Hypervalent Iodine(III) Sulfonate Reagent Mediated Synthesis of 4-Aryl-2-phenyloxazoles in Ionic Liquid

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A new and efficient method for the synthesis of 4-aryl-2-phenyloxazoles is described which is based upon the reaction of α-[(2,4-dinitrobenzene)sulfonyl]oxy ketone intermediates with benzamide in ionic liquid.

Keywords: Hypervalent iodine; Ionic liquid; Oxazoles.

INTRODUCTION

Room temperature ionic liquids (RTIL) are liquids that are composed entirely of ions. In fact, ionic liquids can now be produced which remain liquid at room temperature and below (even as low as -90 °C) and appear to be undemanding and inexpensive to manufacture.[1] Ionic liquids offer an attractive alternative to conventional organic liquids for clean synthesis, as they are easy to recycle, lack flammability, and possess effectively no vapour pressure. Compared with classical molecular solvents, ionic liquids are environmentally benign reaction media.[2] To date some of the more important reactions have been carried out and investigated in ionic liquids, including Friedel-Crafts reaction,[3] alkoxycarbonylation,[4] hydrogenation,[5] Diels-Alder reaction,[6] Wittig reaction,[7] Heck reaction,[8] Trost-Tsuji coupling,[9] ring-closing metathesis (RCM),[10] Suzuki cross-coupling,[11] Fischer indole synthesis,[12] 1,3-dipolar cycloaddition reaction,[13] Beckmann rearrangement,[14] the Knoevenagel condensation, Robinson annulation reactions,[15] etc.

2,4-Substituted oxazoles is a basic building block of several biologically interesting compounds.[16] The reaction of α-halo ketones with amides have been widely used for the preparation of 2,4-substituted oxazoles. However, the method gave only moderate yields with high reaction temperature.[17] Furthermore, it involves the use of α-halo ketones, which are lachrymatory and toxic. Recently, hypervalent iodine(III) reagents have been used extensively in organic synthesis due to their low toxicity, ready availability and easy handling. As a part of our ongoing studies to utilize hypervalent iodine(III) sulfonate reagents in organic synthesis,[18] we now report a new and direct method for the synthesis of 4-aryl-2-phenyloxazoles by the cyclocondensation of benzamide with α-[(2,4-dinitrobenzene)sulfonyl]oxy carbonyl compounds (**2**), formed by the reaction of [hydroxyl(2,4-dinitrobenzenesulfonyloxy)iodo]benzene (HDNIB) with aryl ketones (**1**) (Scheme I). The required HDNIB was prepared in satisfactory yields from the reaction of 2,4-dinitrobenzenesulfonic acid with phenyliodine(III) diacetate (PIDA).[19] Treatment of aromatic ketones with HDNIB in CH_3CN under reflux for 1 h produced the α-[(2,4-dinitrobenzene)sulfonyl]oxy ketone intermediates (**2**). Subsequent cyclocondensation by benzamide in ionic liquid, 1-n-butyl-3-methylimidazolium hexafluorophosphate, [Bmin][PF_6] at 80 °C for 0.5 h gave the corresponding 4-aryl-2-phenyloxazoles (**3**) in good yields.

RESULTS AND DISCUSSION

The 2,4-dinitrobenzenesulfonyloxy group located at the α position to a carbonyl group represents an increasingly important entity in both mechanistic and synthetic organic chemistry. One reason for this importance is that the 2,4-dinitrobenzenesulfonyloxy group is a good leaving group, and this accounts for the considerable synthetic utility associated with these groups in the functionalization of carbonyl compounds.

