Oxidation of 1-Amidoalkyl-2-naphthols Using (Diacetoxyiodo)benzene: Unusual Formation of 1-Arylnaphtho[1,2-*d*]isoxazoles

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Received: 30.09.2013; Accepted after revision: 08.01.2014

Abstract: The reactions of 1-amidoalkyl-2-naphthols with (diacetoxyiodo)benzene results in the unusual formation of 1-arylnaphtho[1,2-*d*]isoxazoles. This procedure demonstrates a useful application of (diacetoxyiodo)benzene for the oxidative formation of an N–O bond.

Key words: 1,2-benzisoxazole, hypervalent iodine, 1-amidoalkyl-2-naphthols, 2-hydroxyaryl ketoximes, phenolic oxidation

The various pharmaceutical and therapeutic agents containing a 1,2-benzisoxazole moiety show a wide spectrum of biological activity including antimicrobial, antithrombotic, anticancer, anti-HIV and antitumor (Figure 1).[1] Zonisamide, an anticonvulsant,[2] and the antipsychotics, risperidone[3] and paliperidone,[4] are the most popular derivatives of 1,2-benzisoxazole, which have been marketed as pharmaceutical drugs. The 1,2-benzisoxazole moiety is structurally isosteric with the indole nucleus, which thus allows it to bind to biologically important enzymes in a manner similar to indole derivatives.[5] Therefore, the 1,2-benzisoxazole unit has been employed widely as a carrier for pharmacophoric moieties in the search for potential drugs.

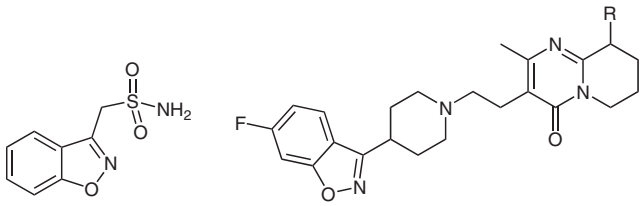
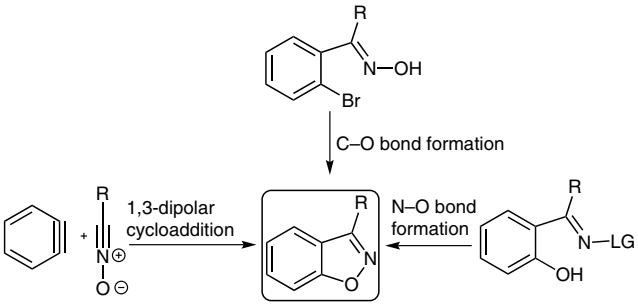


Figure 1 Pharmaceutical drugs containing a 1,2-benzisoxazole moiety

To date, the literature has reported the following methods for the synthesis of 1,2-benzisoxazole derivatives: (a) formation of an N–O bond by intramolecular cyclization of *o*-hydroxybenzyloxime sulfonates or acetates,[6] (b) 1,3-dipolar cycloaddition of in situ generated benzyne with nitrile oxides,[7] and (c) intramolecular C–O cross-coupling reactions of the *Z*-isomer of *o*-haloacetophenone oximes (Scheme 1).[8] Some of these strategies for the synthesis of 1,2-benzisoxazole derivatives have certain limitations such as the requirement for strong basic conditions for intramolecular cyclization,[9] involve competitive Beckmann rearrangement and deoximation side reactions,[10] and the stereochemical requirement for the oxime as the *Z*-isomer, exclusively.[8] Therefore, the development of new methods for the synthesis of 1,2-benzisoxazole derivatives are highly desirable.



