Novel Synthetic Strategy of N-Arylated Heterocycles via Sequential Palladium-Catalyzed Intra- and Inter-Arylation Reactions

Rafik Omar-Amrani, Raphaël Schneider,* Yves Fort*

Synthèse Organométallique et Réactivité, UMR CNRS-UHP 7565, Faculté des Sciences, BP 239, 54506 Vandoeuvre les Nancy Cedex, France
Fax +33(3)83684785; E-mail: Raphael.Schneider@sor.uhp-nancy.fr; Yves.Fort@sor.uhp-nancy.fr

Received 19 May 2004; revised 11 June 2004

Abstract: The use of an in situ generated Pd(0) catalyst associated to \( N,N' \)-bis[2,6-diisopropylphenyl]dihydroimidazol-2-ylidene (SIPr) as a ligand and \( t \)-BuONa as the base for sequential intra- followed by intermolecular aryl amination is described. The method has been applied to the synthesis of N-arylated five-, six- and seven-membered nitrogen heterocycles.

Key words: palladium catalyst, N-heterocyclic carbene ligand, aryl amination reaction, N-arylated heterocycles

N-arylated heterocycles are important scaffolds in medicinal chemistry. Of particular interest are the nitrogen heterocycles shown below (Figure 1). Numerous natural products and important therapeutic agents possessing hypocholesterolemic, hypolipidemic, tuberculostatic, antipsychotic or vasodilator activity contain these core structures. There is thus a considerable interest in developing efficient synthetic protocols for the preparation of these compounds.

Figure 1

In recent years, a growing interest in the application of transition metal promoted processes to the synthesis of heterocyclic systems has been seen. Palladium2- and nickel3-catalyzed sp²-carbon-nitrogen bond-forming reactions have proven to be a valuable synthetic method for the preparation of aromatic amines and have therefore found wide applications in organic synthesis. In particular, intramolecular variant of this reaction has been developed to construct indoline, tetrahydroquinoline, benzazepine and benzimidazole derivatives.4 N-Arylation of nitrogen heterocycles, mainly indoles and tetrahydroquinolines, has also been achieved but no broadly applicable methodology has been described for the synthesis of N-arylated heterocycles.5 Alternatively, transition metal-free base-mediated domino hydroamination-aryne cyclization reactions have recently been developed by Beller and coworkers but this process is limited to the synthesis of N-aryl-2,3-dihydroindoles.6 A general method for the synthesis of N-arylated heterocycles is therefore desirable especially when the N-unsubstituted compound is not readily available.

We envisaged that the cyclization of amino aryl chlorides 1 or 2 via an intramolecular aryl amination followed by an intermolecular coupling could generate the desired N-arylated heterocycles (Scheme 1).

Scheme 1

In this paper, we present a full account of the scope and limitations of the palladium-mediated sequential intra- and intermolecular amination reactions of compounds 1 and 2 with aryl chlorides which enabled us to synthesize a wide range of N-arylated 5-, 6- and 7-membered heterocycles of various classes: indolines, tetrahydroquinolines, 2,3,4,5-tetrahydro-1\(H\)-1-benzazepines, benzoxazines and benzoxazepines.

The synthesis of 2-chlorophenyl alkylamines (\( X = \text{CH}_2 \)) precursors 1 has previously been described.4a Ether-linked precursors 2 were easily prepared by alkylation of 2-chlorophenol with 1,2-dibromoethane or 1,3-dibromopropane,

Scheme 2 Reagents and conditions: (a) BrCH\(_2\)CH\(_2\)Br or BrCH\(_3\), CH\(_2\)\(_3\)Br, NaOH, H\(_2\)O, 100 °C (b) Na\(_2\)S\(_2\)O\(_7\), DMF, 120 °C (c) PPh\(_3\), THF, 0–25 °C

SYNTHESIS 2004, No. 15, pp 2527–2534
Advanced online publication: 02.09.2004
DOI: 10.1055/s-2004-831205; Art ID: Z09504SS
© Georg Thieme Verlag Stuttgart · New York
treatment with sodium azide followed by reduction with triphenylphosphine (Scheme 2).