As shown in Scheme I, our experiments involving a one-pot procedure for the preparation of 4-aryl-2-phenyloxazoles (**3**) by cyclocondensation of benzamide with α-[(2,4-dinitrobenzene)sulfonyl]oxy carbonyl compounds (**2**) in [Bmin][PF_6] at 80 °C were successful. The results are summarized in Table 1. When the reaction was conducted

Scheme I

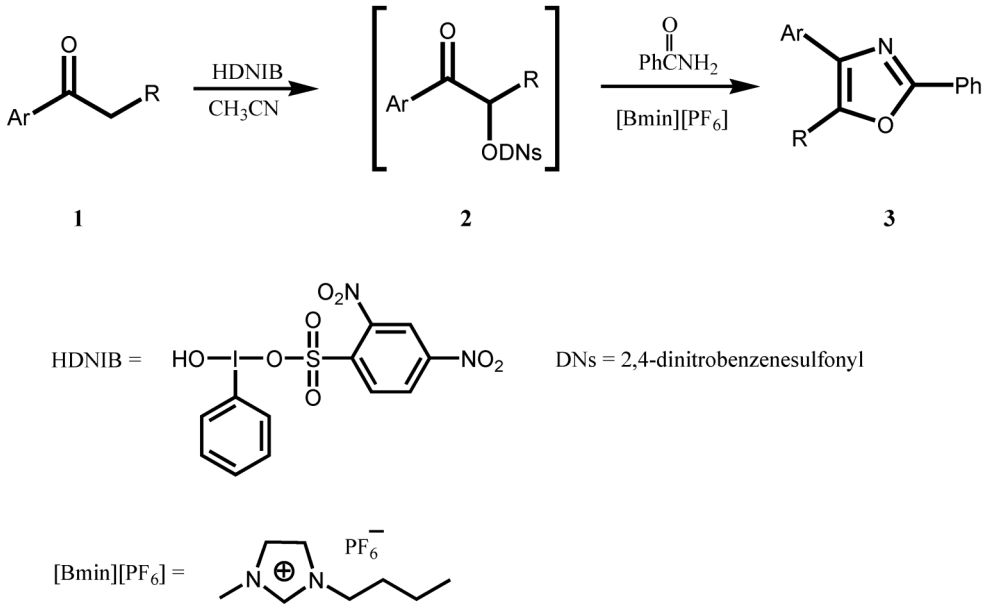

Table 1. Synthesis of 4-aryl-2-phenyloxazole **3a-k**

Entry	Product	Ar	R	Yield (%)
1	**3a**	C_6H_5	H	82
2	**3b**	4-MeC_6H_4	H	77
3	**3c**	4-$MeOC_6H_4$	H	75
4	**3d**	4-FC_6H_4	H	81
5	**3e**	4-ClC_6H_4	H	80
6	**3f**	4-BrC_6H_4	H	83
7	**3g**	3-Furyl	H	76
8	**3h**	3-Thienyl	H	74
9	**3i**	C_6H_5	Me	75
10	**3j**	4-$NO_2C_6H_4$	H	84
11	**3k**	3,4-$Cl_2C_6H_4$	H	82

in the classical molecular solvent, such as acetoniltrile, the preparation of 2,4-diphenyloxazole (**3a**) needs refluxing for 6 h.

The ionic liquid [Bmin][PF_6] can be typically recovered by extracting out the product first and filtering the suspension followed by vacuum drying. The recovered solvent can be reused without any loss of activity.

In summary, our results herein demonstrate that the use of α-[(2,4-dinitrobenzene)sulfonyl]oxy ketone intermediates and benzamide in ionic liquid [Bmin][PF_6] can be performed rapidly to prepare 4-aryl-2-phenyloxazles by cyclocondensation. The ionic liquid plays the dual role of solvent and promoter. Separation of the products from the ionic liquids is very straightforward, as is recycling of the ionic liquid.

EXPERIMENTAL SECTION

All melting points are uncorrected. The IR spectra were recorded on a Shimadzu IR-27 G spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Unity Plus 400 MHz. Chemical shifts (δ) were measured in ppm with respect to TMS. MS were obtained on a JEOL JMS D-300 instrument. Elemental analyses were performed on an EA-1110 instrument.

