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Iodoarene-catalyzed one-pot preparation of 2,4,5-trisubstituted oxazoles from alkyl aryl ketones with *m*CPBA in nitriles

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ABSTRACT

2,4,5-Trisubstituted oxazoles could be easily prepared in moderate yields by the reaction of alkyl aryl ketones, iodoarene, *m*-chloroperbenzoic acid, and trifluoromethanesulfonic acid in acetonitrile, propionitrile, butyronitrile, and isobutyronitrile, respectively. Here, reactive aryliodonium I(III) species is formed in situ by the reaction of iodoarene with *m*CPBA and trifluoromethanesulfonic acid, and the formed aryliodonium I(III) species reacts with alkyl aryl ketone to form β-keto aryliodonium species. This in turn, reacts with nitrile to form the corresponding oxazole. Iodoarene works as a catalyst. However, one equivalent of iodoarene is required because one equivalent of reactive aryliodonium I(III) species must be formed prior to the reaction with alkyl aryl ketone. Then, by introducing an ionic liquid group into iodoarene, to form ionic liquid-supported iodoarene, the isolation procedure of oxazole could be simplified. The addition of ethyl acetate to the reaction mixture, washing of the reaction mixture with aq $NaHCO_3$, removal of ethyl acetate, and extraction of the residue with ether provided oxazoles in moderate purity, and the residual ionic liquid-supported iodoarene could be reused in the same reaction.

1. Introduction

The oxazole group is one of the key units of biologically active natural products, including diazonamides, inthomycins, calyculins, and phorboxazoles, and has been extensively used in medicinal chemistry.[1] One of the simplest and most direct 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] To the best of our knowledge, there are three methods for the direct preparation of oxazoles from ketones with nitriles, which use copper(II) trifluoromethanesulfonate,[2] thallium(III) trifluoromethanesulfonate,[3] and mercury(II) *p*-toluenesulfonate.[4] As less toxic and efficient methods, the preparation of 2,5-disubstituted oxazoles from aryl methyl ketones using (diacetoxyiodo)benzene with trifluoromethanesulfonic acid (TfOH) in acetonitrile[5] and the preparation of 2,4,5-trisubstituted oxazoles from carbonyl compounds using [(hydroxy)(2,4-dinitrobenzenesulfonyloxy)iodo]benzene with amides under solvent-free microwave irradiation conditions[6] were reported recently. In particular, the former method is useful for the direct preparation of 2,4,5-trisubstituted oxazoles in nitrile solvents. On the other hand, recently, PhI-catalyzed reactions with *m*-chloroperbenzoic acid (*m*CPBA) or other oxidants have become popular.[7] We have also reported the direct one-pot preparation of [(hydroxy)(sulfonyloxy)-iodo]arenes from iodoarenes with *m*CPBA and sulfonic acids at room temperature,[8] the PhI-catalyzed α-tosyloxylation of ketones with *m*CPBA and *p*-toluenesulfonic acid,[9] and the efficient conversion of ketones into α-tosyloxyketones with *m*CPBA and *p*-toluenesulfonic acid in the presence of a catalytic amount of IL (ionic liquid)-supported PhI in [emim]OTs (1-ethyl-3-methylimidazolium tosylate).[10]

Here, as part of our series of studies on organic synthesis using PhI-catalyzed systems with *m*CPBA, we would like to report the PhI-catalyzed direct preparation of 2,5-disubstituted and 2,4,5-trisubstituted oxazoles from alkyl aryl ketones with TfOH and *m*CPBA in acetonitrile, propionitrile, butyronitrile, and isobutyronitrile, respectively.[11]

2. Results and disscussion

To an acetonitrile solution were added iodoarene (1.1 equiv), *m*CPBA (1.1 equiv), and TfOH (2.0 equiv), and the mixture was stirred for 0.5 h–2 h depending on the substrate to generate the corresponding arene iodonium species. Then, a solution of acetophene (1.0 equiv) in acetonitrile (2 mL) was added and the obtained mixture was refluxed for 2 h–4 h to provide the corresponding 2-methyl-5-phenyloxazole. First, the effect of iodoarenes with *m*CPBA, acetophenone, and TfOH was studied using iodobenzene, 4-iodotoluene, 4-chloroiodobenzene, 4-iodoanisole, 1-iodonaphthalene, 4,4′-diiodobiphenyl, 1,4-bis(4′-iodophenyl)benzene, and poly(4-iodostyrene), as shown in Table 1 (entries 2–9). In the

