Synthesis V. A. Bodunov et al. Paper

Synthesis of Substituted Indole-3-carboxylates by Iron(II)-Catalyzed Domino Isomerization of 3-Alkyl/aryl-4-aryl-5-methoxyisoxazoles

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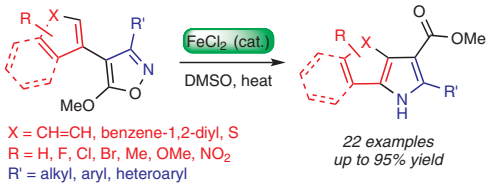

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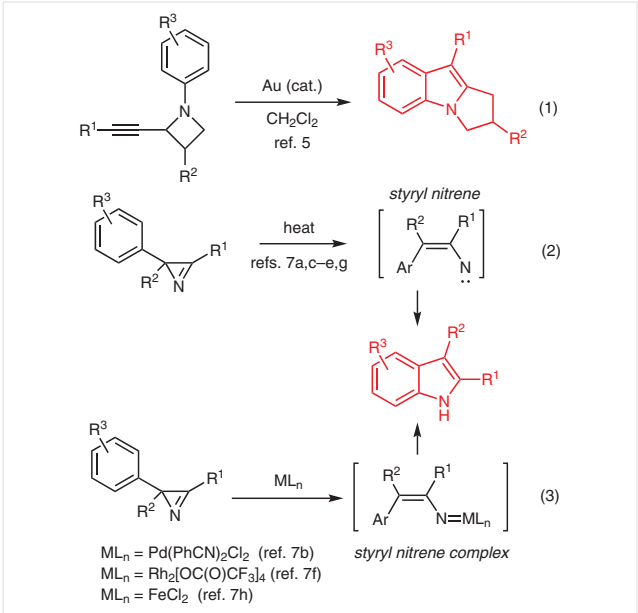
Abstract The iron(II)-catalyzed domino isomerization of 3-alkyl/aryl-4-arylisoxazoles provides a selective access to a wide range of structurally diverse highly substituted indole-3-carboxylates. The operational simplicity, high atom efficiency, and the use of stable starting materials and an inexpensive and low-toxicity catalyst are some of the attractive features of this tandem double ring-opening–ring-closure strategy.

Key words indoles, isoxazoles, isomerization, domino reactions, iron(II) chloride catalysis

The indole moiety is widely present in natural compounds, important marketed medicines, agrochemicals, and progressive materials.[1,2] Accordingly, the development of atom-economical, practical, and safe synthesis of compounds containing an indole ring is of immense interest to synthetic chemists. While numerous methods for the preparation of indoles have been developed,[1,3] there still remains a great need to find new methodologies for the selective preparation of functionalized indoles, substituted in specific positions, from inexpensive and easily available starting materials. The use of ring-to-ring intramolecular isomerization for the preparation of indole derivatives is quite rare,[1] although these processes are 100% atom-economical reactions.[4]

Two types of isomerizations involving ring opening followed by recyclization are known: the gold-catalyzed rearrangement of 2-alkynyl-*N*-arylazetidines to pyrrolo[1,2-*a*]indoles[5] and the rearrangement of 2-aryl-2*H*-azirines to indoles (Scheme 1).[6,7] Since the first report on the thermal rearrangement of 2-phenyl-2*H*-azirine and 3-methyl-2-phenyl-2*H*-azirine to the corresponding indoles,[7a] this reaction has been extended to a series of substituted 2-aryl-2*H*-azirines, making this approach useful for the preparation of some indoles having substituted benzene rings.[7c,d,g] The transformation could also be performed at lower temperatures under $Pd(PhCN)_2Cl_2$,[7b] $Rh_2[OC(O)CF_3]_4$,[7f] and $FeCl_2$[7h] catalysis. Some derivatives of indole-3-carboxylic acid were obtained by both thermal and catalytic isomerization of the corresponding 2*H*-azirines via the 1,5-cyclization of an intermediate styryl nitrene [Scheme 1, eq. 2, R^2 = CN, CO_2Et][7g] or a styryl nitrene complex [Scheme 1, eq. 3, R^2 = morpholinocarbonyl].[7f,h]

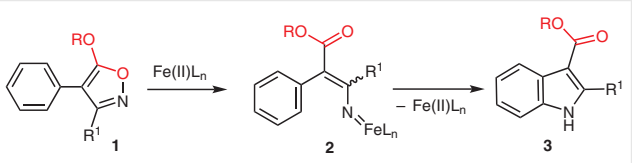


Scheme 1 Different routes for the synthesis of indole derivatives by isomerization

Nitriles of indole-3-carboxylic acids were prepared in high yields by heating 2-aryl-2*H*-azirine-2-carbonitriles at 140 °C in xylene, albeit ethyl 3-benzyl-2-phenyl-2*H*-azirine-2-carboxylate afforded ethyl 2-benzylindole-3-carboxylate in only 42% yield under the same conditions.[7g] The

morpholide of 2-methylindole-3-carboxylic acid was obtained by a $FeCl_2$-catalyzed isomerization of the corresponding azirine in 46% yield[7h] and by $Rh_2[OC(O)CF_3]_4$-catalyzed isomerization in 91% yield.[7f] The above-mentioned isomerization of azirines to indoles depends strongly on the nature of the substituents in the substrates and is applicable mostly to reactive 3-alkyl-substituted 2*H*-azirines. This, along with the limited availability and low stability of some functionalized azirines, necessitates the search for new precursors and catalysts for the generation of styryl nitrenes and their metal complexes.

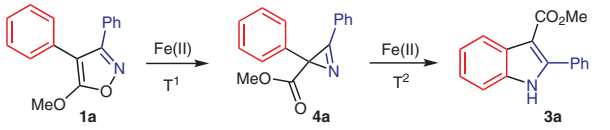
In a search for more effective approaches to indole-3-carboxylates based on nitrenoid-mediated reactions, we turned our attention to 5-alkoxy-4-arylisoxazoles, which can be considered, when using an isoxazole–azirine isomerization,[8a] as synthetic equivalents of difficult-to-access 2-aryl-2*H*-azirine-2-carboxylates. It was previously found that this isomerization is catalyzed by iron(II) compounds,[6,8] which, in turn, can promote isomerization of azirine to indole. Taking into account these prerequisites and especially the relatively low toxicity of many iron species, which is of importance for applications in industry related to healthcare and medicine,[9] we decided to search for conditions for the implementation of a direct domino transformation of isoxazoles into indole-3-carboxylates within the green chemistry framework. We expected that the generation of a nitrene complex **2** from isoxazole, rather than azirine, can prevent some of the secondary processes characteristic for non-complexed azirine-2-carboxylates. This should improve the efficacy of the cyclization of styryl nitrene complexes, leading to indoles and allow the use of higher temperatures, which are necessary for the preparation of 2-arylindole-3-carboxylates, inaccessible until now from the corresponding azirines[6,7] (Scheme 2).



Scheme 2 Route for the synthesis of indole derivatives by isomerization of isoxazoles

In order to find the optimal reaction conditions, we studied the model transformation of 5-methoxy-3,4-diphenylisoxazole (**1a**) and azirine **4a** into methyl 2-phenylindole-3-carboxylate (**3a**) without any catalyst and with typical iron(II) catalysts, $FeCl_2$ and $Fe(NTf_2)_2$,[8] in different solvents and at various temperatures (Table 1). To start, azirine **4a**, prepared by $FeCl_2{\cdot}4H_2O$-catalyzed isomerization of isoxazole **1a**, was heated in xylene. However, even heating at 180 °C for 15 hours without catalyst led to the formation of only traces of **3a** according to NMR analysis, although in other work[7g] heating 2-aryl-2*H*-azirine-2-carbonitriles gave the corresponding 1*H*-indole-3-carbonitriles already at 140 °C. Heating isoxazole **1a** in 1,4-dioxane without catalyst at 170 °C for 20 hours afforded only azirine **4a**. Further experiments, therefore, were performed in the presence iron(II) catalysts.

Table 1 Optimization of Reaction Conditions[a]



Entry	Catalyst	Solvent	Conditions	Yield of **3a** (%)
1	$FeCl_2$	THF	25 °C, 15 h; 70 °C, 30 h	traces
2	$Fe(NTf_2)_2$	THF	25 °C, 15 h; 70 °C, 30 h	traces
3	$Fe(NTf_2)_2$	*o*-$Cl_2C_6H_4$	110 °C, 7 h; 140 °C, 11 h	28
4	$Fe(NTf_2)_2$	*o*-$Cl_2C_6H_4$	200 °C, 0.5 h	40[b]
5	$FeCl_2$	1,4-dioxane	170 °C, 7 h	50
6	$Fe(NTf_2)_2$	1,4-dioxane	170 °C, 7 h	54
7	$Fe(NTf_2)_2$	neat	200 °C, 3 min	13
8	$Fe(NTf_2)_2$	neat	200 °C, 10 min	19
9	$Fe(NTf_2)_2$	neat	200 °C, 1 h	12
10	$FeCl_2$	DMSO	25 °C, 15 h; 165 °C, 5 h	65
11	$FeCl_2$	DMSO	170 °C, 5 h	77[b]

[a] Reaction conditions: **1a** (0.2 mmol), cat. (20 mol%), solvent (2 mL), heat (indicated temperature), time (as shown), screw-capped thick-walled test tube; then reaction mixture cooled down, passed through a short silica pad; reaction progress followed by ^1H NMR spectroscopy (1,1,2,2-tetrabromoethane as internal standard).
[b] Isolated yields.

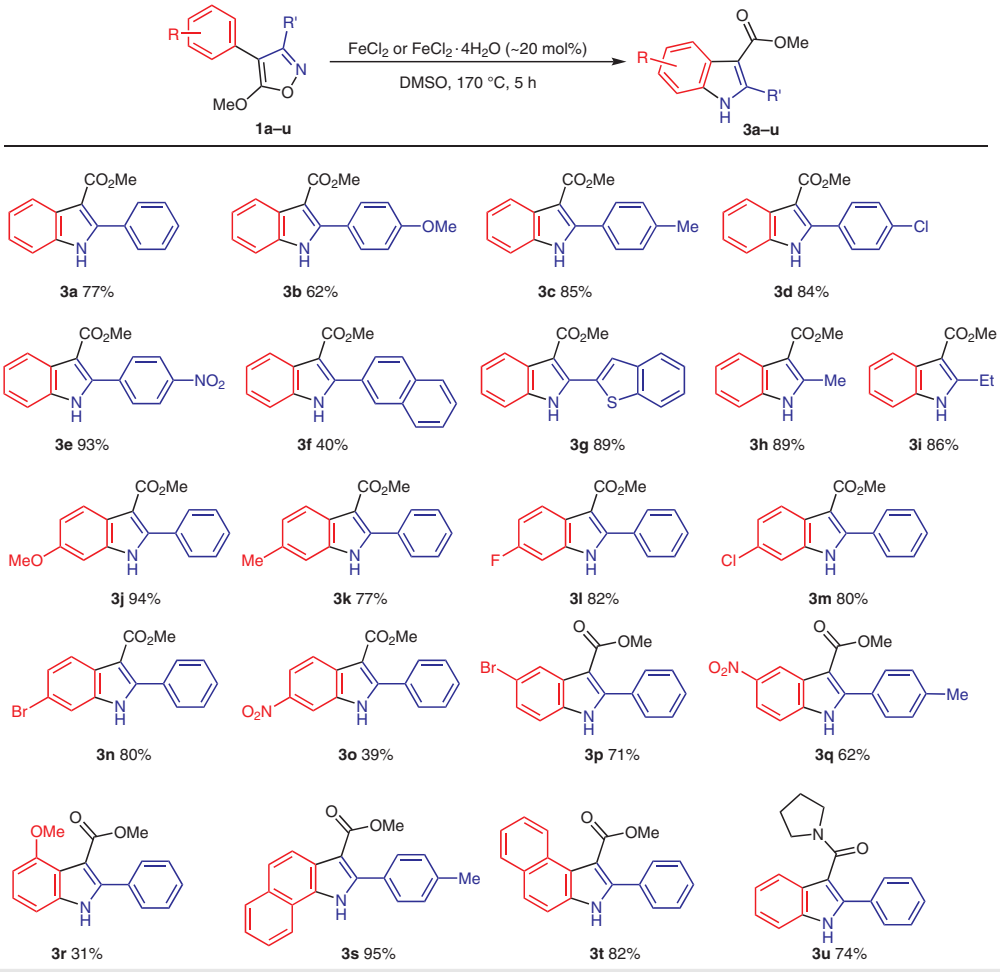
When isoxazole **1a** was stirred at room temperature in the presence of $FeCl_2$ or $Fe(NTf_2)_2$ for the transformation into methyl 2,3-diphenyl-2*H*-azirine-2-carboxylate **4a** and was further heated at 70 °C in THF (the conditions used for the transformation of 3-alkyl-2*H*-azirines into indoles[7h]), only traces of indole **3a** were detected by NMR analysis (Table 1, entries 1 and 2). Increasing the temperature and using *o*-$Cl_2C_6H_4$ or 1,4-dioxane as solvent improved the yield to 54% (entries 3–6). Using solvent-free conditions was unsuccessful, presumably due to decomposition of the product under prolonged heating (entries 7–9). The reaction carried out in DMSO under a dual temperature regime (entry 10) gave **3a** in 65% yield. Finally, the domino reaction of **1a** in the presence of $FeCl_2$ in DMSO at 170 °C for 5 hours gave **3a** in 77% isolated yield (entry 11). Moreover, $FeCl_2{\cdot}4H_2O$ proved to be as effective as anhydrous $FeCl_2$.