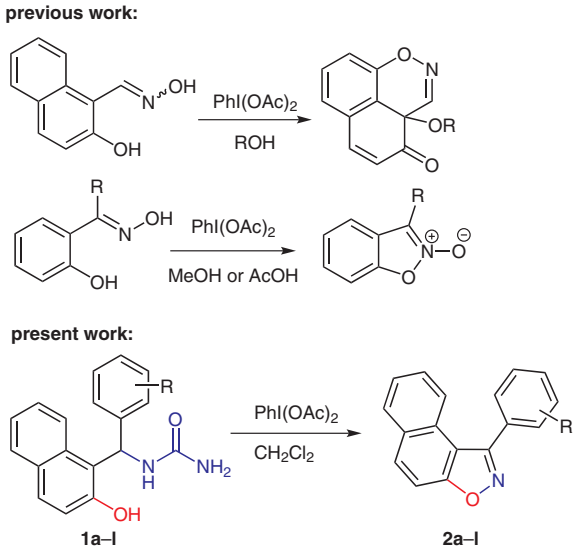
Scheme 1 Reported methods for the preparation of 1,2-benzisoxazoles

Hypervalent iodine reagents have gained considerable popularity in modern organic synthesis due to their commercial availability, mild reaction conditions employed, and their reactivity, which is similar to the heavy metal oxidants (Pb, Hg and Tl), but with fewer toxicity effects.[11] (Diacetoxyiodo)benzene [$PhI(OAc)_2$] is a parent hypervalent iodine(III) reagent, which acts as a two-electron oxidant in a variety of oxidative transformations.[12] The oxidation of phenolic compounds using hypervalent iodine(III) reagents is a very fertile area for the synthesis of highly substituted cyclohexadienones.[13] The appropriate substitution pattern at the *ortho* or *para* positions, with respect to the phenolic group, also permits the synthesis of spiro compounds via intramolecular trapping of the oxidized phenol intermediates with nucleophilic species.[14]

There have been several previous reports on the synthesis of 1-amidoalkyl-2-naphthols via the three component condensation of β-naphthol, an aldehyde and urea under acidic conditions.[15] 1-Amidoalkyl-2-naphthols are typical phenolic compounds with a primary amide-type moiety at the benzylic position. A literature survey revealed that the oxidation of 2-hydroxy-1-naphthaldehyde oxime and 2-hydroxyaryl ketoximes with (diacetoxyiodo)benzene resulted in the formation of alkoxynaphtho[1,8-*de*][1,2]oxazin-4(3a*H*)-ones and 1,2-benzisoxazole 2-oxides,

SYNTHESIS 2014, 46, 0752–0756
Advanced online publication: 07.02.2014
DOI: 10.1055/s-0033-1338590; Art ID: SS-2013-T0651-OP

respectively. Since the structures of 2-hydroxy-1-naphthaldehyde oxime[16] and 2-hydroxyaryl ketoximes[17] are comparable with those of 1-amidoalkyl-2-naphthols, we were interested to discover the outcome of their reactions with (diacetoxyiodo)benzene. We envisaged that the reaction of 1-amidoalkyl-2-naphthols with a hypervalent iodine(III) reagent could induce either a phenolic oxidation followed by trapping of the nucleophilic oxygen of the amide to give a spiro compound, or a Hoffmann-type rearrangement.[18] However, we observed that the reaction of a 1-amidoalkyl-2-naphthol with (diacetoxyiodo)benzene resulted in the formation of an unusual product, a naphtho[1,2-*d*]isoxazole (Scheme 2). Owing to the simplicity of 1-amidoalkyl-2-naphthol synthesis, the present methodology represents a new strategy for the synthesis of naphtho[1,2-*d*]isoxazoles using (diacetoxyiodo)benzene as an oxidant under mild conditions.



