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Direct Synthesis of 2,5-Disubstituted Oxazoles through an Iodine-Catalyzed Decarboxylative Domino Reaction

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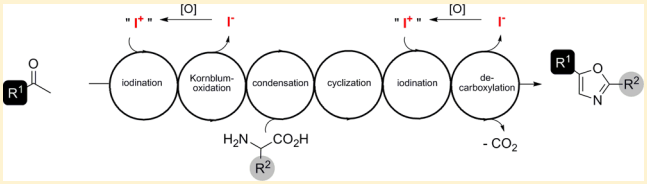
Supporting Information

ABSTRACT: An efficient iodine-catalyzed synthesis of highly substituted oxazoles is presented. Starting from readily available aryl methyl ketones, β-keto esters, or styrenes, in combination with α-amino acids as amine-containing coupling partners, the corresponding 2-alkyl-5-aryl- substituted oxazoles were obtained in up to 80% yield via a decarboxylative domino reaction.



INTRODUCTION

The oxazole motif is a commonly found core structure in pharmaceuticals and natural products. Representative examples are the PPARα/γ agonist aleglitazar,[1] the nonsteroidal anti-inflammatory drug oxaprozin,[2] the peptide alkaloide muscoride A,[3] or the antimycobacterial natural product texaline (Figure 1).[4] As a consequence of the extraordinary abundance of

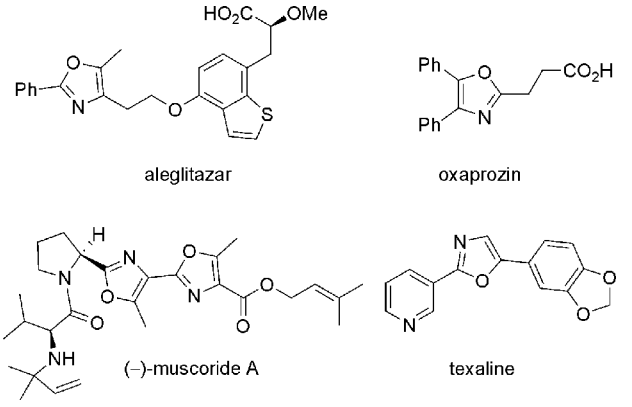


Figure 1. Representative examples of oxazoles in pharmaceuticals and other biologically active compounds.

oxazoles in biologically active compounds, a variety of synthetic procedures yielding highly substituted oxazoles have been developed during the last decades.

Classical routes to the oxazole motif include the cyclodehydration of (α-acylamino)ketones (Robinson–Gabriel Synthesis), the cyclodehydration of (α-acyloxy)ketones in the presence of ammonia, the condensation of cyanhydrines and aromatic aldehydes (Fischer Synthesis), and the annulation of enamides.[5−15] 2-Alkyl-substituted oxazoles are accessible by reactions of aryl alkyl ketones and nitriles using hypervalent iodine reagents,[16−18] mercury-[19] and thallium-salts,[20] by [3 + 2] cycloadditions[21−23] through the cycloisomerization of propargylamides,[24−30] or by a Ritter reaction of α-oxotosylates.[31] However, an underevaluated route to oxazoles, which primarily yields 2,4-disubstituted derivatives, is the cyclocondensation of α-halogenated ketones and carboxamides as initially described by Blümlein and Lewy in the 1880s (Scheme 1a).[32,33] Major drawbacks of this transformation are harsh reaction conditions and the necessity of hazardous α-halo ketones as precursors. The in situ generation of α-halo ketones or synthetic equivalents thereof from α-unsubstituted ketones by in situ halogenation or oxidation and subsequent substitution with an amine and cyclization in a domino process would be much more efficient (Scheme 1b).[34] The utilization of acetophenones for the de novo synthesis of heterocycles via oxidative domino reactions has been studied intensively and resulted in the development of a variety of transformations including the synthesis of 2-acylbenzo[*d*]thiazoles,[35] isoxazoles,[36] quinazolinones,[37] imidazoles and thiazoles,[38,39] imidazo[1,2-*a*]pyridines,[40] and 1,2,3-triaroylindolizines.[41]

However, the synthesis of oxazoles via oxidative domino reactions is less common.[21,22,42,43] For example, Wang and co-workers developed an efficient synthesis of 2,5-disubstituted oxazoles starting from α-amino ketones and aromatic carboxaldehydes.[44] Jiang and co-workers reported an oxidative domino reaction yielding 2,5- or 2,4,5-substituted oxazoles starting from styrenes and benzyl amines. Here, α-halo ketones, as key intermediates, are formed in situ from styrenes by combining molecular iodine and *tert*-butyl hydroperoxide as the co-oxidant.[45] The same authors described an efficient iodine-mediated synthesis of polysubstituted imidazoles.[46] 2-Aryl-4-acyl-substituted oxazoles can be generated by an iodine-catalyzed cascade sp^3 C–H activation starting from alkyl acetoacetates and benzyl amines.[47]

Wu and co-workers presented an iodine-mediated synthesis of oxazoles based on benzoins, aryl methyl ketones, and ammonium acetate by the convergent integration of two self-labor domino sequences.[48]

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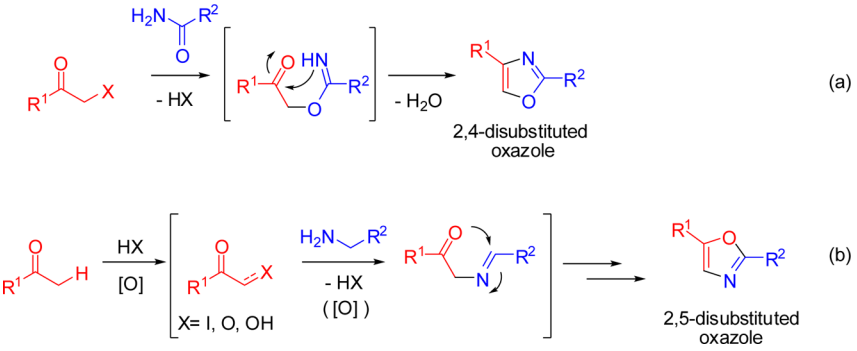
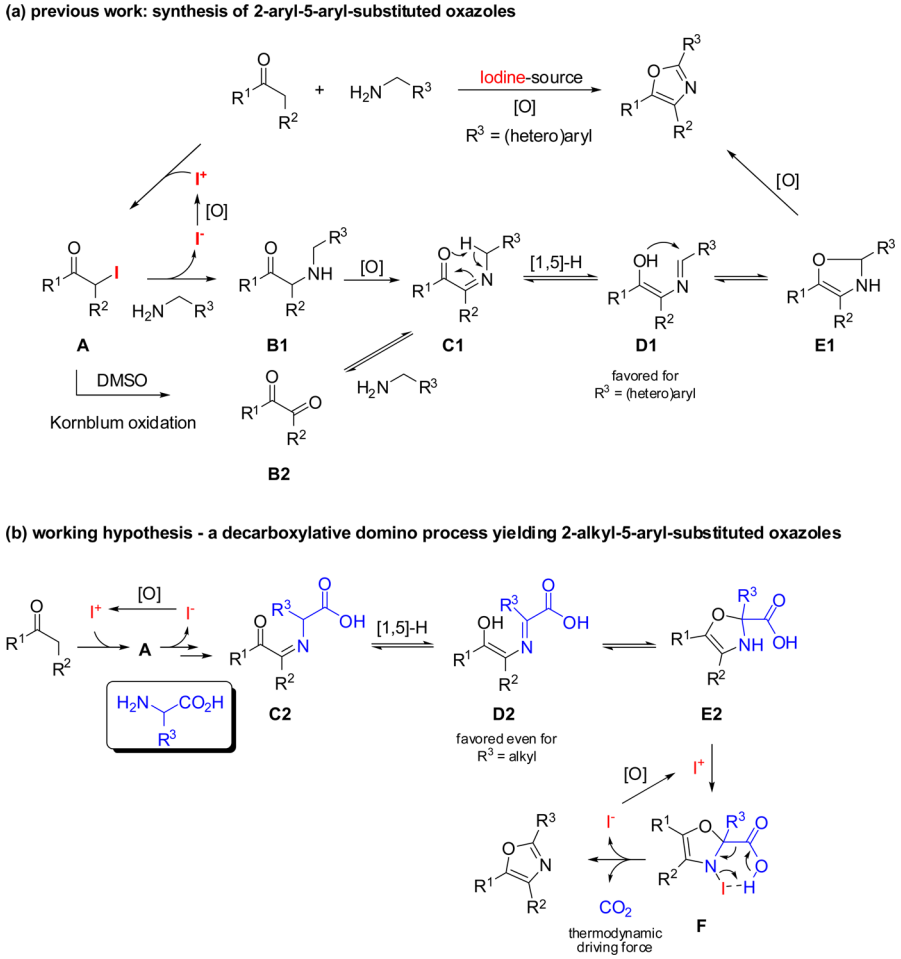
Scheme 1. Synthesis of Oxazoles Starting from (a) α-Halo Ketones and Carboxamides or (b) Ketones and Amines