The latter conditions were used for the preparation of a series of indoles **3a–u** from isoxazoles **1a–u** (Scheme 3). The structures of the isolated products were confirmed by standard spectroscopic methods. The reactions of 5-methoxy-4-phenylisoxazoles bearing 3-phenyl groups with donor or acceptor substituents afforded the corresponding

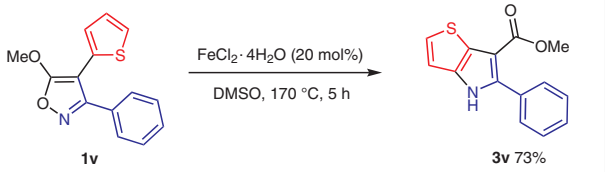
methyl 2-arylindole carboxylates in 62–93% yield. The 3-(2-naphthyl)-substituted isoxazole **1f** gave only 40% yield of indole **3f**, whereas the less bulky 3-(2-benzothienyl)-substituted isoxazole **1g** gave 89% yield of indole **3g**. 3-Alkyl-substituted isoxazoles **1h**,**i** afforded indoles **3h**,**i** in excellent yields. The reaction of 5-methoxy-3-phenylisoxazoles with 4-(*p*-RC_6H_4) groups with R as halogen or MeO substituents afforded the corresponding 6-substituted methyl 2-phenylindole carboxylates **3j**,**l**,**m**,**n** in 80–94% yield, whereas the NO_2 substituent lowered the yield of indole **3o** to 39%.

The reaction of 5-methoxy-3-phenylisoxazoles with 4-(*m*-$NO_2C_6H_4$) and 4-(*m*-BrC_6H_4) substituents led selectively to the corresponding 5-substituted methyl 2-phenylindole carboxylates **3q** and **3p** in 62% and 71% yield, respectively (Scheme 3). 5-Methoxy-4-(2-methoxyphenyl)-3-phenylisoxazole gave 4-substituted methyl 2-phenylindole **3r** in only 31% yield, most likely due to steric congestion in the transition state of the cyclization of the corresponding complex **2**. 5-Methoxy-4-(1/2-naphthyl)-3-(4-tolyl)isoxazoles **1t**,**s** react selectively, affording methyl 2-phenyl-3*H*-benzo[*e*]indole-1-carboxylate **3t** and methyl 2-phenyl-1*H*-benzo[*g*]indole-3-carboxylate **3s** in excellent yields. 5-Aminoisoxazoles are also suitable for the transformation into the corresponding indoles, e.g. isoxazole **1u** gave pyrrolidide of 2-phenylindole-3-carboxylic acid **3u** in 74% yield. All these results demonstrate that the method can be used for the selective synthesis of various 2/4/5/6-substituted indole-3-carboxylates and the benzo[*e*]- and -[*g*]- derivatives.

To verify the applicability of the method for the preparation of hetero analogues of indolecarboxylates, 4-(2-thienyl)-substituted isoxazole **1v** was treated with $FeCl_2$ under the standard reaction conditions to give methyl 5-phenyl-4*H*-thieno[3,2-*b*]pyrrole-6-carboxylate (**3v**) in good yield (Scheme 4).

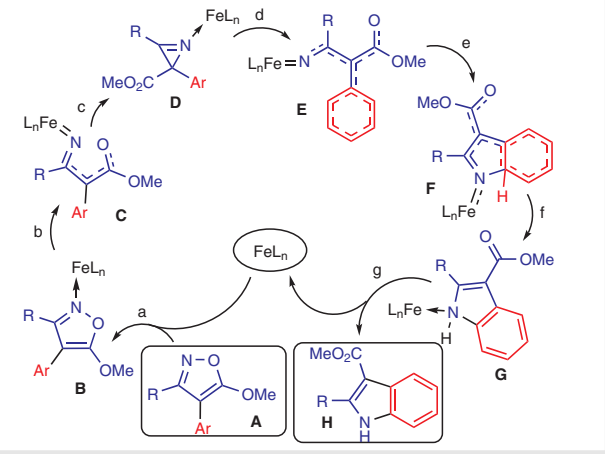


Scheme 3 Reaction scope



Scheme 4 Synthesis of hetero analogue **3v**

On the basis of the obtained results and previous calculations,[8c,d,10] we propose the plausible reaction pathway for the iron(II)-catalyzed domino isomerization of isoxazoles to indoles as shown in Scheme 5. The mechanism includes the following steps: (a) the formation of the isoxazole–Fe complex **B**, (b) opening of the isoxazole ring of the Fe–isoxazole complex **B** via an N–O bond cleavage to form the Fe–nitrene complex **C** having an inappropriate configuration for 1,5-cyclization on the benzene ring, (c) the recyclization of Fe–nitrene complex **C** into the Fe–azirine complex **D**, which, according to calculated data,[8c,d] should occur via a low activation barrier, (d) low-energy conformational transformations in **D** followed by opening of the three-membered ring leading to the Fe–nitrene complex **E** with a configuration providing the possibility of 1,5-cyclization, (e) 1,5-cyclization giving the Fe complex of 7a*H*-indole **F**, and (f) and (g) solvent-assisted[10] H-shift and cleavage of the catalyst to give the final product, indole **H**.



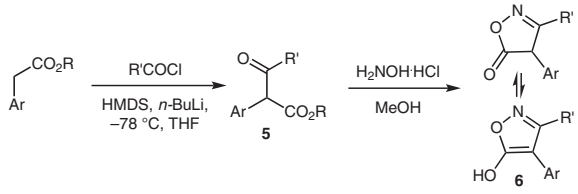
Scheme 5 Plausible reaction mechanism

In summary, a selective, simple, and effective synthesis of highly substituted 2-alkyl/aryl-indole-3-carboxylates based on the isoxazole–azirine-indole domino isomerization under $FeCl_2$ catalysis has been described. This double ring-opening–ring-closure strategy nicely complements existing methods based on the rearrangement of azirines to indoles. The reported method is endowed with several important features, including operational simplicity, high atom-efficiency, and the use of stable starting materials, a green solvent, and an inexpensive and low-toxicity catalyst. The methodology is applicable to the preparation of benzo-fused and hetero analogues of indole-3-carboxylates.

Melting points were determined on a Stuart SMP30 capillary melting point apparatus. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra of $CDCl_3$ or DMSO-d_6 solutions were recorded with a Bruker AVANCE III 400 spectrometer. Chemical shifts (δ) are reported in ppm downfield from TMS (δ = 0.00). ^1H NMR spectra were calibrated according to the residual peak of $CHCl_3$ (δ = 7.26) or DMSO-d_6 (δ = 2.50). $^{13}C\{^1H\}$ and ^{13}C DEPT135 were calibrated according to the peak of $CDCl_3$ (δ = 77.00) or DMSO-d_6 (δ = 39.51). Mass spectra were recorded on a Bruker maXis HRMS-ESI-QTOF, electrospray ionization, positive mode. Thin-layer chromatography (TLC) was conducted on aluminum sheets with 0.2 mm silica gel (fluorescent indicator, Macherey-Nagel) and Macherey-Nagel Silica 60 M was used for column chromatography. THF was distilled from sodium benzophenone-ketyl under argon atmosphere before use. Dimethyl sulfoxide was distilled from calcium hydride under reduced pressure.

Synthesis of Starting Materials

3-Substituted 4-Aryl-5-hydroxyisoxazoles/4-Arylisoxazol-5(4*H*)-ones 6; General Procedure A (Scheme 6)



Scheme 6 Synthesis of 3-substituted 4-aryl-5-hydroxyisoxazoles/4-arylisoxazol-5(4*H*)-ones **6**

A solution of 2.5 M *n*-BuLi in hexane (1.2 equiv) was added dropwise to a solution of HMDS (1.2 equiv) in anhyd THF at –78 °C under argon, and then, after stirring of the mixture for 10 min, a solution of alkyl 2-arylacetate (1 equiv) in THF was added in one portion. The mixture was stirred for 10 min, after which a solution of acyl chloride (1.15 equiv) in THF was added in one portion and the mixture was stirred for 15 min at –78 °C and then overnight at r.t. The reaction mixture was quenched with sat. aq NH_4Cl, extracted with EtOAc or Et_2O, and the organic layer was washed with brine and dried over Na_2SO_4. The solvents were evaporated to give 3-substituted alkyl 2-aryl-3-oxopropanoate **5**, which was used without further purification.

$NH_2OH·HCl$ (2–5 equiv) was added to a solution of **5** in MeOH and the mixture was refluxed for 24 h. The solvent was evaporated, the residue was treated with H_2O, and the precipitate that formed was filtered, washed with H_2O and a mixture of PE/EtOAc (10:1), and then dried in air to give pure 3-substituted 4-aryl-5-hydroxyisoxazole/4-arylisoxazol-5(4*H*)-one **6**. The yields of **6** were calculated for the two steps, and is based on the starting alkyl 2-arylacetate.

3,4-Diphenylisoxazol-5-ol/3,4-Diphenylisoxazol-5(4*H*)-one (6a)

Methyl Propanoate 5a

Pale yellow oil, yield 1.88 g, was prepared from HMDS (1.29 g, 8.0 mmol) in THF (5 mL), *n*-BuLi (3.2 mL, 8.0 mmol), methyl 2-phenylacetate (1.00 g, 6.7 mmol) in THF (5 mL), and benzoyl chloride (1.08 g, 7.7 mmol) in THF (5 mL).

Isoxazol-5-ol 6a

Isoxazol-5-ol **6a** was prepared from compound **5a** (1.88 g) and $NH_2OH{\cdot}HCl$ (2.32 g, 33.5 mmol) in MeOH (40 mL).

Yield: 1.21 g (76%); colorless solid; mp 147–148 °C (MeOH) [Lit.[11] 157 °C ($CHCl_3$)].

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.21–7.25 (m, 1 H), 7.28–7.33 (m, 4 H), 7.44–7.50 (m, 4 H), 7.52–7.56 (m, 1 H), 12.83 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 126.7 (CH), 127.5 (C), 127.9 (CH), 128.2 (CH), 128.3 (CH), 129.0 (CH), 129.8 (C), 131.0 (CH), 160.4 (C), 170.3 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{15}H_{11}NNaO_2^+$: 292.0744; found: 292.0744.

3-(4-Methoxyphenyl)-4-phenylisoxazol-5-ol/3-(4-Methoxyphenyl)-4-phenylisoxazol-5(4H)-one (6b)

Methyl Propanoate 5b

Red semi-solid, yield 1.98 g, was prepared from HMDS (1.29 g, 8.0 mmol) in THF (5 mL), *n*-BuLi (3.2 mL, 8 mmol), methyl 2-phenylacetate (1.00 g, 6.7 mmol) in THF (5 mL), and 4-methoxybenzoyl chloride (1.31 g, 7.7 mmol) in THF (5 mL).

Isoxazol-5-ol 6b

Isoxazol-5-ol **6b** was prepared from compound **5b** (1.98 g) and $NH_2OH{\cdot}HCl$ (2.32 g, 33.5 mmol) in MeOH (13 mL).

Yield: 1.44 g (81%); yellowish solid; mp 147–148 °C (MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.80 (s, 3 H), 7.03 (d, *J* = 8.8 Hz, 2 H), 7.22 – 7.28 (m, 1 H), 7.29 – 7.36 (m, 4 H), 7.39 (d, *J* = 8.8 Hz, 2 H), 12.68 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 55.4 (CH_3), 114.5 (CH), 119.3 (C), 126.7 (CH), 128.3 (CH), 128.3 (CH), 129.4 (CH), 130.1 (C), 160.2 (C), 161.3 (C), 170.5 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{13}NNaO_3^+$: 290.0788; found: 290.0792.

4-Phenyl-3-*p*-tolylisoxazol-5-ol/4-Phenyl-3-*p*-tolylisoxazol-5(4*H*)-one (6c)

Methyl Propanoate 5c

Colorless solid, yield 1.96 g, was prepared from HMDS (1.29 g, 8.0 mmol) in THF (8 mL), *n*-BuLi (3.2 mL, 8.0 mmol), methyl 2-phenylacetate (1.00 g, 6.7 mmol) in THF (10 mL) and 4-methylbenzoyl chloride (1.18 g, 7.7 mmol) in THF (8 mL).

