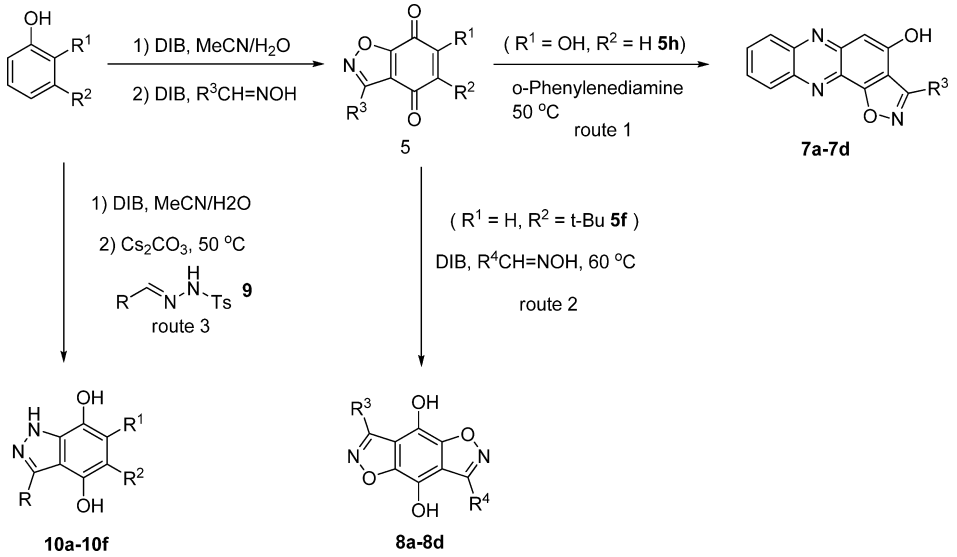
Table 3. Synthesis of 3-Substituted Benz[*d*]isoxazole-4,7-diols with Various Phenols



Entry	Phenol	R	Product	Yield (%) (a:b)*
1	**1b**	2-Pyr	**6a** (R^1 = H, R^2 = Me) + **6b** (R^1 = Me, R^2 = H)	67 (60:40)
2	**1c**	2-Pyr	**6c** (R^1 = R^2 = H)	33
3	**1d**	4-*i*-PrC_6H_4	**6d** (R^1 = H, R^2 = $C_2H_4CO_2H$) + **6e** (R^1 = $C_2H_4CO_2H$, R^2 = H)	25 (86:14)
4	**1d**	2-Pyr	**6f** (R^1 = H, R^2 = $C_2H_4CO_2H$) + **6g** (R^1 = $C_2H_4CO_2H$, R^2 = H)	19 (58:42)
5	**1e**	2-Pyr	**6h** (R^1 = R^2 = -$(CH_2)_4$-)	84
6	**1e**	2- $MeOC_6H_4$	**6i** (R^1 = R^2 = -$(CH_2)_4$-)	71
7	**1e**	4-*i*-PrC_6H_4	**6j** (R^1 = R^2 = -$(CH_2)_4$-)	81
8	**1e**	4-AcNHC_6H_4	**6k** (R^1 = R^2 = -$(CH_2)_4$-)	85
9	**1f**	2-Pyr	**6l** (R^1 = H, R^2 = *t*-Bu) + **6m** (R^1 = *t*-Bu, R^2 = H)	95 (56:44)
10	**1g**	2-Pyr	**6l** (R^1 = H, R^2 = *t*-Bu) + **6m** (R^1 = *t*-Bu, R^2 = H)	89 (56:44)
11	**1f**	3,4,5-$(MeO)_3C_6H_2$	**6n** (R^1 = H, R^2 = *t*-Bu) + **6o** (R^1 = *t*-Bu, R^2 = H)	91 (77:23)
12	**1f**	3-MeO-4-EtO C_6H_3	**6p** (R^1 = H, R^2 = *t*-Bu) + **6q** (R^1 = *t*-Bu, R^2 = H)	82 (60:40)
13	**1f**	3-ClC_6H_4	**6r** (R^1 = H, R^2 = *t*-Bu) + **6s** (R^1 = *t*-Bu, R^2 = H)	79 (93:7)
14	**1f**	2,4-$Cl_2C_6H_3$	**6t** (R^1 = H, R^2 = *t*-Bu) + **6u** (R^1 = *t*-Bu, R^2 = H)	88 (87:13)
15	**1f**	4-AcNHC_6H_4	**6v** (R^1 = H, R^2 = *t*-Bu) + **6w** (R^1 = *t*-Bu, R^2 = H)	89 (91:9)
16	**1f**	$C_6H_5C_2H_4$	**6x** (R^1 = H, R^2 = *t*-Bu) + **6y** (R^1 = *t*-Bu, R^2 = H)	82 (79:21)

*Ratio of mixture determined by the peak areas of 5-H and 6-H in ^{1}H NMR spectroscopy.

Scheme 4. Application for Synthesis of More Complex Molecules



*4-Chlorobenzaldehyde oxime (**2k**):* white solid, 1.44 g, 93% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.35 (s, 1H), 8.15 (s, 1H), 7.61 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H); ESI-MS m/z 156.6 $[M + H]^+$.

*3-Chlorobenzaldehyde oxime (**2l**):* white solid, 1.50 g, 97% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (s, 1H), 7.59 (s, 1H), 7.52 (dd, J = 6.1 Hz, 2.1 Hz, 1H), 7.42−7.34 (m, 2H); ESI-MS m/z 156.5 $[M + H]^+$.

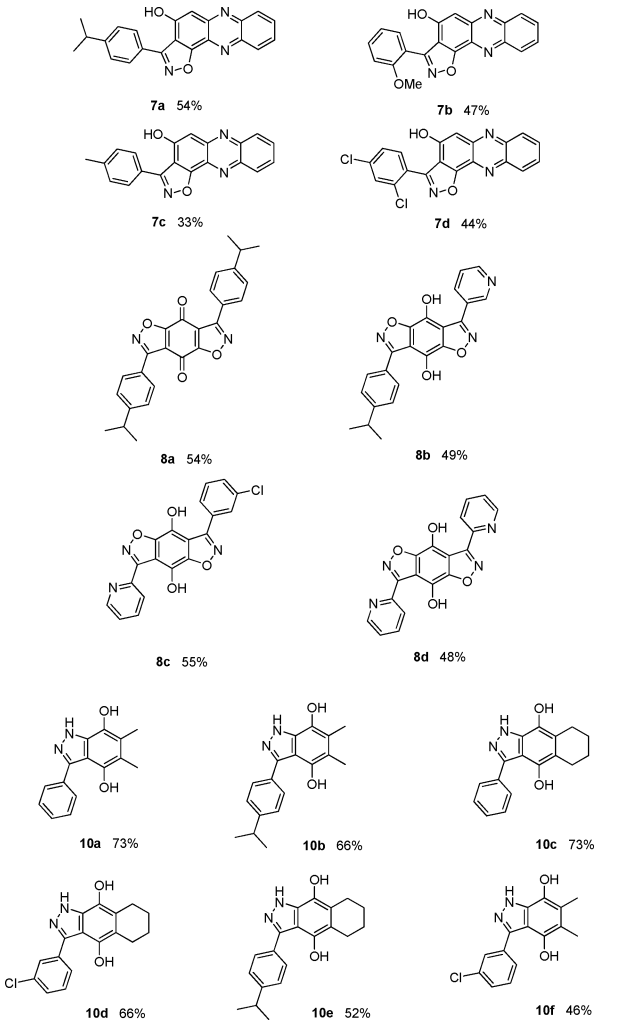
*2,4-Dichlorobenzaldehyde oxime (**2m**):* white solid, 1.73 g, 91% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.95 (s, 1H), 8.29 (s, 1H), 7.80 (d, J = 8.5 Hz, 1H), 7.67 (d, J = 2.0 Hz, 1H), 7.43 (dd, J = 8.5 Hz, 1.7 Hz, 1H); ESI-MS m/z 191.0 $[M + H]^+$.