We have recently reported the use of a Ni(0) catalyst associated with a strong electron-donating and sterically hindered N-heterocyclic carbene \[^7\ \text{[N,N'-bis(2,6-diisopropylphenyl)]dihydroimidazol-2-ylidene, SIPr}}\) (Figure 2) to allow mild amination of aryl chlorides with several classes of amines. \[^8\] Initial sequential couplings were performed using this catalyst associated to Nar-BuO as the base in 1,4-dioxane as these conditions were found to give best results in cycloamination reactions. \[^9\]

![Figure 2 Structure of the SIPr ligand](image)

Using 2-chlorophenylethylamine (1a; \(n = 1\)) and chlorobenzene as substrates, results were disappointing. Despite the utility of the Ni/SIPr catalyst for the amination of aryl chlorides, \[^9\] sequential couplings mediated by this reagent provided a mixture of the desired 1-phenylindoline (5a) and indole, arising from the oxidation of the intermediate indoline, in a nearly 1:1 ratio and with a modest 54% yield. We have subsequently verified in a control experiment with indoline and the Ni/SIPr reagent that the catalyst was responsible of that partial oxidation. We assume that these results are a consequence of the poor efficiency of the Ni/SIPr catalyst during the arylation of primary amines.

Changing the metal to palladium and using SIPr as ligand (Pd/SIPr = 1:1) allowed a significant improvement of the sequential couplings and compound 5a was isolated in 73% yield. Varying the palladium to SIPr ratio from 1:1 to 1:2 gave much better results (92%), especially at low catalyst loadings (1–2 mol%). Several studies on the catalytic properties of palladium/carbene complexes have been recently reported and many of them have displayed outstanding levels of activity. \[^7\]–\[^14\] Due to the strong interaction between palladium and the carbenic carbon of the imidazole moiety, the metal-carbene is robust overtime and these catalysts do not require excess ligand to compensate for metal-ligand bond lability. The optimum palladium-to-ligand ratio was determined to be 1:1. We suppose that for the sequential couplings described herein, the catalyst lifetime is increased using a Pd/SIPr ratio of 1:2. Increasing the Pd/SIPr ratio further (1:3 or 1:4) was found deleterious with essentially a complete loss of catalytic activity. Finally, among Pd\((+2)\) complexes tested for the couplings, Pd(OAc)_2 proved to be the most effective one.

The Pd(0)/SIPr/Nar-BuO catalyst was in situ generated from Pd(OAc)_2 and SIPr-HCl \[^15\] by reduction of Pd(OAc)_2 and deprotonation of the azolium salt using Nar-BuO activated sodium hydride as previously described for Ni catalysts. \[^3\]–\[^10\] The Pd/SIPr combination thus prepared shows very similar activity with Pd/SIPr and Pd/IPr \([\text{IPr} = \text{N,N'-bis(2,6-diisopropylphenyl)]imidazol-2-ylidene}}\) catalysts prepared from Pd(db)\(_2\) \((\text{db} = \text{dibenzyldiene acetone})\), Pd(db)\(_2\) IPr palladacycle or [Pd(IPr)Cl\(_2\)]\(_2\) complexes used by Nolan and Hartwig in NHC mediated amination reactions. \[^11\]–\[^12\]