Scheme 2 Oxidation of 2-hydroxy-1-naphthaldehyde oxime, 2-hydroxyaryl ketoximes and 1-amidoalkyl-2-naphthols with (diacetoxyiodo)benzene

The desired starting materials, 1-amidoalkyl-2-naphthols **1a–l**, were prepared via the three-component condensation of β-naphthol, an aldehyde and urea by employing a well-known literature method.[15a] The reaction of 1-[(2-hydroxynaphthalen-1-yl)(phenyl)methylurea (**1a**) (1 mmol) with (diacetoxyiodo)benzene (1.2 mmol) was studied as a model reaction. Several solvents (CH_2Cl_2, $CHCl_3$, DCE, MeCN and MeOH) were screened and the number of equivalents of (diacetoxyiodo)benzene were also varied in the oxidation reactions of **1a**. The reaction proceeded in all the examined solvents. However, the best solvent proved to be dichloromethane, while the amount of the oxidant required for a satisfactory yield of product was 1.5 equivalents with respect to the substrate (Table 1, entries 1–3).[17] It is important to note that the oxidation of **1a** in a nucleophilic solvent such as methanol (Table 1, entry 8) was also carried out using 1.2 equivalents of (diacetoxyiodo)benzene, and once again **2a** was obtained without formation of any dearomatized or Hofmann-type rearrangement products.

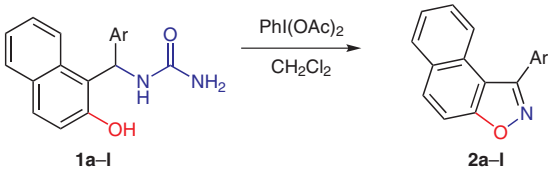
Table 1 Screening of the Conditions for the Oxidation of **1a**

Entry	Solvent	$PhI(OAc)_2$ (equiv)	Time (h)	Yield (%)[a]
1	CH_2Cl_2	1.2	4	67
2	**CH_2Cl_2**	**1.5**	**2**	**72**
3	CH_2Cl_2	1.5	4	72
4	DCE	1.2	4	61
5	DCE	1.5	4	66
6	$CHCl_3$	1.2	6	59
7	MeCN	1.2	6	57
8	MeOH	1.2	8	54

[a] Yield of isolated product.

With these results in hand, we next examined the scope and generality of the method using different 1-amidoalkyl-2-naphthols and dichloromethane as the solvent. As shown in Table 2, this methodology was compatible with a variety of substituents present on the aromatic ring located at position 3. In all the cases, good to excellent yields were obtained.

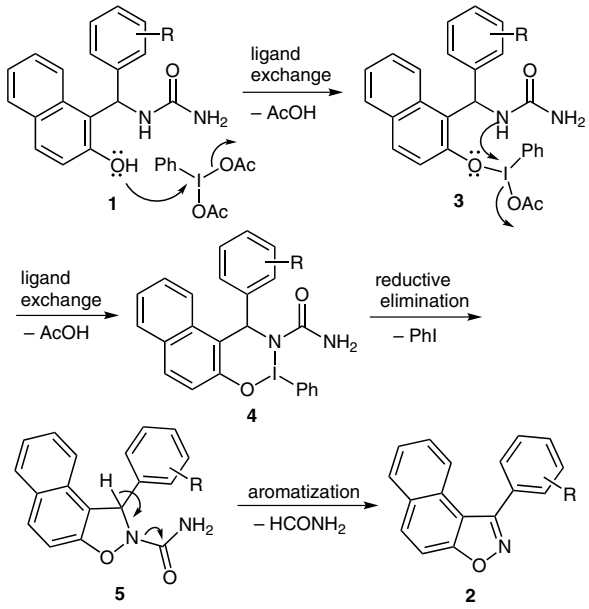
Table 2 Synthesis of 1-Arylnaphtho[1,2-*d*]isoxazoles from 1-Amidoalkyl-2-naphthols Using (Diacetoxyiodo)benzene



Entry	Substrate	Ar	Product	Yield (%)[a]
1	**1a**	C_6H_5	**2a**	71
2	**1b**	2-MeC_6H_4	**2b**	67
3	**1c**	4-MeC_6H_4	**2c**	57
4	**1d**	3-$MeOC_6H_4$	**2d**	70
5	**1e**	3-FC_6H_4	**2e**	68
6	**1f**	2-ClC_6H_4	**2f**	74
7	**1g**	4-ClC_6H_4	**2g**	59
8	**1h**	2-BrC_6H_4	**2h**	63
9	**1i**	3-BrC_6H_4	**2i**	72
10	**1j**	4-BrC_6H_4	**2j**	61
11	**1k**	2,3-$Cl_2C_6H_3$	**2k**	67
12	**1l**	2,4-$Cl_2C_6H_3$	**2l**	74

[a] Yield of isolated product after column chromatography.