*4-Fluorobenzaldehyde oxime (**2n**):* white solid, 1.29 g, 93% yield; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.33 (s, 1H), 8.15 (s, 1H), 7.68 (dd, J = 8.7 Hz, 5.6 Hz, 2H), 7.17 (dd, J = 9.8 Hz, 7.8 Hz, 2H); ESI-MS m/z 140.2 $[M + H]^+$.

*3-Fluorobenzaldehyde oxime (**2o**):* white solid, 1.35 g, 97% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.13 (s, 1H), 7.47−7.32 (m, 3H), 7.23−7.13 (m, 1H); ESI-MS m/z 140.1 $[M + H]^+$.

dx.doi.org/10.1021/jo401077q | J. Org. Chem. XXXX, XXX, XXX−XXX

Table 4. Compounds of 7a−d, 8a−d, and 10a−f



*4-Isopropylbenzaldehyde oxime (**2p**):* white solid, 1.50 g, 92% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.10 (s, 1H), 8.07 (s, 1H), 7.48 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 2.87 (dt, J = 13.8 Hz, 6.9 Hz, 1H), 1.18 (d, J = 6.9 Hz, 6H); ESI-MS m/z 164.2 [M + H]$^+$.

*4-Acetylaminobenzaldehyde oxime (**2q**):* white solid, 1.69 g, 95% yield; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.14 (s, 1H), 8.07 (s, 1H), 7.85 (s, 1H), 7.67 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.7 Hz, 2H), 2.08 (s, 3H); ESI-MS m/z 179.2 [M + H]$^+$.

*4-Hydroxylbenzaldehyde oxime (**2r**):* white solid, 1.27 g, 93% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 9.98 (s, 1H), 9.06 (s, 1H), 8.68 (s, 1H), 7.63−7.37 (m, 2H), 7.06−6.76 (m, 2H); ESI-MS m/z 138.1 [M + H]$^+$.

*1-Naphthaldehyde oxime (**2s**):* white solid, 1.50 g, 88% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 10.53 (s, 1H), 8.78 (s, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.96 (dd, J = 5.6 Hz, 3.2 Hz, 2H), 7.81 (d, J = 7.1 Hz, 1H), 7.62−7.51 (m, 3H); ESI-MS m/z 172.3 [M + H]$^+$.

*Isonicotinaldehyde oxime (**2t**):* white solid, 1.04 g, 85% yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.85 (s, 1H), 8.60 (dd, J = 4.5 Hz, 1.5 Hz, 2H), 8.18 (s, 1H), 7.55 (dd, J = 4.6 Hz, 1.4 Hz, 2H); ESI-MS m/z 123.2 [M + H]$^+$.

*1H-Imidazole-2-carbaldehyde oxime (**2u**):* white solid, 0.92 g, 83% yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.94 (s, 1H), 7.43 (s, 1H), 7.06 (s, 2H); ESI-MS m/z 112.4 [M + H]$^+$.

*3-Phenylpropanal oxime (**2v**):* white solid, 1.32 g, 91% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.82 (s, 1H), 7.34−7.05 (m, 6H), 2.72 (t, J = 7.7 Hz, 2H), 2.53 (t, J = 7.5 Hz, 2H); ESI-MS m/z 150.4 [M + H]$^+$.

Preparation of Ethyl 2-(Hydroxyimino)-3-oxobutanoate (2w). To a solution of ethyl acetoacetate (5.20 g, 40.0 mmol) in 6 mL of AcOH was added a solution of $NaNO_2$ (3.60 g, 52.0 mmol) in 6 mL water at 0 °C. After the mixture was stirred at 0 °C overnight, a saturated aqueous solution of $NaHCO_3$ was added to adjust the pH to 7−8, brine was added, and the mixture was extracted with ethyl acetate, dried by anhydrous Na_2SO_4, concentrated, and then purified by chromatogram on silica gel to afford compound **2w**.

*Ethyl 2-(hydroxyimino)-3-oxobutanoate (**2w**):* colorless oil, 1.19 g, 75% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.23 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 2.33 (s, 3H), 1.21 (t, J = 7.1 Hz, 3H); ESI-MS m/z 160.3 [M + H]$^+$.

Preparation of Benzo[*d*]isoxazole-4,7-diols 4a−w and 6a−y. A mixture of phenol (1.0 mmol) and $PhI(OAc)_2$ (2.0 mmol) was stirred in acetonitrile (4 mL) and water (2 mL) at room temperature until the starting material disappeared. The progress of reaction was monitored by TLC (ethyl acetate/hexane). Then aldehyde oxime (1.5 mmol) was added. After the flask was completely cooled in an ice bath, 2.0 mmol of $PhI(OAc)_2$ solved in acetonitrile (8 mL) and water (4 mL) was added dropwise within 30 min and then the mixture warmed to rt. After the intermediate disappeared, saturated $Na_2S_2O_3$ solution (12 mL) was added, and the mixture stirred at room temperature overnight. The mixture was poured into brine (30 mL) and extracted with ethyl acetate (3 × 50 mL). The combined extract was washed with brine (2 × 50 mL) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the residue was chromatographed by silica gel (ethyl acetate/hexane 1:12) to obtain the desired products. The correct structures of products were characterized by ^{1}H and ^{13}C NMR and mass spectral data.

*7-Methoxy-5,6-dimethyl-3-(pyridin-2-yl)benzo[d]isoxazol-4-ol (**4a**):* yellow oil, 221 mg, 82% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.75 (s, 1H), 8.10−7.96 (m, 2H), 7.59−7.58 (m, 1H), 7.13 (d, J = 1.5 Hz, 1H), 2.95 (s, 3H), 2.13 (d, J = 1.3 Hz, 3H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.7, 176.0, 160.9, 159.3, 150.4, 146.9, 137.5, 125.9, 125.5, 113.2, 110.8, 85.7, 54.1, 25.8, 18.6; ESI-MS m/z 271.1 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{16}N_2O_3$ [M + H]$^+$ 271.1083, found 271.1079.

*5,6-Dimethyl-3-(pyridin-2-yl)benzo[d]isoxazole-4,7-diol (**4b**):* yellow solid, 238 mg, 93% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.77 (d, J = 4.7 Hz, 1H), 8.10−7.97 (m, 2H), 7.64−7.61 (m, 1H), 2.09−1.98 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.0, 175.0, 164.9, 159.2, 150.0, 145.7, 142.9, 139.7, 137.1, 125.6, 125.1, 117.2, 12.6, 11.8; ESI-MS m/z 257.1 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{14}H_{13}N_2O_3$ [M + H]$^+$ 257.0926, found 257.0924; mp 128−130 °C.

*5,6-Dimethyl-3-phenylbenzo[d]isoxazole-4,7-diol (**4c**):* yellow solid, 217 mg, 85% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.01 (dd, J = 7.9 Hz, 1.5 Hz, 2H), 7.66−7.51 (m, 3H), 2.06 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.5, 175.1, 165.1, 159.5, 143.1, 139.6, 131.2, 128.9, 128.7, 126.1, 116.9, 12.7, 11.7; ESI-MS m/z 256.0 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{14}NO_3$ [M + H]$^+$ 256.0974, found 256.0967; mp 122−123 °C.

