Direct nitration of five membered heterocycles


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Dedicated to Dr. A.V. Rama Rao on the occasion of his 70th birthday
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Abstract
Direct nitration of a variety of furans, pyrroles, thiophenes, pyrazoles, imidazoles, isoxazoles and thiazoles (17 compounds) with nitric acid/trifluoroacetic anhydride affords mononitro derivatives in average yield of 60 %.

Keywords: Nitration, nitric acid, trifluoroacetic anhydride, nitrofurans, nitropyrroles, nitrothiophenes, nitropyrazoles, nitroimidazoles, nitroisoxazoles, nitrothiazoles

Introduction
Nitro derivatives of five-membered heterocycles are of considerable interest: some are biologically active¹ with anti-inflammatory or vasodilator activity² others are useful synthetic intermediates for many biologically active compounds; for instance, nitroimidazoles form the basis of nitro-heterocycles analogous to megazol, an antiparasitic agent³.

Nitration of five membered ring heterocycles like furans⁴, pyrroles⁵, thiophenes⁶, pyrazoles⁷, imidazoles⁸, isoxazoles⁹ and thiazoles¹⁰ has usually been carried out using either a mixture of concentrated (or fuming) nitric acid and concentrated sulfuric acid, or in some cases with concentrated nitric acid and acetic anhydride (followed by pyridine in case of furans only). The nitration of some of these heterocycles, for example pyrazoles and imidazoles¹¹, isoxazoles¹²,¹³ and isothiazoles¹² has been studied kinetically. Previous efforts to find milder nitration conditions for direct nitration have included use of cerium (IV) ammonium nitrate¹⁴, montmorillonite impregnated with bismuth nitrate¹⁵ and nitration with dinitrogen pentoxide¹⁶,¹⁷.

In light of our success in the direct nitration of pyridines and pyridine analogs with concentrated nitric acid in trifluoroacetic anhydride, which we believe involves N₂O₅¹⁸ led us to apply this method to nitration of five-membered heterocycles and we discuss our results here.
While the present work was in progress, Shackelford and coworkers reported the use of tetramethylammonium nitrate in triflic anhydride and included results of nitration of aromatics like furans, thiophenes and isoxazoles. Our work complements and significantly extends that of Shackelford group.

**Results and Discussion**

**Furans**

Typically furans have been nitrated using acetyl nitrate to give addition products, which are subsequently converted on treatment with pyridine into 2-nitrofurans. We have now achieved the direct nitration of furan itself and a series of its derivatives with nitric acid in trifluoroacetic anhydride (method A as described in the experimental section) (Scheme 1) (Table 1). Compounds 2a-d were characterized spectroscopically (see Experimental).

![Scheme 1](image)

**Table 1. Nitration of furans**

<table>
<thead>
<tr>
<th>Product</th>
<th>R</th>
<th>Yield %, by method A</th>
<th>Literature methods</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Overall Yield</td>
<td>Method &amp; Reagents</td>
</tr>
<tr>
<td>2a</td>
<td>H</td>
<td>68%</td>
<td>14%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>c</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>c</td>
</tr>
<tr>
<td>2b</td>
<td>CH3</td>
<td>65%</td>
<td>34%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>d</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2c</td>
<td>C(CH3)3</td>
<td>75%</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>c</td>
</tr>
<tr>
<td>2d</td>
<td>CH(OOCOCH3)2</td>
<td>58%a</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>c</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>43%</td>
</tr>
</tbody>
</table>
Method A is described in the Experimental section; a) using method A but replacing TFAA by Ac₂O; b) overall yield is the final yield after multistep conversion to nitrofurans starting with furan; c) cross reference of the compound without reported yield; d) overall yield is 34% following the reaction sequence 2-furfuraldehyde – [80%] – 2-furfuryl alcohol – [76%] – 2-iodomethyl-5-nitrofuran – [56%] – 2-methyl-5-nitrofuran; e) general method of synthesis of nitrofurans from furans in two steps using acetyl nitrate via an addition product which is subsequently converted by pyridine into 2-nitrofurans; f) indirect method starting from 2-iodomethyl-5-nitrofuran using thiophenolate anion as the reagent.

