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Iodoarene-mediated one-pot preparation of 2,5-disubstituted and 2,4,5-trisubstituted oxazoles from alkyl aryl ketones with oxone in nitriles

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ABSTRACT

The reaction of alkyl aryl ketones with Oxone® and trifluoromethanesulfonic acid in the presence of iodoarene in acetonitrile, propionitrile, butyronitrile, and isobutyronitrile, provided directly the corresponding 2,5-disubstituted and 2,4,5-trisubstituted oxazoles, respectively, in moderate yields. Here, reactive aryliodonium I(III) species is formed in situ by the reaction of iodoarene with Oxone® and trifluoromethanesulfonic acid, and the formed aryliodonium I(III) species reacts with alkyl aryl ketone to generate β-keto iodonium species. Then, β-keto iodonium species reacts with nitrile to produce the corresponding oxazole. In principle, iodoarene works as a catalyst. However, 1 equiv of iodoarene is required because 1 equiv of reactive aryliodonium I(III) species must be formed before the reaction with alkyl aryl ketone.

1. Introduction

The oxazole group is one of the important heterocyclic units in biologically active natural products, including diazonamides, inthomycins, calyculins, phorboxazoles, and Oxaprozin® (an anti-inflammatory drug), and has been extensively used in medicinal chemistry.[1] One of the simplest and most common methods for the preparation of the oxazole ring is the cyclodehydration of α-acylamino ketones using dehydrating reagents, such as sulfuric acid, phosphorus pentachloride, polyphosphoric acid, trifluoroacetic anhydride, and trifluoromethanesulfonic anhydride.[1a,b] Recently, another method for the one-pot preparation of 2,5-disubstituted oxazoles was reported using acyl chlorides and alkyl isocyanides, which could be obtained by the reaction of alkyl halides and toxic metal cyanide (AgCN and KCN) in the presence of 2,6-lutidine.[2] To the best of our knowledge, there are few methods for the one-pot preparation of oxazoles from ketones with nitriles, using copper(II) trifluoromethanesulfonate,[3a] thallium(III) trifluoromethanesulfonate,[3b] and mercury(II) *p*-toluenesulfonate.[3c] As a less toxic method, the preparation of 2,5-disubstituted oxazoles from aryl methyl ketones using (diacetoxyiodo)benzene with trifluoromethanesulfonic acid (TfOH) in acetonitrile was reported.[4] On the other hand, recently, PhI-catalyzed synthetic reactions with *m*-chloroperbenzoic acid (*m*CPBA) or peracetic acid,[5] Oxone®,[6] and H_2O_2[7] have become popular. Very recently, we have reported the direct preparation of 2,5-disubstituted and 2,4,5-trisubstituted oxazoles by the reaction of alkyl aryl ketones with TfOH and *m*CPBA in acetonitrile, propionitrile, butyronitrile, and isobutyronitrile.[8]

Here, as part of our studies on organic synthesis using PhI-catalyzed systems with *m*CPBA and Oxone®, we would like to report the iodoarene-mediated direct preparation of 2,5-disubstituted and 2,4,5-trisubstituted oxazoles, which involves the reaction of alkyl aryl ketones with iodoarene, TfOH, and Oxone® in acetonitrile, propionitrile, butyronitrile, and isobutyronitrile, respectively.

2. Results and discussion

The advantages of iodoarene-mediated reactions with Oxone® are that the oxidative reactions can be carried out under metal-free conditions and that Oxone® is an inorganic oxidant and is much less expensive than *m*CPBA.