*3-(4-Methoxyphenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4d**):* yellow solid, 234 mg, 82% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.04 (d, J = 8.8 Hz, 2H), 7.12 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H), 2.07 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.4, 175.0, 165.1, 158.8, 143.1, 139.6, 128.0, 124.6, 122.6, 120.4, 117.0, 115.2, 12.7, 11.7; ESI-MS m/z 287.2 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{16}H_{16}NO_4$ [M + H]$^+$ 286.1079, found 286.1072; mp 94−95 °C.

*3-(3-Methoxyphenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4e**):* yellow solid, 259 mg, 91% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76−7.56 (m, 2H), 7.49 (t, J = 7.9 Hz, 1H), 7.22−7.08 (m, 1H), 3.84 (d, J = 6.0 Hz, 3H), 2.07 (s, 6H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 180.5, 175.1, 165.2, 159.4, 159.2, 143.2, 139.5, 129.9, 127.3, 121.1, 117.0, 116.9, 114.4, 55.3, 12.8, 11.7; ESI-MS m/z 287.3 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{16}H_{16}NO_4$ [M + H]$^+$ 286.1079, found. 286.1070; mp 104−106 °C.

*3-(2-Methoxyphenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4f**):* yellow solid, 228 mg, 80% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.62−7.53 (m, 1H), 7.42 (dd, J = 7.5 Hz, 1.6 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 3.73 (s, 3H), 2.10−1.95 (m,

dx.doi.org/10.1021/jo401077q | J. Org. Chem. XXXX, XXX, XXX−XXX

6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.0, 175.1, 164.0, 157.6, 157.2, 142.3, 139.9, 132.4, 130.4, 120.3, 118.2, 115.1, 111.8, 55.6, 12.4, 11.8; ESI-MS m/z 287.0 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{16}H_{16}NO_4$ [M + H]$^+$ 286.1079, found 286.1077; mp 141−143 °C.

5,6-Dimethyl-3-(2,4,6-trimethoxyphenyl)benzo[d]isoxazole-4,7-diol (**4g**): yellow solid, 300 mg, 97% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.34 (s, 2H), 3.85 (s, 3H), 3.65 (s, 6H), 2.01 (d, J = 1.2 Hz, 3H), 1.95 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.6, 175.4, 164.3, 163.6, 159.6, 154.3, 142.4, 140.6, 119.3, 96.3, 91.5, 56.3, 56.0, 12.7, 12.3; ESI-MS m/z 346.3 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{18}H_{20}NO_6$ [M + H]$^+$ 346.1291, found 346.1281; mp 137−139 °C.

5,6-Dimethyl-3-(3,4,5-trimethoxyphenyl)benzo[d]isoxazole-4,7-diol (**4h**): yellow solid, 293 mg, 85% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.37 (s, 2H), 3.87 (s, 3H), 3.67 (s, 6H), 2.00 (d, J = 24.8 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.6, 175.5, 164.3, 163.6, 159.7, 154.3, 142.4, 140.6, 119.3, 96.3, 91.5, 56.3, 56.0, 12.7, 12.3; ESI-MS m/z 346.2 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{18}H_{18}NO_6$ [M − H]$^-$ 344.1128, found 344.1129; mp 104−106 °C.

3-(4-(Benzyloxy)phenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4j**): yellow solid, 296 mg, 82% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.95 (s, 1H), 8.02 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 15.0 Hz, 2H), 7.56−7.29 (m, 4H), 7.18 (d, J = 8.2 Hz, 1H), 5.20 (s, 2H), 2.05 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.6, 167.4, 165.5, 161.1, 137.1, 132.2, 132.0, 131.0, 129.1,129.0, 128.9, 128.5, 128.3, 118.9, 115.5, 69.9, 13.2, 12.1; ESI-MS m/z 362.4 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{22}H_{18}NO_4$ [M − H]$^-$ 360.1230, found 360.1238; mp 128−129 °C.

3-(4-Chlorophenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4k**): yellow solid, 239 mg, 83% yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.27 (s, 1H), 8.73 (s, 1H), 8.08 (d, J = 8.4, 1H), 7.96 (d, J = 8.4, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 8.4 Hz, 1H), 2.18 (d, J = 20.4, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.5, 175.0, 165.1, 158.5, 153.4, 143.1, 140.4, 136.1, 131.4, 124.9, 119.1, 12.7, 11.7; ESI-MS m/z 290.0 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{13}ClNO_3$ [M + H]$^+$ 290.0584, found 290.0576; mp 136−138 °C.

3-(3-Chlorophenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4l**): yellow solid, 216 mg, 75% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.45 (s, 1H), 8.32 (d, J = 7.7 Hz, 1H), 7.99 (d, J = 7.8 Hz, 1H), 7.99 (t, J = 7.8 Hz, 1H), 2.07 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.9, 175.5, 165.7, 163.6, 161.2, 143.6, 140.2, 131.5, 128.6, 125.4, 118.7, 117.4, 116.3, 12.8, 11.8; ESI-MS m/z 290.2 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{13}ClNO_3$ [M + H]$^+$ 290.0584, found 290.0577; mp 120−121 °C.

3-(2,4-Dichlorophenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4m**): yellow solid, 260 mg, 81% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.92 (d, J = 1.2 Hz, 1H), 7.65 (d, J = 2.1 Hz, 2H), 2.08 (d, J = 1.1 Hz, 3H), 2.02 (d, J = 1.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.5, 175.3, 164.8, 157.2, 142.6, 141.0, 136.9, 134.4, 133.4, 129.9, 128.2, 125, 118.5, 12.7, 12.4; ESI-MS m/z 324.0 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{12}Cl_2NO_3$ [M + H]$^+$ 324.0194, found 324.0188; mp 135−136 °C.

3-(4-Fluorophenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4n**): yellow solid, 123 mg, 45% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.32−8.20 (m, 2H), 7.37 (dd, J = 9.9 Hz, 7.9 Hz, 2H), 2.25−2.13 (m, 6H); ^{13}C NMR (100 MHz, acetone-d_6) δ 180.8, 175.3, 165.7, 163.2, 159.0, 143.7, 140.0, 131.6 (d, J = 8.8 Hz), 123.1 (d, J = 3.3 Hz), 117.3, 115.6, 12.1, 11.0; ESI-MS m/z 274.1 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{13}FNO_3$ [M + H]$^+$ 274.0879, found 274.0872; mp 109−110 °C.

3-(3-Fluorophenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4o**): yellow solid, 177 mg, 65% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.00−7.88 (m, 2H), 7.68−7.62 (m, 1H), 7.57−7.39 (m, 1H), 2.07 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.4, 165.6, 163.6, 161.1, 158.9 (d, J = 2.6 Hz), 143.7, 140.1, 131.5 (d, J = 8.3 Hz), 128.5 (d, J = 8.8 Hz), 125.4 (d, J = 3.0 Hz), 118.7, 117.4, 116.3, 13.2, 12.2; ESI-MS m/z 274.2 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{13}FNO_3$ [M + H]$^+$ 274.0879, found 274.0871; mp 115−116 °C.

3-(4-Isopropylphenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4p**): yellow solid, 243 mg, 82% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.07 (d, J = 8.3 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 3.02 (dt, J = 13.8 Hz, 6.9 Hz, 1H), 2.14 (d, J = 2.8 Hz, 6H), 1.30 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.5, 175.0, 165.0, 159.4, 151.8, 143.1, 139.5, 128.9, 126.8, 123.5, 116.8, 33.4, 23.6, 12.7, 11.7; ESI-MS m/z 298.3 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{18}H_{20}NO_3$ [M + H]$^+$ 298.1443, found 298.1435; mp 122−124 °C.