Isoxazol-5-ol 6c

Compound **6c** was prepared from compound **5c** (1.96 g) and $NH_2OH{\cdot}HCl$ (1.35 g, 19.4 mmol) in MeOH (13 mL).

Yield: 1.43 g (86%); colorless solid; mp 162–163 °C (MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.35 (s, 3 H), 7.20–7.39 (m, 9 H), 12.67 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.0 (CH_3), 124.7 (C), 126.5 (CH), 127.8 (CH), 128.1 (CH), 128.3 (CH), 129.6 (CH), 130.2 (C), 140.9 (C), 160.4 (C), 170.6 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{13}NNaO_2^+$: 274.0838; found: 274.0842.

3-(4-Chlorophenyl)-4-phenylisoxazol-5-ol/3-(4-Chlorophenyl)-4-phenylisoxazol-5(4*H*)-one (6d)

Methyl Propanoate 5d

Pale green oil, yield 2.05 g, was prepared from HMDS (1.30 g, 8 mmol) in THF (5 mL), *n*-BuLi (3.2 mL, 8 mmol), methyl 2-phenylacetate (1.00 g, 6.7 mmol) in THF (5 mL), and 4-chlorobenzoyl chloride (1.35 mg, 7.7 mmol) in THF (5 mL).

Isoxazol-5-ol 6d

Compound **6d** was prepared from compound **5d** (2.05 g) and $NH_2OH{\cdot}HCl$ (2.09 g, 30 mmol) in MeOH (13 mL).

Yield: 1.41 g (78%); colorless solid; mp 141–142 °C (MeOH) [Lit.[11] 154 °C ($CHCl_3$)].

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.20–7.39 (m, 5 H), 7.46 (d, *J* = 8.4 Hz, 2 H), 7.56 (d, *J* = 8.4 Hz, 2 H), 12.66 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 126.6 (C), 126.8 (CH), 128.3 (CH), 128.4 (CH), 129.2 (CH), 129.6 (C), 129.8 (CH), 135.7 (C), 159.4 (C), 170.3 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{15}H_{10}{}^{35}ClNNaO_2^+$: 294.0292; found: 294.0295.

3-(4-Nitrophenyl)-4-phenylisoxazol-5-ol/3-(4-Nitrophenyl)-4-phenyl-5(4*H*)-one (6e)

Methyl Propanoate 5e

Yellowish solid, yield 2.00 g, was prepared from HMDS (1.16 g, 7.2 mmol) in THF (9 mL), *n*-BuLi (2.9 mL, 7.2 mmol), methyl 2-phenylacetate (901 mg, 6.0 mmol) in THF (11 mL), and 4-nitrobenzoyl chloride (1.28 g, 6.9 mmol) in THF (10 mL).

Isoxazol-5-ol 6e

Compound **6e** was prepared from compound **5e** (2.00 g) and $NH_2OH{\cdot}HCl$ (1.05 g, 15.2 mmol) in MeOH (12 mL).

Yield: 1.35 g (82%); colorless solid; mp 154–155 °C (MeOH) [Lit.[11] 159 °C ($CHCl_3$)].

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.24–7.28 (m, 3 H), 7.31–7.35 (m, 2 H), 7.69–7.72 (m, 2 H), 8.31 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 95.8 (C), 124.1 (CH), 126.9 (CH), 128.4 (CH), 128.5 (CH), 129.3 (C), 129.5 (CH), 134.5 (C), 148.5 (C), 159.0 (C), 170.3 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{15}H_{10}N_2NaO_4^+$: 305.0533; found: 305.0529.

3-(2-Naphthyl)-4-phenylisoxazol-5-ol/3-(2-Naphthyl)-4-phenylisoxazol-5(4*H*)-one (6f)

Methyl Propanoate 5f

Colorless solid, yield 1.80 g, was prepared from HMDS (1.07 g, 6.6 mmol) in THF (8 mL), *n*-BuLi (2.6 mL, 6.6 mmol), methyl phenylacetate (826 mg, 5.5 mmol) in THF (9 mL), and 2-naphthoyl chloride (1.21 g, 6.3 mmol) in THF (13 mL).

Isoxazol-5-ol 6f

Compound **6f** was prepared from compound **5f** (1.80 g) and $NH_2OH{\cdot}HCl$ (1.81 g, 26.0 mmol) in EtOH (20 mL) for 2 d. After evaporation of MeOH and addition of H_2O, the product was extracted with Et_2O, and the organic layer was washed with H_2O and extracted with 5% aq KOH. The aqueous solution was washed with Et_2O and acidified with HCl. The precipitate was collected by filtration, washed with H_2O, and dried in air to give pure product.

Yield: 1.27g (80%); gray solid; mp 159–160 °C (H_2O).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.22–7.34 (m, 5 H), 7.41–7.43 (m, 1 H), 7.58–7.65 (m, 2 H), 7.97–7.99 (m, 3 H), 8.16 (s, 1 H), 13.00 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 96.8 (br s, C), 124.7 (CH), 125.0 (br s, C), 126.7 (CH), 127.1 (CH), 127.76 (CH), 127.82 (CH), 127.9 (CH), 128.1 (CH), 128.3 (CH), 128.5 (CH), 128.6 (CH), 129.9 (C), 132.4 (C), 133.7 (C), 160.5 (C), 170.4 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{19}H_{14}NO_2^+$: 288.1019; found: 288.1006.

3-(Benzo[*b*]thiophen-2-yl)-4-phenylisoxazol-5-ol/3-(Benzo[*b*]thiophen-2-yl)-4-phenylisoxazol-5(4*H*)-one (6g)

Methyl Propanoate 5g

Compound **5g** was prepared from HMDS (1.16 g, 7.2 mmol) in THF (10 mL), *n*-BuLi (2.9 mL, 7.2 mmol), methyl 2-phenylacetate (901 mg, 6.0 mmol) in THF (8 mL), and benzo[*b*]thiophene-2-carbonyl chloride (1.36 g, 6.9 mmol) in THF (10 mL). Compound **5g** was recrystallized from MeOH.

Yield 1.57 g (84%); colorless solid; mp 150–151 °C (MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.70 (s, 3 H), 6.23 (s, 1 H), 7.32–7.55 (m, 7 H), 8.02–8.06 (m, 2 H), 8.57 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 52.6 (CH_3), 58.9 (CH), 123.2 (CH), 125.5 (CH), 126.6 (CH), 128.0 (CH), 128.3 (CH), 128.6 (CH), 129.5 (CH), 132.6 (CH), 133.2 (C), 138.8 (C), 141.6 (C), 142.0 (C), 168.8 (C), 188.4 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{18}H_{14}NaO_3S^+$: 333.0556; found: 333.0561.

Isoxazol-5-ol 6g

Compound **6g** was prepared from compound **5g** (1.35 g, 4.4 mmol) and $NH_2OH{\cdot}HCl$ (1.41 g, 20.3 mmol) in EtOH (26 mL) under reflux for 3 d.

Yield: 986 mg (77%, 65% over two steps); yellowish solid; mp 138–139 °C (EtOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.34–7.46 (m, 7 H), 7.66 (s, 1 H), 7.89–7.91 (m, 1 H), 8.00–8.02 (m, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 122.6 (CH), 124.7 (CH), 125.1 (CH), 125.9 (CH), 126.2 (CH), 127.6 (CH), 128.5 (CH), 129.1 (C), 129.4 (CH), 138.5 (C), 139.7 (C), 155.5 (C), 170.5 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{17}H_{12}NO_2S^+$: 294.0583; found: 294.0594.

3-Methyl-4-phenylisoxazol-5-ol/3-Methyl-4-phenylisoxazol-5(4*H*)-one (6h)

Methyl Propanoate 5h

Colorless oil, yield 1.50 g, was prepared from HMDS (1.29 g, 8.0 mmol) in THF (5 mL), *n*-BuLi (3.2 mL, 8 mmol), methyl 2-phenylacetate (1.00 g, 6.7 mmol) in THF (5 mL), and acetyl chloride (604 mg, 7.7 mmol) in THF (5 mL).

Isoxazol-5-ol 6h

Compound **6h** was prepared from compound **5h** (1.50 g) and $NH_2OH{\cdot}HCl$ (2.32 g, 33.5 mmol) in MeOH (15 mL). After evaporation of MeOH and addition of H_2O, the product was extracted with Et_2O, and the organic layer was washed with H_2O and extracted with 5% aq KOH. The aqueous solution was washed with Et_2O and acidified with HCl. The precipitate was filtered, washed with H_2O, and dried in air to give pure product.

Yield: 552 mg (47%); yellowish solid; mp 106–107 °C (H_2O).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.31 (s, 3 H), 7.21–7.25 (m, 1 H), 7.36–7.40 (m, 2 H), 7.53–7.56 (m, 2 H), 11.78 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 12.0 (CH_3), 95.4 (C), 125.9 (CH), 126.8 (CH), 128.3 (CH), 130.8 (C), 159.4 (C), 170.1 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{10}H_9NO_2^+$: 176.0706; found: 176.0714.

3-Ethyl-4-phenylisoxazol-5-ol/3-Ethyl-4-phenylisoxazol-5(4*H*)-one (6i)

Methyl Propanoate 5i

Red oil, yield 1.57 g, was prepared from HMDS (1.29 g, 8.0 mmol) in THF (5 mL), *n*-BuLi (3.2 mL, 8 mmol), methyl 2-phenylacetate (1.00 g, 6.7 mmol) in THF (5 mL), and propionic anhydride (1.00 g, 7.7 mmol) in THF (5 mL).

Isoxazol-5-ol 6i

Compound **6i** was prepared from compound **5i** (1.57 g) and $NH_2OH{\cdot}HCl$ (2.32 g, 33.5 mmol) in MeOH (15 mL). After evaporation of MeOH and addition of H_2O, the product was extracted with Et_2O, and the organic layer was washed with H_2O and extracted with 5% aq KOH. The aqueous solution was washed with Et_2O and acidified with HCl. The precipitate was collected by filtration, washed with H_2O, and dried in air to give pure product.

Yield: 728 mg (58%); light rose solid; mp 96–97 °C (H_2O).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.15 (q, *J* = 7.6 Hz, 3 H), 2.73 (t, *J* = 7.6 Hz, 2 H), 7.26–7.27 (m, 1 H), 7.37–7.41 (m, 2 H), 7.48–7.50 (m, 2 H), 12.77 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 11.1 (CH_3), 19.2 (CH_2), 126.2 (CH), 127.3 (CH), 128.4 (CH), 130.5 (C), 163.9 (C), 170.0 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{11}H_{11}NNaO_2^+$: 212.0682; found: 212.0691.

4-(4-Methoxyphenyl)-3-phenylisoxazol-5-ol/4-(4-Methoxyphenyl)-3-phenylisoxazol-5(4*H*)-one (6j)

Methyl Propanoate 5j

Pale yellow oil, yield 880 mg, was prepared from HMDS (549 mg, 3.4 mmol) in THF (5 mL), *n*-BuLi (1.4 mL, 3.4 mmol), methyl 2-(4-methoxyphenyl)acetate (500 mg, 2.8 mmol) in THF (5 mL), and benzoyl chloride (450 mg, 3.2 mmol) in THF (5 mL).

Isoxazol-5-ol 6j

Compound **6j** was prepared from compound **5j** (880 mg) and $NH_2OH{\cdot}HCl$ (970 mg, 14.0 mmol) in MeOH (20 mL).

Yield: 530 mg (71%); light yellow solid; 151–152 °C (MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.74 (s, 3 H), 6.89 (d, *J* = 8.7 Hz, 2 H), 7.21 (d, *J* = 8.7 Hz, 2 H), 12.7 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 55.0 (CH_3), 113.9 (CH), 121.8 (C), 127.7 (C), 127.8 (CH), 129.0 (CH), 129.5 (CH), 130.9 (CH), 158.1 (C), 160.0 (C), 170.6 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{13}NNaO_3^+$: 290.0788; found: 290.0786.

3-Phenyl-4-*p*-tolylisoxazol-5-ol/3-Phenyl-4-*p*-tolylisoxazol-5(4*H*)-one (6k)

Methyl Propanoate 5k

Colorless oily solid, yield 2.72 g, was prepared from HMDS (1.89 g, 11.7 mmol) in THF (10 mL), *n*-BuLi (4.7 mL, 11.7 mmol), methyl 2-(4-methylphenyl)acetate (1.46 g, 9.8 mmol) in THF (12 mL), and benzoyl chloride (1.58 g, 11.2 mmol) in THF (9 mL).

Isoxazol-5-ol 6k

Compound **6k** was prepared from compound **5k** (2.72 g) and $NH_2OH{\cdot}HCl$ (1.51 g, 21.7 mmol) in MeOH (13 mL).