To an acetonitrile solution were added PhI (1.1 equiv), Oxone®, and TfOH (2.0 equiv), and the mixture was stirred for 2 h to generate the corresponding aryliodonium species. Then, a solution of acetophenone (1.0 equiv) in acetonitrile (2 mL) was added

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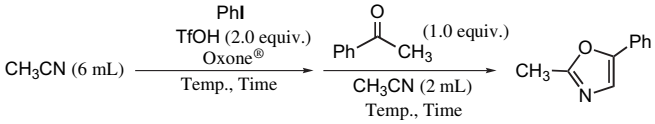
and the obtained mixture was refluxed to provide the corresponding 2-methyl-5-phenyloxazole. As shown in Table 1, entries 9 and 10 showed the best results (63% and 66%) when 1.5 equiv of Oxone® was used. Surprisingly, in the absence of PhI, 2-methyl-5-phenyloxazole was obtained in 12% yield and acetophenone was consumed completely (entry 11). While, in the presence of 0.5 equiv of PhI, 2-methyl-5-phenyloxazole was obtained only in 18% yield and acetophenone was completely consumed (entry 12). We believe that a small amount of α-hydroxyacetophenone is formed by the reaction of acetophenone and Oxone® in the presence of TfOH, and acetonitrile reacts with α-hydroxyacetophenone in acidic conditions to provide 2-methyl-5-phenyloxazole. Practically, preparation of α-hydroxyalkyl aryl ketones by the reaction of alkyl aryl ketones with Oxone® and TFAA in the presence of PhI in a mixture of H_2O and CH_3CN at 90 °C was reported.[6c]

When the effects of iodoarenes, such as iodobenzene, 4-methyliodobenzene, 4-chloroiodobenzene, 4-methoxyiodobenzene, 4-iodobenzoic acid, and 3-trifluoromethyliodobenzene, were compared, iodobenzene and 4-chloroiodobenzene were found to give the best yields, as shown in Table 2 (entries 1–6). 4-Chloroiodobenzene was recovered in high yield together with 2-methyl-5-phenyloxazole, which was produced in 58% yield (entry 3). This suggests that iodoarene works as a catalyst in the present oxazole formation. When 4-methoxyiodobenzene was used, the electron-rich aromatic ring might have reacted with reactive aryliodonium species (entry 4). In contrast, when 4-iodobenzoic acid was used, aryliodonium species might be not formed effectively because of the electron-deficient aromatic ring (entry 5). These are the possible reasons why the yield of 2-methyl-5-phenyloxazole was extremely low, when 4-methoxyiodobenzene and 4-iodobenzoic acid were used. Practically, the black tar was obtained in the former reaction (entry 4). Then, the preparation of 2-methyl-5-aryloxazoles and 2-methyl-4-alkyl-5-aryloxazoles was carried out using various alkyl aryl ketones with iodobenzene and 4-chloroiodobenzene, and 2-methyl-5-(4′-methylphenyl)oxazole, 2-methyl-5-(4′-chlorophenyl)oxazole, 2-methyl-5-(4′-nitrophenyl)oxazole, and 2,4-dimethyl-5-phenyloxazole were obtained in moderate yields (entries 7–12). However, the yield of 2-methyl-4-heptyl-5-phenyloxazole was low, when nonanophenone was used (entries 13 and 14). This may be because the ketone has steric hindrance for cyclization to oxazole. Under the present conditions, dialkyl ketones gave the corresponding oxazoles in low yields (~10%). Moreover, when silyl ethers, prepared from the reaction of ketones with trimethylsilyl chloride and triethylamine, were used instead of ketones, the yields of oxazoles were again low (~20%).

When the same reaction was carried out in propionitrile instead of acetonitrile, 2-ethyl-5-phenyloxazole, 2-ethyl-5-(4′-methylphenyl)oxazole, 2-ethyl-5-(4′-chlorophenyl)oxazole, 2-ethyl-5-(4′-nitrophenyl)oxazole, and 2-ethyl-4-methyl-5-phenyloxazole were obtained in moderate yields from acetophenone, 4-methylacetophenone, 4-chloroacetophenone, 4-nitroacetophenone, and

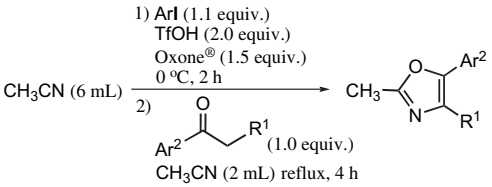
Table 1
Preparation of 2-methyl-5-phenyloxazole from acetophenone in acetonitrile