Typical procedure for the preparation of 2,4-diphenyloxazole (3a)

To a solution of acetophenone (**1a**) (120 mg, 1.0 mmol) in actonitrile (30 mL) was added HDNIB (561 mg, 1.2 mmol) and stirred under refluxing for 1 h. After removing the solvent, benzamide (0.36 g, 3 mmol) was added to [Bmin][PF_6] (2 mL) at 80 °C for 0.5 h. Subsequently, the reaction mixture was extracted with AcOEt. The extract was dried over $MgSO_4$. The solvent was evaporated off and the residue was purified by chromatography on a silica gel column eluting with AcOEt-*n*-hexane (1:5) to give 0.18 g (82%) of **3a**, mp 105-106 °C (lit.[20], 105-106 °C). IR (KBr) ν: 1606, 1551, 1444, 1068, 927, 780, 754, 717, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.97 (s, 1H), 7.31-7.36 (m, 1H), 7.41-7.51 (m, 5H), 7.81-7.84 (m, 2H), 8.10-8.15 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 125.6, 126.5, 127.5, 128.1, 128.7, 130.4, 131.1, 133.4, 141.9, 161.9; EI-MS *m/z* (rela-

tive intensity) 221 (M^+), 193, 164, 166, 90.

4-(4-Methylphenyl)-2-phenyloxazole (3b)

mp 110-112 °C. IR (KBr) ν: 3140, 1604, 1482, 1066, 822, 781, 722, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.39 (s, 3H), 7.93 (s, 1H), 7.23-7.26 (m, 2H), 7.46-7.49 (m, 3H), 7.72 (d, J = 8.4 Hz, 2H), 8.11-8.13 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 21.3, 125.5, 126.5, 127.6, 128.3, 128.7, 129.4, 130.3, 133.0, 137.9, 142.0, 161.8.; EI-MS *m/z* (relative intensity) 235 (M^+), 208, 207, 206, 192, 165, 78; Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.74; H, 5.62; N, 5.83.

4-(4-Methoxyphenyl)-2-phenyloxazole (3c)

mp 106-108 °C. IR (KBr) ν: 3129, 1617, 1503, 1068, 834, 762, 712, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 3.85 (s, 3H), 7.88 (s, 1H), 6.95-6.99 (m, 2H), 7.45-7.51 (m, 3H), 7.76 (td, J = 3.2, 8.4 Hz, 2H), 8.10-8.13 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 55.3, 114.1, 114.2, 123.8, 126.4, 126.9, 127.5, 128.7, 130.3, 132.4, 141.7, 159.5, 161.8; EI-MS *m/z* (relative intensity) 251 (M^+), 223, 208, 180, 91; Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57. Found: C, 76.51; H, 5.38; N, 5.63.

4-(4-Fluorophenyl)-2-phenyloxazole (3d)

mp 103-104 °C. IR (KBr) ν: 3129, 1608, 1496, 1064, 843, 777, 727, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.92 (s, 1H), 7.10-7.16 (m, 2H), 7.47-7.51 (m, 3H), 7.78-7.83 (m, 2H), 8.09-8.14 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 115.6, 115.8, 126.5, 127.3, 127.4, 128.8, 130.5, 133.0, 141.1, 161.4, 163.8; EI-MS *m/z* (relative intensity) 239 (M^+), 212, 184, 183, 107, 89; Anal. Calcd for $C_{15}H_{10}FNO$: C, 75.30; H, 4.21; N, 5.85. Found: C, 75.48; H, 4.35; N, 5.97.

4-(4-Chlorophenyl)-2-phenyloxazole (3e)

mp 126-128 °C (lit.[21], 126-128 °C). IR (KBr) ν: 3123, 1607, 1482, 1065, 841, 778, 722, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.96 (s, 1H), 7.39-7.42 (m, 2H), 7.47-7.50 (m, 3H), 7.77 (td, J = 2.4, 8.8 Hz, 2H), 8.10-8.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 126.8, 126.9, 127.3, 128.8, 128.9, 130.5, 133.5, 133.8; EI-MS *m/z* (relative intensity) 257 (M^++2), 255 (M^+), 228, 227, 192, 165, 89.

4-(4-Bromophenyl)-2-phenyloxazole (3f)

mp 134-136 °C. IR (KBr) ν: 3166, 1607, 1479, 1068, 841, 777, 721, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.97 (s, 1H), 7.47-7.57 (m, 5H), 7.70 (td, J = 2.4, 8.4 Hz, 2H), 8.09-8.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 121.9, 123.3, 126.5, 127.2, 128.8, 130.1, 130.6, 131.9, 133.6, 141.0, 160.1; EI-MS *m/z* (relative intensity) 301 (M^++2), 299 (M^+), 273, 271, 192, 165, 89; Anal. Calcd for $C_{15}H_{10}{}^{79}BrNO$: C, 60.02; H, 3.36; N, 4.67. Found: C, 60.18; H, 3.16; N, 4.52.