Scheme 2. Mechanistic Proposal for (a) Known Oxidative Domino Synthesis of 2-Aryl-5-aryl-disubstituted Oxazoles from Aryl Methyl Ketones and Benzyl Amines and (b) Decarboxylative Domino Reaction Based on α-Amino Acids



Very recently, the same group developed an iodine-mediated and peroxide-free oxidative domino synthesis of 2-aryl-5-aryl-disubstituted oxazoles utilizing aryl methyl ketones and benzyl amines as substrates.[49] However, all oxidative domino sequences described above give 2-aryl-substituted oxazoles exclusively. The complementary 2-alkyl-substituted derivatives are not accessible via these iodine-mediated oxidative domino sequences.[21,25,50,51] An efficient synthetic approach toward 2-alkyl-substituted oxazoles was reported by Martínez-Alvarez and co-workers through the reaction of 1-(methylthio)acetone with nitriles in the presence of triflic acid.[52] However, an explanation for the preferred 2-aryl substituent in iodine-mediated oxidative domino sequences for the synthesis of oxazoles is given in Scheme 2a. In either case, the α-iodinated ketone **A** is generated by in situ iodination. **A** reacts with the corresponding amine to the aza enone **C1** either by a substitution/oxidation mechanism through the α-amino ketone **B1** or, depending on the reaction conditions, via a Kornblum oxidation through a 1,2-dicarbonyl intermediate **B2**. However, for the key cyclization step, **C1** must isomerize via a [1,5]-H-shift to compound **D1**, which after cyclization to **E1** and subsequent oxidation gives the desired oxazole. Looking at this cascade reaction, it seems obvious that formation of **D1** is highly favored for R^3 being a (hetero)aromatic residue due to

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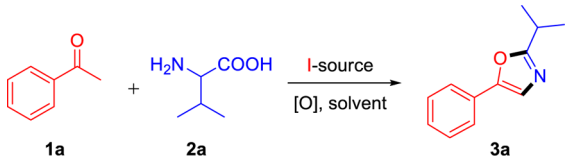
Table 1. Optimization Studies[a]



1a 2a 3a

entry	cat (mol %)	oxidant (equiv)	solvent	t [°C]	t [h]	yield **3a** [%][a,b]
1	I_2 (20)	TBHP (2.5)[c]	DMSO	95	2	27
2	I_2 (20)	NaOCl (2.5)[d]	DMSO	95	2	0
3	I_2 (20)	H_2O_2 (2.5)[e]	DMSO	95	2	0
4	I_2 (20)	oxone (2.5)	DMSO	95	2	53
5	TBAI (20)	oxone (2.5)	DMSO	95	2	trace
6	I_2 (20)	oxone (2.5)	DMF	95	2	trace
7	I_2 (20)	oxone (2.5)	CH_3CN	95	2	trace
8[f]	I_2 (20)[c]	oxone (2.5)	DMSO	95	2	53
9[g]	I_2 (20)[d]	oxone (2.5)	DMSO	95	2	53
10[h]	I_2 (20)[e]	oxone (2.5)	DMSO	95	2	57
11	I_2 (20)	oxone (3.0)	DMSO	95	2	80
12	I_2 (20)	oxone (3.5)	DMSO	95	2	74
13	I_2 (20)	oxone (3.0)	DMSO	75	2	60
14	I_2 (20)	oxone (3.0)	DMSO	115	2	67

[a]General reaction conditions: 0.4 mmol (1 equiv) acetophenone **1a**, 1.2 mmol (3 equiv) DL-valine **2a**, and catalyst in 3 mL of solvent. [b]Isolated yield after flash column chromatography. [c]70% aq solution. [d]30% aq solution. [e]5% aq solution. [f]2 equiv of K_2CO_3 was added. [g]2 equiv of Na_2CO_3 was added. [h]2 equiv of AcOH was added.

the generation of a highly conjugated π-system explaining the high preference for benzyl amines in this transformation. Inspired by the mechanism shown in Scheme 2a, we intended to introduce aliphatic residues in the 2-position of the oxazole by using α-amino acids in a decarboxylative process (Scheme 2b). The carboxylic acid would act as a directing group that has two positive effects on this domino process: (1) intermediate **D2** would be favored, even for an aliphatic residue at R^3 due to a conjugation with the carboxylic acid, and (2) an iodine-mediated oxidative decarboxylation can be formulated (**F**) generating the oxazole directly through the oxidative loss of CO_2. Our working hypothesis was strongly supported by two recently published articles describing iodine-mediated decarboxylative domino reactions based on α-amino acids for the construction of highly substituted pyridines and quinazolines by Wang and co-workers.[53,54] On the basis of this proposal and recent results of our group and others in iodine-mediated oxidative couplings, halogenations, and domino reactions,[55−63] we herein report the first iodine-catalyzed synthesis of 2-alkyl-substituted oxazoles by a decarboxylative domino reaction starting from aryl methyl ketones or styrenes and α-amino acids.

RESULTS AND DISCUSSION

In initial experiments, we investigated the reaction between acetophenone **1a** and DL-valine **2a** in the presence of an iodine source and a co-oxidant. Because it is well-known that the combination of I_2 and the co-oxidant TBHP (*tert*-butyl hydroperoxide) gives undesired α-ketoamides from acetophenones and amines,[64] it was not surprising to us that initial experiments using the common co-oxidant TBHP gave the desired oxazole **3a** in only low yields of 27% (Table 1, entry 1). Other oxidants such as NaOCl or H_2O_2 did not yield **3a** at all (Table 1, entries 2 and 3). To our great delight, the co-oxidant Oxone ($2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$) gave **3a** in a promising isolated yield of 53% (Table 1, entry 4). Switching the iodine source from molecular iodine to tetrabutylammonium iodide (TBAI) resulted in an almost complete loss of reactivity (Table 1, entry 5). For a mechanistic discussion, it is important to note that the reaction can be exclusively performed in DMSO. Other polar aprotic solvents such as DMF and CH_3CN gave the desired product only in trace amounts (Table 1, entries 6 and 7). The reason for this solvent dependency is most likely a Kornblum oxidation giving 1,2-diketone of type **B2** as discussed in Scheme 2. Addition of base additives such as K_2CO_3 or Na_2CO_3, as well as acid additives such as acetic acid, did not improve yields significantly (Table 1, entries 8−10). However, when the amount of co-oxidant was increased from 2.5 to 3 equiv, the isolated yield of **3a** could be increased from 53 to 80%, respectively (Table 1, entry 11).