Inspection of Table 1 clearly shows the advantage of our new method. In most published nitration procedures for furan, nitroacetate intermediates had to be isolated. Our one step nitration procedure produces much higher yields without isolation of any intermediate.

**Pyrroles**
Again acetyl nitrate has been used for the nitration of pyrrole\(^3\), to give mainly the 2-nitro derivatives (55%). Our nitration method B, gave novel compounds 4a-b from 3a-b respectively (Scheme 2), structures were confirmed spectroscopically (see Experimental).

![Scheme 2](image_url)

**Thiophenes**
Thiophenes are easy to nitrate compared to other five membered heterocycles. They react with mild nitrating agents such as copper nitrate\(^4\), usually in the 2-position. Thiophene (5), on nitration with our reagent gave a 78% yield of 2-nitroderivative (6) by method B (Scheme 3) (Table 2). Shackelford reported the nitration of methyl 2-thiophenecarboxylate to give a mixture of 2- and 4- nitro derivatives (1.6:1) in 91% yield\(^1\).

![Scheme 3](image_url)
Table 2. Nitration of thiophenes

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield %, by method B</th>
<th>Literature methods</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall Yield %</td>
<td>Method / Reagents</td>
</tr>
<tr>
<td>6 2-nitro</td>
<td>78%</td>
<td>Cu(NO₃)₂/Ac₂O</td>
</tr>
<tr>
<td></td>
<td>70%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>K10 clay; HNO₃</td>
</tr>
<tr>
<td></td>
<td>23%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NH₄NO₃/Tf₂O</td>
</tr>
<tr>
<td>8 3-bromo-2-nitro</td>
<td>58%</td>
<td>HNO₃</td>
</tr>
</tbody>
</table>

Method: B as described in the Experimental section; <sup>a</sup>yield from thiophene; <sup>b</sup>yield from thiophene 2-boronic acid; <sup>c</sup>yield from 3-bromothiophene.

We found that the nitration of 3-bromo-thiophene (7) gave a complicated mixture with the main product (8) (58%). The other component were found to be 9, 10a-b, and 11. The structure of 10a was not unambiguously diffretiated from the structure 10b (Scheme 4).

Scheme 4

Pyrazoles

Acetyl nitrate has been employed to nitrate pyrazoles at one of the nitrogen atoms and subsequent rearrangement at 140 °C has been observed to give 3- or 5-nitropyrazoles, sometimes as a mixture. Pyrazole (12) on treatment with our nitrating system following method B gave a 41% yield of the 3,4-dinitrated derivative (13) while N-methylpyrazole under the same reaction condition gave a 65% yield of the 3-nitro product (13). This orientation was confirmed by nOe experiments (Scheme 5) (Table 3).
Method B as described in the Experimental section; a overall yield is the final yield after multistep conversion to nitropyrazole starting with pyrazole as starting material; b overall yield is 68% following the reaction sequence as pyrazole – [80%] – 3-nitropyrazole – [86%] – 3,4-dinitropyrazole; c overall yield is 28% following the reaction sequence as pyrazole – [90%] – 1-methylpyrazole – [32%] – 3,4-dinitropyrazole; d overall yield is 53% following the reaction sequence as 3,5-dimethylpyrazole – [94%] – 4-bromo-3,5-dimethylpyrazole – [53%] – 3,5-dimethyl-4-nitropyrazole; e cross reference of the compound without reported yield; f direct conversion of pyrazole or its derivatives to nitropyrazole; g ring cyclization to pyrazole using dinitromethane as one of the reactants.