Yield: 1.69 mg (69%); colorless solid; mp 173–174 °C (MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.28 (s, 3 H), 7.12 (d, *J* = 8.1 Hz, 2 H), 7.18 (d, *J* = 8.1 Hz, 2 H), 7.43–7.55 (m, 5 H), 12.78 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 20.7 (CH_3), 126.8 (C), 127.6 (C), 127.9 (CH), 128.1 (CH), 128.9 (CH), 129.0 (CH), 130.9 (CH), 136.0 (C), 160.3 (C), 170.5 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{13}NNaO_2^+$: 274.0838; found: 274.0842.

4-(4-Fluorophenyl)-3-phenylisoxazol-5-ol/4-(4-Fluorophenyl)-3-phenylisoxazol-5(4*H*)-one (6l)

Methyl Propanoate 5l

Colorless oily solid, yield 1.32 g, was prepared from HMDS (872 mg, 5.4 mmol) in THF (5 mL), *n*-BuLi (2.7 mL, 5.4 mmol), methyl 2-(4-fluorophenyl)acetate (750 mg, 4.5 mmol) in THF (5 mL), and benzoyl chloride (730 mg, 5.2 mmol) in THF (3 mL).

Isoxazol-5-ol 6l

Compound **6l** was prepared from compound **5l** (1.32 g) and $NH_2OH{\cdot}HCl$ (1.56 g, 22.5 mmol) in MeOH (35 mL).

Yield: 820 mg (72%); colorless solid; 162–163 °C (MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.13–7.18 (m, 2 H), 7.29–7.33 (m, 2 H), 7.44–7.55 (m, 5 H), 12.89 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 115.3 (d, *J* = 21.5 Hz, CH), 126.2 (d, *J* = 3.2 Hz, C), 127.4 (C), 127.9 (CH), 129.1 (CH), 130.1 (d, *J* = 8.1 Hz, CH), 131.0 (CH), 160.3 (C), 160.9 (d, *J* = 244 Hz, C), 170.3 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{15}H_{10}FNNaO_2^+$: 278.0588; found: 278.0600.

4-(4-Chlorophenyl)-3-phenylisoxazol-5-ol/4-(4-Chlorophenyl)-3-phenylisoxazol-5(4*H*)-one (6m)

Methyl Propanoate 5m

Colorless oily solid, yield 1.19 g, was prepared from HMDS (775 mg, 4.8 mmol) in THF (5 mL), *n*-BuLi (2.4 mL, 4.8 mmol), methyl 2-(4-chlorophenyl)acetate (750 mg, 4.0 mmol) in THF (4 mL), and benzoyl chloride (650 mg, 4.6 mmol) in THF (3 mL).

Isoxazol-5-ol 6m

Compound **6m** was prepared from compound **5m** (1190 mg) and $NH_2OH{\cdot}HCl$ (1390 mg, 20.0 mmol) in MeOH (30 mL).

Yield: 760 mg (70%); colorless solid; mp 157–158 °C (MeOH) [Lit.[11] 159 °C ($CHCl_3$)].

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.29–7.31 (m, 2 H), 7.36–7.38 (m, 2 H), 7.45–7.58 (m, 5 H), 12.80 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 94.9 (C), 127.3 (C), 128.0 (CH), 128.4 (CH), 128.9 (C), 129.2 (CH), 129.6 (CH), 131.1 (CH), 160.4 (C), 170.1 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{15}H_{10}{}^{35}ClNNaO_2^+$: 294.0292; found: 294.0298.

4-(4-Bromophenyl)-3-phenylisoxazol-5-ol/4-(4-Bromophenyl)-3-phenylisoxazol-5(4*H*)-one (6n)

Methyl Propanoate 5n

Light yellow oil, yield 2.45 g, was prepared from HMDS (1.34 g, 8.3 mmol) in THF (10 mL), *n*-BuLi (3.3 mL, 8.3 mmol), methyl 2-(4-bromophenyl)acetate (1.59 g, 6.9 mmol) in THF (14 mL), and benzoyl chloride (1.12 g, 8.0 mmol) in THF (11 mL).

Isoxazol-5-ol 6n

Compound **6n** was prepared from compound **5n** (2.45 g) and $NH_2OH{\cdot}HCl$ (1.66 g, 23.9 mmol) in MeOH (15 mL).

Yield: 1.75 g (80%); colorless solid; mp 157–158 °C (MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.22–7.26 (m, 2 H), 7.45–7.58 (m, 7 H), 12.85 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 94.9 (C), 119.6 (C), 127.3 (C), 128.0 (CH), 129.2 (CH), 129.3 (C), 129.9 (CH), 131.1 (CH), 131.3 (CH), 160.4 (C), 170.0 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{15}H_{10}{}^{79}BrNNaO_2^+$: 337.9787; found: 337.9802.

4-(4-Nitrophenyl)-3-phenylisoxazol-5-ol/4-(4-Nitrophenyl)-3-phenylisoxazol-5(4*H*)-one (6o)

Methyl Propanoate 5o

Red oil, yield 790 mg, was prepared from HMDS (500 mg, 3.1 mmol) in THF (2 mL), *n*-BuLi (1.2 mL, 3.1 mmol), methyl 2-(4-nitrophenyl)acetate (500 mg, 2.6 mmol) in THF (3 mL), and benzoyl chloride (420 mg, 3.0 mmol) in THF (2 mL).

Isoxazol-5-ol 6o

Compound **6o** was prepared from compound **5o** (790 mg) and $NH_2OH·HCl$ (900 mg, 13.0 mmol) in MeOH (20 mL).

Yield: 520 mg (70%); yellow solid; 184–185 °C (MeOH).

^1H NMR (400 MHz, DMSO-d_6): δ = 7.49–7.62 (m, 7 H), 8.12 (d, J = 8.9 Hz, 2 H), 12.17 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 92.5 (C), 123.6 (CH), 127.3 (CH), 127.4, 128.2 (CH), 129.3 (CH), 131.2 (CH), 138.3, 144.7, 160.7, 169.9.

HRMS-ESI: m/z [M + Na]$^+$ calcd for $C_{15}H_{10}N_2NaO_4^+$: 305.0533; found: 305.0544.

4-(3-Bromophenyl)-3-phenylisoxazol-5-ol/4-(3-Bromophenyl)-3-phenylisoxazol-5(4*H*)-one (6p)

Methyl Propanoate 5p

Light yellow solid, yield 2.46 g, was prepared from HMDS (1.37 g, 8.5 mmol) in THF (10 mL), *n*-BuLi (3.4 mL, 8.5 mmol), methyl 2-(3-bromophenyl)acetate (1.51 g, 6.6 mmol) in THF (8 mL), and benzoyl chloride (1.14 g, 8.1 mmol) in THF (8 mL).

Isoxazol-5-ol 6p

Compound **6p** was prepared from compound **5p** (2.46 g) and $NH_2OH·HCl$ (1.51 g, 21.7 mmol) in MeOH (13 mL).

Yield: 1.59 g (71%); yellowish solid; mp 142–143 °C (MeOH).

^1H NMR (400 MHz, DMSO-d_6): δ = 7.22–7.24 (m, 2 H), 7.40–7.41 (m, 1 H), 7.48–7.58 (m, 6 H), 12.07 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 94.1 (C), 121.6 (C), 126.6 (CH), 127.2 (C), 128.0 (CH), 129.1 (CH), 129.1 (CH), 130.1 (CH), 130.3 (CH), 131.2 (CH), 132.6 (C), 160.5 (C), 170.0 (C).

HRMS-ESI: m/z [M + H]$^+$ calcd for $C_{15}H_{11}{}^{79}BrNO_2^+$: 315.9968; found: 315.9983.

4-(3-Nitrophenyl)-3-*p*-tolylisoxazol-5-ol/4-(3-Nitrophenyl)-3-*p*-tolylisoxazol-5(4*H*)-one (6q)

Methyl Propanoate 5q

Brown oil, yield 1.43 g, was prepared from HMDS (780 mg, 4.8 mmol) in THF (6 mL), *n*-BuLi (1.9 mL, 4.8 mmol), methyl 2-(3-nitrophenyl)acetate (786 mg, 4.0 mmol) in THF (11 mL) and 4-methylbenzoyl chloride (716 mg, 4.6 mmol) in THF (8 mL).

Isoxazol-5-ol 6q

Compound **6q** was prepared from compound **5q** (1.43 g) and $NH_2OH·HCl$ (996 mg, 14.3 mmol) in MeOH (11 mL).

Yield: 992 mg (83%); yellowish solid; mp 162–163 °C (MeOH).

^1H NMR (400 MHz, DMSO-d_6): δ = 2.38 (s, 3 H), 7.34 (d, J = 8.1 Hz, 2 H), 7.40 (d, J = 8.1 Hz, 2 H), 7.54–7.67 (m, 2 H), 8.04–8.06 (m, 1 H), 8.25 (m, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.0 (CH_3), 92.0 (C), 120.9 (CH), 121.6 (CH), 124.0 (C), 127.9 (CH), 129.7 (CH), 129.9 (CH), 132.3 (C), 133.6 (CH), 141.4 (C), 147.8 (C), 160.5 (C), 170.0 (C).

HRMS-ESI: m/z [M + H]$^+$ calcd for $C_{16}H_{13}N_2O_4^+$: 297.0870; found: 297.0877.

4-(2-Methoxyphenyl)-3-phenylisoxazol-5-ol/4-(2-Methoxyphenyl)-3-phenyl-5(4*H*)-one (6r)

Methyl Propanoate 5r

Brown oil, yield 550 mg, was prepared from HMDS (322 mg, 2 mmol) in THF (2 mL), *n*-BuLi (0.8 mL, 2 mmol), methyl 2-(2-methoxyphenyl)acetate (300 mg, 1.7 mmol) in THF (3 mL), and benzoyl chloride (270 mg, 1.9 mmol) in THF (2 mL).

Isoxazol-5-ol 6r

Compound **6r** was prepared from compound **5r** (550 mg) and $NH_2OH·HCl$ (590 mg, 8.5 mmol) in MeOH (10 mL).

Yield: 280 mg (63%); creamy solid; mp 141–142 °C (MeOH).

^1H NMR (400 MHz, DMSO-d_6): δ = 3.44 (s, 3 H), 6.96–7.01 (m, 2 H), 7.23–7.25 (m, 1 H), 7.31–7.35 (m, 3 H), 7.38–7.42 (m, 2 H), 7.45–7.48 (m, 1 H), 12.69 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 54.9 (CH_3), 111.5 (CH), 118.6 (C), 120.4 (CH), 126.6 (CH), 128.7 (CH), 129.3 (CH), 130.7 (CH), 131.6 (CH), 157.0 (C), 161.2 (C), 170.6 (C).

HRMS-ESI: m/z [M + Na]$^+$ calcd for $C_{16}H_{13}NNaO_3^+$: 290.0788; found: 290.0798.

4-(2-Naphthyl)-3-*p*-tolylisoxazol-5-ol/4-(2-Naphthyl)-3-*p*-tolylisoxazol-5(4*H*)-one (6s)

Methyl Propanoate 5s

Colorless solid, yield 1.72 g, was prepared from HMDS (947 mg, 5.9 mmol) in THF (8 mL), *n*-BuLi (2.4 mL, 5.9 mmol), methyl 2-(2-naphthyl)acetate (950 mg, 4.8 mmol) in THF (6 mL), and 4-methylbenzoyl chloride (869 mg, 5.6 mmol) in THF (7 mL).

Isoxazol-5-ol 6s

Compound **6s** was prepared from compound **5s** (1.72 g) and $NH_2OH·HCl$ (1.53 g, 22.0 mmol) in MeOH (20 mL).

Yield: 1.10 g (75%); yellowish solid; mp 160–161 °C (MeOH).

^1H NMR (400 MHz, DMSO-d_6): δ = 2.34 (s, 3 H), 7.27–7.31 (m, 3 H), 7.37–7.39 (m, 2 H), 7.47–7.50 (m, 2 H), 7.79–7.87 (m, 3 H), 7.96 (s, 1 H), 12.90 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.0 (CH_3), 95.7 (C), 124.9 (C), 125.7 (CH), 126.2 (CH), 126.44 (CH), 126.50 (CH), 127.46 (CH), 127.52 (CH), 127.58 (CH), 127.8 (CH), 128.0 (C), 129.6 (CH), 131.6 (C), 133.0 (C), 141.0 (C), 160.5 (C), 170.8 (C).

HRMS-ESI: m/z [M + Na]$^+$ calcd for $C_{20}H_{15}NNaO_2^+$: 324.0995; found: 324.1005.