When 3.5 equiv of Oxone was used, yields dropped again (Table 1, entry 12). The initially chosen 95 °C seemed to be the ideal reaction temperature since increasing or lowering the reaction temperature resulted in a significant drop in yields (Table 1, entries 13 and 14). Having these optimized reaction conditions in hand, we tested the reactivity of a variety of aryl methyl ketones and α-amino acids in this novel domino reaction (Scheme 3). Besides valine, other aliphatic amino acids, in particular, leucine and isoleucine, reacted smoothly to give the desired oxazoles **3b** and **3c** in 70 and 52% yield, respectively.

To our surprise, yields dropped significantly to 20% when unbranched aliphatic α-amino acids such as alanine or norvaline were used as substrates (**3d** and **3e**). Furthermore, it is worth mentioning that enantiopure (2*S*,3*S*)-isoleucine gave the corresponding oxazole **3c** as a racemic mixture. Electron-rich aryl methyl ketones such as 4-methoxy acetophenone or 2′,5′-dimethylacetophenone gave oxazoles **3f−3j** in good yields of up to 63%. Here, α-aryl-substituted amino acids such as phenyl glycine could be used as substrates, as well. A variety of *ortho*-, *meta*- , and *para*-halogenated acetophenones could be utilized giving **3k−3o** in up to 70% yield. 4-Nitro and 4-CF_3-substituted

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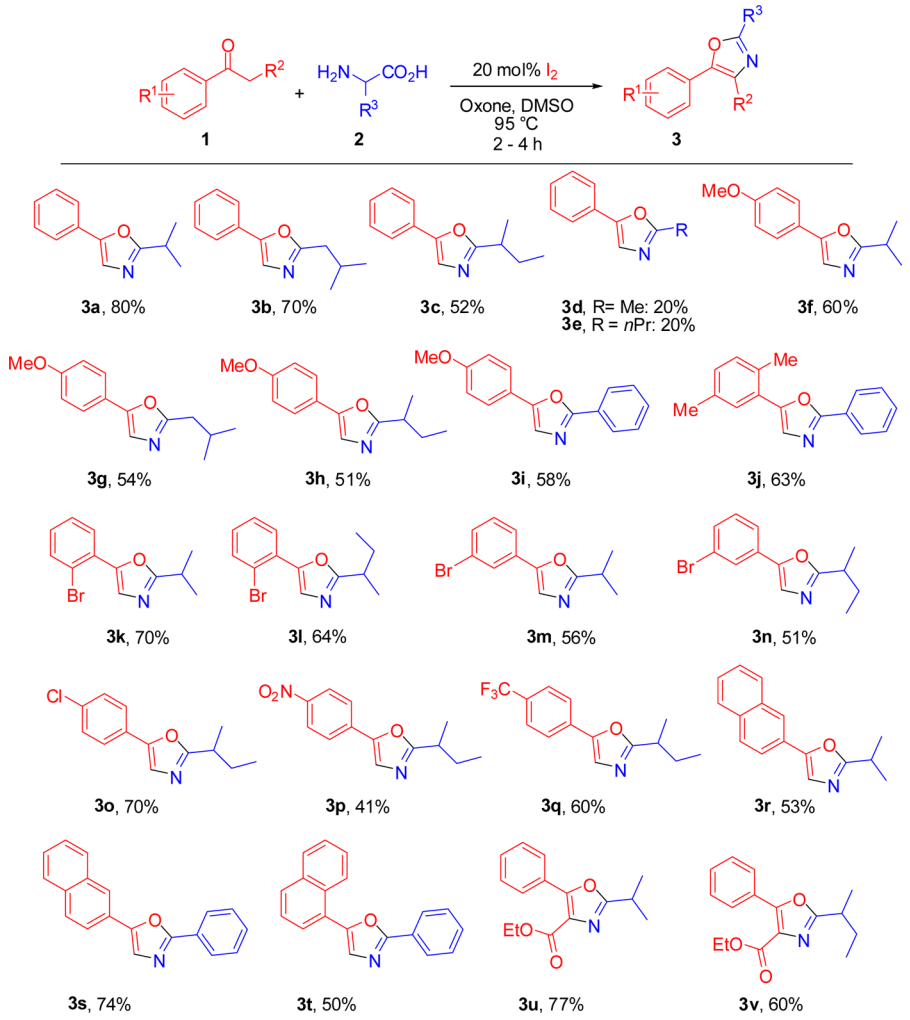
Scheme 3. Reaction of Various Aryl Methyl Ketones with α-Amino Acids[a]



[a]General reaction conditions: 0.4 mmol (1 equiv) **1**, 1.2 mmol (3 equiv) **2** , 0.08 mmol (20 mol%) I_2, 1.2 mmol (3 equiv) Oxone, and 3 mL of DMSO. Isolated yield after flash column chromatography.

acetophenones yielded oxazoles **3p** and **3q** in 41 and 60% yield, respectively. 1- and 2-Naphthalenones resulted in formation of 5-(1-naphthyl) and 5-(2-naphthyl)-substituted oxazoles **3r**−**3t** in 53−74% yield. Finally, the 1,3-dicarbonyl compound ethyl benzoyl acetate was tested in this domino process. Reaction with valine and isoleucine gave the 2,4,5-trisubstituted oxazoles **3u** and **3v** in 77 and 60% yield, respectively. However, it is worth mentioning that other higher-substituted aryl alkyl ketones such as propiophenone, which would give access to 2,4,5-trisubstituted oxazoles, cannot be used under our optimized reaction conditions. Aliphatic ketones such as cyclopentanone or butan-2-one also showed no reactivity. To gain detailed information into the mechanism of our newly developed domino reaction, we intended to isolate side products and reaction intermediates formed during the reaction cascade (Scheme 4). First, we isolated the α-hydroxylated 1-naphthalenone **4** (Scheme 4 (1)), which is formed by hydrolysis of the α-iodoketone. Subsequently, **4** was shown to react with valine to the desired oxazole **3r** in 75% yield under the same optimized reaction conditions previously found in Table 1. Thus, **4** can be seen as an intermediate which is formed in a constructive side pathway coexistent to the Kornblum oxidation pathway. Since an excess of the corresponding amino acid (relative to the ketone) is needed, an undesired decomposition of the amino acid was expected. As a control experiment, phenylglycine was treated with molecular iodine in the presence of Oxone, without the addition of the corresponding ketone.