3, 5-Dimethylpyrazole (14), on the other hand, gives only 3,5-dimethyl-4-nitropyrazole in 76% yield (Scheme 6) (Table 3).
**Imidazoles**

Imidazoles unsubstituted at nitrogen are easily nitrated by mixed acid nitration\(^{46,47}\). The direct nitration of N-substituted imidazoles is more difficult and most nitro-N-methylimidazoles have been prepared by the N-methylation of the corresponding nitroimidazoles.

A mixture of 4-nitro- (17a) and 5-nitroimidazoles (17b) was obtained by the action of concentrated nitric acid on 1-methylimidazole (16) in trifluoroacetic anhydride at 0-5°C for 12.0 h according to method B (Scheme 7) (Table 4). Yields quoted for (17) and (19) are that of pure isomers isolated by column chromatography.

\[
\text{Imidazole} + (\text{CF}_3\text{CO})_2\text{O} + \text{HNO}_3 \rightarrow \text{Nitroimidazole, 61%} + \text{Nitroimidazole, 28%}
\]

**Scheme 7**

Similarly, a mixture of 1,2-dimethyl-4-nitroimidazole (19a) and 1,2-dimethyl-5-nitroimidazoles (19b) was obtained by the action of concentrated nitric acid on 1,2-dimethylimidazole (18) in trifluoroacetic anhydride at 0-5°C for 12.0 h according to method B (Scheme 8).

\[
\text{Imidazole} + (\text{CF}_3\text{CO})_2\text{O} + \text{HNO}_3 \rightarrow \text{Nitroimidazole, 58%} + \text{Nitroimidazole, 35%}
\]

**Scheme 8**
Table 4. Nitration of imidazoles

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield %, by method B</th>
<th>Overall Yielda %</th>
<th>Method / Reagent</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>17a 1-methyl-4-nitro</td>
<td>61%</td>
<td>22%b</td>
<td>Me₂SO₄/ range of catalyst.</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>44%c</td>
<td>Me₂SO₄</td>
<td>49</td>
</tr>
<tr>
<td>17b 1-methyl-5-nitro</td>
<td>28%</td>
<td>34%d</td>
<td>Me₂SO₄/ range of catalyst.</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>57%</td>
<td>Dimethyl carbonate/18-Crown-6 / K₂CO₃</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>59%</td>
<td>t-BuOK; Reflux in DMF</td>
<td>51</td>
</tr>
<tr>
<td>19a 1,2-dimethyl-4-nitro</td>
<td>58%</td>
<td>47%c</td>
<td>Dimethyl carbonate/18-Crown-6 / K₂CO₃</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25%</td>
<td>Me₂SO₄</td>
<td>52</td>
</tr>
<tr>
<td>19b 1,2-dimethyl-4-nitro</td>
<td>35%</td>
<td>80%</td>
<td>Me₂SO₄</td>
<td>53</td>
</tr>
</tbody>
</table>

Method B as described in the Experimental section. 

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield %, by method B</th>
<th>Overall Yielda %</th>
<th>Method / Reagent</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>17a 1-methyl-4-nitro</td>
<td>61%</td>
<td>22%b</td>
<td>Me₂SO₄/ range of catalyst.</td>
<td>48</td>
</tr>
<tr>
<td>17b 1-methyl-5-nitro</td>
<td>28%</td>
<td>34%d</td>
<td>Me₂SO₄/ range of catalyst.</td>
<td>48</td>
</tr>
<tr>
<td>19a 1,2-dimethyl-4-nitro</td>
<td>58%</td>
<td>47%c</td>
<td>Dimethyl carbonate/18-Crown-6 / K₂CO₃</td>
<td>50</td>
</tr>
<tr>
<td>19b 1,2-dimethyl-4-nitro</td>
<td>35%</td>
<td>80%</td>
<td>Me₂SO₄</td>
<td>53</td>
</tr>
</tbody>
</table>

Method B as described in the Experimental section. 