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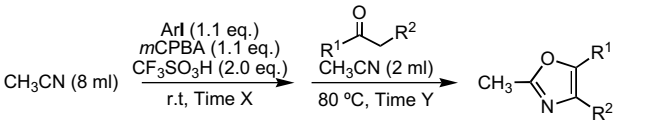
Table 1
Preparation of oxazoles from ketones in acetonitrile

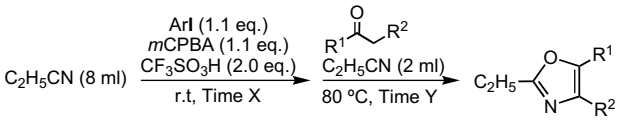


Entry	ArI	R^1	R^2	Time *X* (h)	Time *Y* (h)	Yield[a] (%)
1	—	Ph	H	0.5	2	0
2	PhI	Ph	H	0.5	2	56
3	4-$CH_3C_6H_4I$	Ph	H	2	2	60
4	4-ClC_6H_4I	Ph	H	1	2	54
5	4-$CH_3OC_6H_4I$	Ph	H	2	2	0
6		Ph	H	2	2	0
7		Ph	H	2	2	17
8		Ph	H	2	2	14
9		Ph	H	2	2	35
10	PhI	4-$CH_3C_6H_4$	H	0.5	2	64
11	4-$CH_3C_6H_4I$	4-$CH_3C_6H_4$	H	2	2	58
12	4-ClC_6H_4I	4-$CH_3C_6H_4$	H	1	2	63
13	PhI	4-ClC_6H_4	H	0.5	2	61
14	4-$CH_3C_6H_4I$	4-ClC_6H_4	H	2	2	54
15	4-ClC_6H_4I	4-ClC_6H_4	H	1	2	57
16	PhI	4-$O_2NC_6H_4$	H	0.5	2	77
17	4-$CH_3C_6H_4I$	4-$O_2NC_6H_4$	H	2	2	48
18	4-ClC_6H_4I	4-$O_2NC_6H_4$	H	1	2	68[b]
19	PhI	Ph	CH_3	0.5	2	66
20	4-$CH_3C_6H_4I$	Ph	CH_3	2	2	58
21	4-ClC_6H_4I	Ph	CH_3	1	2	55
22	PhI	Ph	C_7H_{15}	0.5	3	50
23	4-$CH_3C_6H_4I$	Ph	C_7H_{15}	2	3	44
24	4-ClC_6H_4I	Ph	C_7H_{15}	1	3	45

[a] Isolated yield.
[b] 4-Chloroiodobenzene was recovered in 100% yield.

absence of iodoarene, 2-methyl-5-phenyloxazole was not formed at all and acetophenone was recovered in ca. 70% yield (entry 1). However, in the presence of iodoarene, 2-methyl-5-phenyloxazole was formed in moderate yields (54–60%) in a one-pot manner, especially with iodobenzene, 4-iodotoluene, and 4-chloroiodobenzene (entries 2–4). When 4-iodoanisole or 1-iodonaphthalene was used, the reaction generated black tar species without the formation of 2-methyl-5-phenyloxazole, whereas when 4,4′-diiodobiphenyl, 1,4-bis(4′-iodophenyl)benzene, or poly(4-iodostyrene) was used, the yield of 2-methyl-5-phenyloxazole was low due to the low solubility in acetonitrile. Based on these results, 2-methyl-5-(4′-methylphenyl)oxazole (entries 10–12), 2-methyl-5-(4′-chlorophenyl)oxazole (entries 13–15), and 2-methyl-5-(4′-nitrophenyl)oxazole (entries 16–18) were obtained in moderate yields from 4-methylacetophenone, 4-chloroacetophenone, and 4-nitroacetophenone, respectively. When propiophenone and nonanophenone were used under the same conditions, 2,4-dimethyl-5-phenyloxazole (entries 19–21) and 2-methyl-4-heptyl-5-phenyloxazole (entries 22–24) were obtained in moderate yields. Here, iodoarene worked as a catalyst and in the reaction of 4-chloroiodobenzene, *m*CPBA, and TfOH with 4-nitroacetophenone in acetonitrile, 4-chloroiodobenzene was recovered in 100% yield, together with 2-methyl-5-(4′-nitrophenyl)oxazole (entry 18). Other iodoarenes, such as iodobenzene and 4-iodotoluene, were