N-(4-(4,7-Dihydroxy-5,6-dimethylbenzo[d]isoxazol-3-yl)phenyl)-acetamide (**4q**): yellow solid, 246 mg, 79% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.22 (s, 1H), 8.01 (d, J = 8.6 Hz, 2H), 7.75 (d, J = 8.8 Hz, 2H), 2.10 (s, 3H), 2.06 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.9, 181.0, 175.6, 169.3, 165.5, 159.5, 143.6, 142.4, 139.9, 130.1, 120.7, 119.0, 24.6, 13.2, 12.2; ESI-MS m/z 313.4 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{17}H_{15}N_2O_4$ [M − H]$^-$ 311.1026, found 311.1028; mp 158−160 °C.

3-(4-Hydroxyphenyl)-5,6-dimethylbenzo[d]isoxazole-4,7-diol (**4r**): yellow solid, 178 mg, 66% yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.12 (s, 1H), 7.94 (d, J = 8.7 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 2.06 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.7, 175.2, 165.0, 160.2, 159.3, 143.1, 139.4, 130.7, 116.7, 116.6, 115.5, 12.8, 11.7; ESI-MS m/z 272.1 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{14}NO_4$ [M + H]$^+$ 272.0923, found 272.0913; mp 123−125 °C.

5,6-Dimethyl-3-(naphthalen-1-yl)benzo[d]isoxazole-4,7-diol (**4s**): yellow solid, 105 mg, 32% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.75 (s, 1H), 8.16 (d, J = 8.1 Hz, 1H), 8.06 (d, J = 8.1 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 7.0 Hz, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.61 (dd, J = 14.3 Hz, 7.3 Hz, 1H), 7.55−7.49 (m, 1H), 1.97 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 154.1, 151.5, 143.0, 133.5, 131.4, 131.2, 129.2, 128.9, 127.6, 127.0, 125.6, 125.5, 124.0, 115.9, 12.8, 12.3; ESI-MS m/z 306.3 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{19}H_{15}NO_3Na$ [M + Na]$^+$ 328.0950, found 328.0945; mp 123−124 °C.

5,6-Dimethyl-3-(pyridin-4-yl)benzo[d]isoxazole-4,7-diol (**4t**): yellow solid, 228 mg, 89% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.76 (s, 1H), 9.31 (s, 1H), 8.80 (d, J = 4.7 Hz, 2H), 7.99 (d, J = 4.7 Hz, 2H), 2.15−2.00 (m, 6H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.5, 154.0, 150.8, 150.1, 140.8, 131.9, 128.1, 124.4, 120.0, 110.3, 13.4, 13.1; ESI-MS m/z 257.0 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{14}H_{13}N_2O_3$ [M + H]$^+$ 257.0926, found 257.0924; mp 115−116 °C.

5,6-Dimethyl-3-(imidazol-2-yl)benzo[d]isoxazole-4,7-diol (**4u**): yellow solid, 208 mg, 85% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.86 (s, 1H), 13.86 (s, 1H), 13.25 (s, 1H), 9.10 (s, 1H), 7.54 (s, 1H), 7.37 (s, 1H), 2.23 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.0, 149.1, 141.6, 137.2, 130.1, 129.5, 128.5, 121.1, 117.2, 107.5, 13.3, 12.4; ESI-MS m/z 246.2 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{12}H_{12}N_3O_3$ [M + H]$^+$ 246.0873, found 246.0865; mp 133−135 °C.

5,6-Dimethyl-3-phenethylbenzo[d]isoxazole-4,7-diol (**4v**): yellow solid, 249 mg, 85% yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.28 (d, J = 7.5 Hz, 5H), 3.19 (t, J = 7.7 Hz, 2H), 3.01 (t, J = 7.4 Hz, 2H), 2.05 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.1, 175.8, 164.7, 160.6, 142.7, 140.9, 129.1, 129.0, 126.9, 118.4, 110.0, 33.2, 27.4, 12.9, 12.5; ESI-MS m/z 284.1 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{17}H_{18}NO_3$ [M + H]$^+$ 284.1287, found 284.1279; mp 100−102 °C.

Ethyl 5,6-dimethyl-4,7-diol-4,7-dihydrobenzo[d]isoxazole-3-carboxylate (**4w**): yellow solid, 118 mg, 47% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.39 (s, 1H), 9.34 (s, 1H), 4.52 (d, J = 7.0 Hz, 2H), 2.18 (d, J = 32.3 Hz, 6H), 1.39 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.3, 153.9, 151.5, 139.9, 131.0, 129.6, 118.7, 108.3, 64.0, 14.3, 13.3, 12.3; ESI-MS m/z 252.1 [M + H]$^+$; HRMS (ESI-TOF) calcd for $C_{12}H_{14}NO_5$ [M + H]$^+$ 252.0872, found 252.0889; mp 108−110 °C.

5-Methyl-3-(pyridin-2-yl)benzo[d]isoxazole-4,7-diol and 6-Methyl-3-(pyridin-2-yl)benzo[d]isoxazole-4,7-diol (**6a** *and* **6b**, **6a:6b** = *1:0.67*): yellow solid, 162 mg, 67% yield; ^{1}H NMR (400 MHz, DMSO-d_6) (**6a**) δ 12.99 (s, 1H), 12.73 (s, 1H), 9.61 (s, 1H), 8.84 (s, 2H), 8.41 (d, J = 7.4 Hz, 2H), 6.86 (s, 1H), 2.25 (s, 3H), 2.18 (s, 3H); ^{1}H NMR (400 MHz, DMSO-d_6) (**6b**) δ 12.99 (s, 1H), 12.73 (s, 1H), 9.12 (s, 1H), 8.41 (d, J = 7.4 Hz, 2H), 7.72 (s, 2H), 6.50 (s, 1H), 2.25 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) (**6a** + **6b**) δ 156.7, 156.3, 155.3, 152.8, 148.3, 148.2, 146.8, 146.6, 143.8, 141.2,

dx.doi.org/10.1021/jo401077q | J. Org. Chem. XXXX, XXX, XXX−XXX

140.0, 140.00, 132.4, 130.3, 129.6, 126.4, 126.3, 122.4, 120.0, 117.0, 111.1, 110.0, 108.2, 15.9, 15.3; ESI-MS m/z 243.0 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{13}H_{11}N_2O_3$ $[M + H]^+$ 243.0770, found 243.0763.

*3-(Pyridin-2-yl)benzo[d]isoxazole-4,7-diol (**6c**):* yellow solid, 75 mg, 33% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.81 (s, 1H), 9.74 (s, 1H), 8.84(d, J = 4.4 Hz, 1H), 8.22−8.17 (m, 1H), 7.73 (dd, J = 7.6 Hz, 5.0 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 6.53 (d, J = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.0, 154.7, 150.2, 148.7, 147.0, 144.7, 140.5, 133.7, 126.9, 122.9, 118.4, 109.2; ESI-MS m/z 229.0 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{12}H_9N_2O_3$ $[M + H]^+$ 229.0608, found 229.0602; mp 122−123 °C.