Isoxazoles

Nitroisoxazoles have been synthesized using various nitrating agents like nitronium fluoroborate54, ammonium nitrate/TFAA 55 or just nitration with mixed acid 56. Our nitration method A when applied to nitration of isoxazole (20a), 5-methylisoxazole (20b) and 3,5-dimethylisoxazole (20c); 2-nitroisoxazole (21a), 5-methyl-3-nitroisoxazole (21b) and 3,5-dimethyl-4-nitroisoxazole (21c) were obtained in the yield of 73%, 64%, and 72% respectively. (Scheme 9) (Table 5). Shackelford 19 found that 3,5-dimethylisoxazole was converted to the 4-nitro derivatives in 96% isolated yield using tetramethylammonium nitrate in triflic anhydride.

Scheme 9
**Table 5. Nitration of isoxazoles**

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield %, by method B</th>
<th>Literature methods</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall Yielda %</td>
<td>Method / Reagent</td>
</tr>
<tr>
<td><strong>21a 4-nitro</strong></td>
<td>73%</td>
<td>NH₄NO₃ / TFA</td>
</tr>
<tr>
<td></td>
<td>51%</td>
<td>HNO₃ / H₂SO₄</td>
</tr>
<tr>
<td></td>
<td>3.5%</td>
<td>HNO₃ / H₂SO₄</td>
</tr>
<tr>
<td></td>
<td>35%</td>
<td>NO₂BF₄</td>
</tr>
<tr>
<td></td>
<td>63%</td>
<td>NH₄NO₃ / TFA</td>
</tr>
<tr>
<td><strong>21b 5-methyl-4-nitro</strong></td>
<td>64%</td>
<td>HNO₃ / H₂SO₄</td>
</tr>
<tr>
<td></td>
<td>67%</td>
<td>HNO₃ / H₂SO₄</td>
</tr>
<tr>
<td></td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>96%</td>
<td>(CH₃)₄NNO₃/Tf₂O</td>
</tr>
<tr>
<td><strong>21c 3,5-dimethyl-4-nitro</strong></td>
<td>72%</td>
<td>HNO₃ / H₂SO₄</td>
</tr>
<tr>
<td></td>
<td>20%</td>
<td></td>
</tr>
</tbody>
</table>

Method B as described in the Experimental section. aoverall yield is the final yield of the conversion to nitroisoxazole starting with isoxazole as starting material. bcross reference of the compound without reported yield. dcirect nitration method of isoxazole to nitrooxazole by using different reagents. dring closure method to synthesize nitrooxazole.

**Thiazoles**

Nitration of thiazoles had not previously been studied extensively.60 2,5-Dimethylthiazole (22), gave 2,5-dimethyl-4-nitrothiazole (23) in 67% yield (Scheme 10), which was characterized spectroscopically (see Experimental). We did not study the nitration of thiazole because it was insoluble in our nitration system.

![Scheme 10](image)

**Experimental Section**

**General Procedures.** Melting points are uncorrected. ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were recorded in CDCl₃ (with TMS for ¹H and chloroform-d for ¹³C as the internal reference) unless specified otherwise.
General method of preparation of nitro derivatives of five membered heterocycles

**Method A.** A mixture of trifluoroacetic anhydride (10 mL) and fuming nitric acid (2.4 mL) was chilled at −15°C and after 1 h a solution of (10 mmol) in trifluoroacetic anhydride (2 mL) was slowly added to the reaction mixture keeping the temperature at -15°C. The reaction mixture was stirred at -15°C for 2 h and then the solvents were removed and pyridine (2 mL) was added to the reaction mixture, stirred for 15 min. And then the solvent was again removed and the oily residue was poured in ice and extracted with diethyl ether. The crude product was then purified over a silica gel column to give pure nitro derivatives.