A plausible mechanism is depicted in Scheme 3 for the formation of unusual product **2**. The more nucleophilic phenolic oxygen of **1** may undergo ligand association/dissociation to form intermediate **3**. The dearomatization of **3** is inhibited due to the formation of **4**.[19] The propensity for compound **4** to undergo reductive elimination of iodobenzene results in the creation of the key N–O bond to yield **5**, which finally undergoes aromatization along with the elimination of formamide to give the isoxazole **2**.



Scheme 3 A plausible mechanism

In conclusion, we have described an unusual, but direct and useful method for the synthesis of 1-arylnaphtho[1,2-*d*]isoxazoles starting from 1-amidoalkyl-2-naphthols using (diacetoxyiodo)benzene as the oxidant. This procedure exemplifies another application of (diacetoxyiodo)benzene, demonstrating direct N–O bond formation, in contrast to the earlier reports on oxidations of 2-hydroxy-1-naphthaldehyde oxime and 2-hydroxyaryl ketoximes.

Unless otherwise stated, all chemicals and reagents were used as received. Petroleum ether (PE) refers to the fraction boiling in the 60–80 °C range. All reactions were monitored by thin-layer chromatography using Merck silica gel 60 F254 pre-coated plates (0.25 mm), and samples were made visual under UV light. Flash column chromatography was performed using Rankem silica gel (230–400 mesh, particle size 0.040–0.063 mm). Reaction samples were analyzed on a Shimadzu LC 2010 LC–MS using a C18 column. Melting points were obtained using an MIC melting point apparatus. IR spectra were recorded on a Bruker Alpha T spectrophotometer in ATR mode; wavenumbers are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance II 400 NMR spectrometer. Data for ^1H NMR spectra are reported as follows: chemical shift (ppm), multiplicity, coupling constant (Hz), integration. Multiplicity qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. HRMS was performed using a Thermo Fisher HRMS-Q Exactive (ORBITRAP) spectrometer.

Oxidation; General Procedure

To a stirred solution of the appropriate 1-amidoalkyl-2-naphthol **1a–l** (2 mmol) in CH_2Cl_2 (15 mL) was added $PhI(OAc)_2$ (3 mmol), and the mixture was stirred for 2 h at r.t. The progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (EtOAc–PE, 0.5:99.5) to afford products **2a–l**.

1-Phenylnaphtho[1,2-*d*]isoxazole (2a)

Yield: 71% (353 mg); white solid; mp 172–174 °C.

IR (neat): 3046, 1635, 1587, 1486, 1236, 816, 772 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.52 (m, 4 H), 7.62–7.68 (m, 2 H), 7.74 (d, *J* = 8.8 Hz, 1 H), 7.92 (d, *J* = 8.2 Hz, 1 H), 8.28–8.30 (m, 2 H), 8.57 (d, *J* = 8.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.8, 122.3, 125.4, 126.0, 126.6, 126.9, 127.3, 127.5, 128.6, 128.9, 131.0, 131.2, 137.6, 148.0, 162.3.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{12}NO$: 246.09134; found: 246.20585.

1-(*o*-Tolyl)naphtho[1,2-*d*]isoxazole (2b)

Yield: 67% (347 mg); white solid; mp 78–80 °C.