Entry	First step				Second step		
	PhI (equiv)	Oxone (equiv)	Temp	Time	Temp	Time	Yield[a] (%)
1	1.1	1.1	rt	30 min	Reflux	Overnight	10
2	1.1	1.1	0 °C	30 min	Reflux	Overnight	41
3	1.1	1.1	0 °C	2 h	Reflux	Overnight	65
4	1.1	1.1	0 °C	3 h	Reflux	Overnight	38
5	1.1	1.1	0 °C	2 h	60 °C	Overnight	52
6	1.1	1.1	0 °C	2 h	Reflux	2 h	40
7	1.5	1.5	0 °C	2 h	Reflux	2 h	55
8	1.1	1.1	0 °C	2 h	Reflux	4 h	49
9	1.1	1.5	0 °C	2 h	Reflux	4 h	63
10	1.5	1.5	0 °C	2 h	Reflux	7 h	66
11	0	1.5	0 °C	2 h	Reflux	4 h	12
12	0.5	1.5	0 °C	2 h	Reflux	4 h	18
13	1.1	1.5	0 °C	2 h	Reflux	7 h	45
14	1.5	1.5	0 °C	2 h	Reflux	4 h	42

[a] Isolated yield.

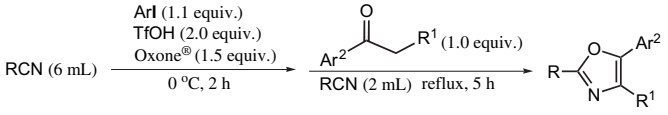
Table 2
Preparation of oxazoles from ketones in acetonitrile



Entry	ArI	R^1	Ar^2	Yield[a] (%)
1	PhI	H	Ph	63
2	4-$CH_3C_6H_4I$			47
3	4-ClC_6H_4I			58 (80)[b]
4	4-$CH_3OC_6H_4I$			0
5	4-$HO_2CC_6H_4I$			<5
6	3-$CF_3C_6H_4I$			45
7	PhI	H	4-$CH_3C_6H_4$	65
8	PhI	H	4-ClC_6H_4	38
9	4-ClC_6H_4I	H	4-ClC_6H_4	58
10	PhI	H	4-$O_2NC_6H_4$	44
11	4-ClC_6H_4I	H	4-$O_2NC_6H_4$	47
12	PhI	CH_3	Ph	70
13	PhI	$CH_3(CH_2)_6$	Ph	34
14	4-ClC_6H_4I	$CH_3(CH_2)_6$	Ph	32

[a] Isolated yield.
[b] Yield of recovered 4-chloroiodobenzene.