In this experiment, we observed benzaldehyde as the only side product in 30% yield, most likely due to an iodine-mediated decarboxylation and the subsequent hydrolysis of the emerging imine (Scheme 4 (2)). During our investigations toward the substrate scope, we already recognized that phenylalanine was a surprisingly poor substrate for our domino reaction. A remarkable side reaction was observed when phenylalanine reacted with Oxone in the presence of iodine. As the only product, the unexpected 2-acyl oxazole **5** was isolated in 50% yield (Scheme 4 (3)). Here, a benzylic oxidation of phenylalanine to its β-oxo derivative **A** is proposed. **A** must be prone to two convergent decomposition processes yielding 1,2-diketone **C** via an iodine-mediated oxidative decarboxylation. Simultaneously, decarboxylation of the β-keto acid **A** gives α-amino acetophenone **D**. Condensation of both substrates finally yields 2-acyl-5-aryl oxazole **5**. Finally, we tried to elucidate the poor reactivity of higher-substituted aryl alkyl ketones. When propiophenone was reacted under our

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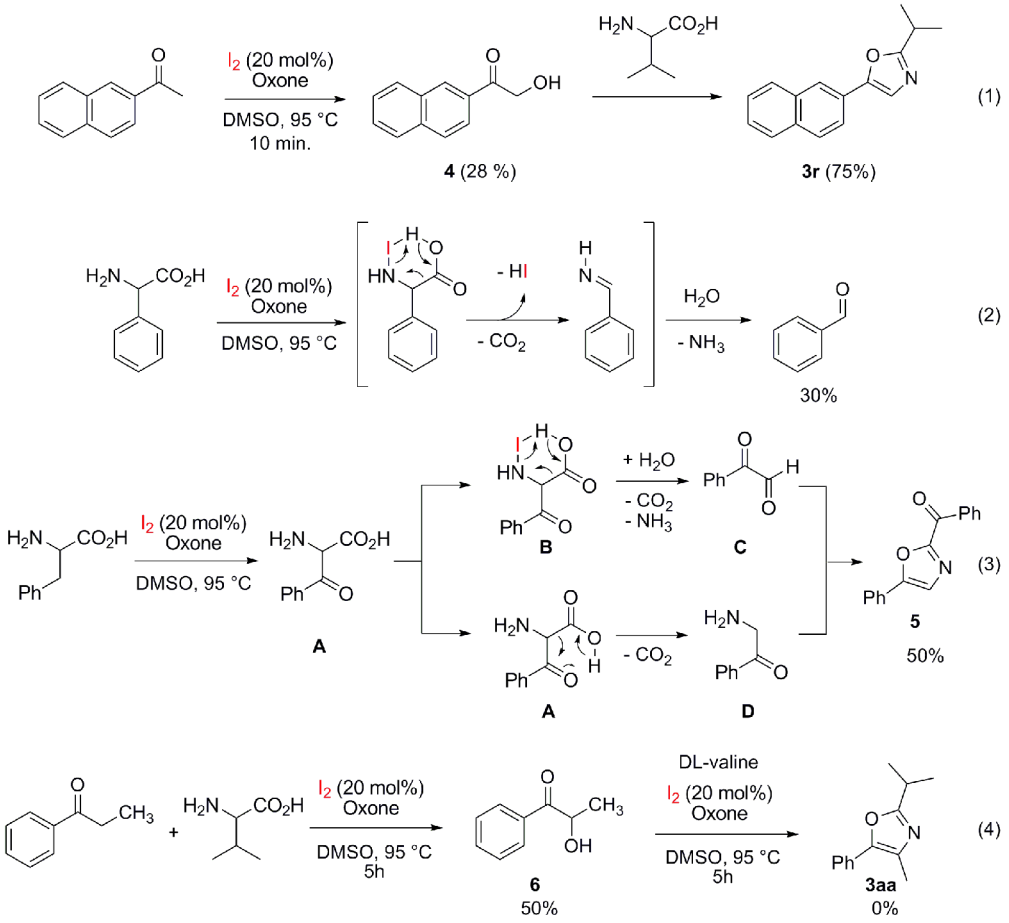
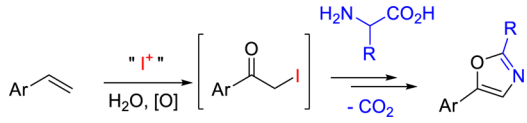
Scheme 4. Decomposition Pathways



optimized reaction conditions, no oxazole formation was observed. Instead, we could only isolate the corresponding α-hydroxlated derivative **6** in 50% yield upon reaction with valine. In contrast to the primary alcohol **4**, this secondary hydroxyl group can obviously not be further oxidized to the corresponding 1,2-diketone since further reaction of isolated **6** with valine under the same reaction conditions did not result in the formation of desired 2,4,5-trisubstituted oxazole **3aa**. Next, we investigated an even more ambitious domino reaction. The conversion of styrenes into the corresponding α-iodoketones with electrophilic iodine reagents is well-known.[35,38,39,65−71] Thus, a direct conversion of styrenes to oxazoles with I_2 and a co-oxidant should be possible, as well. One example for such a reaction was reported in 2010 by Jiang and co-workers.[45] However, stoichiometric amounts of molecular iodine were necessary, and again only 2-aryl-substituted oxazoles are accessible via this method. Therefore, we wondered whether we could extend the substrate scope of our decarboxylative domino reaction sequence to styrenes, as well (Scheme 5). Initial optimization studies for the reaction between styrene and valine revealed that this reaction can be performed under similar reaction conditions as described in Table 1 (data not shown). The only significant difference is a previously not-observed positive effect of acetic acid as an additive.

Finally, oxazole **3a** could be isolated in only a moderate yield of 36% (Scheme 6), which was significantly lower in comparison with the same reaction based on acetophenone as a substrate (80%). However, we observed that the reaction

Scheme 5. Reaction of Styrene with an α-Amino Acid To Give 2-Alkyl-5-aryl Oxazoles via a Decarboxylative Domino Reaction



with styrenes is in general significantly slower, leading to a substantial negative influence of the amino acid decomposition pathways as described in Scheme 4, which explains the significant drop in yield. Furthermore, undesired side reactions of the styrene, such as epoxidations and/or iodohydroxylations, cannot be ruled out.

Even dropwise addition of the amino acid and/or styrene did not improve product yields. Electron-poor styrenes such as 2-chlorostyrene reacted uncleanly, and the desired oxazole **3z** could not be isolated in significant amounts. However, moderately electron-rich styrenes, such as *para*-methyl styrene, yielded the desired oxazoles **3w**−**3y** in up to a 48% yield.

In summary, we have developed an efficient synthesis of 2-alkyl-5-aryl oxazoles starting from acetophenones and α-amino acids on the basis of an iodine-catalyzed decarboxylative domino reaction. The reaction must be conducted in DMSO, which strongly supports an initial Kornblum oxidation pathway. With only 20 mol % of molecular iodine and Oxone as a cheap and readily available co-oxidant, a variety of 2-alkyl-5-aryl-substituted oxazoles could be isolated in excellent yields of up

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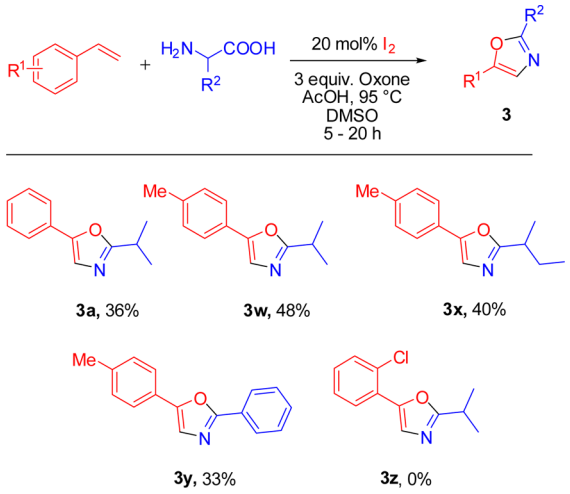
Scheme 6. Reaction of Styrenes with α-Amino Acids[a]



[a]General reaction conditions: 0.3 mmol **1**, 0.6 mmol (2 equiv) styrene, 0.06 mmol (20 mol %) I_2, 0.9 mmol (3 equiv) AcOH, and 0.75 mmol (2.5 equiv) Oxone in 2 mL of DMSO. Isolated yield after flash column chromatography.

to 80% using a variety of alkyl-substituted amino acids. Finally, this domino reaction could be extended to styrenes as substrates, as well, however with significantly lower yields.