The optimal protocol \([\text{Pd} \ (2 \ \text{mol%}), \ \text{SIPr} \ (4 \ \text{mol%}), \ \text{Nar-BuO} \ (3 \ \text{equiv}), \ 1,4\)-dioxane, 100 °C\] was then applied to the sequential intra- and intermolecular coupling of compounds 1 and 2 with aryl chlorides. The indoline, tetrahydroquinoline, 1-benzazepine, benzoazene and benzoxazepine skeletons were first prepared by a Pd/SIPr-catalyzed cycloamination reaction. Upon completion of the first coupling \([3–4 \ h \ \text{for substrates} \ 1\text{a} \ (n = 1), \ 1\text{b} \ (n = 2) \ \text{and} \ 2\text{a}, \ 7–8 \ h \ \text{for compounds} \ 1\text{c} \ \text{and} \ 2\text{b} \ \text{as judged by GC–MS analysis}]\), a second aryl chloride was added and the reaction was further heated to allow for the second coupling to occur. The yields of the N-arylated heterocycles obtained by this method were comparable to those obtained when the non-arylated intermediate was isolated prior to the second coupling. For instance, 1-(4-methoxyphenyl)indoline \(5\text{b}\) was obtained in 91% yield following the ‘one-pot’ protocol while indoline was converted to \(5\text{b}\) in 93% yield using the Pd/SIPr catalyst and 4-chloroanisole. Due to the clean conversion of the starting materials during the synthesis and arylation of 5- and 6-membered heterocycles, the only purification required in order to obtain analytically pure products was concentration and removal of the catalyst and sodium salts by chromatography through a short plug of silica gel. The arylation of 7-membered heterocycles required longer reaction times \([9–15 \ h \ \text{the conversion being incomplete even after heating for 24 h}]\) and gave slightly lower yields. As shown in Table 1, the reaction tolerates a great number of substituents on the aryl chloride used as second partner. Electronically deactivated and/or sterically hindered substrates generally required longer reaction times of up to 17 h (entries d–f and l). Dehalogenation of the starting material or of the aryl chloride used in the second coupling was only a minor reaction in all cases \(< 2\%\). Compared to simple aryl substrates, the coupling of 3-chloropyridine is slower probably due to a competition with the carbene for coordination to palladium thereby inhibiting the amination reaction (entry g).