Table 3
Preparation of oxazoles from ketones in nitriles

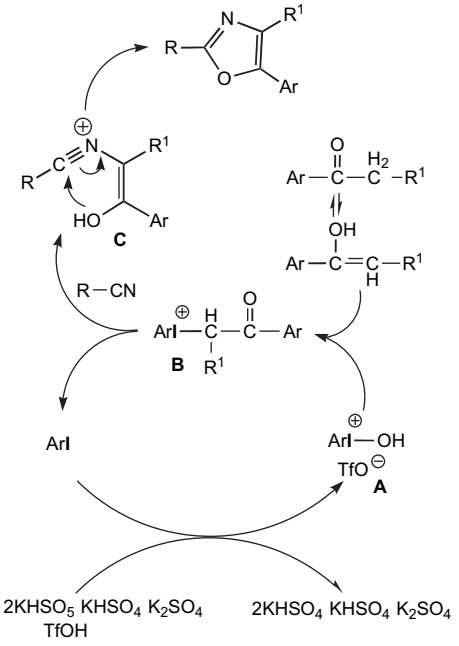


Entry	ArI	RCN	R^1	Ar^2	Yield[a] (%)
1	PhI	CH_3CH_2CN	H	Ph	59
2	PhI	CH_3CH_2CN	H	4-$CH_3C_6H_4$	63
3	4-ClC_6H_4I	CH_3CH_2CN	H	4-ClC_6H_4	59
4	4-ClC_6H_4I	CH_3CH_2CN	H	4-$O_2NC_6H_4$	55
5	PhI	CH_3CH_2CN	CH_3	Ph	67
6	PhI	CH_3CH_2CN	$CH_3(CH_2)_6$	Ph	38
7	4-ClC_6H_4I	$CH_3CH_2CH_2CN$	H	Ph	42
8	PhI	$CH_3CH_2CH_2CN$	H	4-$CH_3C_6H_4$	48
9	4-ClC_6H_4I	$CH_3CH_2CH_2CN$	H	4-ClC_6H_4	56
10	4-ClC_6H_4I	$CH_3CH_2CH_2CN$	H	4-$O_2NC_6H_4$	56
11	PhI	$CH_3CH_2CH_2CN$	CH_3	Ph	44
12	PhI	$CH_3CH_2CH_2CN$	$CH_3(CH_2)_6$	Ph	22
13	PhI	$(CH_3)_2CHCN$	H	Ph	43
14	PhI	$(CH_3)_2CHCN$	H	4-$CH_3C_6H_4$	43
15	4-ClC_6H_4I	$(CH_3)_2CHCN$	H	4-ClC_6H_4	48
16	4-ClC_6H_4I	$(CH_3)_2CHCN$	H	4-$O_2NC_6H_4$	50
17	PhI	$(CH_3)_2CHCN$	CH_3	Ph	26
18	PhI	$(CH_3)_2CHCN$	$CH_3(CH_2)_6$	Ph	28
19[b]	PhI	PhCN	H	Ph	14

[a] Isolated yield.
[b] Reaction temperature was 150 °C.

propiophenone, respectively, as shown in Table 3 (entries 1–5). However, the same treatment with nonanophenone gave 2-ethyl-4-heptyl-5-phenyloxazole in low yield (entry 6). When butyronitrile and isobutyronitrile, instead of acetonitrile, were used under the same conditions, the corresponding 2-propyl-5-aryloxazoles and 2-isopropyl-5-aryloxazoles were obtained in moderate yields (entries 7–18). Again, the same treatment with nonanophenone provided 2-propyl-4-heptyl-5-phenyloxazole and 2-isopropyl-4-heptyl-5-phenyloxazole in low yields, respectively (entries 12 and 18). When benzonitrile was used as the nitrile source, the yield of 2,5-diphenyloxazole was low due to the low nucleophilicity of the nitrogen atom in benzonitrile even if the reaction was conducted at high temperature (entry 19).

The proposed reaction mechanism is shown in Scheme 1. Iodoarene is oxidized to aryliodonium species **A** by Oxone® and TfOH, and **A** reacts with the enolate form of ketone to generate the corresponding β-keto iodonium species **B**. Then, β-keto iodonium species **B** reacts with nitrile to provide the oxazole through intermediate **C**. As an evidence for the formation of β-keto iodonium species **B**, α-tosyloxyacetophenone was obtained in 84% yield, when a mixture of PhI (1 mmol), Oxone® (1.5 mmol), acetophenone (1 mmol), and *p*-TsOH·H_2O (5 mmol) in acetonitrile (4 mL) was warmed at 60 °C for 5 h.



Scheme 1. Proposed reaction mechanism.

3. Conclusion

2-Methyl-5-aryloxazoles, 2-ethyl-5-aryloxazoles, 2-propyl-5-aryloxazoles, 2-isopropyl-5-aryloxazoles, and 2,4-disubstituted 5-aryloxazoles were efficiently obtained in moderate yields in a one-pot manner from the reaction of alkyl aryl ketones with Oxone® and TfOH in the presence of iodoarene in acetonitrile, propionitrile, butyronitrile, and isobutyronitrile, respectively. Here, iodoarene worked as a catalyst. The advantages of iodoarene-mediated reactions with Oxone® are that the oxidative reactions can be carried out under metal-free conditions and that Oxone® is an inorganic oxidant and is much less expensive than *m*CPBA.