*3-(4,7-Dihydroxy-3-(4-isopropylphenyl)benzo[d]isoxazol-5-yl)-propanoic acid and 3-(4,7-dihydroxy-3-(4-isopropylphenyl)benzo-[d]isoxazol-6-yl)propanoic acid (**6d** and **6e**, **6d**:**6e** = 1:0.15):* yellow solid, 85 mg, 25% yield; ^{1}H NMR (400 MHz, DMSO-d_6) (**6d**) δ 10.19 (s, 1H), 9.50 (s, 1H), 7.89 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 6.72 (s, 1H), 3.04−2.85 (m, 1H), 2.72−2.58 (m, 2H), 2.37−2.19 (m, 2H), 1.24 (d, J = 6.9 Hz, 6H), ^{1}H NMR (400 MHz, DMSO-d_6) (**6e**) δ 10.19 (s, 1H), 9.50 (s, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H), 6.59 (s, 1H), 3.04−2.85 (m, 1H), 2.72−2.58 (m, 2H), 2.37−2.19 (m, 2H), 1.24 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) (**6d**) δ 179.3, 173.3, 160.3, 151.8, 130.0, 129.8, 126.9, 126.6, 124.5, 114.9, 68.3, 33.9, 33.8, 33.5, 28.6, 24.1; ESI-MS m/z 342.2 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{19}H_{20}NO_5$ $[M + H]^+$ 342.1336, found 342.1335.

*3-(4,7-Dihydroxy-3-(pyridin-2-yl)benzo[d]isoxazol-5-yl)propanoic acid and 3-(4,7-Dihydroxy-3- (pyridin-2-yl)benzo[d]isoxazol-6-yl)-propanoic acid (**6f** and **6g**, **6f**:**6g** = 1:0.72):* yellow solid, 57 mg, 19% yield; ^{1}H NMR (600 MHz, DMSO-d_6), **6f**: δ 13.13 (s, 1H), 12.75 (s, 1H), 8.85 (s, 1H), 7.72 (m, 2H), 7.14 (m, 1H), 6.89 (s, 1H), 2.82 (d, J = 7.4 Hz, 2H), 1.95 (d, J = 24.0 Hz, 2H); ^{1}H NMR (600 MHz, DMSO-d_6) (**6g**) δ 13.13 (s, 1H), 12.75 (s, 1H), 8.41 (m, 1H), 8.19 (m, 2H), 6.79 (m, 1H), 6.51 (s, 1H), 2.82 (d, J = 7.4 Hz, 2H), 1.95 (d, J = 24.0 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) (**6f** + **6g**) δ 173.9, 159.4, 156.4, 153.1, 152.0, 149.7, 149.4, 148.9, 148.3, 148.1, 146.6, 141.2, 140.0, 139.9, 137.3, 136.9, 136.7, 132.5, 127.7, 126.3, 125.2, 123.9, 122.4, 120.3, 119.7, 119.3, 110.3, 110.1, 34.0, 25.2; ESI-MS m/z 301.1 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{13}N_2O_5$ $[M + H]^+$ 301.0819, found 301.0806.

*3-(Pyridin-2-yl)-5,6,7,8-tetrahydronaphtho[2,3-d]isoxazole-4,9-diol (**6h**):* yellow solid, 237 mg, 84% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.99 (s, 1H), 9.03 (s, 1H), 8.86 (d, J = 4.1 Hz, 1H), 8.41 (d, J = 7.9 Hz, 1H), 8.19 (t, J = 7.4 Hz, 1H), 7.81−7.65 (m, 1H), 2.70 (d, J = 27.6 Hz, 4H), 1.72 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.3, 152.7, 148.2, 146.8, 141.1, 139.9, 129.6, 129.1, 126.2, 122.3, 117.7, 107.0, 24.0, 23.3, 22.0, 21.9; ESI-MS m/z 283.1 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_3$ $[M + H]^+$ 283.1077, found 283.1073; mp 149−151 °C.

*3-(2-Methoxyphenyl)-5,6,7,8-tetrahydronaphtho[2,3-d]-isoxazole-4,9-diol (**6i**):* yellow solid, 221 mg, 71% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.63−7.52 (m, 1H), 7.42 (dd, J = 7.5 Hz, 1.7 Hz, 1H), 7.22 (d, J = 8.3 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 3.73 (s, 3H), 2.42 (d, J = 25.1 Hz, 4H), 1.66 (d, J = 2.7 Hz, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.1, 175.1, 164.1, 157.6, 157.2, 143.5, 143.3, 132.4, 130.4, 120.3, 118.2, 115.1, 111.8, 55.7, 22.7, 22.0, 20.5, 18.6; ESI-MS m/z 312.2 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{18}H_{18}NO_4$ $[M + H]^+$ 312.1236, found 312.1229; mp 129−131 °C.

*3-(4-Isopropylphenyl)-5,6,7,8-tetrahydronaphtho[2,3-d]-isoxazole-4,9-diol (**6j**):* yellow solid, 261 mg, 81% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.92 (d, J = 8.1 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 2.95 (dt, J = 13.5 Hz, 6.7 Hz, 1H), 2.42 (d, J = 25.1 Hz, 4H), 2.39 (s, 4H), 1.62 (s, 2H), 1.22 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.6, 175.0, 165.1, 159.3, 151.8, 144.3, 140.9, 128.9, 126.6, 123.5, 116.8, 109.3, 33.4, 23.6, 22.9, 21.9, 20.5; ESI-MS m/z 324.3 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{20}H_{22}NO_3$ $[M + H]^+$ 324.1600, found 324.1609; mp 143−144 °C.

*N-(4-(4,9-Dihydroxy-5,6,7,8-tetrahydronaphtho[2,3-d]isoxazol-3-yl)phenyl)acetamide (**6k**):* yellow solid, 287 mg, 85% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.27 (s, 1H), 8.02 (d, J = 8.7 Hz, 2H), 7.77 (d, J = 8.6 Hz, 2H), 2.51 (s, 4H), 2.10 (s, 3H), 1.68 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.6, 157.8, 154.7, 152.5, 140.7, 130.7, 127.6, 125.8, 123.4, 121.9, 119.3, 110.5, 24.1, 22.1, 21.8, 21.6, 21.0; ESI-MS m/z 339.2 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{19}H_{19}N_2O_4$ $[M + H]^+$ 339.1345, found 339.1338; mp 162−164 °C.

*5-tert-Butyl-3-(pyridin-2-yl)benzo[d]isoxazole-4,7-diol and 6-tert-butyl-3-(pyridin-2-yl) benzo[d]isoxazole-4,7-diol (**6l** and **6m**, **6l**:**6m** = 1:0.78):* yellow solid, 269 mg, 95% yield; ^{1}H NMR (400 MHz, DMSO-d_6), **6l**: δ 13.42 (s, 1H), 12.61 (s, 1H), 9.56 (s, 1H), 8.92−8.83 (m, 1H), 8.43 (t, J = 9.2 Hz, 1H), 7.05 (s, 1H), 1.42 (s, 9H); ^{1}H NMR (400 MHz, DMSO-d_6) (**6m**) δ 13.42 (s, 1H), 12.61 (s, 1H), 9.30 (s, 1H), 8.21 (t, J = 7.0 Hz, 1H), 7.84−7.66 (m, 1H), 6.62 (s, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) (**6l** + **6m**) δ 156.6, 156.2, 152.4, 150.1, 148.4, 147.9, 146.8, 143.3, 142.2, 141.0, 140.0, 137.3, 134.0, 131.8, 130.6, 128.9, 126.4, 125.1, 122.5, 122.4, 116.7, 111.1, 107.9, 107.5, 35.00, 34.4, 29.5; ESI-MS m/z 285.4 $[M + H]^+$. HRMS (ESI-TOF) calcd for $C_{16}H_{17}N_2O_3$ $[M + H]^+$ 285.1239, found 285.1229.