**Method B.** Trifluoroacetic anhydride [10 mL] was chilled in an ice bath and the substrate heterocycle [17 mmol] was slowly added. After 1 h, concentrated nitric acid [3.0 mL] was added dropwise with cooling. After stirring for 12 h at room temperature, the excess trifluoroacetic acid and nitric acid were removed under vacuum to get the nitro derivatives, which were purified by column chromatography.

**Compound characterization**

**2-Nitrofuran (2a).** Yellowish microcrystals (68 %), mp 28.0–29.0 °C (lit.61 mp 28.8–29.2 °C). 1H NMR: δ 6.68 (dd, J = 3.6, 1.8 Hz, 1H), 7.34 (dd, J = 3.6, 1.0 Hz, 1H), 7.57 (dd, J = 1.8, 1.0 Hz, 1H); 13C NMR: δ 111.43, 113.35, 144.95, 152.71.

**2-Methyl-5-nitrofuran (2b).** White prisms (65 %), mp 42.5-43.5 ºC (lit.62 mp 43.5 ºC). 1H NMR: δ 2.46 (dd, J = 0.9, 0.5 Hz, 3H), 6.31 (dq, J = 3.6, 0.9 Hz, 1H), 7.26 (dq, J = 3.6, 0.5 Hz, 1H); 13C NMR: δ 13.98, 110.01, 113.19, 151.26, 156.84.

**2-(tert-Butyl)-5-nitrofuran (2c).** Yellowish prisms (75 %), mp 56.0-57.0 ºC. 1H NMR: δ 1.36 (s, 9H), 6.24 (d, J = 3.8 Hz, 1H), 7.23 (d, J = 3.8 Hz, 1H); 13C NMR: δ 28.52, 33.45, 106.39, 112.75, 151.19, 168.30. Anal. Calcd for C8H11NO3 (169.18): C, 56.80; H, 6.55; N, 8.28. Found: C, 56.74; H, 6.75; N, 8.08.

**(Acetyloxy)(5-nitro-2-furyl) methyl acetate (2d).** White prisms (58 %), mp 88.6-90.0 °C (lit.30 mp 91.0-92.0 °C). 1H NMR: δ 2.18 (s, 6H), 6.74 (d, J = 3.7 Hz, 1H), 7.30 (d, J = 3.7 Hz, 1H), 7.72 (s, 1H); 13C NMR: δ 20.53, 82.45, 111.45, 112.29, 150.37, 168.05. Anal. Calcd for C9H9NO7 (243.17): C, 44.45; H, 3.73; N, 5.76. Found: C, 44.68; H, 3.67; N, 5.68.

**2,2,2-Trifluoro-1-(4-nitro-1H-pyrrol-2-yl)-1-ethanone (4a).** White prisms (81 %), mp 112.0–113.0 ºC. 1H NMR: δ 7.64 (q, J = 1.8 Hz, 1H), 8.48 (d, J = 1.5 Hz, 1H), 13.86 (br s, 1H); 13C NMR: δ 116.14 (q, Jc,F = 289.7 Hz), 114.68 (q, Jc,F = 3.4 Hz), 124.22, 129.14, 137.76, 170.15 (q, Jc,F =36.1 Hz). Anal. Calcd for C6H3F3N2O3 (208.10): C, 34.63; H, 1.45; N, 13.46. Found C, 34.71; H, 1.22; N, 13.26.

**2,2,2-Trifluoro-1-(1-methyl-4-nitro-1H-pyrrol-2-yl)-1-ethanone (4b).** White prisms (72 %), mp 63.5-64.5 ºC. 1H NMR: δ 4.08 (d, J = 0.5 Hz, 3H), 7.69 (q, J = 1.8 Hz, 1H), 7.84 ( dq, J = 1.8, 0.6 Hz, 1H); 13C NMR: δ 38.99, 116.11, 117.29, 123.69, 131.28, 136.07, 171.33. Anal. Calcd for C7H5F3N2O3 (222.12): C, 37.85; H, 2.27; N, 12.61. Found C, 38.01; H, 2.13; N, 12.34.