4. Experimental section

4.1. General

^{1}H NMR and ^{13}C NMR spectra were obtained with JEOL-JNM-GSX-400, JEOL-JNM-LA-400, and JEOL-JNM-LA-500 spectrometers. Chemical shifts are expressed in parts per million downfield from TMS in δ units. Mass spectra were recorded on JEOL-HX-110 and JEOL-JMS-ATII15 spectrometers. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel 60 (Kanto Kagaku Co.) was used for column chromatography and Wakogel B-5F was used for preparative TLC.

4.2. Typical procedure for one-pot preparation of 2-methyl-5-phenyloxazole with iodobenzene and Oxone® in acetonitrile

To a mixture of iodobenzene (purity 98%, 1.1 mmol, 228 mg) and Oxone® ($KHSO_5$ 45%, 1.5 mmol, 507 mg) in CH_3CN (6 mL) was added TfOH (2.0 mmol, 0.17 mL) at 0 °C. The obtained mixture was stirred for 2 h at 0 °C under an argon atmosphere. Then, a solution of acetophenone (purity 98.5%, 1.0 mmol, 122 mg) in CH_3CN (2 mL) was added and the mixture was stirred for 4 h under refluxing conditions. After the reaction, the reaction mixture was poured into satd aq Na_2SO_3 solution and extracted with $CHCl_3$ (3×20 mL). The organic layer was dried over Na_2SO_4. After filtration and removal of the solvent under reduced pressure, the residue was purified by preparative TLC on silica gel (eluent: hexane–EtOAc=5:1) to give 2-methyl-5-phenyloxazole in 63% yield.

4.2.1. 2-Methyl-5-phenyloxazole. Mp 57–58.5 °C (lit.[9] mp 57–58 °C). IR (KBr): 1580, 1560, 1480 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.53 (s, 3H), 7.20 (s, 1H), 7.30 (tt, *J*=1.5, 7.8 Hz, 1H), 7.40 (t, *J*=7.8 Hz, 2H), 7.60 (dd, *J*=1.5, 7.8 Hz, 2H). MS (FAB): *m*/*z*=160 [M+H].

4.2.2. 2-Methyl-5-(4′-chlorophenyl)oxazole. Mp 71–72 °C (lit.[10] mp 74–75.5 °C). IR (KBr): 3060, 1580, 1560, 1480, 1090, 820 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.53 (s, 3H, s), 7.20 (s, 1H), 7.38 (d, *J*=8.9 Hz, 2H), 7.54 (d, *J*=8.9 Hz, 2H).

4.2.3. 2-Methyl-5-(4′-nitrophenyl)oxazole. Mp 161–162 °C (lit.[11] mp 167–168 °C). IR (KBr): 3020, 1610, 1560, 1500, 1350, 1330, 1130, 1110, 1060, 940, 850, 760 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.58 (s, 3H), 7.42 (s, 1H), 7.76 (d, *J*=9.0 Hz, 2H), 8.28 (d, *J*=9.0 Hz, 2H). MS (FAB): *m*/*z*=205 [M+H].

4.2.4. 2-Methyl-5-(4′-methylphenyl)oxazole. Mp 54–55 °C (lit.[11] mp 56–57 °C). IR (KBr): 1580, 1560, 1500, 1460, 1380 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.37 (s, 3H), 2.52 (s, 3H), 7.15 (s, 1H), 7.21 (d, *J*=8.1 Hz, 2H), 7.49 (d, *J*=8.1 Hz, 2H).

4.2.5. 2,4-Dimethyl-5-phenyloxazole. Mp 43–44 °C. IR (Nujol): 1450, 1380, 770, 760, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.37 (s, 3H), 2.48 (s, 3H), 7.29 (t, *J*=7.5 Hz, 1H), 7.42 (t, *J*=7.5 Hz, 2H), 7.57 (d, *J*=7.5 Hz, 2H). MS (FAB): *m*/*z*=174 [M+H]. HRMS: calcd for $C_{13}H_{24}NO$: 174.0913; found: 174.0913.