In conclusion, we have developed a new palladium-catalyzed methodology for sequential intra- and intermolecular amination reactions, which allows in one pot the synthesis of a wide range of \(N\)-arylated nitrogen heterocycles. The simplicity of the process and the relative lack of methods to prepare \(N\)-arylated nitrogen heterocycles should render this method of great use to synthetic chemists.
### Table 1  Palladium(0)-Catalyzed Sequential Intra- and Intermolecular Amination Reactions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reagents</th>
<th>FG</th>
<th>Product 5*</th>
<th>Time 1 (h)b,c</th>
<th>Time 2 (h)d</th>
<th>Yield (%)e</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>H</td>
<td>Cl</td>
<td><img src="image1.png" alt="Image" /></td>
<td>4</td>
<td>6</td>
<td>92</td>
</tr>
<tr>
<td>b</td>
<td>4-OMe</td>
<td>Cl</td>
<td><img src="image2.png" alt="Image" /></td>
<td>4</td>
<td>5</td>
<td>91</td>
</tr>
<tr>
<td>c</td>
<td>3-OMe</td>
<td>Cl</td>
<td><img src="image3.png" alt="Image" /></td>
<td>4</td>
<td>4</td>
<td>91</td>
</tr>
<tr>
<td>d</td>
<td>2-OMe</td>
<td>Cl</td>
<td><img src="image4.png" alt="Image" /></td>
<td>4</td>
<td>7</td>
<td>67</td>
</tr>
<tr>
<td>e</td>
<td>2,5-Me₂</td>
<td>Cl</td>
<td><img src="image5.png" alt="Image" /></td>
<td>4</td>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td>f</td>
<td>2,6-Me₂</td>
<td>Cl</td>
<td><img src="image6.png" alt="Image" /></td>
<td>4</td>
<td>17</td>
<td>41</td>
</tr>
<tr>
<td>g</td>
<td>H, X = N</td>
<td>Cl</td>
<td><img src="image7.png" alt="Image" /></td>
<td>4</td>
<td>10</td>
<td>45</td>
</tr>
<tr>
<td>h</td>
<td>H</td>
<td>Cl</td>
<td><img src="image8.png" alt="Image" /></td>
<td>3</td>
<td>5</td>
<td>96</td>
</tr>
<tr>
<td>i</td>
<td>4-CN</td>
<td>Cl</td>
<td><img src="image9.png" alt="Image" /></td>
<td>3</td>
<td>4</td>
<td>92</td>
</tr>
<tr>
<td>j</td>
<td>H</td>
<td>Cl</td>
<td><img src="image10.png" alt="Image" /></td>
<td>7</td>
<td>10</td>
<td>52</td>
</tr>
<tr>
<td>k</td>
<td>4-CF₃</td>
<td>Cl</td>
<td><img src="image11.png" alt="Image" /></td>
<td>7</td>
<td>9</td>
<td>54</td>
</tr>
<tr>
<td>l</td>
<td>2,4-Me₂</td>
<td>Cl</td>
<td><img src="image12.png" alt="Image" /></td>
<td>7</td>
<td>15</td>
<td>51</td>
</tr>
<tr>
<td>m</td>
<td>H</td>
<td>Cl</td>
<td><img src="image13.png" alt="Image" /></td>
<td>4</td>
<td>4</td>
<td>97</td>
</tr>
<tr>
<td>n</td>
<td>4-OMe</td>
<td>Cl</td>
<td><img src="image14.png" alt="Image" /></td>
<td>4</td>
<td>7</td>
<td>99</td>
</tr>
<tr>
<td>o</td>
<td>3-OMe</td>
<td>Cl</td>
<td><img src="image15.png" alt="Image" /></td>
<td>4</td>
<td>4</td>
<td>96</td>
</tr>
<tr>
<td>p</td>
<td>4-COPh</td>
<td>Cl</td>
<td><img src="image16.png" alt="Image" /></td>
<td>4</td>
<td>6</td>
<td>81</td>
</tr>
</tbody>
</table>
Melting points were taken on a Tottoli apparatus and were uncorrected. Products yields are given for purified compounds. IR spectra were recorded using NaCl cells or mixtures of compounds/KBr. The 1H NMR spectra were recorded at 400 MHz or 200 MHz using CDCl3 as solvent. The 13C NMR spectra were recorded at 100 MHz or 50 MHz using CDCl3 as solvent. Chemical shifts are reported in ppm from internal TMS. 1,4-Dioxane, THF, hexanes and EtOAc were distilled and dried according to standard procedures.16 tert-BuOH was distilled from sodium before use. Sodium hydride (65% in mineral oil) was purchased from Fluka and used after two washings in THF. All reagents were of reagent grade and were used without purification. Mass spectra were obtained on a GC–MS Shimadzu QP-5050 (EI, 70 eV). TLC was performed on precoated 5 × 20 silica gel plates (Macherey-Nagel) with detection by UV light. Column chromatography was carried out on silica gel (E. Merck, 0.063-0.2 mm). Microanalyses were performed at the SRSMC Laboratory, Université Henri Poincaré, France.

Preparation of 1-Azido-2-chlorobenzenes 4; General Procedure

To a solution of 2-chlorophenol (50 mmol) in water (40 mL) was added 1,2-dibromoethane or 1,3-dibromopropane (62.5 mmol) and the mixture was allowed to warm to r.t. After ca. 15 h, H2O (36 mmol) was added and the mixture was further stirred at r.t. for 3 h. The reaction mixture was evaporated, acidified with HCl (2 N) and the aqueous layer was extracted with Et2O (2 × 50 mL). The aqueous layer was basified to pH = 11 with NaOH (2 N) and extracted with CH2Cl2 (3 × 100 mL). The organic phases were combined, dried over MgSO4 and evaporated under vacuum to give compounds 1. Compounds were used without further purification for the sequential aryl amination reactions.

Preparation of 1-(3-Azidopropoxy)-2-chlorobenzene (4b)

Yield: 82%; colorless oil.