EXPERIMENTAL SECTION

^{1}H NMR spectra were recorded on a commercial instrument at 400 MHz. Chemical shifts for ^{1}H NMR were reported as δ parts per million (ppm) relative to the signal of $CHCl_3$ at 7.26(s) ppm. Chemical shifts for ^{13}C NMR were reported as δ ppm relative to the $CDCl_3$ triplet at 77.0 ppm. The following abbreviations were used to describe splitting patterns: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet. Coupling constants J are given in Hz. Mass spectra were recorded using the EI ionization method with a quadrupole mass analyzer. High-resolution mass spectra were recorded using ESI ionization method with a FT-ICR mass analyzer.

Unless otherwise stated, all chemicals were either used as received from their commercial supplier or purified according to *Purification of Common Laboratory Chemicals*.[72] Solvents for flash column and thin layer chromatography, including cyclohexane, ethyl acetate, toluene, and diethyl ether, were distilled prior to use. DMSO was 99.5% pure and used without further drying or purification. Thin layer chromatography was performed on fluorescence indicator-marked precoated silica gel 60 plates and visualized by UV light (254 nm/366 nm). Flash column chromatography was performed on silica gel (0.040−0.063 mm). Melting points are uncorrected.

General Experimental Procedure 1 for Preparation of 2-Alkyl-5-aryl Oxazoles from Aryl Ketones. A solution of the corresponding acetophenone **1** (0.40 mmol, 1 equiv), the α-amino acid (1.2 mmol, 3 equiv), Oxone (1.2 mmol, 3 equiv), and iodine (0.08 mmol, 0.2 equiv) in DMSO (3 mL) was heated to 95 °C. The resulting mixture was stirred at 95 °C until the starting material was completely converted. The reaction mixture was allowed to cool to rt and then treated with saturated aqueous solutions of $Na_2S_2O_3$ and $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 times), and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel to afford **3a**−**v**.

General Experimental Procedure 2 for Preparation of 2-Alkyl-5-aryl Oxazoles from Styrenes. A solution of the corresponding styrene (0.30 mmol, 1 equiv), the α-amino acid (0.90 mmol, 3 equiv), Oxone (0.75 mmol, 2.5 equiv), iodine (0.06 mmol, 0.2 equiv), and acetic acid (0.90 mmol, 3 equiv) in DMSO (2 mL) was heated to 95 °C. The resulting mixture was stirred at 95 °C until the starting material was completely converted. The reaction mixture was allowed to cool to rt and then treated with saturated aqueous solutions of $Na_2S_2O_3$ and $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 times), and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel to afford **3a**, **3w**−**3z**.

*2-Isopropyl-5-phenyloxazole (**3a**):* Prepared from acetophenone and valine following general experimental procedure 1; Yield, 60 mg (80%). Prepared from styrene and valine following general experimental procedure 2;yield, 20 mg (36%), yellow liquid; eluent, petroleum ether/ethyl acetate (7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dt, J = 8.1, 1.6 Hz, 2H), 7.34−7.31 (m, 2H), 7.24−7.20 (m, 1H), 7.15 (s, 1H), 3.08 (hept, J = 7.0 Hz, 1H), 1.34 (d, J = 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 150.6, 128.7, 128.2, 128.0, 123.9, 121.5, 28.4, 20.4; IR (neat) 2974, 1691, 1552, 1489, 1363, 1273, 1203, 1139, 943, 823, 762, 712, 657, 613 (cm^{-1}); MS (EI) m/z 187.1 (100) $[M]^{+\bullet}$, 172.1 (87) $[M - CH_3]^{+\bullet}$, 105.1 (9) $[M - C_5H_8N]^{+\bullet}$, 82.2 (12) $[M - C_7H_5O]^{+\bullet}$, 77.1 (16) $[M - C_6H_8NO]^{+\bullet}$. The spectral data were in good agreement with the literature.[17]

*2-Isobutyl-5-phenyloxazole (**3b**):* Prepared from acetophenone and leucine following general experimental procedure 1; yield, 42 mg (70%), yellow liquid; eluent, petroleum ether/ethyl acetate (8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 7.2 Hz, 2H), 7.57 (t, J = 7.7 Hz, 2H), 7.49−7.44 (m, 1H), 7.40 (s, 1H), 2.88 (d, J = 7.1 Hz, 2H), 2.43−2.33 (m, 1H), 1.19 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 150.8, 128.8, 128.3, 128.0, 123.9, 121.7, 37.1, 27.6, 22.3; IR (neat) 2958, 1554, 1137, 1082, 940, 822, 759, 690, 671 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{15}NO$ $[M + H]^+$ 202.1226, found 202.1225.

*2-(1-Methylpropyl)-5-phenyloxazole (**3c**):* Prepared from acetophenone and isoleucine following general experimental procedure 1; yield, 42 mg (52%), yellow liquid; eluent, petroleum ether/ethyl acetate (8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, J = 5.2, 3.3 Hz, 2H), 7.42−7.38 (m, 2H), 7.32−7.27 (m, 1H), 7.22 (s, 1H), 2.97 (h, J = 7.0 Hz, 1H), 1.92−1.84 (m, 1H), 1.74−1.69 (m, 1H), 1.38 (d, J = 7.0 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 150.6, 128.8, 128.3, 128.0, 123.9, 121.5, 35.3, 28.2, 18.0, 11.6; IR (neat) 2967, 1552, 1449, 1138, 1055, 955, 822, 761, 742, 689 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{15}NO$ $[M + H]^+$ 202.1226, found 202.1226.

*2-Methyl-5-phenyloxazole (**3d**):* Prepared from acetophenone and alanine following general experimental procedure 1; yield, 13 mg (20%), yellow solid; eluent, petroleum ether/ethyl acetate (8:1); mp 56.0−58.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.59 (m, 2H), 7.40 (t, J = 7.6 Hz, 2H), 7.30 (tt, J = 8.0 Hz, 2.0 Hz, 1H), 7.21 (s, 1H), 2.54 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 151.1, 128.8, 128.1, 128.1, 123.9, 121.6, 14.1; IR (neat) 3119, 1754, 1668, 1558, 1484, 1304, 1214, 1130, 1061, 942, 834, 760, 692 (cm^{-1}); MS (EI) m/z 159.1 (100) $[M]^{+\bullet}$, 130.1 (50) $[M - C_2H_5]^{+\bullet}$, 104.2 (28) $[M - C_2H_1NO]^{+\bullet}$. The spectral data were in good agreement with the literature.[21]

*2-Propyl-5-phenyloxazole (**3e**):* Prepared from acetophenone and norvaline following general experimental procedure 1; yield, 15 mg (20%), pale yellow liquid; eluent, petroleum ether/ethyl acetate (7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.54 (m, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.24 (t, J = 7.4 Hz, 1H), 7.17 (s, 1H), 2.77 (t, J = 7.5 Hz, 2H), 1.84−1.75 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.9, 130.84, 128.8, 128.2, 128.0, 123.9, 121.7, 30.1, 20.5, 13.7; IR (neat) 2964, 1556, 1448, 1133, 1026, 941, 760, 709, 690, 665 cm^{-1}; MS (EI) m/z 187.2 (36) $[M]^{+\bullet}$, 172.1 (13) $[M - CH_3]^{+\bullet}$, 159.1 (100) $[M - C_2H_6]^{+\bullet}$, 105.1 (6) $[M - C_5H_8N]^{+\bullet}$, 77.1 (7) $[M - C_6H_8NO]^{+\bullet}$. The spectral data were in good agreement with the literature.[17]

*2-Isopropyl-5-(4-methoxyphenyl)oxazole (**3f**):* Prepared from 4-methoxyacetophenone and valine following general experimental procedure 1; yield, 52 mg (60%), yellow liquid; eluent, petroleum ether/ethyl acetate (8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.51 (m, 2H), 7.07 (s, 1H), 6.94−6.90 (m, 2H), 3.82 (s, 3H), 3.12 (dt, J =

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13.9, 7.0 Hz, 1H), 1.38 (d, J = 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 159.4, 150.6, 125.4, 121.2, 120.0, 114.2, 55.3, 28.4, 20.4; IR (neat) 2970, 1557, 1503, 1304, 1248, 115, 1137, 1029, 960, 831, 737, 685, 604 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{15}NO_2$ [M + H]$^+$ 218.1176, found 218.1175.