IR (neat): 2919, 2849, 1544, 1471, 1371, 1271, 1231, 1203, 1084, 1027, 1008, 922, 873, 802, 773, 752, 725, 702, 627, 561 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.86 (s, 3 H), 7.31–7.37 (m, 3 H), 7.51 (t, *J* = 8.0 Hz, 1 H), 7.64 (t, *J* = 8.0 Hz, 1 H), 7.75 (d, *J* = 8.8 Hz, 1 H), 7.79 (d, *J* = 8.0 Hz, 1 H), 7.93 (d, *J* = 8.0 Hz, 1 H), 8.21 (d, *J* = 8.0 Hz, 1 H), 8.58 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.3, 110.8, 122.3, 125.3, 125.9, 126.1, 126.5, 126.7, 126.9, 128.5, 129.7, 130.5, 131.1, 131.8, 137.5, 138.6, 147.5, 162.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{14}NO$: 260.1070; found: 260.1067.

1-(*p*-Tolyl)naphtho[1,2-*d*]isoxazole (2c)

Yield: 57% (296 mg); white solid; mp 146–148 °C.

IR (neat): 2919, 2849, 1544, 1488, 1455, 1371, 1271, 1231, 1203, 1163, 1084, 1027, 1008, 922, 867, 773, 752, 725, 702, 554 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 7.53 (t, *J* = 8.0 Hz, 1 H), 7.65 (t, *J* = 8.0 Hz, 1 H), 7.70 (d, *J* = 8.0 Hz, 1 H), 7.77 (d, *J* = 8.0 Hz, 1 H), 7.95 (d, *J* = 8.0 Hz, 1 H), 8.20 (d, *J* = 8.0 Hz, 2 H), 8.58 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 110.8, 122.2, 124.7, 125.3, 125.7, 126.5, 126.9, 127.3, 128.5, 129.2, 129.6, 130.2, 131.2, 137.6, 141.5, 147.9, 162.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{14}NO$: 260.1070; found: 260.1068.

1-(3-Methoxyphenyl)naphtho[1,2-*d*]isoxazole (2d)

Yield: 70% (385 mg); white solid; mp 126–128 °C.

IR (neat): 2919, 2851, 1557, 1489, 1373, 1271, 1236, 1175, 1088, 1052, 1016, 928, 877, 815, 761, 739, 724, 642 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3 H), 7.00 (d, *J* = 8.0 Hz, 1 H), 7.37 (t, *J* = 8.0 Hz, 1 H), 7.48 (t, *J* = 8.0 Hz, 1 H), 7.62 (t, *J* = 8.0 Hz, 2 H), 7.71 (d, *J* = 8.0 Hz, 1 H), 7.79 (s, 1 H), 7.84–7.90 (m, 2 H), 8.56 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5, 110.8, 111.7, 117.7, 119.8, 122.3, 125.3, 126.0, 126.5, 126.9, 128.6, 128.7, 130.0, 131.2, 137.6, 148.0, 159.9, 162.2.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{14}NO_2$: 276.1019; found: 276.1018.

1-(3-Fluorophenyl)naphtho[1,2-*d*]isoxazole (2e)

Yield: 68% (358 mg); white solid; mp 144–148 °C.

IR (neat): 3069, 3050, 2922, 1615, 1592, 1553, 1473, 1446, 1372, 1300, 1248, 1202, 1087, 1061, 1008, 947, 884, 859, 819, 791, 760, 745, 724, 662, 626, 571 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.20 (t, *J* = 8.9 Hz, 1 H), 7.45–7.55 (m, 2 H), 7.64–7.69 (m, 2 H), 7.78 (d, *J* = 8.0 Hz, 1 H), 7.93–8.00 (m, 2 H), 8.07 (d, *J* = 8.0 Hz, 1 H), 8.55 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.7, 114.1, 114.3, 117.9, 118.1, 122.2, 123.0, 125.5, 126.4, 126.5, 127.1, 128.6, 130.5, 131.2, 137.5, 148.1, 161.7 (d, *J* = 70 Hz), 164.2.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{11}FNO$: 264.0819; found: 264.0817.