4.2.6. 2-Methyl-4-heptyl-5-phenyloxazole. Oil. IR (neat): 2930, 2860, 1720, 1240, 760, 690 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.87 (t, *J*=6.9 Hz, 3H), δ=1.20–1.43 (m, 8H), 1.72 (m, 2H), δ=2.49 (s, 3H), 2.60 (t, *J*=7.9 Hz, 2H), 7.30 (t, *J*=7.4 Hz, 1H), 7.42 (t, *J*=7.4 Hz, 2H), 7.56 (d, *J*=7.4 Hz, 2H). MS (FAB): *m*/*z*=258 [M+H]. HRMS: calcd for $C_{17}H_{24}NO$: 258.1858; found: 258.1864.

4.2.7. 2-Ethyl-5-phenyloxazole. Oil. IR (neat): 3060, 2980, 2940, 1580, 1560, 1490, 1450, 760, 690 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$):

δ=1.40 (t, J=7.6 Hz, 3H), 2.86 (q, J=7.6 Hz, 2H), 7.22 (s, 1H), 7.30 (tt, J=1.4, 7.6 Hz, 1H), 7.40 (dd, J=7.6, 8.0 Hz, 2H), 7.61 (dd, J=1.4, 8.0 Hz, 2H). HRMS: m/z [M+H] calcd for $C_{11}H_{12}NO$: 174.0919; found: 174.0922.

4.2.8. 2-Ethyl-5-(4′-chlorophenyl)oxazole. Oil. IR (neat): 1570, 1560, 1490, 1130, 1090, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.38 (t, J=7.7 Hz, 3H), 2.85 (q, J=7.7 Hz, 2H), 7.20 (s, 1H), 7.37 (d, J=8.5 Hz, 2H), 7.53 (d, J=8.5 Hz, 2H). MS (FAB): m/z=210 [M+H]. HRMS: m/z [M+H] calcd for $C_{12}H_{12}NOCl$: 208.0529; found: 208.0521.

4.2.9. 2-Ethyl-5-(4′-nitrophenyl)oxazole. Mp 81–82 °C (lit.[9] mp 85–86 °C). IR (KBr): 3120, 2990, 1620, 1560, 1500, 1330, 750 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.42 (t, J=7.6 Hz, 3H), 2.90 (q, J=7.6 Hz, 2H), 7.44 (s, 1H), 7.76 (d, J=9.0 Hz, 2H), 8.28 (d, J=9.0 Hz, 2H).

4.2.10. 2-Ethyl-5-(4′-methylphenyl)oxazole. Mp 54–55 °C (lit.[11] mp 56–57 °C). IR (KBr): 1580, 1560, 1500, 1460, 1380 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.40 (t, J=7.6 Hz, 3H), 2.37 (s, 3H), 2.85 (q, J=7.6 Hz, 2H), 7.16 (s, 1H), 7.21 (d, J=8.1 Hz, 2H), 7.49 (d, J=8.1 Hz, 2H). MS (FAB) m/z=188 [M+H]. HRMS: m/z [M+H] calcd for $C_{13}H_{15}NO$: 188.1075; found: 188.1063.

4.2.11. 2-Ethyl-4-methyl-5-phenyloxazole. Oil. IR (neat): 1570, 1500, 1240, 1020, 760, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.38 (t, J=7.6 Hz, 3H), 2.38 (s, 3H), 2.82 (q, J=7.6 Hz, 2H), 7.29 (t, J=8.0 Hz, 1H), 7.42 (t, J=8.0 Hz, 2H), 7.58 (d, J=8.0 Hz, 2H). MS (FAB): m/z=188 [M+H]. HRMS: m/z [M+H] calcd for $C_{13}H_{15}NO$: 188.1075; found: 188.1073.