4-(1-Naphthyl)-3-phenylisoxazol-5-ol/4-(1-Naphthyl)-3-phenylisoxazol-5(4*H*)-one (6t)

Methyl Propanoate 5t

Colorless solid, yield 1.52 g, was prepared from HMDS (1.13 g, 7.0 mmol) in THF (6 mL), *n*-BuLi (2.8 mL, 7.0 mmol), methyl 2-(1-naphthyl)acetate (901 mg, 4.6 mmol) in THF (5 mL) and benzoyl chloride (717 mg, 5.1 mmol) in THF (5 mL).

Isoxazol-5-ol 6t

Compound **6t** was prepared from compound **5t** (1.52 g) and $NH_2OH·HCl$ (1.38 g, 19.9 mmol) in MeOH (50 mL).

Yield: 926 mg (69%); yellowish solid; mp 158–159 °C (MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.28–7.32 (m, 4 H), 7.35–7.46 (m, 3 H), 7.50–7.54 (m, 2 H), 7.71–7.73 (m, 1 H), 7.95–7.98 (m, 2 H), 13.07 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 125.1 (CH), 125.7 (CH), 126.0 (CH), 126.3 (CH), 127.2 (CH), 127.4 (C), 128.3 (CH), 128.4 (CH), 128.8 (CH), 129.3 (CH), 130.9 (CH), 131.8 (C), 133.4 (C), 161.4 (C), 170.7 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{19}H_{14}NO_2^+$: 288.1019; found: 288.1026.

3-Phenyl-4-(2-thienyl)isoxazol-5-ol/3-Phenyl-4-(2-thienyl)isoxazol-5(4*H*)-one (6v)

Methyl Propanoate 5v

Yellow oil, yield 1.86 g, was prepared from HMDS (1.28 g, 7.9 mmol) in THF (5 mL), *n*-BuLi (3.2 mL, 7.9 mmol), methyl 2-(2-thienyl)acetate (1.03 g, 6.59 mmol) in THF (10 mL), and benzoyl chloride (1.06 g, 7.6 mmol) in THF (5 mL).

Isoxazol-5-ol 6v

Compound **6v** was prepared from compound **5v** (1.86 g) and $NH_2OH{\cdot}HCl$ (1.28 g, 20.0 mmol) in MeOH (15 mL). After evaporation of MeOH and addition of H_2O, the product was extracted with Et_2O, and the organic layer was washed with H_2O and extracted with 5% aq KOH. The aqueous solution was washed with Et_2O and acidified with HCl. The precipitate was collected by filtration, washed with H_2O and dried in air to give **6v**, which was used freshly prepared and without further purification because of instability.

Yield: 1.16 g (72 %); violet solid; mp 95–96 °C (H_2O).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{13}H_{10}NO_2S^+$: 244.0427; found: 244.0430.

3-Substituted 4-Aryl-5-methoxyisoxazoles 1a–v; General Procedure B

A THF suspension/solution of the appropriate **6** (1 equiv) was cooled to 0 °C and treated portionwise with a solution of diazomethane in Et_2O [prepared from *N*-methyl-*N*-nitrosourea (MNU) (2.5–3.0 equiv) and a 40% solution of KOH (10–20 equiv)]. The reaction mixture was stirred at r.t. for 1 h and quenched by AcOH. The solvents were evaporated in vacuo, and the residue was dissolved in CH_2Cl_2 and purified by column chromatography (silica gel, PE/EtOAc, 10:1 to 5:1).

5-Methoxy-3,4-diphenylisoxazole (1a)

Isoxazole **1a** was prepared from compound **6a** (1.00 g, 4.2 mmol) in THF (5 mL) and MNU (1.08 g, 10.5 mmol) in Et_2O (35 mL).

Yield: 750 mg (71%); colorless solid; mp 81–82 °C (PE/EtOAc) (Lit.[12] 81–83 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.18 (s, 3 H), 7.22–7.41 (m, 8 H), 7.46–7.49 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.0 (CH_3), 93.5 (C), 126.9 (CH), 128.36 (CH), 128.43 (CH), 128.5 (CH), 129.0 (CH), 129.1 (C), 129.6 (CH), 129.6 (C), 163.6 (C), 168.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{13}NNaO_2^+$: 274.0838; found: 274.0835.

5-Methoxy-3-(4-methoxyphenyl)-4-phenylisoxazole (1b)

Isoxazole **1b** was prepared from compound **6b** (418 mg, 1.6 mmol) in THF (11 mL) and MNU (532 mg, 4.1 mmol) in Et_2O (24 mL).

Yield: 370 mg (84%); colorless solid; mp 68–69 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.82 (s, 3 H), 4.16 (s, 3 H), 6.86–6.89 (m, 2 H), 7.23–7.26 (m, 3 H), 7.29–7.33 (m, 2 H), 7.39–7.43 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2 (CH_3), 57.9 (CH_3), 93.3 (C), 113.9 (CH), 121.9 (C), 126.8 (CH), 128.4 (CH), 129.1 (CH), 129.3 (C), 129.8 (CH), 160.6 (C), 163.2 (C), 168.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_3^+$: 304.0944; found: 304.0952.

5-Methoxy-4-phenyl-3-*p*-tolylisoxazole (1c)

Isoxazole **1c** was prepared from compound **6c** (616 mg, 2.5 mmol) in THF (17 mL) and MNU (655 mg, 6.4 mmol) in Et_2O (21 mL).

Yield: 438 mg (67%); colorless solid; mp 59–60 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.37 (s, 3 H), 4.17 (s, 3 H), 7.16 (d, *J* = 8.1 Hz, 2 H), 7.23–7.26 (m, 3 H), 7.29–7.33 (m, 2 H), 7.37 (d, *J* = 8.1 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 58.0 (CH_3), 93.4 (C), 126.7 (C), 126.8 (CH), 128.30 (CH), 128.34 (CH), 129.0 (CH), 129.2 (CH), 129.3 (C), 139.6 (C), 163.6 (C), 168.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_2^+$: 288.0995; found: 288.1001.

3-(4-Chlorophenyl)-5-methoxy-4-phenylisoxazole (1d)

Isoxazole **1d** was prepared from compound **6d** (350 mg, 1.3 mmol) in THF (2 mL) and MNU (340 mg, 3.3 mmol) in Et_2O (14 mL).

Yield: 272 mg (74%); colorless solid; mp 100–101 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.17 (s, 3 H), 7.19–7.23 (m, 2 H), 7.26–7.36 (m, 5 H), 7.40–7.44 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.1 (CH_3), 93.5 (C), 127.1 (CH), 128.1 (C), 128.5 (CH), 128.79 (C), 128.82 (CH), 129.0 (CH), 129.7 (CH), 135.8 (C), 162.5 (C), 169.1 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}ClNNaO_2^+$: 308.0449; found: 308.0451.

5-Methoxy-3-(4-nitrophenyl)-4-phenylisoxazole (1e)

Isoxazole **1e** was prepared from compound **6e** (506 mg, 1.8 mmol) in THF (16 mL) and MNU (481 mg, 4.7 mmol) in Et_2O (25 mL).

Yield: 445 mg (83%); colorless solid; mp 124–125 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.20 (s, 3 H), 7.18–7.21 (m, 2 H), 7.28–7.36 (m, 3 H), 7.66 (d, *J* = 8.8 Hz, 2 H), 8.21 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.3 (CH_3), 93.9 (C), 123.7 (CH), 127.5 (CH), 128.29 (C), 128.7 (CH), 129.1 (CH), 129.3 (CH), 136.09 (C), 148.59 (C), 161.69 (C), 169.59 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}N_2NaO_4^+$: 319.0689; found: 319.0704.

5-Methoxy-3-(2-naphthyl)-4-phenylisoxazole (1f)

Isoxazole **1f** was prepared from compound **6f** (650 mg, 2.3 mmol) in THF (4 mL) and MNU (588 mg, 5.7 mmol) in Et_2O (25 mL).

Yield: 408 mg (60%); colorless solid; mp 75–76 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.21 (s, 3 H), 7.24–7.33 (m, 5 H), 7.47–7.56 (m, 3 H), 7.78–7.87 (m, 3 H), 8.04 (*pseudo*-s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.1 (CH_3), 93.7 (C), 125.6 (CH), 126.3 (CH), 126.88 (CH), 126,92 (CH), 127.0 (C), 127.7 (CH), 128.16 (CH), 128.20 (CH), 128.40 (CH), 128.49 (CH), 129.0 (CH), 129.1 (C), 133.0 (C), 133.7 (C), 163.6 (C), 169.0 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{20}H_{15}NNaO_2^+$: 324.0995; found: 324.1009.

3-(Benzo[*b*]thiophen-2-yl)-5-methoxy-4-phenylisoxazole (1g)

Isoxazole **1g** was prepared from compound **6g** (565 mg, 1.9 mmol) in THF (10 mL) and MNU (515 mg, 5.0 mmol) in Et_2O (25 mL).

Yield: 440 mg (74%); colorless solid; mp 99–100 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.15 (s, 3 H), 7.31–7.42 (m, 8 H), 7.66–7.68 (m, 1 H), 7.82–7.84 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.2 (CH_3), 93.8 (C), 122.3 (CH), 124.2 (CH), 124.5 (CH), 125.2 (CH), 125.4 (CH), 127.8 (CH), 128.5 (C), 128.6 (CH), 130.0 (CH), 130.8 (C), 135.3 (C), 140.0 (C), 158.4 (C), 169.3 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{18}H_{13}NNaO_2S^+$: 330.0559; found: 330.0568.

5-Methoxy-3-methyl-4-phenylisoxazole (1h)

Isoxazole **1h** was prepared from compound **6h** (300 mg, 1.7 mmol) in THF (4 mL) and MNU (440 mg, 4.3 mmol) in Et_2O (15 mL).

Yield: 195 mg (60%); orange solid; mp 31–32 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 4.13 (s, 3 H), 7.24–7.31 (m, 1 H), 7.37–7.42 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.4 (CH_3), 57.8 (CH_3), 93.9 (C), 126.6 (CH), 127.8 (CH), 128.6 (CH), 129.6 (C), 161.3 (C), 168.4 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{11}H_{12}NO_2^+$: 190.0863; found: 190.0862.

3-Ethyl-5-methoxy-4-phenylisoxazole (1i)

Isoxazole **1i** was prepared from compound **6i** (518 mg, 2.7 mmol) in THF (7 mL) and MNU (742 mg, 7.2 mmol) in Et_2O (28 mL).

Yield: 378 mg (68%); rose oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 7.5 Hz, 3 H), 2.75 (q, *J* = 7.5 Hz, 2 H), 4.11 (s, 3 H), 7.25–7.30 (m, 1 H), 7.36–7.41 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.6 (CH_3), 20.2 (CH_2), 57.8 (CH_3), 93.4 (C), 126.7 (CH), 128.1 (CH), 128.6 (CH), 129.6 (C), 166.0 (C), 168.4 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{12}H_{14}NO_2^+$: 204.1019; found: 204.1025.

5-Methoxy-4-(4-methoxyphenyl)-3-phenylisoxazole (1j)

Isoxazole **1j** was prepared from compound **6j** (200 mg, 0.8 mmol) in THF (2 mL) and MNU (206 mg, 2 mmol) in Et_2O (10 mL).

Yield: 150 mg (71%); colorless solid; mp 78–79°C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 3 H), 4.16 (s, 3 H), 6.83–6.87 (m, 2 H), 7.13–7.17 (m, 2 H), 7.33–7.42 (m, 3 H), 7.46–7.49 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2 (CH_3), 58.0 (CH_3), 93.2 (C), 113.9 (CH), 121.3 (C), 128.4 (CH), 128.5 (CH), 129.5 (CH), 129.7 (C), 130.3 (CH), 158.6 (C), 163.5 (C), 168.8 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_3^+$: 304.0944; found: 304.0953.

5-Methoxy-3-phenyl-4-*p*-tolylisoxazole (1k)

Isoxazole **1k** was prepared from compound **6k** (624 mg, 2.5 mmol) in THF (20 mL) and MNU (670 mg, 6.5 mmol) in Et_2O (23 mL).

Yield: 561 mg (85%); colorless solid; mp 80–81 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3 H), 4.16 (s, 3 H), 7.12 (*pseudo*-s, 4 H), 7.33–7.43 (m, 3 H), 7.48–7.50 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 (CH_3), 58.0 (CH_3), 93.5 (C), 126.1 (C), 128.41 (CH), 128.45 (CH), 128.9 (CH), 129.1 (CH), 129.5 (CH), 129.7 (C), 136.7 (C), 163.6 (C), 168.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_2^+$: 288.0995; found: 288.0994.

4-(4-Fluorophenyl)-5-methoxy-3-phenylisoxazole (1l)

Isoxazole **1l** was prepared from compound **6l** (600 mg, 2.4 mmol) in THF (8 mL) and MNU (618 mg, 6 mmol) in Et_2O (24 mL).