Table 2
Preparation of oxazoles from ketones in propionitrile



Entry	ArI	R^1	R^2	Time *X* (h)	Time *Y* (h)	Yield[a] (%)
1	PhI	Ph	H	0.5	2	51
2	4-$CH_3C_6H_4I$	Ph	H	2	2	68
3	4-ClC_6H_4I	Ph	H	1	2	61
4	PhI	4-$CH_3C_6H_4$	H	0.5	2	33
5	4-$CH_3C_6H_4I$	4-$CH_3C_6H_4$	H	2	2	45
6	4-ClC_6H_4I	4-$CH_3C_6H_4$	H	1	2	39
7	PhI	4-ClC_6H_4	H	0.5	2	48
8	4-$CH_3C_6H_4I$	4-ClC_6H_4	H	2	2	42
9	4-ClC_6H_4I	4-ClC_6H_4	H	1	2	63
10	PhI	4-$O_2NC_6H_4$	H	0.5	2	40
11	4-$CH_3C_6H_4I$	4-$O_2NC_6H_4$	H	2	2	55
12	4-ClC_6H_4I	4-$O_2NC_6H_4$	H	1	2	78[b]
13	PhI	Ph	CH_3	0.5	2	59
14	4-$CH_3C_6H_4I$	Ph	CH_3	2	2	55
15	4-ClC_6H_4I	Ph	CH_3	1	2	52
16	PhI	Ph	C_7H_{15}	0.5	2	22
17	4-$CH_3C_6H_4I$	Ph	C_7H_{15}	2	2	36
18	4-ClC_6H_4I	Ph	C_7H_{15}	1	2	30

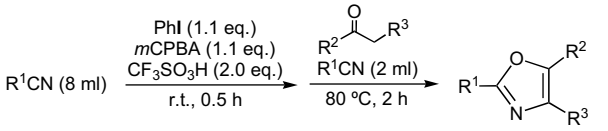
[a] Isolated yield.
[b] 4-Chloroiodobenzene was recovered in 97% yield.

also recovered in high yields. Under the present conditions, dialkyl ketones gave the corresponding oxazoles in low yields (~10%).

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, and 2-ethyl-5-(4′-nitrophenyl)oxazole were obtained in moderate yields from acetophenone, 4-methylacetophenone, 4-chloroacetophenone, and 4-nitroacetophenone, respectively, as shown in Table 2 (entries 1–12). 2-Ethyl-4-methyl-5-phenyloxazole and 2-ethyl-4-heptyl-5-phenyloxazole were obtained in moderate yields when propiophenone and nonanophenone were used instead of aryl methyl ketones under the same conditions (entries 13–18). In entry 12, 4-chloroiodobenzene was recovered in 97% yield as a catalyst, together with 2-ethyl-5-(4′-nitrophenyl)oxazole in 78% yield.

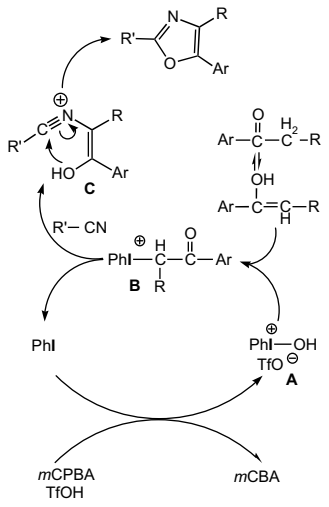
The same reaction was carried out in butyronitrile and isobutyronitrile instead of acetonitrile using iodobenzene and *m*CPBA, as shown in Table 3. Corresponding 2-propyl-5-aryloxazoles were obtained in moderate yields; however, 2-isopropyl-5-aryloxazoles were obtained in moderate to low yields, probably due to steric hindrance.