2-Isobutyl-5-(4-methoxyphenyl)oxazole (**3g**): Prepared from 4-methoxyacetophenone and leucine following general experimental procedure 1; yield, 50 mg (54%), yellow liquid; eluent, petroleum ether/ethyl acetate (8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.45 (m, 2H), 7.03 (s, 1H), 6.87−6.84 (m, 2H), 3.76 (s, 3H), 2.62 (d, J = 7.1 Hz, 2H), 2.13 (dp, J = 13.6, 6.8 Hz, 1H), 0.95 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 159.4, 150.8, 125.4, 121.2, 120.1, 114.2, 55.3, 37.1, 27.5, 22.3; IR (neat) 2957, 1620, 1558, 1503, 1463, 1295, 1250, 1174, 1028, 831, 796, 681, 608 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{17}NO_2$ [M + H]$^+$ 232.1332, found 232.1332.

2-(1-Methylpropyl)-5-(4-methoxyphenyl)oxazole (**3h**): Prepared from 4-methoxyacetophenone and isoleucine following general experimental procedure 1; yield, 47 mg (51%), yellow liquid; eluent, petroleum ether/ethyl acetate (8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54−7.51 (m, 2H), 7.08 (s, 1H), 6.93−6.90 (m, 2H), 3.81 (s, 3H), 2.93 (h, J = 7.0 Hz, 1H), 1.89−1.82 (m, 1H), 1.71−1.66 (m, 1H), 1.36 (d, J = 7.0 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 159.4, 150.5, 125.4, 121.2, 119.9, 114.2, 55.2, 35.2, 28.2, 17.9, 11.5; IR (neat) 2967, 1556, 1503, 1460, 1291, 1246, 1175, 1028, 831, 799, 742, 610 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{17}NO_2$ [M + H]$^+$ 232.1332, found 232.1333.

2-Phenyl-5-(4-methoxyl)oxazole (**3i**): Prepared from 4-methoxyacetophenone and phenylglycine following general experimental procedure 1; yield, 58 mg (58%), pale yellow solid; eluent, petroleum ether/ethyl acetate (8:1); mp 77.0−78.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (dt, J = 8.3, 2.2 Hz, 2H), 7.65−7.63 (m, 2H), 7.48−7.46 (m, 3H), 7.32 (s, 1H), 6.98−6.95 (m, 2H), 3.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 159.7, 151.2, 130.0, 128.7, 127.5, 126.1, 125.7, 121.8, 120.8, 114.3, 55.3; IR (neat) 2973, 1498, 1300, 1250, 1021, 951, 823, 772, 705, 614 cm^{-1}; MS (ESI) m/z [M]+ 251.1. The spectral data were in good agreement with the literature.[73]

2-Phenyl-5-(2,5-dimethylphenyl)oxazole (**3j**): Prepared from 2,5-dimethylacetophenone and phenylglycine following general experimental procedure 1; yield, 62 mg (63%), white solid; eluent, petroleum ether/ethyl acetate (15:1); mp 79.0−80.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, J = 8.0, 1.7 Hz, 2H), 7.59 (s, 1H), 7.52−7.46 (m, 3H), 7.34 (s, 1H), 7.18 (d, J = 7.7 Hz, 1H), 7.09 (dd, J = 7.7, 1.3 Hz, 1H), 2.50 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 150.9, 135.7, 131.8, 131.2, 130.2, 129.2 128.8, 127.4, 127.2, 127.0, 126.2, 126.0, 21.4, 21.0; IR (neat) 2921, 1538, 1494, 1445, 1066, 963, 811, 772, 704, 687 cm^{-1}; HRMS (ESI) m/z calcd for $C_{17}H_{15}NO$ [M + H]$^+$ 250.1226, found 250.1225.

2-Isopropyl-5-(2-bromophenyl)oxazole (**3k**): Prepared from 2-bromoacetophenone and valine following general experimental procedure 1; yield, 74 mg (70%), pale yellow liquid; eluent, petroleum ether/ethyl acetate (10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72−7.70 (m, 2H), 7.63 (dd, J = 8.0, 1.2 Hz, 1H), 7.35 (td, J = 7.7, 1.2 Hz, 1H), 7.15−7.11 (m, 1H), 3.15 (hept, J = 7.0 Hz, 1H), 1.40 (d, J = 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 148.1, 134.0, 128.9, 128,9, 128.3, 127.4, 126.3 119.7, 28.4, 20.4; IR (neat) 2972, 1562, 1469, 1146, 1021, 939, 833, 756, 710, 638 cm^{-1}; HRMS (ESI) m/z calcd for $C_{12}H_{12}BrNO$ [M + H]$^+$ 266.0175, found 266.0175.

2-(1-Methylpropyl)-5-(2-bromophenyl)oxazole (**3l**): Prepared from 2-bromoacetophenone and isoleucine following general experimental procedure 1; yield, 71 mg (64%), yellow liquid; eluent, petroleum ether/ethyl acetate (6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72−7.70 (m, 2H), 7.64 (dd, J = 8.0, 1.0 Hz, 1H), 7.38−7.34 (m, 1H), 7.14 (td, J = 7.8, 1.6 Hz, 1H), 2.97 (h, J = 7.0 Hz, 1H), 1.91−1.84 (m, 1H), 1.69 (dt, J = 14.0, 7.3 Hz, 1H), 1.38 (d, J = 7.0 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 148.0, 134.0, 129.0, 128.9, 128.3, 127.4, 126.3, 119.7, 35.3, 28.2, 17.9, 11.6; IR (neat) 2967, 1562, 1548, 1469, 1146, 1021, 939, 833, 756, 711, 640 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{14}BrNO$ [M + H]$^+$ 280.0332, found 280.0334.

2-Isopropyl-5-(3-bromophenyl)oxazole (**3m**): Prepared from 3-bromoacetophenone and valine following general experimental procedure 1; yield, 59 mg (56%), yellow liquid; eluent, petroleum ether/ethyl acetate (8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (t, J = 1.7 Hz, 1H), 7.53−7.50 (m, 1H), 7.41 (m, 1H), 7.27−7.25 (m, 1H), 7.23 (d, J = 1.9 Hz, 1H), 3.14 (hept, J = 7.0 Hz, 1H), 1.40 (d, J = 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 149.2, 130.9, 130.3, 130.2, 126.8, 122.9, 122.6, 122.4, 28.5, 20.4; IR (neat) 2974, 1582, 1549, 1472, 1281, 1139, 1074, 963, 825, 781, 684, 612 cm^{-1}; HRMS (ESI) m/z calcd for for $C_{12}H_{12}BrNO$ [M + H]$^+$ 266.0175, found 266.0174.