Yield: 490 mg (76%); colorless solid; mp 79–80 °C (PE/EtOAc),

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.18 (s, 3H), 6.96–7.03 (m, 2H), 7.16–7.22 (m, 2H), 7.34–7.48 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.0 (CH_3), 92.6 (C), 115.4 (d, *J* = 21.7 Hz, CH), 125.1 (d, *J* = 3.2 Hz, C), 128.4 (CH), 128.6 (CH), 129.4 (C), 129.7 (CH), 130.7 (d, *J* = 8.0 Hz, CH), 161.7 (d, *J* = 246.8 Hz, C), 163.5 (C), 168.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}FNNaO_2^+$: 292.0744; found: 292.0748.

4-(4-Chlorophenyl)-5-methoxy-3-phenylisoxazole (1m)

Isoxazole **1m** was prepared from compound **6m** (500 mg, 1.8 mmol) in THF (4 mL) and MNU (464 mg, 4.5 mmol) in Et_2O (19 mL).

Yield: 380 mg (74%); colorless solid; mp 111–112 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.19 (s, 3 H), 7.14–7.17 (m, 2 H), 7.25–7.28 (m, 2 H), 7.36–7.47 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.0 (CH_3), 92.4 (C), 127.6 (C), 128.4 (CH), 128.59 (CH), 128.60 (CH), 129.3 (C), 129.7 (CH), 130.1 (CH), 132.6 (C), 163.5 (C), 168.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}{}^{35}ClNNaO_2^+$: 308.0449; found: 308.0453.

4-(4-Bromophenyl)-5-methoxy-3-phenylisoxazole (1n)

Isoxazole **1n** was prepared from compound **6n** (545 mg, 1.7 mmol) in THF (9 mL) and MNU (464 mg, 4.5 mmol) in Et_2O (20 mL).

Yield: 413 mg (73%); colorless solid; mp 103–104 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.19 (s, 3 H), 7.08–7.11 (m, 2 H), 7.36–7.47 (m, 7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.1 (CH_3), 92.5 (C), 120.8(C), 128.1 (C), 128.4 (CH), 128.6 (CH), 129.3 (C), 129.8 (CH), 130.4 (CH), 131.6 (CH), 163.4 (C), 168.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}{}^{79}BrNNaO_2^+$: 351.9944; found: 351.9951.

5-Methoxy-4-(4-nitrophenyl)-3-phenylisoxazole (1o)

Isoxazole **1o** was prepared from compound **6o** (120 mg, 0.4 mmol) in THF (6 mL) and MNU (103 mg, 1 mmol) in Et_2O (6 mL).

Yield: 90 mg (70%); yellowish solid; mp 133–134 °C (PE/EtOAc).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.24 (s, 3 H), 7.42 (d, *J* = 8.9 Hz, 2 H), 7.40–7.43 (m, 2 H), 7.46–7.56 (m, 3 H), 8.19 (d, *J* = 8.9 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 58.9 (CH_3), 91.4 (C), 123.7 (CH), 128.2 (CH), 128.6 (C), 128.9 (CH), 129.0 (CH), 130.2 (CH), 136.0 (C), 145.7 (C), 162.9 (C), 169.4 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}N_2NaO_4^+$: 319.0700; found: 319.0697.

4-(3-Bromophenyl)-5-methoxy-3-phenylisoxazole (1p)

Isoxazole **1p** was prepared from compound **6p** (500 mg, 1.6 mmol) in THF (3 mL) and MNU (412 mg, 4 mmol) in Et_2O (17 mL).

Yield: 443 mg (84%); light yellow-green oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.21 (s, 3 H), 7.06–7.16 (M, 2 H), 7.35–7.48 (m, 7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.1 (CH_3), 92.2 (C), 122.4 (C), 127.4 (CH), 128.4 (CH), 128.6 (CH), 129.2 (C), 129.78 (CH), 129.80 (CH), 131.3 (C), 131.5 (CH), 163.5 (C), 169.0 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{16}H_{13}{}^{79}BrNO_2^+$: 330.0124; found: 330.0125.

5-Methoxy-4-(3-nitrophenyl)-3-*p*-tolylisoxazole (1q)

Isoxazole **1q** was prepared from compound **6q** (505 mg, 1.7 mmol) in THF (22 mL) and MNU (464 mg, 4.5 mmol) in Et_2O (25 mL).

Yield: 387 mg (68%); colorless solid; mp 100–101 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 4.25 (s, 3 H), 7.20 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 7.41 (t, *J* = 8.0 Hz, 1 H), 7.47 (dt, *J* = 7.7, 1.2 Hz, 1 H), 8.06 (ddd, *J* = 8.0, 2.0, 1.2 Hz, 1 H), 8.17 (t, *J* = 2.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 58.2 (CH_3), 91.4 (C), 121.4 (CH), 123.2 (CH), 125.9 (C), 128.3 (CH), 129.1 (CH), 129.5 (CH), 131.3 (C), 134.3 (CH), 140.2 (C), 148.4 (C), 163.5 (C), 169.2 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{14}N_2NaO_4^+$: 333.0846; found: 333.0846.

5-Methoxy-4-(2-methoxyphenyl)-3-phenylisoxazole (1r)

Isoxazole **1r** was prepared from compound **6r** (200 mg, 0.8 mmol) in THF (2 mL) and MNU (206 mg, 2 mmol) in Et_2O (10 mL).

Yield: 150 mg (71%); creamy solid; mp 97–98 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.45 (s, 3 H), 4.10 (s, 3 H), 6.85–6.87 (m, 1 H), 6.95–6.99 (m, 1 H), 7.21–7.24 (m, 1 H), 7.26–7.36 (m, 4 H), 7.41–7.43 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.0 (CH_3), 58.0 (CH_3), 90.1 (C), 111.2 (CH), 118.2 (C), 120.6 (CH), 127.2 (CH), 128.2 (CH), 129.1 (CH), 129.3 (CH), 130.7 (C), 131.9 (CH), 157.3 (C), 164.2 (C), 169.1 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_3^+$: 304.0944; found: 304.0945.

5-Methoxy-4-(2-naphthyl)-3-*p*-tolylisoxazole (1s)

Isoxazole **1s** was prepared from compound **6s** (400 mg, 1.3 mmol) in THF (3 mL) and MNU (342 mg, 3.3 mmol) in Et_2O (15 mL).

Yield: 300 mg (72%); light yellow oil; mp 89–90 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 4.20 (s, 3 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.29–7.33 (m, 1 H), 7.41 (d, *J* = 8.0 Hz, 2 H), 7.45–7.49 (m, 2 H), 7.74–7.79 (m, 3 H), 7.80–7.84 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 58.0 (CH_3), 93.4 (C), 125.9 (CH), 126.1 (CH), 126.6 (C), 126.7 (C), 127.1 (CH), 127.6 (CH), 127,82 (CH), 127.84 (CH), 128.3 (CH), 129.2 (CH), 132.2 (C), 133.3 (C), 139.7 (C), 163.6 (C), 169.1 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNaO_2^+$: 338.1151; found: 338.1152.

5-Methoxy-4-(1-naphthyl)-3-phenylisoxazole (1t)

Isoxazole **1t** was prepared from compound **6t** (400 mg, 1.4 mmol) in THF (10 mL) and MNU (402 mg, 3.9 mmol) in Et_2O (18 mL).

Yield: 321 mg (77%); colorless solid; mp 128–129 °C (PE/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.05 (s, 3 H), 7.15–7.19 (m, 2 H), 7.24–7.28 (m, 1 H), 7.36–7.38 (m, 3 H), 7.40–7.51 (m, 3 H), 7.75–7.77 (m, 1 H), 7.87–7.90 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.1 (CH_3), 91.5 (C), 125.4 (CH), 125.5 (CH), 126.0 (CH), 126.4 (CH), 126.6 (C), 127.6 (CH), 128.36 (CH), 128.40 (CH), 128.7 (CH), 129.46 (C), 129.48 (CH), 129.51 (CH), 132.6 (C), 133.8 (C), 164.1 (C), 169.6 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{20}H_{15}NNaO_2^+$: 324.0995; found: 324.1007.

3,4-Diphenyl-5-(pyrrolidin-1-yl)isoxazole (1u)

5-Chloro-3,4-diphenylisoxazole

5-Chloro-3,4-diphenylisoxazole was prepared according to a modified procedure.[11] A mixture of 3,4-diphenylisoxazol-5(4*H*)-one **6a** (880 mg, 3.7 mmol) and phosphorus oxychloride (3.4 mL, 37 mmol) was stirred at 0 °C and Et_3N (0.3 mL, 2.1 mmol) was added dropwise. The solution was stirred at 0 °C for 20 min, slowly heated to r.t., and then was heated under stirring at 80 °C for 4 d. After the mixture had cooled to r.t., it was quenched with ice, and the precipitate that formed was filtered and washed with H_2O. The residue was dissolved in EtOAc, and the solution was dried with Na_2SO_4, filtered, and concentrated to an oil that was crystallized after the addition of pentane.

Yield: 710 mg (74%); colorless solid; mp 85–86 °C (pentane) [Lit.[11] 72 °C (PE)].

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.29 (m, 2 H), 7.32–7.45 (m, 8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 114.6 (C), 127.8 (C), 128.2 (C), 128.3 (CH), 128.5 (CH), 128.6 (CH), 128.7 (CH), 129.5 (CH), 130.0 (CH), 152.2 (C), 162.9 (C).

HRMS-ESI: *m/z* [M + Ag]$^+$ calcd for $C_{15}H_{10}{}^{35}ClNOAg^+$: 361.9496; found: 361.9513.

Isoxazole 1u

A mixture of 5-chloro-3,4-diphenylisoxazole (180 mg, 0.70 mmol), pyrrolidine (600 mg, 8.4 mmol), and K_2CO_3 (146 mg, 1.1 mmol) in THF (4 mL) was refluxed under stirring for 4 h (monitoring by TLC). The solvent was evaporated, H_2O was added to the reaction mixture, and the residue was filtered, washed with H_2O, and dried in air to give pure **1u**.

Yield: 192 mg (94%); colorless solid; mp 157–158 °C (H_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84–1.88 (m, 4 H), 3.28–3.31 (m, 4 H), 7.20–7.31 (m, 8 H), 7.34–7.36 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.3 (CH_2), 48.3 (CH_2), 92.1 (C), 126.9 (CH), 127.8 (CH), 128.1 (CH), 128.4 (CH), 128.8 (CH), 130.2 (C), 131.6 (C), 132.0 (C), 162.9 (C), 165.2 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{19}H_{19}N_2O^+$: 291.1492; found: 291.1504.

5-Methoxy-3-phenyl-4-(2-thienyl)isoxazole (1v)

Isoxazole **1v** was prepared from compound **6v** (500 mg, 2 mmol) in THF (5 mL) and MNU (620 mg, 6 mmol) in Et_2O (20 mL).

Yield: 133 mg (25%); light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.21 (s, 3 H), 6.90 (dd, *J* = 3.6, 1.1 Hz, 1 H), 6.98 (dd, *J* = 5.2, 3.6 Hz, 1 H), 7.23 (dd, *J* = 5.2, 1.1 Hz, 1 H), 7.38–7.46 (m, 3 H), 7.52–7.57 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.2 (CH_3), 88.4 (C), 124.9 (CH), 126.2 (CH), 126.9 (CH), 128.5 (CH), 128.6 (CH), 129.2 (C), 129.8 (CH), 129.9 (C), 163.5 (C), 168.7 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}NO_2S^+$: 258.0583; found: 258.0579.

Methyl 2,3-Diphenyl-2*H*-azirine-2-carboxylate (4a)

$FeCl_2$ (11 mg, 25 mol%) was added to a solution of **1a** (85 mg, 0.34 mmol) in 0.5 mL anhyd DMSO under an argon atmosphere. After stirring for 4 h at r.t., the reaction mixture was poured into H_2O, and extracted with EtOAc; the combined organic layer was washed with brine and dried over Na_2SO_4. The solvent was evaporated and the residue was filtered (silica gel, PE/EtOAc, 5:1).

Yield: 84 mg (99%); colorless solid; mp 67–68 °C (PE/EtOAc) (Lit.[13] 70–71 °C for *R*-isomer).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.75 (s, 3 H), 7.27–7.36 (m, 3 H), 7.47–7.52 (m, 2 H), 7.55–7.61 (m, 2 H), 7.62–7.67 (m, 1 H), 7.91–7.96 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.1 (C), 52.6 (CH_3), 122.0 (C), 127.7 (CH), 128.1 (CH), 128.2 (CH), 129.4 (CH), 130.4 (CH), 133.9 (CH), 136.2 (C), 160.7 (C), 171.6 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{16}H_{13}NNaO_2^+$: 274.0838; found: 274.0849.