Table 3
Preparation of oxazoles from ketones in butyronitrile and isobutyronitrile



Entry	R^1	R^2	R^3	Yield[a] (%)
1	$CH_3CH_2CH_2$	Ph	H	74
2	$CH_3CH_2CH_2$	Ph	CH_3	50
3	$CH_3CH_2CH_2$	4-$CH_3C_6H_4$	H	74
4	$CH_3CH_2CH_2$	4-ClC_6H_4	H	48
5	$CH_3CH_2CH_2$	4-$O_2NC_6H_4$	H	59
6	$(CH_3)_2CH$	Ph	H	36
7	$(CH_3)_2CH$	Ph	CH_3	41
8	$(CH_3)_2CH$	4-$CH_3C_6H_4$	H	27
9	$(CH_3)_2CH$	4-ClC_6H_4	H	38
10	$(CH_3)_2CH$	4-$O_2NC_6H_4$	H	28

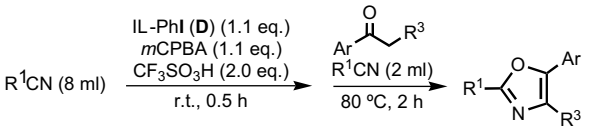
[a] Isolated yield.



Scheme 1. Proposed reaction pathway.

The proposed reaction pathway is shown in Scheme 1. Iodoarene is oxidized to aryliodonium species **A** by *m*CPBA and TfOH, and **A** reacts with the enolate form of ketone to form corresponding α-keto iodonium species **B**. Finally, β-keto iodonium species **B** reacts with nitrile to provide the oxazole through intermediate **C**.

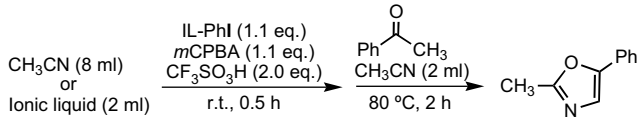
Table 5
Preparation of Oxazoles Using IL-Supported PhI **D**



Entry	R^1	R^2	R^3	Yield[a] (%)
1	CH_3	Ph	CH_3	62
2	CH_3	4-$CH_3C_6H_4$	H	57
3	CH_3	4-ClC_6H_4	H	61
4	CH_3	4-$O_2NC_6H_4$	H	73
5	CH_3	Ph	$(CH_2)_6CH_3$	29
6	CH_3CH_2	Ph	H	45
7	CH_3CH_2	Ph	CH_3	49
8	CH_3CH_2	4-$CH_3C_6H_4$	H	45
9	CH_3CH_2	4-ClC_6H_4	H	78
10	CH_3CH_2	4-$O_2NC_6H_4$	H	59
11	$CH_3CH_2CH_2$	Ph	H	58
12	$CH_3CH_2CH_2$	Ph	CH_3	64
13	$CH_3CH_2CH_2$	4-$CH_3C_6H_4$	H	42
14	$CH_3CH_2CH_2$	4-ClC_6H_4	H	38
15	$CH_3CH_2CH_2$	4-$O_2NC_6H_4$	H	73
16	$(CH_3)_2CH$	Ph	H	51
17	$(CH_3)_2CH$	Ph	CH_3	69
18	$(CH_3)_2CH$	4-$CH_3C_6H_4$	H	41
19	$(CH_3)_2CH$	4-ClC_6H_4	H	55
20	$(CH_3)_2CH$	4-$O_2NC_6H_4$	H	59