2-(1-Methylpropyl)-5-(3-bromophenyl)oxazole (**3n**): Prepared from 3-bromoacetophenone and isoleucine following general experimental procedure 1; yield, 57 mg (51%), colorless liquid; eluent, petroleum ether/ethyl acetate (7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (t, J = 1.7 Hz, 1H), 7.54−7.51 (m, 1H), 7.42−7.39 (m, 1H), 7.27−7.23 (m, 2H), 2.96 (h, J = 7.0 Hz, 1H), 1.93−1.80 (m, 1H), 1.73−1.68 (m, 1H), 1.37 (d, J = 7.0 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 149.1, 130.8, 130.3, 130.2, 126.8, 122.9, 122.5, 122.4, 35.3, 28.2, 17.9, 11.6; IR (neat) 2967, 1697, 1547, 1472, 1211, 1138, 1075, 958, 782, 737, 684 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{14}BrNO$ [M + H]$^+$ 280.0332, found 280.0332.

2-(1-Methylpropyl)-5-(4-chlorophenyl)oxazole (**3o**): Prepared from 4-chloroacetophenone isoleucine following general experimental procedure 1; yield, 66 mg (70%), pale yellow liquid; eluent, petroleum ether/ethyl acetate (7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.6 Hz, 2H), 7.35 (d, J = 8.6 Hz, 2H), 7.20 (s, 1H), 2.99−2.90 (m, 1H), 1.91−1.80 (m, 1H), 1.74−1.64 (m, 1H), 1.36 (d, J = 7.0 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 168.2, 149.6, 133.7, 129.0, 126.8, 125.1, 121.9, 35.3, 28.1, 17.9, 11.5; IR (neat) 2967, 1549, 1485, 1139, 1092, 1012, 820, 737 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{14}ClNO$ [M + H]$^+$ 236.0837, found 236.0836.

2-(1-Methylpropyl)-5-(4-nitrylphenyl)oxazole (**3p**): Prepared from 4-nitroacetophenone and isoleucine following general experimental procedure 1; yield, 40 mg (41%), yellow liquid; eluent, petroleum ether/ethyl acetate (6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.24 (m, 2H), 7.75−7.73 (m, 2H), 7.43 (s, 1H), 2.99 (h, J = 7.0 Hz, 1H), 1.91−1.84 (m, 1H), 1.75−1.70 (m, 1H), 1.38 (d, J = 7.0 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 148.6, 146.8, 134.0, 125.1, 124.4, 124.2, 35.4, 28.1, 17.8, 11.5; IR (neat) 2968, 1607, 1548, 1514, 1457, 1332, 1108, 1073, 956, 851, 752, 691 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O_3$ [M + H]$^+$ 247.1077, found 247.1078.

2-(1-Methylpropyl)-5-(4-trifluoromethyl)oxazole (**3q**): Prepared from 4-(trifluoromethyl)acetophenone and isoleucine following general experimental procedure 1; yield, 64 mg (60%), pale yellow liquid; eluent, petroleum ether/ethyl acetate (8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.77 (d, J = 7.1 Hz, 1H), 7.54−7.49 (m, 2H), 7.31 (s, 1H), 2.97 (h, J = 7.0 Hz, 1H), 1.92−1.85 (m, 1H), 1.74−1.69 (m, 1H), 1.38 (d, J = 7.0 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 149.3, 131.4 (q, J = 32.3 Hz), 129.3, 129.1, 126.9, 145.5 (q, J = 4.0 Hz), 123.8 (q, J = 272.7 Hz), 122.8, 120.6 (q, J = 4.0 Hz), 35.4, 28.2, 17.9, 11.5; IR (neat) 2971, 1553, 1454, 1334, 1266, 1166, 1123, 1096, 960, 897, 829, 799, 745, 696, 651 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{14}F_3NO$ [M + H]$^+$ 270.1100, found 270.1099.

2-Isopropyl-5-(2-naphthyl)oxazole (**3r**): Prepared from 2-acetylnaphthalene and valine following general experimental procedure 1; yield, 50 mg (53%), pale yellow solid; eluent, petroleum ether/ethyl acetate (10:1); mp 59.0−61.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.79−7.72 (m, 3H), 7.60 (dd, J = 7.2, 1.1 Hz, 1H), 7.43−7.38 (m, 2H), 7.24 (s, 1H), 3.11 (hept, J = 6.9 Hz, 1H), 1.36 (d, J = 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 150.8, 133.4, 132.9, 128.6, 128.1, 127.8, 126.7, 126.3, 125.6, 122.5, 122.1, 122.0, 28.6, 20.5; IR (neat) 2967, 1570, 1508, 1129,1104, 1049, 897, 865, 818, 752, 737, 675 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{15}NO$ [M + H]+ 238.1226, found 238.1227.

2-Phenyl-5-(2-naphthyl)oxazole (**3s**): Prepared from 2-acetylnaphthalene and phenylglycine following general experimental procedure 1;

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yield, 80 mg (74%), pale yellow solid; eluent, petroleum ether/ethyl acetate (8:1); mp 100.0−102.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18−8.16 (m, 3H), 7.91−7.83 (m, 3H), 7.76 (dd, J = 8.5, 1.7 Hz, 1H), 7.55−7.47 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 151.3, 133.3, 133.0, 130.3, 128.8, 128.7, 128.2, 127.8, 127.4, 126.7, 126.4, 126.3, 125.2, 123.9, 122.8, 122.0; IR (neat) 3091, 1562, 1485, 1137, 973, 891, 857, 819, 744 706, 618 cm^{-1}; MS (EI) m/z 271.1 (100) $[M]^{+\bullet}$, 243.2 (22) $[M - CH_2N]^{+\bullet}$, 127.1 (12) $[M - C_9H_6NO]^{+\bullet}$. The spectral data were in good agreement with the literature.[45]

*2-Phenyl-5-(1-naphthyl)oxazole (**3t**):* Prepared from 1-acetylnaphthalene and phenylglycine following general experimental procedure 1; yield, 54 mg (50%); pale yellow solid; eluent, petroleum ether/ethyl acetate (15:1); mp 113.0−114.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.4 Hz, 1H), 8.20−8.17 (m, 2H), 7.92 (t, J = 8.3 Hz, 2H), 7.84 (dd, J = 7.2, 1.1 Hz, 1H), 7.63−7.49 (m, 7H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 150.5, 133.8, 130.4, 130.0, 129.5, 128.8, 128.7, 127.4, 127.1, 126.7, 126.4, 126.3, 126.2, 125.3, 125.3, 124.8; IR (neat) 3053, 1589, 1485, 1397, 1233, 1119, 990, 925, 839, 767, 703, 684, 655, 623, 601 cm^{-1}; MS (EI) m/z 271.1 (100) $[M]^{+\bullet}$, 243.2 (25) $[M - CH_2N]^{+\bullet}$. The spectral data were in good agreement with the literature.[45]

*2-Isopropyl-4-(carboxylic acid ethyl ester)-5-phenyloxazole (**3u**):* Prepared from ethyl benzoylacetate and valine following general experimental procedure 1; yield, 80 mg (77%), pale yellow solid; eluent, petroleum ether/ethyl acetate (5:1); mp 41.0−42.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−7.98 (m, 2H), 7.42 (m, 3H), 4.38 (d, J = 21.4 Hz, 2H), 3.18 (hept, J = 7.0 Hz, 1H), 1.40−1.34 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 162.2, 154.7, 129.9, 128.2, 128.1, 127.2, 126.6, 61.1, 28.4, 20.2, 14.2; IR (neat) 2980, 1710, 1585, 1450, 1371, 1240, 1205, 1157, 1025, 835, 768, 693 cm^{-1}; HRMS (ESI) m/z calcd for $C_{15}H_{17}NO_3$ $[M + H]^+$ 260.1281, found 260.1271