Substituted Indole-3-carboxylates 3a–v; General Procedure C

A mixture of the appropriate isoxazole **1** (1 mmol) and $FeCl_2{\cdot}4H_2O$ or $FeCl_2$ (20–30 mol%) in DMSO (2–3 mL) was stirred at 170 °C in a screw-cap thick-wall test tube until the reaction reached completion (TLC monitoring). The reaction mixture was cooled and H_2O was added. The precipitate that formed was filtered, washed with H_2O, and dried to give pure indole **3**. If a precipitate was not formed, the mixture was extracted with EtOAc or Et_2O, the organic layer was washed with brine and dried over Na_2SO_4, the solvent was evaporated, and the residue was purified by column chromatography (silica gel, EtOAc, CH_2Cl_2 or PE/EtOAc).

Methyl 2-Phenyl-1*H*-indole-3-carboxylate (3a)

Indole-3-carboxylate **3a** was prepared from isoxazole **1a** (90 mg, 0.36 mmol) and $FeCl_2$ (11 mg 0.085 mmol, 24 mol%) in DMSO (0.5 mL) for 5 h.

Yield: 69 mg (77%); light orange solid; mp 146–147 °C (EtOAc) (Lit.[14] 137–139 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.82 (s, 3 H), 7.24–7.31 (m, 2 H), 7.33–7.38 (m, 1 H), 7.41–7.46 (m, 3 H), 7.61–7.66 (m, 2 H), 8.20–8.23 (m, 1 H), 8.66 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.8 (CH_3), 104.4 (C), 111.0 (CH), 122.07 (CH), 122.11 (CH), 123.2 (CH), 127.5 (C), 128.1 (CH), 129.2 (CH), 129.5 (CH), 131.9 (C), 135.1 (C), 144.6 (C), 165.8 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{13}NNaO_2^+$: 274.0838; found: 274.0844.

Methyl 2-(4-Methoxyphenyl)-1*H*-indole-3-carboxylate (3b)

Indole-3-carboxylate **3b** was prepared from isoxazole **1b** (98 mg, 0.35 mmol) and $FeCl_2{\cdot}4H_2O$ (15 mg 0.07 mmol, 20 mol%) in DMSO (1.0 mL) for 5 h.

Yield: 68 mg (62%); colorless solid; mp 144–145 °C (CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H), 3.84 (s, 3 H), 6.92 (d, *J* = 8.1 Hz, 2 H), 7.26–7.35 (m, 3 H), 7.57 (d, *J* = 8.1 Hz, 2 H), 8.18–8.20 (m, 1 H), 8.63 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.8 (CH_3), 55.3 (CH_3), 103.8 (C), 110.9 (CH), 113.6 (CH), 121.96 (CH), 122.00 (CH), 123.0 (CH), 124.1 (C), 127.6 (C), 130.8 (CH), 135.0 (C), 144.8 (C), 160.3 (C), 166.0 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_3^+$: 304.0944; found: 304.0949.

Methyl 2-*p*-Tolyl-1*H*-indole-3-carboxylate (3c)

Indole-3-carboxylate **3c** was prepared from isoxazole **1c** (106 mg, 0.29 mmol) and $FeCl_2{\cdot}4H_2O$ (12 mg, 0.06 mmol, 21 mol%) in DMSO (2 mL) for 4 h.

Yield: 90 mg (85%); colorless solid; mp 148–149 °C (PE/EtOAc) (Lit.[14] 148–149 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 3.84 (s, 3 H), 7.21–7.23 (m, 2 H), 7.25–7.30 (m, 2 H), 7.34–7.36 (m, 1 H), 8.19–8.24 (m, 1 H), 8.60 (br s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (CH_3), 50.8 (CH_3), 104.2 (C), 111.0 (CH), 122.0 (CH), 122.1 (CH), 123.1 (CH), 127.6 (C), 128.85 (CH), 128.93 (C), 129.3 (CH), 135.1 (C), 139.3 (C), 145.9 (C), 166.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_2^+$: 288.0995; found: 288.1002.

Methyl 2-(4-Chlorophenyl)-1*H*-indole-3-carboxylate (3d)

Indole-3-carboxylate **3d** was prepared from isoxazole **1d** (110 mg, 0.39 mmol) and $FeCl_2{\cdot}4H_2O$ (15 mg 0.075 mmol, 20 mol%) in DMSO (1.5 mL) for 3.5 h.

Yield: 82 mg (84%); colorless solid; mp 172–173 °C (CH_2Cl_2) (Lit.[14] 166–167 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 7.27–7.31 (m, 2 H), 7.34–7.39 (m, 3 H), 7.54–7.57 (m, 2 H), 8.18–8.21 (m, 1 H), 8.66 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.9 (CH_3), 104.8 (C), 111.1 (CH), 122.2 (CH), 122.3 (CH), 123.5 (CH), 127.4 (C), 128.4 (CH), 130.3 (C), 130.8 (CH), 135.2 (C), 135.3 (C), 143.2 (C), 165.8 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}{}^{35}ClNNaO_2^+$: 308.0449; found: 308.0459.

Methyl 2-(4-Nitrophenyl)-1*H*-indole-3-carboxylate (3e)

Indole-3-carboxylate **3e** was prepared from isoxazole **1e** (137 mg, 0.46 mmol) and $FeCl_2{\cdot}4H_2O$ (19 mg, 0.095 mmol, 20 mol%) in DMSO (2 mL) for 3.5 h.

Yield: 128 mg (93%); bright yellow solid; mp 192–193 °C (CH_2Cl_2).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.76 (s, 3 H), 7.22–7.30 (m, 2 H), 7.51 (d, *J* = 7.6 Hz, 1 H), 7.97–7.99 (m, 2 H), 8.08 (d, *J* = 8.0 Hz, 1 H), 8.35 (d, *J* = 8.9 Hz, 2 H), 12.41 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.7 (CH_3), 104.2 (C), 112.1 (CH), 121.5 (CH), 121.8 (CH), 122.9 (CH), 123.3 (CH), 127.0 (C), 131.2 (CH), 135.9 (C), 138.2 (C), 141.6 (C), 147.4 (C), 164.7 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}N_2NaO_4^+$: 319.0689; found: 319.0705.

Methyl 2-(2-Naphthyl)-1*H*-indole-3-carboxylate (3f)

Indole-3-carboxylate **3f** was prepared from isoxazole **1f** (100 mg, 0.33 mmol) and $FeCl_2{\cdot}4H_2O$ (7 mg, 0.035 mmol, 11 mol%) in DMSO (1 mL) for 7 h.

Yield: 40 mg (40%); orange solid; mp 133–134 °C (EtOAc) (Lit.[14] 140–141 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 7.28–7.33 (m, 2 H), 7.39–7.44 (m, 1 H), 7.50–7.57 (m, 2 H), 7.75–7.79 (m, 1 H), 7.85–7.93 (m, 3 H), 8.09 (*pseudo*-s, 1 H), 8.21–8.27 (m, 1 H), 8.62 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.9 (CH_3), 104.9 (C), 110.9 (CH), 122.18 (CH), 122.20 (CH), 123.3 (CH), 126.5 (CH), 126.9 (CH), 127.3 (CH), 127.65 (CH), 127.66 (C), 127.8 (CH), 128.3 (CH), 128.5 (CH), 129.5 (C), 132.9 (C), 133.5 (C), 135.2 (C), 144.4 (C), 165.7 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{20}H_{15}NNaO_2^+$: 324.0995; found: 324.1007.

Methyl 2-(Benzo[*b*]thiophen-2-yl)-1*H*-indole-3-carboxylate (3g)

Indole-3-carboxylate **3g** was prepared from isoxazole **1g** (121 mg, 0.39 mmol) and $FeCl_2{\cdot}4H_2O$ (16 mg, 0.08 mmol, 20 mol%) in DMSO (1.5 mL) for 3.5 h.

Yield: 86 mg (71%); light yellow solid; mp 174–175 °C (CH_2Cl_2).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.87 (s, 3 H), 7.21–7.30 (m, 2 H), 7.41–7.47 (m, 2 H), 7.51–7.53 (m, 1 H), 7.95–7.99 (m, 1 H), 8.03–8.07 (m, 2 H), 8.12 (s, 1 H), 12.36 (s, 1 H).

^{13}C NMR (DMSO-d, 100 MHz): δ = 50.8 (CH_3), 104.0 (C), 111.9 (CH), 112.5 (C),121.5 (CH), 121.7 (CH), 122.2 (CH), 123.4 (CH), 124.1 (CH), 124.8 (CH), 125.3 (CH), 126.1 (CH), 127.0 (C), 132.5 (C), 135.8 (C), 136.6 (C), 138.8 (C), 140.1 (C), 164.7 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{18}H_{13}NNaO_2S^+$: 330.0559; found: 330.0564.

Methyl 2-Methyl-1*H*-indole-3-carboxylate (3h)

Indole-3-carboxylate **3h** was prepared from isoxazole **1h** (95 mg, 0.50 mmol) and $FeCl_2{\cdot}4H_2O$ (20 mg, 0.10 mmol, 20 mol%) in DMSO (1.0 mL) for 4 h.

Yield: 85 mg (89%); colorless solid; mp 164–165 °C (CH_2Cl_2) (Lit.[15] 154 °C, decomp.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.74 (s, 3 H), 3.94 (s, 3 H), 7.18–7.25 (m, 2 H), 7.29–7.31 (m, 1 H), 8.09–8.11 (m, 1 H), 8.51 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH_3), 50.8 (CH_3), 104.5 (C), 110.5 (CH), 121.2 (CH), 121.7 (CH), 122.4 (CH), 127.1 (C), 134.5 (C), 144.0 (C), 166.6 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{11}H_{11}NNaO_2^+$: 212.0682; found: 212.0684.

Methyl 2-Ethyl-1*H*-indole-3-carboxylate (3i)

Indole-3-carboxylate **3i** was prepared from isoxazole **1i** (146 mg, 0.70 mmol) and $FeCl_2{\cdot}4H_2O$ (28 mg, 0.140 mmol, 20 mol%) in DMSO (0.8 mL) for 4 h.

Yield: 126 mg (86%); rose solid; mp 72–73 °C (CH_2Cl_2) (Lit.[16] 72–73 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (t, *J* = 7.6 Hz, 3 H), 3.20 (q, *J* = 7.6 Hz, 2 H), 3.95 (s, 3 H), 7.18–7.26 (m, 2 H), 7.31–7.34 (m, 1 H), 8.12–8.14 (m, 1 H), 8.63 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.2 (CH_3), 21.3 (CH_2), 50.8 (CH_3), 103.4 (C), 110.7 (CH), 121.4 (CH), 121.7 (CH), 122.3 (CH), 127.2 (C), 134.5 (C), 149.7 (C), 166.4 (C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{12}H_{14}NO_2^+$: 204.1019; found: 204.1024.

Methyl 6-Methoxy-2-phenyl-1*H*-indole-3-carboxylate (3j)

Indole-3-carboxylate **3j** was prepared from isoxazole **1j** (85 mg, 0.3 mmol) and $FeCl_2$ (16 mg, 0.08 mmol, 26 mol%) in DMSO (1.5 mL) for 4 h.

Yield: 80 mg (94%); colorless solid; mp 143–144 °C (EtOAc) [Lit.[17] 147–149 °C (EtOAc)].

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 3 H), 3.86 (s, 3 H), 6.86–6.87 (m, 1 H), 6.93–6.95 (m, 1 H), 7.41–7.48 (m, 3 H), 7.63–7.66 (m, 2 H), 8.07–8.09 (m, 1 H), 8.36 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.4 (CH_3), 55.2 (CH_3), 94.5 (CH), 102.6 (C), 111.4 (CH), 121.2 (C), 122.0 (CH), 127.8 (CH), 128.6 (CH), 129.7 (CH), 131.9 (C), 136.3 (C), 143.4 (C), 156.2 (C), 164.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_3^+$: 304.0944; found: 304.0945.

Methyl 6-Methyl-2-phenyl-1*H*-indole-3-carboxylate (3k)

Indole-3-carboxylate **3k** was prepared from isoxazole **1k** (110 mg, 0.42 mmol) and $FeCl_2{\cdot}4H_2O$ (17 mg, 0.085 mmol, 20 mol%) in DMSO (1.5 mL) for 6.5 h.

Yield: 85 mg (77%); colorless solid; mp 146–147 °C (PE/EtOAc).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.42 (s, 3 H), 3.72 (s, 3 H), 7.01–7.04 (m, 1 H), 7.24 (s, 1 H), 7.44–7.52 (m, 3 H), 7.66–7.69 (m, 2 H), 7.90–7.92 (m, 1 H), 11.96 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.2 (CH_3), 50.4 (CH_3), 102.5 (C), 111.5 (CH), 121.0 (CH), 123.1 (CH), 125.1 (C), 127.8 (CH), 128.7 (CH), 129.8 (CH), 131.8 (C), 131.9 (C), 135.9 (C), 144.0 (C), 164.9 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_2^+$: 288.0995; found: 288.0999.