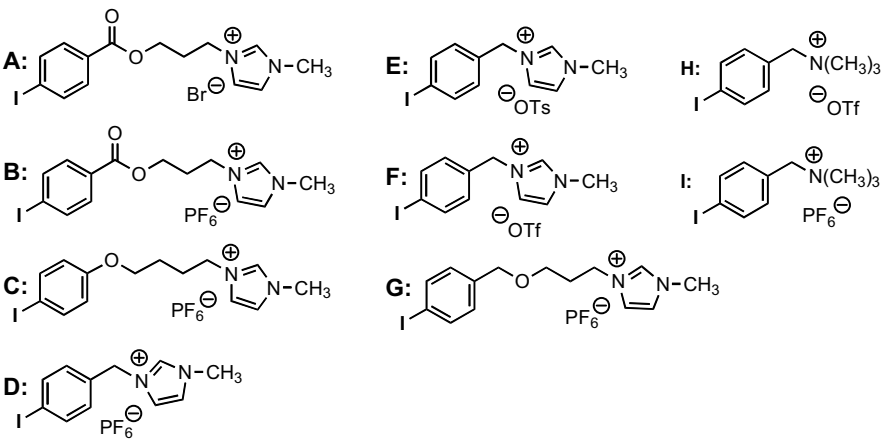
[a] Isolated yield.

Table 4
Preparation of oxazoles using IL-supported PhI



Entry	Solvent	IL-PhI	Yield[a] (%)
1	CH_3CN	**A**	0
2	CH_3CN	**B**	44
3	CH_3CN	**C**	0
4	CH_3CN	**D**	59, 50[b]
5	CH_3CN	**E**	<5
6	CH_3CN	**F**	23
7	CH_3CN	**G**	39
8	CH_3CN	**H**	34
9	CH_3CN	**I**	48
10	[emim]OTs	**D**	0
11	[bmim]PF_6	**D**	33
12	[bmpy]NTf_2	**D**	45

[a] Isolated yield.
[b] First recovered IL-PhI was used.



To extend this catalytic reaction, the one-pot preparation of oxazoles with IL-supported PhI was carried out. Ionic liquids (ILs) have become very popular as organic reaction media due to their ability to promote ionic reactions and their recyclability. ILs possess interesting and useful advantages for organic reactions, such as low vapor pressure, low flammability, high thermal stability, easy reusability, and easy separation of product from reaction media.[12]

The results of the reactions of acetonitrile, *m*CPBA, TfOH, and acetophenone are shown in Table 4, using various IL-supported iodoarenes (IL-supported PhIs). The reactivities of IL-supported PhIs **A**–**I** are shown in entries 1–9, and IL-suppported PhI **D** showed the best reactivity. Instead of acetonitrile as solvent, room temperature ILs, such as [emim]OTs, [bmim]PF_6, and [bmpy]NTf_2, were used in the present IL-supported PhI **D** (entries 10–12). However, [emim]OTs did not promote the oxazole formation at all, while [bmim]PF_6 and [bmpy]NTf_2 provided the oxazole in moderate to low yields. Thus, use of acetonitrile as solvent yielded the best reactivity as compared with these ILs.

Based on the above results, alkyl aryl ketones were treated with *m*CPBA and TfOH in the presence of IL-supported PhI **D** in acetonitrile, propionitrile, butyronitrile, and isobutyronitrile, to provide the corresponding oxazoles in moderate yields, as shown in Table 5. Here, the addition of ethyl acetate to the reaction mixture, washing with aq $NaHCO_3$, the removal of ethyl acetate, and the extraction of the residue with ether provided oxazoles in moderate purity (>70%), and the residual IL-supported PhI could be reused in the same reaction to obtain a moderate yield of oxazole, as shown in Table 4 (entry 4). Here, purity of the recovered IL-supported PhI was over 90%.

3. Conclusion

In conclusion, 2-methyl-5-aryloxazoles, 2-ethyl-5-aryloxazoles, 2-propyl-5-aryloxazoles, 2-isopropyl-5-aryloxazoles, and 2,4-disubstituted 5-aryloxazoles were smoothly and efficiently obtained in moderate yields in a one-pot manner from the reaction of alkyl aryl ketones with iodoarene, *m*CPBA, and TfOH in acetonitrile, propionitrile, butyronitrile, and isobutyronitrile, respectively. Here, iodoarene worked as a catalyst. IL-supported PhI could be also used in the same preparation of oxazoles from ketones and could be reused in the same reaction to obtain moderate yields of oxazoles.