*5-tert-Butyl-3-(3,4,5-trimethoxyphenyl)benzo[d]isoxazole-4,7-diol and 6-tert-butyl-3-(3,4,5- trimethoxyphenyl)benzo[d]isoxazole-4,7-diol (**6n** and **6o**, **6n**:**6o** = 1:0.3):* yellow solid, 339 mg, 91% yield; ^{1}H NMR (400 MHz, DMSO-d_6) (**6n**) δ 10.05 (s, 1H), 9.22 (s, 1H), 7.41 (s, 2H), 6.70 (s, 1H), 3.85 (s, 6H), 3.74 (s, 3H), 1.40 (s, 9H); ^{1}H NMR (400 MHz, DMSO-d_6) (**6o**) δ 10.05 (s, 1H), 9.22 (s, 1H), 7.33 (s, 2H), 6.89 (s, 1H), 3.85 (s, 6H), 3.74 (s, 3H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) (**6n**) δ 157.3, 156.4, 153.1, 143.4, 139.0, 131.2, 123.7, 108.3, 107.6, 106.9, 103.7, 60.1, 55.9, 34.9, 29.5; ESI-MS m/z 374.2 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{20}H_{24}NO_6$ $[M + H]^+$ 374.1604, found 374.1627.

*5-tert-Butyl-3-(4-ethoxy-3-methoxyphenyl)benzo[d]isoxazole-4,7-diol and 6-tert-butyl-3-(4-ethoxy- 3-methoxyphenyl)benzo[d]-isoxazole-4,7-diol (**6p** and **6q**, **6p**:**6q** =1:0.67):* yellow solid, 292 mg, 82% yield; ^{1}H NMR (400 MHz, DMSO-d_6) (**6p**) δ 9.96 (s, 1H), 9.71 (s, 1H), 9.18 (s, 1H), 7.68−7.59 (m, 1H), 7.13−7.06 (m, 1H), 6.99 (s, 1H), 4.10 (q, J = 6.9 Hz, 2H), 3.82 (s, 3H), 1.38 (dd, J = 9.4 Hz, 4.7 Hz, 12H); ^{1}H NMR (400 MHz, DMSO-d_6) (**6q**) δ 9.96 (s, 1H, OH), 9.71 (s, 1H), 8.10 (s, 1H), 7.50−7.43 (m, 1H), 7.13−7.06 (m, 1H), 6.99 (s, 1H), 4.10 (q, J = 6.9 Hz, 2H), 3.82 (s, 3H), 1.38 (dd, J = 9.4 Hz, 4.7 Hz, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) (**6p** + **6q**) δ 157.9, 157.2, 156.3, 151.9, 149.4, 149.3, 148.5, 148.4, 143.5, 140.6, 138.9, 134.3, 131.1, 122.4, 122.1, 121.1, 120.8, 115.4, 114.8, 113.2, 113.1, 112.4, 112.3, 108.4, 107.3, 63.8, 63.7, 55.5, 55.4, 34.8, 34.4, 30.3, 29.5, 29.4, 26.3, 14.7; ESI-MS m/z 358.3 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{20}H_{24}NO_5$ $[M + H]^+$ 358.1654, found 358.1646.

*5-tert-Butyl-3-(3-chlorophenyl)benzo[d]isoxazole-4,7-diol and 6-tert-butyl-3-(3- chlorophenyl) benzo[d]isoxazole-4,7-diol (**6r** and **6s**, **6r**:**6s** = 1:0.08):* yellow solid, 250 mg, 79% yield; ^{1}H NMR (400 MHz, DMSO-d_6), **6r**: δ 10.04 (s, 1H), 9.27 (s, 1H), 8.08 (s, 1H), 7.95 (d, J = 7.3 Hz, 1H), 7.63−7.45 (m, 2H), 6.68 (s, 1H), 1.38 (s, 9H,); ^{1}H NMR (400 MHz, DMSO-d_6) (**6s**) δ 10.04 (s, 1H), 9.27 (s, 1H), 8.16, (s, 1H), 8.04 (d, J = 7.3 Hz, 1H), 7.72−7.65 (m, 2H), 6.75 (s, 1H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) (**6r**) δ 156.4, 156.3, 143.4, 139.4, 133.0, 131.2, 130.6, 130.3, 129.8, 129.1, 127.8, 108.1, 107.5, 34.9, 29.5; ESI-MS m/z 318.1 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{17}H_{17}ClNO_3$ $[M + H]^+$ 318.0897, found 318.0890.

*5-tert-Butyl-3-(2,4-dichlorophenyl)benzo[d]isoxazole-4,7-diol and 6-tert-butyl-3-(2,4- dichlorophenyl)benzo[d]isoxazole-4,7-diol (**6t** and **6u**, **6t**:**6u** = 1:0.15):* yellow solid, 309 mg, 88% yield; ^{1}H NMR (400 MHz, DMSO-d_6) (**6t**) δ 9.63 (s, 1H), 9.30 (s, 1H), 7.63−7.55 (m, 3H), 6.64 (s, 1H), 1.40 (s, 9H); ^{1}H NMR (400 MHz, DMSO-d_6) (**6u**) δ 9.63 (s, 1H), 9.30 (s, 1H), 7.63−7.55 (m, 3H), 6.64 (s, 1H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) (**6t**) δ 155.5, 154.8, 143.8, 140.2, 139.5, 135.3, 134.4, 132.9, 131.0, 129.1, 127.3, 110.0, 107.3, 35.0, 29.6; ESI-MS m/z 352.2 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{17}H_{16}Cl_2NO_3$ $[M + H]^+$ 352.0507, found 352.0517.

*N-(4-(5-tert-Butyl-4,7-dihydroxybenzo[d]isoxazol-3-yl)phenyl)-acetamide and N-(4-(6-tert-butyl-4,7- dihydroxybenzo[d]isoxazol-3-yl)phenyl)acetamide (**6v** and **6w**, **6v**:**6w** = 1:0.1):* yellow solid, 302 mg, 89% yield; ^{1}H NMR (400 MHz, DMSO-d_6) (**6v**) δ 10.15 (s, 1H), 9.91 (s, 1H), 9.19 (s, 1H), 7.95 (d, J = 8.5 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 0,2H), 6.67 (s, 1H), 2.09 (s, 3H), 1.40 (s, 9H); ^{1}H NMR (400 MHz, DMSO-d_6) (**6w**) δ 10.15 (s, 1H), 9.91 (s,

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1H), 9.19 (s, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.00 (s, 1H), 2.05 (s, 3H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) (**6v**) δ 168.6, 157.2, 156.3, 143.6, 140.8, 138.9, 131.1, 129.9, 123.0, 118.4, 108.3, 107.2, 34.9, 29.5, 24.1; ESI-MS m/z 341.3 $[M + H]^+$. HRMS (ESI-TOF) calcd for $C_{19}H_{20}N_2O_4$ $[M + H]^+$ 341.1501, found 341.1492.

*5-tert-Butyl-3-phenethylbenzo[d]isoxazole-4,7-diol and 6-tert-butyl-3-phenethylbenzo[d]isoxazole-4,7-diol (**6x** and **6y**, **6x**:**6y** = 1:0.27):* yellow solid, 255 mg, 82% yield; ^{1}H NMR (400 MHz, DMSO-d_6) (**6x**) δ 7.29−7.25 (m, 5H), 6.65 (s, 1H), 3.20 (t, J = 6.0 Hz, 2H), 2.99 (t, J = 7.7 Hz, 2H), 1.29 (s, 9H); ^{1}H NMR (400 MHz, DMSO-d_6) (**6y**) δ 7.23−7.16 (m, 5H), 6.58 (s, 1H), 3.15 (t, J = 6.0 Hz, 2H), 2.99 (t, J = 7.7 Hz, 2H), 1.29 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) (**6x**) δ 182.0, 175.2, 160.7, 157.1, 140.2, 131.3, 128.4, 126.5, 126.2, 119.7, 35.4, 32.5, 29.5, 29.2, 26.6; ESI-MS m/z 312.3 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{19}H_{22}NO_3$ $[M + H]^+$ 312.1600, found 312.1594.