Methyl 6-Fluoro-2-phenyl-1*H*-indole-3-carboxylate (3l)

Indole-3-carboxylate **3l** was prepared from isoxazole **1l** (85 mg, 0.32 mmol) and $FeCl_2$ (22 mg, 0.11 mmol, 33 mol%) in DMSO (1 mL) for 5 h.

Yield: 65 mg (82%); colorless solid; mp 201–202 °C (EtOAc) [Lit.[17] 202–205 °C (EtOAc)].

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 7.02–7.09 (m, 2 H), 7.46–7.50 (m, 3 H), 7.64–7.66 (m, 2 H), 8.13–8.17 (m, 1 H), 8.42 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.6 (CH_3), 97.8 (d, *J* = 25.7 Hz, CH), 102.7 (C), 109.8 (d, *J* = 24.0 Hz, CH), 122.5 (d, *J* = 9.9 Hz, CH), 123.8 (C), 127.9 (CH), 129.0 (CH), 129.7 (CH), 131.5 (C), 135.5 (d, *J* = 12.7 Hz, C), 145.2 (d, *J* = 2.5 Hz, C), 159.1 (d, *J* = 237.0 Hz, C), 164.6 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}FNNaO_2^+$: 292.0744; found: 292.0744.

Methyl 6-Chloro-2-phenyl-1*H*-indole-3-carboxylate (3m)

Indole-3-carboxylate **3m** was prepared from 4-(4-chlorophenyl)-5-methoxy-3-phenylisoxazole **1m** (85 mg, 0.29 mmol) and $FeCl_2$ (20 mg, 0.10 mmol, 33 mol%) in DMSO (1.5 mL) for 3.5 h.

Yield: 60 mg (70%); colorless solid; mp 229–230 °C (EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 7.24–7.25 (m, 1 H), 7.39–7.40 (m, 1 H), 7.47–7.50 (m, 3 H), 7.65–7.67 (m, 2 H), 8.12–8.14 (m, 1 H), 8.40 (br s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.6 (CH_3), 102.8 (C), 111.4 (CH), 121.7 (C), 122.6 (CH), 125.9 (C), 127.1 (C), 127.9 (CH), 129.1 (CH), 129.8 (CH), 131.3 (C), 135.9 (C), 145.4 (C), 164.5 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}{}^{35}ClNNaO_2^+$: 308.0449; found: 308.0453.

Methyl 6-Bromo-2-phenyl-1*H*-indole-3-carboxylate (3n)

Indole-3-carboxylate **3n** was prepared from isoxazole **1n** (176 mg, 0.53 mmol) and $FeCl_2·4H_2O$ (21 mg, 0.11 mmol, 20 mol%) in DMSO (2.0 mL) for 4 h.

Yield: 141 mg (80%); colorless solid; mp 235–236 °C (CH_2Cl_2).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.73 (s, 3 H), 7.34 (dd, *J* = 8.6, 1.6 Hz, 1 H), 7.47–7.54 (m, 3 H), 7.60 (d, *J* = 1.6 Hz, 1 H), 7.68–7.70 (m, 2 H), 7.98 (d, *J* = 8.6 Hz, 1 H), 12.27 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.6 (CH_3), 102.9, 114.3 (CH), 115.1 (C), 123.0 (CH), 124.3 (CH), 126.2 (C), 127.9 (CH), 129.2 (CH), 129.8 (CH), 131.3 (C), 136.4 (C), 145.3 (C), 164.5 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}{}^{79}BrNNaO_2^+$: 351.9944; found: 351.9950.

Methyl 6-Nitro-2-phenyl-1*H*-indole-3-carboxylate (3o)

Indole-3-carboxylate **3o** was prepared from isoxazole **1o** (85 mg, 0.29 mmol) and $FeCl_2$ (16 mg, 0.080 mmol, 28 mol%) in DMSO (1.0 mL) for 5 h.

Yield: 33 mg (39%); yellow solid; mp 268–269 °C (EtOAc).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.77 (s, 3 H), 7.54–7.56 (m, 3 H), 7.73–7.75 (m, 2 H), 8.08–8.11 (m, 1 H), 8.20–8.22 (m, 1 H), 8.30–8.31 (m, 1 H), 12.84 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 50.9 (CH_3), 103.8 (C), 108.2 (CH), 116.4 (CH), 121.5 (CH), 128.1 (CH), 129.76 (CH), 129.82 (CH), 130.7 (C), 132.1 (C), 134.1 (C), 142.8 (C), 149.6 (C), 164.1 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}N_2NaO_4^+$: 319.0700; found: 319.0689.

Methyl 5-Bromo-2-phenyl-1*H*-indole-3-carboxylate (3p)

Indole-3-carboxylate **3p** was prepared from isoxazole **1p** (138 mg, 0.42 mmol) and $FeCl_2·4H_2O$ (17 mg, 0.085 mmol, 20 mol%) in DMSO (2.0 mL) for 8 h.

Yield: 96 mg (71%); colorless solid; mp 175–176 °C (CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 7.24 (d, *J* = 8.6 Hz, 1 H), 7.36 (dd, *J* = 8.6, 1.8 Hz, 1 H), 7.43–7.46 (m, 3 H), 7.62–7.65 (m, 2 H), 8.34 (d, *J* = 1.8 Hz, 1 H), 8.59 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.0 (CH_3), 112.4 (CH), 115.6 (C), 124.8 (CH), 126.2 (CH), 128.3 (CH), 129.2 (C), 129.46 (CH), 129.54 (CH), 131.4 (C), 133.7 (C), 145.5 (C), 165.3 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{16}H_{12}{}^{79}BrNNaO_2^+$: 351.9944; found: 351.9951.

Methyl 5-Nitro-2-*p*-tolyl-1*H*-indole-3-carboxylate (3q)

Indole-3-carboxylate **3q** was prepared from isoxazole **1q** (134 mg, 0.43 mmol) and $FeCl_2·4H_2O$ (18 mg, 0.09 mmol, 20 mol%) in DMSO (1.5 mL) for 6 h.

Yield: 83 mg (62%); yellowish solid; mp 258–259 °C (CH_2Cl_2).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.41 (s, 3 H), 3.77 (s, 3 H), 7.34 (d, *J* = 7.9 Hz, 2 H), 7.59 (dd, *J* = 8.9, 1.6 Hz, 1 H), 7.63 (d, *J* = 7.9 Hz, 2 H), 8.09 (dd, *J* = 8.9, 1.7 Hz, 1 H), 8.87 (d, *J* = 1.7 Hz, 1 H), 12.68 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 21.0 (CH_3), 50.9 (CH_3), 104.1 (C), 112.4 (CH), 117.6 (CH), 117.9 (CH), 126.6 (C), 127.7 (C), 128.6 (CH), 129.8 (CH), 138.7 (C), 139.4 (C), 142.3 (C), 148.0 (C), 164.1 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{14}N_2NaO_4^+$: 333.0846; found: 333.0862.

Methyl 4-Methoxy-2-phenyl-1*H*-indole-3-carboxylate (3r)

Indole-3-carboxylate **3r** was prepared from isoxazole **1r** (80 mg, 0.28 mmol) and $FeCl_2$ (15 mg 0.075 mmol, 28 mol%) in DMSO (1 mL) for 7 h.

Yield: 25 mg (31%); yellowish solid; mp 142–143 °C (EtOAc).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.74 (s, 3 H), 3.84 (s, 3 H), 6.59–6.61 (m, 1 H), 7.04–7.06 (m, 1 H), 7.10–7.14 (m, 1 H), 7.39–7.42 (m, 1 H), 7.47–7.51 (m, 2 H), 7.61–7.62 (m, 2 H), 11.83 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 51.5 (CH_3), 55.5 (CH_3), 101.1 (CH), 104.8 (CH), 104.9 (C), 116.6 (C), 123.5 (CH), 127.7 (CH), 128.3 (CH), 128.6 (CH), 131.4 (C), 136.8 (C), 138.9 (C), 152.9 (C), 167.2 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{17}H_{15}NNaO_3^+$: 304.0944; found: 304.0945.

Methyl 2-*p*-Tolyl-1*H*-benzo[*g*]indole-3-carboxylate (3s)

Indole-3-carboxylate **3s** was prepared from isoxazole **1s** (130 mg, 0.60 mmol) and $FeCl_2·4H_2O$ (24 mg, 0.12 mmol, 20 mol%) in DMSO (2 mL) for 4 h.

Yield: 124 mg (95%); colorless solid; mp 217–218 °C (CH_2Cl_2).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.41 (s, 3 H), 3.76 (s, 3 H), 7.31–7.37 (m, 2 H), 7.44–7.51 (m, 1 H), 7.56–7.61 (m, 1 H), 7.61–7.68 (m, 3 H), 7.94–8.00 (m, 1 H), 8.16–8.21 (m, 1 H), 8.56–8.62 (m, 1 H), 12.67 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 20.9 (CH_3), 50.5 (CH_3), 104.4 (C), 120.7 (CH), 121.14 (CH), 121.5 (C), 121,9 (CH), 123.5 (C), 124.4 (CH), 125.8 (CH), 128.3 (CH), 128.4 (CH), 129.0 (C), 130.0 (CH), 130.3 (C), 138.2 (C), 142.8 (C), 165.0 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{21}H_{17}NNaO_2^+$: 338.1151; found: 338.1162.

Methyl 2-Phenyl-3*H*-benzo[*e*]indole-1-carboxylate (3t)

Indole-3-carboxylate **3t** was prepared from isoxazole **1t** (203 mg, 0.67 mmol) and $FeCl_2·4H_2O$ (28 mg, 0.14 mmol, 20 mol%) in DMSO (2.5 mL) for 3.5 h.

Yield: 166 mg (82%); yellowish solid; mp 183–184 °C (EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H), 7.37 (m, 7 H), 7.56–7.59 (m, 1 H), 7.63–7.66 (m, 1 H), 7.90–7.92 (m, 1 H), 8.79 (br s, 1 H), 8.90–8.92 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.6 (CH_3), 108.3 (C), 112.1 (CH), 121.0 (C), 124.0 (CH), 124.8 (CH), 125.2 (CH), 126.1 (CH), 128.0 (C), 128.4 (CH), 128.54 (CH), 128.56 (CH), 128.8 (CH), 130.5 (C), 132.48 (C), 132.5 (C), 139.8 (C), 168.0 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{20}H_{15}NNaO_2^+$: 324.0995; found: 324.1010

(2-Phenyl-1*H*-indol-3-yl)(pyrrolidin-1-yl)methanone (3u)

Indole-3-carboxylate **3u** was prepared from isoxazole **1u** (113 mg, 0.39 mmol) and $FeCl_2·4H_2O$ (8 mg, 0.04 mmol, 20 mol%) in DMSO (2 mL) for 6 h.

Yield: 84 mg (74%); colorless solid; mp 254–255 °C (EtOAc/CH_2Cl_2).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.61–1.64 (m, 2 H), 1.77–1.81 (m, 1 H), 2.94–2.97 (m, 2 H), 3.52–3.55 (m, 2 H), 7.05–7.09 (m, 1 H), 7.14–7.19 (m, 1 H), 7.36–7.41 (m, 1 H), 7.43–7.50 (m, 4 H), 7.67–7.69 (m, 1 H), 11.69 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 24.1 (CH_2), 25.4 (CH_2), 45.3 (CH_2), 47.3 (CH_2), 110.0 (C), 111.6 (CH), 119.2 (CH), 120.0 (CH), 122.2 (CH), 126.6 (C), 126.8 (CH), 128.1 (CH), 128.9 (CH), 131.8 (C), 134.9 (C), 135.7 (C), 165.5(C).

HRMS-ESI: *m/z* [M + H]$^+$ calcd for $C_{19}H_{19}N_2O^+$: 291.1492; found: 291.1505.

Methyl 5-Phenyl-4*H*-thieno[3,2-*b*]pyrrole-6-carboxylate (3v)

Indole-3-carboxylate **3v** was prepared from isoxazole **1v** (130 mg, 0.50 mmol) and $FeCl_2{\cdot}4H_2O$ (20 mg, 0.10 mmol, 20 mol%) in DMSO (1.5 mL) for 4 h.

Yield: 95 mg (73%); light brown solid; mp 37–38 °C (EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 6.95 (d, *J* = 5.3 Hz, 1 H), 7.19 (d, *J* = 5.3 Hz, 1 H), 7.38–7.44 (m, 3 H), 7.65–7.67 (m, 2 H), 8.72 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.3 (CH_3), 105.6 (C), 111.0 (CH), 125.7 (CH), 126.6 (C), 128.3 (CH), 128.8 (CH), 129.1 (CH), 131.8 (C), 136.9 (C), 142.0 (C), 164.5 (C).

HRMS-ESI: *m/z* [M + Na]$^+$ calcd for $C_{14}H_{11}NNaO_2S^+$: 280.0403; found: 280.0415.

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Supporting Information

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