4-(3-Furyl)-2-phenyloxazole (3g)

mp 64-66 °C. IR (KBr) ν: 1647, 1555, 1533, 1481, 1212, 1085, 1001 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.90 (s, 1H), 6.49-6.50 (m, 1H), 6.80 (d, J = 3.2 Hz, 1H), 7.45-7.49 (m, 4H), 8.09-8.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 107.4, 111.6, 126.8, 127.4, 129.0, 130.9, 133.4, 134.7, 142.4, 147.1, 162.3; EI-MS *m/z* (relative intensity) 211 (M^+), 183, 155, 154, 52; Anal. Calcd for $C_{13}H_9NO_2$: C, 73.92; H, 4.29; N, 6.63. Found: C, 73.83; H, 4.38; N, 6.57.

2-Phenyl-4-(3-thienyl)oxazole (3h)

mp 77-79 °C. IR (KBr) ν: 1653, 1552, 1481, 1445, 1268, 1113, 1060, 906 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.88 (s, 1H), 7.09-7.11 (m, 1H), 7.31-7.32 (m, 1H), 7.42-7.43 (m, 1H), 7.46-7.49 (m, 3H), 8.10-8.13 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 124.2, 125.0, 126.6, 127.1, 127.6, 128.7, 130.5, 132.6, 133.8, 137.0, 161.8; EI-MS *m/z* (relative intensity) 227 (M^+), 199, 198, 171, 96, 70; Anal. Calcd for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16. Found: C, 68.62; H, 3.81; N, 6.28.

5-Methyl-2,4-diphenyloxazole (3i)

Oily compound. IR (neat) ν: 1620, 1597, 1557, 1495, 1447, 1206, 1069, 1014, 964 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.61 (s, 3H), 7.33-7.38 (m, 1H), 7.43-7.51 (m, 5H), 7.78-7.80 (m, 2H), 8.11-8.14 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 11.9, 125.9, 126.7, 127.2, 128.5, 128.6, 129.8, 132.3, 135.8, 137.3, 143.8, 159.2; EI-MS *m/z* (relative intensity) 235 (M^+), 220, 191, 165, 78; HRMS *m/z* Calcd for $C_{16}H_{13}NO$: 235.0997. Found 235.0995.

4-(4-Nitrophenyl)-2-phenyloxazole (3j)

mp 175-176 °C. IR (KBr) ν: 3149, 1516, 1334, 854, 747, 715, 689 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 8.13 (s, 1H), 7.50-7.52 (m, 3H), 8.00 (d, J = 8.8 Hz, 2H), 8.12-8.14 (m, 2H), 8.29-8.31 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 124.2, 126.1, 126.6, 126.9, 128.9, 130.9, 135.4, 137.4, 140.2, 147.3, 162.6; EI-MS *m/z* (relative intensity) 266 (M^+), 238, 192, 165, 89, 63; Anal. Calcd for $C_{15}H_{10}N_2O_3$: C, 67.67; H, 3.79; N, 10.52. Found: C, 67.75; H, 3.62; N, 10.43.

4-(3,4-Dichlorophenyl)-2-phenyloxazole (3k)

mp 117-118 °C. IR (KBr) ν: 1608, 1557, 1446, 1286, 1061, 1024, 927 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 7.97 (s, 1H), 7.47-7.50 (m, 4H), 7.63 (dd, J = 2.0, 8.0 Hz, 1H), 7.94 (d, J = 2.0 Hz, 1H), 8.10-8.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 124.7, 126.5, 127.1, 127.4, 128.8, 130.7, 131.2, 131.8, 132.9, 134.0, 140.0, 162.2; EI-MS *m/z* (relative intensity) 293 (M^++4), 291 (M^++2), 289 (M^+), 263, 261, 226, 191, 123, 89; Anal. Calcd for $C_{15}H_9Cl_2NO$: C, 62.09; H,

3.13; N, 4.83. Found: C, 62.23; H, 3.26; N, 4.71.

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