4.2.12. 2-Ethyl-4-heptyl-5-phenyloxazole. Oil. IR (neat): 2960, 2930, 2860, 1460, 760, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=0.89 (t, J=7.9 Hz, 3H), 1.20–1.45 (m, 11H), 1.72 (m, 2H), 2.71 (t, J=7.9 Hz, 2H), 2.82 (q, J=7.6 Hz, 2H), 7.49 (t, J=7.6 Hz, 1H), 7.42 (t, J=7.6 Hz, 2H), 7.56 (d, J=7.6 Hz, 2H). MS (FAB): m/z=272 [M+H]. HRMS: m/z [M+H] calcd for $C_{18}H_{25}NO$: 272.2014; found: 272.2013.

4.2.13. 2-Propyl-5-phenyloxazole. Oil. IR (neat): 2970, 1560, 760, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.04 (t, J=7.3 Hz, 3H), 1.85 (m, 2H), 2.81 (t, J=7.4 Hz, 2H), 7.22 (s, 1H), 7.30 (t, J=7.5 Hz, 1H), 7.40 (t, J=7.5 Hz, 2H), 7.62 (d, J=7.5 Hz, 2H). MS (FAB): m/z=188 [M+H]. HRMS: m/z [M+H] calcd for $C_{12}H_{14}NO$: 188.1075; found: 188.1064.

4.2.14. 2-Propyl-5-(4′-chlorophenyl)oxazole. Mp 29–30 °C. IR (Nujol): 1560, 1490, 1460, 1020, 1090, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.04 (t, J=7.3 Hz, 3H), 1.85 (m, 2H), 2.80 (t, J=7.6 Hz, 2H), 7.22 (s, 1H), 7.38 (d, J=8.6 Hz, 2H), 7.54 (d, J=8.6 Hz, 2H). MS (FAB): m/z=222 [M+H]. HRMS: m/z [M+H] calcd for $C_{12}H_{13}NOCl$: 222.0686; found: 222.0697.

4.2.15. 2-Propyl-5-(4′-nitrophenyl)oxazole. Mp 74–75 °C. IR (Nujol): 1610, 1510, 1460, 1330, 850 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.05 (t, J=7.4 Hz, 3H), 1.88 (m, 2H), 2.85 (t, J=7.5 Hz, 2H), 7.44 (s, 1H), 7.76 (d, J=7.9 Hz, 2H), 7.58 (d, J=7.9 Hz, 2H). MS (FAB): m/z=233 [M+H]. HRMS: m/z [M+H] calcd for $C_{12}H_{13}N_2O_3$: 233.0926; found: 233.0927.

4.2.16. 2-Propyl-5-(4′-methylphenyl)oxazole. Oil. IR (neat): 3130, 1700, 1500, 810 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.03 (t, J=7.5 Hz, 3H), 1.85 (m, 2H), 2.37 (s, 3H), 2.80 (t, J=7.6 Hz, 2H), 7.16 (s, 1H), 7.21 (d, J=8.0 Hz, 2H), 7.50 (d, J=8.0 Hz, 2H). MS (FAB): m/z=202 [M+H]. HRMS: m/z [M+H] calcd for $C_{13}H_{16}NO$: 202.1226; found: 202.1226.

4.2.17. 2-Propyl-4-methyl-5-phenyloxazole. Oil. IR (neat): 2970, 1700, 1570, 1020, 760, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.03 (t, J=7.3 Hz, 3H), 1.85 (m, 2H), 2.41 (s, 3H), 2.78 (t, J=7.6 Hz, 2H), 7.30 (t, J=7.5 Hz, 1H), 7.42 (t, J=7.5 Hz, 2H), 7.58 (d, J=7.5 Hz, 2H). MS (FAB): m/z=202 [M+H]. HRMS: m/z [M+H] calcd for $C_{13}H_{16}NO$: 202.1226; found: 202.1226.