Preparation of Isoxazolo[5,4-*a*]phenazines (7a−d). A mixture of resorcinol (1.0 mmol) and 2.0 mmol of $PhI(OAc)_2$ was stirred in acetonitrile (4 mL) and water (2 mL) at rt until the starting material disappeared. The progress of the reaction was monitored by TLC (ethyl acetate/hexane). Then aldehyde oxime (1.5 mmol) was added. After the flask was cooled in an ice bath, an additional 2.0 mmol of $PhI(OAc)_2$ dissolved in acetonitrile (8 mL) and water (4 mL) was added dropwise over 30 min and then the mixture warmed to rt. After the intermediate disappeared, *o*-phenylenediamine (2.0 mmol) was added and the mixture heated at 50 °C for 8 h. The mixture was poured into brine (30 mL) and extracted with ethyl acetate (3 × 50 mL). The combined extract was washed with brine (2 × 50 mL) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the residue was chromatographed by silica gel (methanol/dichloromethane 1:20) to obtain the desired products. The correct structures of the products were characterized by ^{1}H and ^{13}C NMR and mass spectral data.

*3-(4-Isopropylphenyl)isoxazolo[5,4-a]phenazin-4-ol (**7a**):* yellow solid, 191 mg, 54% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (d, J = 8.1 Hz, 2H), 8.16 (d, J = 8.3 Hz, 1H), 8.08 (d, J = 8.1 Hz, 1H), 7.90 (d, J = 6.7 Hz, 1H), 7.85 (d, J = 6.7 Hz, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.46 (s, 1H), 3.09−3.03 (m, 1H), 1.33 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.6, 159.9, 151.2, 148.0, 144.7, 141.5, 139.2, 135.6, 130.4, 129.3, 129.0, 128.4, 126.3, 125.5, 125.0, 114.4, 109.4, 33.6, 23.9; ESI-MS m/z 356.3 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{22}H_{18}N_3O_2$ $[M + H]^+$ (356.1399), found 356.1381; mp 218−219 °C.

*3-(2-Methoxylphenyl)isoxazolo[5,4-a]phenazin-4-ol (**7b**):* yellow solid, 161 mg, 47% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.18 (s, 1H), 8.14 (d, J = 8.3 Hz, 1H), 7.89−7.75 (m, 3H), 7.65 (t, J = 7.3 Hz, 1H), 7.58 (d, J = 7.3 Hz, 1H), 7.44 (s, 1H), 7.31 (d, J = 8.3 Hz, 1H), 7.13 (t, J = 7.4 Hz, 1H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.7, 159.0, 158.1, 149.2, 144.9, 141.8, 140.2, 136.0, 132.4, 131.2, 130.5, 129.6, 129.3, 128.9, 120.5, 117.8, 116.4, 112.0, 109.4, 55.9; ESI-MS m/z 344.5 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{20}H_{14}N_3O_3$ $[M + H]^+$ 344.1035, found 344.1019; mp 250−252 °C.

*3-(4-Methylphenyl)isoxazolo[5,4-a]phenazin-4-ol (**7c**):* yellow solid, 108 mg, 33% yield; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.30 (d, J = 8.1 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.89−7.85 (m, 1H), 7.84−7.79 (m, 1H), 7.46 (d, J = 7.9 Hz, 2H), 7.38 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.7, 160.4, 147.9, 142.2, 140.8, 130.6, 129.9, 129.4, 129.3, 126.1, 125.7, 125.4, 124.1, 116.6, 116.3, 114.9, 111.6, 110.3, 109.9, 23.8; ESI-MS m/z 328.2 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{20}H_{14}N_3O_2$ $[M + H]^+$ 328.1068, found 328.1068; mp 213−214 °C.

*3-(2,4-Dichlorophenyl)isoxazolo[5,4-a]phenazin-4-ol (**7d**):* yellow solid, 167 mg, 44% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.31 (d, J = 8.0 Hz, 2H), 8.17 (d, J = 7.8 Hz, 1H), 8.08 (d, J = 8.2 Hz, 1H), 7.90 (dd, J = 17.1 Hz, 8.8 Hz, 2H), 7.47 (d, J = 7.9 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.2, 157.5, 144.9, 140.0, 136.3, 135.4, 135.2, 133.8, 130.8, 129.7, 129.4, 128.8, 127.9, 127.2, 119.1, 117.9, 116.1, 115.2, 109.9; ESI-MS m/z 382.0 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{19}H_{10}Cl_2N_3O_2$ $[M + H]^+$ 382.0144, found 382.0143; mp 165−167 °C.

Preparation of Benzodiisoxazole-4,8-diols (8a−d). A mixture of phenol (1.0 mmol) and $PhI(OAc)_2$ (2.0 mmol) was stirred in acetonitrile (4 mL) and water (2 mL) at rt until the starting material disappeared. Then aldehyde oxime (1.5 mmol) was added. After the flask was cooled in an ice bath, 2.0 mmol of $PhI(OAc)_2$ dissolved in acetonitrile (8 mL) and water (4 mL) was added dropwise over 30 min and then warmed to rt. After the intermediate disappeared, another aldehyde oxime (1.5 mmol) was added followed by addition of 2.0 mmol of $PhI(OAc)_2$ in acetonitrile (8 mL) and water (4 mL) dropwise over 30 min. After the mixture was heated under stirring at 60 °C for 24 h, saturated sodium thiosulfate solution (12 mL) was added and the mixture stirred at rt overnight. The mixture was added to brine (30 mL) and extracted with ethyl acetate (3 × 50 mL). The combined extract was washed with brine (2 × 50 mL) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the residue was chromatographed by silica gel (ethyl acetate/hexane 1:30) to obtain the desired products. The correct structures of products were characterized by ^{1}H and ^{13}C NMR and mass spectral data.

*3,7-Di(4-isopropylphenyl)benzodiisoxazole-4,8-dione (**8a**):* yellow solid, 230 mg, 54% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.94−7.78 (m, 4H), 7.49−7.36 (m, 4H), 2.97 (dd, J = 15.3 Hz, 7.2 Hz, 2H), 1.23 (dt, J = 11.5 Hz, 5.8 Hz, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 178.0, 159.6, 152.0, 151.3, 129.4, 127.2, 126.4, 124.0, 33.4, 23.7; ESI-MS m/z 427.3 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{26}H_{23}N_2O_4$ $[M + H]^+$ 427.1658, found 427.1650; mp 119−120 °C.

*3-(Pyrdin-2-yl)-7-(4-isopropylphenyl)benzodiisoxazole-4,8-diol (**8b**):* yellow solid, 188 mg, 49% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 14.87 (s, 1H), 8.97 (s, 1H), 8.91 (d, J = 4.9 Hz, 1H), 8.54 (d, J = 8.0 Hz, 1H), 8.32−8.28 (m, 1H), 8.04−7.98 (m, 2H), 7.82 (dd, J = 7.0 Hz, 5.6 Hz, 1H), 7.47 (d, J = 8.2 Hz, 2H), 3.06 (dt, J = 13.8 Hz, 6.9 Hz, 1H), 1.35 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, acetone-d_6) δ 158.9, 157.4, 156.2, 155.3, 150.8, 147.7, 146.9, 141.0, 140.2, 129.8, 126.5, 126.3, 126.2, 122.7, 115.6, 107.8, 107.1, 33.9, 23.3; ESI-MS m/z 386.1 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{22}H_{16}N_3O_4$ $[M + H]^+$ 386.1141, found 386.1135; mp 191−192 °C.