1H NMR (400 MHz, CDCl3); δ = 7.35 (dd, J = 8.0, 1.2 Hz, 1 H), 7.20 (dd, J = 8.0, 8.0, 1.2 Hz, 1 H), 6.92 (d, J = 8.0 Hz, 1 H), 6.91 (dd, J = 8.0, 8.0, 1.2 Hz, 1 H), 4.10 (t, J = 6.0 Hz, 2 H), 3.58 (t, J = 6.8 Hz, 2 H), 2.12–2.05 (m, 2 H).

13C NMR (100 MHz, CDCl3); δ = 154.1, 130.2, 128.4, 127.7, 121.6, 113.4, 65.5, 48.0, 28.6.

EI–MS: m/z = 211 [M].


Preparation of 2-Chlorophenoxy-1-alkylamines 2; General Procedure

To the 1-azidoalkoxy-2-chlorobenzene 4 (20 mmol) dissolved in anhyd THF (50 mL) at 0 °C was added slowly triphenylphosphine (21.6 mmol) and the mixture was allowed to warm to r.t. After ca. 15 h, H2O (36 mmol) was added and the mixture was further stirred at r.t. for 3 h. The reaction mixture was evaporated, acidified with HCl (2 N) and the aqueous layer was extracted with Et2O (2 × 50 mL). The aqueous layer was basified to pH = 11 with NaOH (2 N) and extracted with CH2Cl2 (3 × 100 mL). The organic phases were combined, dried over MgSO4 and evaporated under vacuum to give compounds 2. Compounds 2 were used without further purification for the sequential aryl amination reactions.

Table 1 Palladium(0)-Catalyzed Sequential Intra- and Intermolecular Amination Reactions (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reagents FG</th>
<th>Product S</th>
<th>Time 1 (h)c</th>
<th>Time 2 (h)d</th>
<th>Yield (%)e</th>
</tr>
</thead>
<tbody>
<tr>
<td>q</td>
<td>H</td>
<td></td>
<td>8</td>
<td>10</td>
<td>53</td>
</tr>
<tr>
<td>r</td>
<td>4-CN</td>
<td>8</td>
<td>12</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>s</td>
<td>3-OMe</td>
<td>8</td>
<td>15</td>
<td>52</td>
<td></td>
</tr>
</tbody>
</table>

a All products were characterized by 1H and 13C NMR, IR, mass spectroscopy and elemental analysis.
b Determined by GC–MS analysis.
c Reaction time for the first coupling.
d Reaction time for the second coupling.
e Isolated yields.

Synthesis 2004, No. 15, 2527–2534 © Thieme Stuttgart · New York
Hz. 1 H), 4.09 (t, J = 6.0 Hz, 2 H), 2.94 (t, J = 6.4 Hz, 2 H), 2.02–1.91 (m, 2 H), 1.43 (2 H, NH).

\(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 157.7, 130.5, 128.0, 123.1, 121.6, 113.5, 67.51, 39.6, 33.1.\)

EI-MS: \(m/z = 186 [M].\)

Anal. Calcd for C\(_8\)H\(_8\)N\(_4\): C, 79.79; H, 6.71; N, 6.22; O, 7.10. Found: C, 79.79; H, 6.65; N, 6.33.

\(\text{N-(2-Methoxyphenyl)indoline (5d)}\)

Yield: 54%; pale yellow oil.

IR (NaCl): 2941, 2836, 1591, 1458, 1486, 1246, 1223, 1152, 1028, 741 cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.27–7.00 (m, 4 H), 6.93–6.68 (m, 3 H), 6.50 (ddd, J = 8.2, 2.4, 0.6 Hz, 1 H), 3.88 (t, J = 8.4 Hz, 2 H), 3.77 (s, 3 H), 3.05 (t, J = 8.4 Hz, 2 H).\)

\(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 158.0, 146.7, 145.2, 131.2, 130.0, 129.7, 126.9, 124.9, 118.8, 110.0, 108.3, 105.8, 103.5, 55.0, 51.9, 27.9.\)

EI-MS: \(m/z = 225 [M].\)

\(\text{N-(2,6-Dimethylphenyl)indoline (5e)}\)

Yield: 41%; pale yellow oil.