4.2.18. 2-Propyl-4-heptyl-5-phenyloxazole. Oil. IR (neat): 2928, 2856, 1568, 1495, 1464, 1283, 1011, 764, 693 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=0.87 (t, J=6.8 Hz, 3H), 1.02 (t, J=7.5 Hz, 3H), 1.21–1.45 (m, 8H), 1.72 (m, 2H), 1.84 (m, 2H), 2.71 (t, J=8.0 Hz, 2H), 2.76 (t, J=7.4 Hz, 2H), 7.29 (t, J=7.5 Hz, 1H), 7.42 (t, J=8.0 Hz, 2H), 7.56 (d, J=7.0 Hz, 2H). HRMS: m/z [M+H] calcd for $C_{19}H_{28}NO$: 286.2171; found: 286.2160.

4.2.19. 2-Isopropyl-5-phenyloxazole. Oil. IR (neat): 2970, 1560, 1240, 760, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.41 (d, J=7.0 Hz, 6H), 3.15 (septet, J=7.0 Hz, 1H), 7.21 (s, 1H), 7.30 (t, J=7.5 Hz, 1H), 7.40 (t, J=7.5 Hz, 2H), 7.62 (d, J=7.5 Hz, 2H). MS (FAB): m/z=188 [M+H]. HRMS: m/z [M+H] calcd for $C_{12}H_{14}NO$: 188.1075; found: 188.1068.

4.2.20. 2-Isopropyl-5-(4′-chlorophenyl)oxazole. Oil. IR (neat): 2970, 1550, 1490, 1090, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.40 (d, J=7.7 Hz, 6H), 3.15 (septet, J=7.7 Hz, 1H), 7.21 (s, 1H), 7.38 (t, J=8.8 Hz, 2H), 7.55 (t, J=8.8 Hz, 2H). MS (FAB): m/z=222 [M+H]. HRMS: m/z [M+H] calcd for $C_{12}H_{13}NOCl$: 222.0686; found: 222.0698.

4.2.21. 2-Isopropyl-5-(4′-nitrophenyl)oxazole. Mp 52–53 °C. IR (Nujol): 1580, 1460, 1350, 850 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.43 (d, J=7.1 Hz, 6H), 3.20 (septet, J=7.1 Hz, 1H), 7.44 (s, 1H), 7.77 (d, J=8.0 Hz, 2H), 8.28 (d, J=8.0 Hz, 2H). MS (FAB): m/z=233 [M+H]. HRMS: m/z [M+H] calcd for $C_{12}H_{13}N_2O_3$: 233.0926; found: 233.0919.

4.2.22. 2-Isopropyl-5-(4′-methylphenyl)oxazole. Oil. IR (neat): 2970, 1700, 1560, 1510, 810 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.39 (d, J=7.3 Hz, 6H), 2.40 (s, 3H), 3.11 (septet, J=7.3 Hz, 1H), 7.28 (t, J=7.3 Hz, 1H), 7.42 (t, J=7.9 Hz, 2H), 7.58 (d, J=7.9 Hz, 2H). MS (FAB): m/z=202 [M+H]. HRMS: m/z [M+H] calcd for $C_{13}H_{16}NO$: 202.1226; found: 202.1226.

4.2.23. 2-Isopropyl-4-methyl-5-phenyloxazole. Oil. IR (neat): 2970, 1560, 760, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=1.38 (d, J=7.0 Hz, 6H), 2.40 (s, 3H), 3.10 (septet, J=7.0 Hz, 1H), 7.28 (t, J=7.8 Hz, 1H), 7.42 (t, J=7.8 Hz, 2H), 7.54 (d, J=7.8 Hz, 2H). MS (FAB): m/z=202 [M+H]. HRMS: m/z [M+H] calcd for $C_{13}H_{16}NO$: 202.1226.

4.2.24. 2,5-Diphenyloxazole. Mp 61 °C (lit.[12] mp 72 °C). IR (Nujol): 1589, 1546, 1446, 1349, 1247, 1133, 1070, 1027, 953, 822, 758, 711 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=7.35 (t, J=7.5 Hz, 1H), 7.41–7.52 (m, 6H), 7.73 (d, J=7.3 Hz, 2H), 8.12 (dd, J=1.7, 8.1 Hz, 2H).

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