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

To a mixture of iodobenzene (purity 98%, 1.1 mmol, 228 mg) and *m*CPBA (purity 65%, 292 mg) in CH_3CN (8 mL) was added TfOH (2.0 mmol, 0.17 mL). The obtained mixture was stirred for 0.5 h at rt 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 2 h under refluxing conditions. After the reaction, the reaction mixture was poured into satd aq $NaHCO_3$ solution and extracted with $CHCl_3$ (3×30 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 56% yield.

4.3. Typical procedure for one-pot preparation of 2-methyl-5-phenyloxazole with IL-supported PhI D

To a mixture of IL-supported PhI **D** (1.1 mmol, 488 mg) and *m*CPBA (purity 65%, 292 mg) in CH_3CN (8 mL) was added TfOH (2.0 mmol, 0.17 mL). The obtained mixture was stirred for 0.5 h at rt 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 2 h under refluxing conditions. After the reaction, the reaction mixture was poured into satd aq $NaHCO_3$ solution and extracted with AcOEt (3×30 mL). The organic layer was dried over Na_2SO_4. After filtration and removal of the solvent under reduced pressure, the residue was extracted with Et_2O (10×5 mL) to give crude 2-methyl-5-phenyloxazole (purity>70%). Pure 2-methyl-5-phenyloxazole was obtained in 59% yield by preparative TLC on silica gel (eluent: hexane-EtOAc=5:1).

4.4. Typical procedure for recycling IL-supported PhI D

To a mixture of IL-supported PhI **D** (1.1 mmol, 488 mg) and *m*CPBA (purity 65%, 292 mg) in CH_3CN (8 mL) was added TfOH (2.0 mmol, 0.17 mL). The obtained mixture was stirred for 0.5 h at rt 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 2 h under refluxing conditions. After the reaction, the reaction mixture was poured into satd aq $NaHCO_3$ solution and extracted with AcOEt (3×30 mL). The organic layer was dried over Na_2SO_4. After filtration and removal of the solvent under reduced pressure, the residue was extracted with Et_2O (10×5 mL) to give crude 2-methyl-5-phenyloxazole (purity>70%). The residual IL-supported PhI **D** was dried by a vacuum pump for 1 h, and it was reused in the same reaction, as mentioned above.

4.4.1. 2-Methyl-5-phenyloxazole

Mp 57–58.5 °C (lit.[13] 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].

4.4.2. 2-Methyl-5-(4′-chlorophenyl)oxazole

Mp 71–72 °C (lit.[14] 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).

4.4.3. 2-Methyl-5-(4′-nitrophenyl)oxazole

Mp 161–162 °C (lit.[15] 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].

4.4.4. 2-Methyl-5-(4′-methylphenyl)oxazole

Mp 54–55 °C (lit.[15] 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).

4.4.5. 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.

4.4.6. 2-Methyl-4-heptyl-5-phenyloxazole

Oil. IR (neat): 2930, 2860, 1720, 1240, 760, 690 cm^{-1}. ^1H 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: 250.1864.

4.4.7. 2-Ethyl-5-phenyloxazole

Oil. IR (neat): 3060, 2980, 2940, 1580, 1560, 1490, 1450, 760, 690 cm^{-1}. ^1H 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.

4.4.8. 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.

4.4.9. 2-Ethyl-5-(4′-nitrophenyl)oxazole

Mp 81–82 °C (lit.[13] 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).

4.4.10. 2-Ethyl-5-(4′-methylphenyl)oxazole

Mp 54–55 °C (lit.[15] 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.

4.4.11. 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.

4.4.12. 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.

4.4.13. 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.

4.4.14. 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.

4.4.15. 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.

4.4.16. 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.

4.4.17. 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), δ=1.85 (m, 2H), δ=2.41 (s, 3H), δ=2.78 (t, J=7.6 Hz, 2H), δ=7.30 (t, J=7.5 Hz, 1H), δ=7.42 (t, J=7.5 Hz, 2H), δ=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.

4.4.18. 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.

4.4.19. 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.

4.4.20. 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.

4.4.21. 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), δ=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.

4.4.22. 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; found: 202.1226.