IR (NaCl): 2941, 2836, 1591, 1458, 1486, 1246, 1223, 1152, 1028, 741 cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.25–6.90 (m, 6 H), 6.59 (dd, J = 7.6, 7.6 Hz, 1 H), 6.59 (dd, J = 7.6, 7.6 Hz, 1 H).\)

\(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 138.2, 129.6, 128.8, 128.5, 127.8, 127.4, 126.9, 126.8, 124.5, 121.8, 116.0, 105.3, 51.5, 47.7, 34.9, 28.7.\)

EI-MS: \(m/z = 223 [M].\)

Anal. Calcd for C\(_{16}\)H\(_{17}\)N: C, 85.89; H, 7.56; N, 6.38.

\(\text{1-(2-Pyridinyl)indoline (5g)}\)

Yield: 45%; pale yellow oil.

IR (NaCl): 2956, 2851, 1594, 1485, 1460, 1339, 1280, 1110, 735 cm\(^{-1}\).

\(^1\)H NMR (200 MHz, CDCl\(_3\)): \(\delta = 8.56 (br s, 1 H), 8.19 (d, J = 4.0 Hz, 1 H), 7.52 (br dd, 1 H), 7.28–7.05 (m, 4 H), 6.80 (dd, J = 7.0, 7.0, 2.2 Hz, 1 H), 3.96 (t, J = 8.0 Hz, 2 H), 2.15 (s, 3 H), 2.16 (s, 3 H).\)

\(^1\)C NMR (50 MHz, CDCl\(_3\)): \(\delta = 145.9, 145.8, 141.6, 140.5, 139.6, 131.2, 127.1, 125.8, 126.3, 124.5, 121.0, 116.0, 105.3, 51.5, 47.7, 34.9, 28.7.\)

EI-MS: \(m/z = 195 [M^+].\)


1-Phenyl-1,2,3,4-tetrahydroquinoline (5h)

Yield: 96%; pale yellow oil.

IR (NaCl): 3059, 2946, 1591, 1495, 1310, 1238, 854, 748, 695 cm\(^{-1}\).
1H NMR (400 MHz, CDCl3): δ = 7.30 (dd, J = 7.2, 7.2 Hz, 1 H), 7.23–7.01 (m, 5 H), 6.97–6.85 (m, 1 H), 6.95 (d, J = 8.4 Hz, 1 H), 3.59 (t, J = 5.6 Hz, 2 H), 2.81 (t, J = 6.4 Hz, 2 H), 2.04–1.92 (m, 2 H).

13C NMR (100 MHz, CDCl3): δ = 148.7, 148.3, 129.8, 129.6, 125.02, 123.9, 121.6, 121.3, 118.2, 116.2, 51.2, 28.1, 23.1.

EI–MS: m/z = 209 [M].

4-[3,4-Dihydro-1(2H)-quinoxalin-5(4H)]benzonitrile (5i)

Yield: 92%; pale yellow oil.

IR (NaCl): 3036, 2963, 2927, 2868, 1588, 1493, 1467, 1337, 1253, 1212, 1059, 746, 698 cm–1.

1H NMR (400 MHz, CDCl3): δ = 7.34 (dd, J = 7.2, 7.2 Hz, 2 H), 7.22 (d, J = 8.4 Hz, 2 H), 7.08 (dd, J = 7.2, 7.2 Hz, 1 H), 6.94–6.85 (m, 2 H), 6.79–6.71 (m, 2 H), 4.30 (t, J = 4.3 Hz, 2 H), 3.71 (t, J = 4.3 Hz, 2 H).