*3-(Pyrdin-2-yl)-7-(3-chlorophenyl)benzodiisoxazole-4,8-diol (**8c**):* yellow solid, 208 mg, 55% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.28 (s, 1H), 8.85 (d, J = 4.1 Hz, 1H), 8.40 (d, J = 7.8 Hz, 1H), 8.23 (t, J = 7.6 Hz, 1H), 8.10−7.86 (m, 2H), 7.80−7.53 (m, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 158.1, 157.8, 156.3, 155.6, 148.5, 146.3, 141.2, 140.5, 137.6, 132.2, 131.0, 130.7, 130.1, 129.8, 129.0, 127.5, 123.3, 116.3, 110.9; ESI-MS m/z 380.2 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{19}H_{11}ClN_3O_4$ $[M + H]^+$ 380.0438, found 380.0431; mp 151−153 °C.

*3,7-Di(pyridin-2-yl)benzodiisoxazole-4,8-dione (**8d**):* yellow solid, 166 mg, 48% yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.85 (d, J = 3.8 Hz, 1H), 8.79 (d, J = 4.3 Hz, 1H), 8.35 (d, J = 7.8 Hz, 1H), 8.22−8.02 (m, 3H), 7.74 (dd, J = 6.7, 4.8 Hz, 1H), 7.69−7.58 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.9, 151.1, 146.0, 143.2, 138.7, 128.0, 126.7, 125.7, 123.9; ESI-MS m/z 347.1 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{18}H_{11}N_4O_4$ $[M + H]^+$ 347.0780, found 347.0773; mp 212−213 °C.

Preparation of Indazole-4,7-diols (10a−f). A mixture of resorcinol (1.0 mmol) and $PhI(OAc)_2$ (2.0 mmol) was stirred in acetonitrile (4 mL) and water (2 mL) at until the starting material disappeared. Then K_2CO_3 (2.5 mmol) was added. After the mixture was stirred for 1 h, *N*′-benzylidene-4-methylbenzenesulfonohydrazide (1.5 mmol) was added. Heating continued at 50 °C for 24 h. The mixture was added to brine (30 mL) and extracted with ethyl acetate (3 × 50 mL). The combined extract was washed with brine (2 × 50 mL) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the residue was chromatographed by silica gel (ethyl acetate/hexane 1:6) to obtain the desired products. The structure of products were confirmed by ^{1}H and ^{13}C NMR and mass spectral data.

*5,6-Dimethyl-3-phenyl-1H-indazole-4,7-diol (**10a**):* yellow solid, 185 mg, 73% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.04 (s, 2H), 7.74−7.38 (m, 3H), 2.04 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.8, 146.8, 144.2, 143.0, 135.9, 134.3, 130.3, 129.2, 127.4, 120.3,

dx.doi.org/10.1021/jo401077q | J. Org. Chem. XXXX, XXX, XXX−XXX

111.4, 13.5, 12.9; ESI-MS m/z 255.6 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{15}N_2O_2$ $[M + H]^+$ 255.1134, found 255.1142; mp 168−170 °C.

*5,6-Dimethyl-3-(4-isopropyl)phenyl-1H-indazole-4,7-diol (**10b**):* yellow solid, 195 mg, 73% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.81 (s, 1H), 8.24 (s, 1H), 7.80 (d, J = 8.1 Hz, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.42 (d, J = 8.1 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 7.12 (s, 1H), 2.86 (dt, J = 13.7 Hz, 6.9 Hz, 1H), 2.08 (d, J = 19.2 Hz, 6H), 1.16 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.4, 148.3, 146.5, 142.8, 135.4, 131.5, 129.4, 128.3, 127.0, 119.9, 110.8, 33.3, 23.6, 13.0, 12.5; ESI-MS m/z 297.2 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{18}H_{21}N_2O_2$ $[M + H]^+$ 297.1603, found 297.1595; mp 159−160 °C.

*3-Phenyl-5,6,7,8-tetrahydro-1H-benzo[f]indazole-4,9-diol (**10c**):* yellow solid, 204 mg, 73% yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.89 (d, J = 7.9 Hz, 2H), 7.51 (d, J = 7.8 Hz, 2H), 7.30 (s, 1H), 2.62 (d, J = 16.8 Hz, 4H), 1.74 (s, 4H); ^{13}C NMR (100 MHz, acetone-d_6) δ 148.6, 146.0, 144.1, 129.8, 133.1, 130.1, 129.2, 128.1, 124.5, 109.8, 24.4, 24.0, 22.2, 21.9, 21.7; ESI-MS m/z 281.1 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_2$ $[M + H]^+$ 281.1290, found 281.1286; mp 124−126 °C.

*3-(3-Chlorophenyl)-5,6,7,8-tetrahydro-1H-benzo[f]indazole-4,9-diol (**10d**):* yellow solid, 207 mg, 66% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.53 (s, 1H), 7.56 (d, J = 8.3 Hz, 1H), 7.14 (d, J = 8.1 Hz, 2H), 6.72 (s, 1H), 2.33 (d, J = 5.2 Hz, 4H), 1.53−1.36 (m, 4H); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.0, 147.4, 145.5, 140.4, 135.1, 132.0, 130.9, 130.0, 129.6, 129.2, 127.7, 120.8, 109.7, 24.7, 24.0, 22.5, 22.4; ESI-MS m/z 315.3 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{17}H_{16}ClN_2O_2$ $[M + H]^+$ 315.0895, found 315.0895; mp 131−132 °C.

*3-(4-Isopropylphenyl)-5,6,7,8-tetrahydro-1H-benzo[f]indazole-4,9-diol (**10e**):* yellow solid, 167 mg, 52% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.82 (s, 1H), 8.24 (s, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 8.2 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 5.91 (s, 1H), 2.88 (dt, J = 13.7 Hz, 6.9 Hz, 1H), 2.64−2.44 (m, 4H), 1.69 (s, 4H), 1.16 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.3, 148.0, 146.2, 143.7, 142.7, 135.5, 131.6, 129.5, 127.4, 119.0, 109.9, 33.3, 24.5, 24.1, 21.9, 21.7, 21.1; ESI-MS m/z 323.3 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{20}H_{23}N_2O_2$ $[M + H]^+$ 323.1760, found 323.1752; mp 105−106 °C.

*5,6-Dimethyl-3-(3-chlorophenyl)-1H-indazole-4,7-diol (**10f**):* yellow solid, 132 mg, 46% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.85 (d, J = 0.9 Hz, 1H), 8.24 (d, J = 1.0 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.68−7.51 (m, 1H), 7.41 (dd, J = 18.9 Hz, 6.4 Hz, 2H), 6.02 (s, 1H), 2.14 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.1, 146.9, 144.6, 141.5, 137.0, 136.5, 134.2, 131.3, 129.0, 126.1, 120.3, 112.6, 111.7, 13.7, 13.2; ESI-MS m/z 289.6 $[M + H]^+$; HRMS (ESI-TOF) calcd for $C_{15}H_{14}ClN_2O_2$ $[M + H]^+$ 289.0744, found 289.0739; mp 130−132 °C.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: gangliu27@tsinghua.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge financial support from the National Natural Science Foundation of China (Grant Nos. 91213303 and 81273364). We thank Yi Dong, Xiao Hu, and Qifei Zhong for their great assistance in the resynthesis of some compounds and for confirming all data for compound characterization.

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