1-(2-Chlorophenyl)naphtho[1,2-*d*]isoxazole (2f)
Yield: 74% (418 mg); white solid; mp 96–98 °C.

IR (neat): 2917, 2848, 1633, 1601, 1543, 1475, 1398, 1370, 1270, 1235, 1179, 1113, 1084, 1049, 1005, 924, 878, 842, 800, 753, 727, 695 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.47 (m, 2 H), 7.54–7.59 (m, 2 H), 7.69 (t, *J* = 6.0 Hz, 1 H), 7.76 (d, *J* = 8.0 Hz, 1 H), 7.84 (d, *J* = 8.0 Hz, 1 H), 7.98 (d, *J* = 8.0 Hz, 1 H), 8.22–8.25 (m, 1 H), 8.61 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.9, 122.3, 125.5, 126.5, 126.6, 126.9, 127.1, 128.6, 131.2, 131.3, 131.6, 131.8, 133.2, 137.1, 148.1, 160.3.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{11}ClNO$: 280.0524; found: 280.0524.

1-(4-Chlorophenyl)naphtho[1,2-*d*]isoxazole (2g)
Yield: 59% (330 mg); white solid; mp 184–186 °C.

IR (neat): 2920, 2851, 1705, 1596, 1471, 1453, 1369, 1269, 1234, 1203, 1083, 1048, 1003, 878, 832, 798, 742, 725, 693, 632 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.59 (t, *J* = 8.0 Hz, 1 H), 7.63 (d, *J* = 8.0 Hz, 2 H), 7.71 (t, *J* = 8.0 Hz, 1 H), 7.89 (d, *J* = 8.0 Hz, 1 H), 7.94 (d, *J* = 8.0 Hz, 1 H), 8.07 (d, *J* = 8.0 Hz, 1 H), 8.27 (d, *J* = 8.0 Hz, 2 H), 8.47 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 110.9, 121.5, 125.4, 125.5, 125.7, 126.3, 127.0, 128.4, 128.6, 129.2, 130.8, 136.4, 136.7, 147.6, 160.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{11}ClNO$: 280.0524; found: 280.0522.

1-(2-Bromophenyl)naphtho[1,2-*d*]isoxazole (2h)
Yield: 63% (407 mg); white solid; mp 104–106 °C.

IR (neat): 2921, 2852, 1538, 1455, 1373, 1315, 1231, 1095, 1076, 1022, 1003, 931, 802, 755, 726, 687, 642 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.36 (t, *J* = 8.0 Hz, 1 H), 7.48 (t, *J* = 8.0 Hz, 1 H), 7.56 (t, *J* = 8.0 Hz, 1 H), 7.68 (t, *J* = 8.0 Hz, 1 H), 7.77 (t, *J* = 8.0 Hz, 2 H), 7.84 (d, *J* = 8.0 Hz, 1 H), 7.98 (d, *J* = 8.0 Hz, 1 H), 8.16 (d, *J* = 8.0 Hz, 1 H), 8.60 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.9, 121.8, 122.3, 125.5, 126.5, 126.6, 127.1, 127.4, 128.6, 128.7, 131.2, 131.7, 132.1, 134.6, 137.1, 148.1, 160.8.

HRMS (ESI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{11}{}^{81}BrNO$: 324.0019; found: 324.0020.

1-(3-Bromophenyl)naphtho[1,2-*d*]isoxazole (2i)
Yield: 72% (472 mg); white solid; mp 180–182 °C.