*2-(1-Methylpropyl)-4-(carboxylic acid ethyl ester)-5-phenyloxazole (**3v**):* Prepared from ethyl benzoylacetate and isoleucine following general experimental procedure 1; yield, 65 mg (60%), colorless liquid; eluent, petroleum ether/ethyl acetate (10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dt, J = 8.5, 2.3 Hz, 2H), 7.47−7.40 (m, 3H), 4.40 (q, J = 7.1 Hz, 2H), 3.01 (h, J = 7.0 Hz, 1H), 1.92−1.84 (m, 1H), 1.74−1.68 (m, 1H), 1.38 (dt, J = 7.1, 3.6 Hz, 6H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 162.3, 154.8, 129.9, 128.3, 128.2, 127.3, 126.6, 61.2, 35.3, 28.0, 17.8, 14.3, 11.7; IR (neat) 2971, 2360, 1716, 1492, 1372, 1230, 1185, 1089, 1038, 837, 766, 690 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{19}NO_3$ $[M + Na]^+$ 296.1257, found 296.1258.

*2-Isopropyl-5-(4-methylphenyl)oxazole (**3w**):* Prepared from 4-methylstyrene and valine following general experimental procedure 2; yield, 29 mg (48%), yellow liquid; eluent, petroleum ether/diethyl ether (10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 8.3 Hz, 2H), 7.15 (s, 1H), 3.14 (hept, J = 7.0 Hz, 2H), 2.37 (m, 3H), 1.40 (d, J = 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 150.8, 138.0, 129.5, 125.6, 123.9, 120.9, 28.5, 21.3, 20.5; IR (neat) 2974, 1556, 1504, 1138, 1106, 1065, 1053, 940, 812, 738 cm^{-1}; HRMS (ESI/TOF) m/z calcd for $C_{13}H_{15}NO$ $[M + H]^+$ 202.12264, found 202.12269.

*2-(1-Methylpropyl)-5-(4-methylphenyl)oxazole (**3x**):* Prepared from 4-methylstyrene and isoleucine following general experimental procedure 2; yield, 26 mg (40%), yellow liquid; eluent, petroleum ether/diethyl ether (10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.17 (s, 1H), 2.96 (hext, J = 7.0 Hz, 1H), 2.37 (s, 3H), 1.89−1.84 (m, 1H), 1.72−1.70 (m, 1H), 1.38 (d, J = 7.0 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 150.9, 138.1, 129.5, 125.5, 124.0, 120.6, 35.3, 28.2, 21.3, 18.0, 11.6; IR (neat) 2966, 1554, 1504, 1455, 1137, 1111, 1053, 955, 812 cm^{-1}; HRMS (ESI/TOF) m/z calcd for $C_{14}H_{17}NO$ $[M + H]^+$ 216.13829, found 216.13813.

*2-Phenyl-5-(4-methylphenyl)oxazole (**3y**):* Prepared from 4-methylstyrene and phenylglycine following general experimental procedure 2; yield, 23 mg (33%), yellow liquid; eluent, petroleum ether/diethyl ether (10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12−8.10 (m, 2H), 7.62 (d, J = 8.2 Hz, 2H), 7.50−7.40 (m, 3H), 7.26 (d, J = 8.0 Hz, 2H), 7.25 (s, 1H), 2.40 (s, 3H)) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 151.5, 138.5, 130.2, 129.6, 128.8, 127.5, 126.2, 125.3, 124.2, 122.7, 21.4; IR (neat) 2965, 2923, 1675, 1504, 1068, 1018, 814 cm^{-1}; HRMS (ESI/TOF) m/z calcd for $C_{16}H_{13}NO$ $[M + H]^+$ 236.10699, found 236.10705.

*2-Hydroxy-1-naphthalen-2-yl-ethanone (**4**).* A solution of 2-acetylnaphthalene (0.4 mmol, 1 equiv), valine (1.2 mmol, 3 equiv), iodine (0.08 mmol, 0.2 equiv), and Oxone (1.2 mmol, 3 equiv) in DMSO (3 mL) was heated to 95 °C for 10 min. The reaction mixture was allowed to cool to rt and then treated with saturated aqueous solutions of $Na_2S_2O_3$ and $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 times), and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel to afford **4**: yield, 21 mg (28%), white solid; eluent, petroleum ether/ethyl acetate (7:1); mp 117.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.99−7.88 (m, 4H), 7.66−7.56 (m, 2H), 5.02 (s, 2H), 3.62 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 136.1, 132.4, 130.6, 129.6, 129.5, 129.0, 128.9, 127.9, 127.1, 123.0, 65.5; IR (neat) 3422, 1678, 1406, 1245, 1185, 1100, 938, 821, 749, 603 cm^{-1}; MS (EI) m/z 186.1 (12) $[M]^{+\bullet}$, 155.1 (100) $[M - CH_3O]^{+\bullet}$, 127.1 (80) $[M - C_2H_3O_2]^{+\bullet}$. The spectral data were in good agreement with the literature.[74]

*Phenyl(5-phenyloxazol-2-yl)methanone (**5**).* A solution of phenylalanine (0.6 mmol, 1 equiv), iodine (0.06 mmol, 0.10 equiv), and Oxone (0.75 mmol, 3 equiv) in DMSO (3 mL) was heated to 95 °C. The resulting mixture was stirred at 95 °C until the starting material was completely converted. The reaction mixture was allowed to cool to rt and then treated with saturated aqueous solutions of $Na_2S_2O_3$ and $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 times), and the combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel to afford **5**: yield, 75 mg (50%), yellow solid; eluent, petroleum ether/diethyl ether (10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50−8.48 (m, 2H), 7.84−7.81 (m, 2H), 7.67−7.63 (m, 1H), 7.61 (s, 1H), 7.56−7.52 (m, 2H), 7.50−7.42 (m, 3H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.7, 157.0, 154.2, 135.3, 133.7, 130.7, 130.0, 129.1, 128.4, 126.6, 125.4, 123.9; IR (neat) 3068, 1650, 1473, 1446, 1361, 1256, 1171, 947, 904, 764, 685, 638 cm^{-1}; MS (EI) m/z 249.1 (36) $[M]^{+\bullet}$, 221.1 (24) $[M - CH_2N]^{+\bullet}$, 105.1 (100) $[M - C_9H_6NO]^{+\bullet}$, 77.1 (46) $[M - C_{10}H_6NO_2]^{+\bullet}$. The spectral data were in good agreement with the literature.[75]

*2-Hydroxy-1-phenyl-1-propanone (**6**).* Prepared from propiophenone and valine following general experimental procedure 1: yield 30 mg (50%), pale yellow liquid; eluent, petroleum ether/ethyl acetate (7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dt, J = 8.5, 1.6 Hz, 2H), 7.64−7.58 (m, 1H), 7.54−7.46 (m, 2H), 5.16 (q, J = 7.0 Hz, 1H), 4.17−3.17 (m, 1H), 1.44 (d, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.3, 133.9, 133.3, 128.8, 128.6, 69.3, 22.2; MS (EI) m/z $[M]^{+\bullet}$ 151.1. The spectral data were in good agreement with the following literature.[76]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of oxazoles **3a**−**y** and compounds **4**, **5**, and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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