4.4.23. IL-supported PhI ***D***

Mp 99–100 °C. IR (Nujol): 1440, 1380, 1160, 840, 820, 750, 560 cm^{-1}. ^1H NMR (400 MHz, Acetone-d_6): δ=3.95 (s, 3H), 5.45 (s, 2H), 7.19 (d, J=8.5 Hz 2H), 7.63 (d, J=3.4 Hz, 1H), 7.66 (d, J=3.4 Hz, 1H), 7.70 (d, J=8.5 Hz, 2H), 9.00 (s, 1H). E.A Calcd for $C_{11}H_{12}F_6IN_2P$: C, 29.75; H, 2.72; N, 6.31; found: C, 29.88; H, 2.49; N, 6.28.

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References and notes

1. (a) *Comprehensive Heterocyclic Chemistry*; Boyd, G. V., Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 6, Chapter 4.18; (b) *Comprehensive Heterocyclic Chemistry II*; Hartner, F. W., Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Elsevier Science: Oxford, 1996; Vol. 3, Chapter 3.04; (c) Pattenden, G. *J. Heterocycl. Chem.* **1992**, *29*, 607; (d) Michael, J. P.; Pattenden, G. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1; (e) Wipf, P. *Chem. Rev.* **1995**, *95*, 2115; (f) Vedejs, E.; Monahan, S. D. *J. Org. Chem.* **1996**, *61*, 5192; (g) Brain, C. T.; Paul, J. M. *Synlett* **1999**, 1642; (h) Yeh, V. S. C. *Tetrahedron* **2004**, *60*, 11995; (i) Thalhammer, A.; Mecinovic, J.; Schofield, C. J. *Tetrahedron Lett.* **2009**, *50*, 1045.
2. Nagayoshi, K.; Sato, T. *Chem. Lett.* **1983**, *12*, 1355.
3. Lee, J. C.; Hong, T. *Tetrahedron Lett.* **1997**, *38*, 8959.
4. Lee, J. C.; Song, I. G. *Tetrahedron Lett.* **2000**, *41*, 5891.
5. Varma, R. S.; Kumar, D. *J. Heterocycl. Chem.* **1998**, *35*, 1533.
6. Lee, J. C.; Choi, H. J.; Lee, Y. C. *Tetrahedron Lett.* **2003**, *44*, 123.
7. (a) Ochiai, M.; Takeuchi, Y.; Katayama, T.; Sueda, T.; Miyamoto, K. *J. Am. Chem. Soc.* **2005**, *127*, 12244; (b) Dohi, T.; Maruyama, A.; Yoshimura, M.; Morimoto, K.; Tohma, H.; Kita, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 6193; (c) Ochiai, M.; Miyamoto, K. *Eur. J. Org. Chem.* **2008**, 4229.
8. Yamamoto, Y.; Togo, H. *Synlett* **2005**, 2486.
9. (a) Yamamoto, Y.; Togo, H. *Synlett* **2006**, 798; (b) Yamamoto, Y.; Kawano, Y.; Toy, P. H.; Togo, H. *Tetrahedron* **2007**, *63*, 4680.
10. Akiike, J.; Yamamoto, Y.; Togo, H. *Synlett* **2007**, 2168.
11. As a preliminary report: Kawano, Y.; Togo, H. *Synlett* **2008**, 217.
12. Reviews: (a) Welton, T. *Chem. Rev.* **1999**, *99*, 2071; (b) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772; (c) Sheldon, R. *Chem. Commun.* **2001**, 2399; (d) Sheldon, R. A. *Pure Appl. Chem.* **2002**, *72*, 1233; (e) Earle, M. J.; Seddon, K. R. *Pure Appl. Chem.* **2000**, *72*, 1391; (f) Zhao, H.; Malhotra, S. V. *Aldrichimica Acta* **2002**, *35*, 75; (g) Lee, S. *Chem. Commun.* **2006**, 1049; (h) Macfarlane, D. R.; Pringle, J. M.; Johansson, K. M.; Forsyth, S. A.; Forsyth, M. *Chem. Commun.* **2006**, 1905.
13. Lamattina, J. L. *J. Org. Chem.* **1980**, *45*, 2261.
14. Houwing, H. A.; Wildeman, J.; Leusen, A. M. *Tetrahedron Lett.* **1976**, *17*, 143.
15. Ibata, T.; Sato, R. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3597.