IR (neat): 3065, 1633, 1580, 1229, 716 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.43 (t, *J* = 7.9 Hz, 1 H), 7.58 (t, *J* = 7.0 Hz, 1 H), 7.66–7.69 (m, 1 H), 7.72 (d, *J* = 7.0 Hz, 1 H), 7.75 (d, *J* = 8.9 Hz, 1 H), 7.84 (d, *J* = 8.9 Hz, 1 H), 8.01 (d, *J* = 8.2 Hz, 1 H), 8.27 (d, *J* = 7.8 Hz, 1 H), 8.50–8.51 (m, 1 H), 8.59 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.8, 122.2, 123.0, 125.5, 125.8, 126.5, 127.1, 128.6, 129.4, 130.1, 130.4, 131.2, 133.9, 137.5, 148.1, 160.7.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{11}{}^{81}BrNO$: 324.00185; Found: 324.29729.

1-(4-Bromophenyl)naphtho[1,2-*d*]isoxazole (2j)
Yield: 61% (394 mg); white solid; mp 194–198 °C.

IR (neat): 2919, 1595, 1475, 1372, 1270, 1235, 1202, 1087, 1071, 1048, 1004, 877, 834, 806, 745, 723, 682 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.55 (t, *J* = 8.0 Hz, 1 H), 7.66–7.73 (m, 4 H), 7.81 (d, *J* = 8.0 Hz, 1 H), 7.97 (d, *J* = 8.0 Hz, 1 H), 8.18 (d, *J* = 8.5 Hz, 2 H), 8.56 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.7, 122.2, 125.5, 125.7, 126.3, 126.4, 126.5, 127.1, 128.6, 128.7, 131.2, 132.2, 137.5, 148.1, 161.4.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{11}{}^{81}BrNO$: 325.9998; found: 325.9987.

1-(2,3-Dichlorophenyl)naphtho[1,2-*d*]isoxazole (2k)
Yield: 67% (291 mg); white solid; mp 170–172 °C.

IR (neat): 3056, 1662, 1558, 1516, 1442, 1313, 1187, 1155, 1122, 1064, 1008, 1003, 941, 882, 801, 779, 742, 726, 701, 632, 563 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.55 (t, *J* = 8.0 Hz, 1 H), 7.61 (t, *J* = 8.0 Hz, 1 H), 7.72 (t, *J* = 8.0 Hz, 1 H), 7.81 (d, *J* = 8.0 Hz, 1 H), 7.90 (d, *J* = 8.9 Hz, 1 H), 7.98 (d, *J* = 8.9 Hz, 1 H), 8.08 (d, *J* = 8.0 Hz, 1 H), 8.17 (d, *J* = 8.0 Hz, 1 H), 8.48 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 110.9, 121.5, 125.5, 125.8, 126.9, 127.1, 128.0, 128.0, 128.3, 130.2, 130.4, 130.7, 132.5, 133.9, 136.3, 147.6, 158.8.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{10}Cl_2NO$: 314.0134; found: 314.0133.

1-(2,4-Dichlorophenyl)naphtho[1,2-*d*]isoxazole (2l)
Yield: 74% (321 mg); white solid; mp 162–164 °C.

IR (neat): 2964, 1680, 1653, 1558, 1506, 1456, 1378, 1314, 1209, 1186, 1096, 1033, 1007, 944, 864, 826, 797, 762, 729, 693, 639 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.60 (t, *J* = 8.0 Hz, 2 H), 7.70 (d, *J* = 8.0 Hz, 1 H), 7.73 (s, 1 H), 7.88 (d, *J* = 8.9 Hz, 1 H), 7.96 (d, *J* = 8.9 Hz, 1 H), 8.07 (d, *J* = 8.0 Hz, 1 H), 8.17 (d, *J* = 7.9 Hz, 1 H), 8.47 (d, *J* = 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 110.8, 121.5, 124.4, 125.4, 125.8, 126.7, 127.1, 127.6, 128.5, 130.7, 132.5, 133.0, 136.3, 136.4, 147.5, 158.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{10}Cl_2NO$: 314.0134; found: 314.0128.

Acknowledgment

The authors are thankful to the Department of Science and Technology, New Delhi, India (No. SR/S1/OC-72/2009) for the financial support. The authors are also grateful to SAIF, Punjab University, Chandigarh, India, for recording the NMR spectra.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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