13C NMR (100 MHz, CDCl3): δ = 147.3, 177.0, 144.9, 129.4, 124.3, 124.4, 123.3, 120.8, 120.2, 117.0, 116.9, 64.4, 48.6.

EI–MS: m/z = 211 [M].

Anal. Calcld for C18H15NO: C, 79.59; H, 6.20; N, 6.63; O, 7.57. Found: C, 80.05; H, 6.87; N, 6.99.

4-(Methoxyphenyl)-3,4-dihydro-2H,1,4-benzoxazine (5m)

Yield: 99%; pale yellow oil.

IR (NaCl): 3036, 2960, 2870, 1578, 1482, 1469, 1340, 1255, 1100, 1056, 830, 749, 693 cm–1.

1H NMR (400 MHz, CDCl3): δ = 7.16 (dd, J = 8.8 Hz, 2 H), 6.91 (d, J = 8.8 Hz, 2 H), 6.88–6.81 (m, 2 H), 6.71–6.60 (m, 2 H), 4.31 (t, J = 4.4 Hz, 2 H), 3.81 (s, 3 H), 3.64 (t, J = 4.4 Hz, 2 H).

13C NMR (100 MHz, CDCl3): δ = 156.0, 148.9, 145.6, 132.5, 130.5, 121.2, 120.9, 117.8, 117.5, 115.9, 109.4, 109.1, 64.8, 55.7, 48.9.

EI–MS: m/z = 241 [M].

Anal. Calcld for C18H15NO: C, 74.67; H, 6.27; N, 5.81; O, 13.2. Found: C, 74.60; H, 6.39; N, 5.78.

4-(3-Methoxyphenyl)-3,4-dihydro-2H,1,4-benzoxazine (5o)

Yield: 94%; pale yellow oil.

IR (NaCl): 3035, 2960, 2870, 1578, 1482, 1469, 1340, 1255, 1209, 1100, 1056, 830, 749, 693 cm–1.

1H NMR (400 MHz, CDCl3): δ = 7.22 (dd, J = 8.4, 8.4 Hz, 1 H), 6.98–6.55 (m, 7 H), 4.26 (t, J = 4.4 Hz, 2 H), 3.76 (s, 3 H), 3.68 (t, J = 4.4 Hz, 2 H).

13C NMR (100 MHz, CDCl3): δ = 166.7, 150.4, 145.8, 132.5, 130.5, 121.2, 120.9, 117.8, 117.5, 115.9, 109.4, 109.1, 64.8, 55.7, 48.9.

EI–MS: m/z = 241 [M].

Anal. Calcld for C18H15NO: C, 74.67; H, 6.27; N, 5.81; O, 13.2. Found: C, 74.56; H, 6.12; N, 5.96.
**5-Phenyl-2,3,4,5-tetrahydro-1,5-benzoxazepine (5q)**

Yield: 51%; yellow oil.

IR (KBr): 3058, 2941, 2868, 1588, 1488, 1362, 1289, 1241, 1197, 1281, 1237, 1229, 1205, 1140, 100.0, 70.2, 47.8, 27.5.

EI–MS: \( m/z = 315 \) [M].

Anal. Calcd for \( \text{C}_{16}\text{H}_{14}\text{N}_{2}\text{O} \): C, 76.78; H, 5.64; N, 11.19; O, 6.39.

Found: C, 78.86; H, 6.58; N, 5.42.

EI–MS: \( m/z = 225 \) [M].

Anal. Calcd for \( \text{C}_{15}\text{H}_{15}\text{NO} \): C, 79.97; H, 6.71; N, 6.22; O, 7.10.

Found: C, 79.77; H, 6.95; N, 6.10.

EI–MS: \( m/z = 253 \) [M].

Anal. Calcd for \( \text{C}_{14}\text{H}_{12}\text{N}_{2} \): C, 77.72; H, 5.44; N, 16.84.

Found: C, 77.86; H, 5.39; N, 16.89.

References


(15) SIPr·HCl is commercially available from Strem Chemicals Inc.