**2-Nitrothiophene (6).** White prisms (78 %), mp 42.0–43.0 ºC (lit.63 mp 45.5 ºC). 1H NMR: δ 7.07 (q, J = 4.1, 5.3 Hz, 1H), 7.55 (dd, J = 1.6, 5.3 Hz, 1H), 7.93 (dd, J =1.6, 4.1Hz, 1H); 13C
NMR: δ 126.97, 128.54, 132.50, 152.58. Anal. Calcd for C₄H₃NO₂S (129.14): C, 37.20; H, 2.34; N, 10.85. Found C, 37.33; H, 2.22; N, 10.70.

3-Bromo-2-nitrothiophene (8). Yellowish prisms (58 %); mp 79.0-80.0 °C (lit.37 mp 81.0-83.0 oC). ^1H NMR: δ 7.13 (d, J = 5.6 Hz, 1H), 7.54 (d, J = 5.6 Hz, 1H); ^13C NMR: δ 112.95, 130.97, 132.54, 146.54. Anal. Calcd for C₄H₂BrNO₂S (208.03): C, 23.09; H, 0.97; N, 6.73. Found C, 23.38; H, 0.78; N, 6.53.

3-Bromo-5-nitrothiophene (9). Yellowish prisms (8 %); mp 45.0-46.0 °C (lit.64 mp 46-47.0 oC). ^1H NMR: δ 7.47 (d, J = 1.9 Hz, 1H), 7.85 (d, J = 1.9 Hz, 1H); ^13C NMR: δ 109.98, 129.46, 130.55, 152.06.

3-Bromo-4,5-dinitro-thiophene (10a or 10b). Yellow prisms (4 %); mp 178-180.0ºC (lit.65 mp 165-166ºC for 10b); ^1H NMR: δ 7.95 (s, 1H); ^13C NMR: δ 112.82, 131.26, 133.17, 152.03.

3-Bromo-2,5-dinitro-thiophene (11). Yellow microcrystals prisms (10 %); m.p.: 111-112ºC (lit.67 m.p.: 112-113ºC); ^1H NMR: δ 7.89 (s, 1H); ^13C NMR: δ 111.28, 131.46, 148.40, 151.70.

3,4-Dinitro-1H-pyrazole (13a). White prisms (41 %); mp 90-91ºC (lit. 40 mp 87.5-88.5). ^1H NMR: δ 8.57 (s, 1H); ^13C NMR: δ 132.38, 133.58, 135.38.

1-Methyl-3-nitro-1H-pyrazole (13b). White prisms (65 %), mp 81.0–82.0 ºC (lit. 41 mp 80.0-84.0 ºC). ^1H NMR: δ 4.02 (s, 3H), 6.89 (d, J = 2.4 Hz, 1H), 7.44 (dq, J = 2.4, 0.3 Hz, 1H). ^13C NMR: δ 40.42, 103.14, 132.64, 155.37. Anal. Calcd for C₄H₅N₃O₂ (127.10): C, 37.80; H, 3.97; N, 33.06. Found C, 38.16; H, 3.79; N, 32.79.

3,5-Dimethyl-4-nitro-1H-pyrazole (15). Brownish needles (76%), mp 122.0–123.0 ºC (lit.43 mp 126.0–127.0 ºC). ^1H NMR: δ 2.46 (s, 6H); ^13C NMR: δ 12.69, 130.04, 143.46. Anal. Calcd for C₅H₇N₃O₂ (141.13): C, 42.55; H, 5.00; N, 29.77. Found C, 42.67; H, 5.02; N, 29.43.

1-Methyl-4-nitro-1H-imidazole (17a). White prisms (39 %), mp 133.0–134.0 ºC (lit.48 mp 134 ºC). ^1H NMR: δ 3.83 (s, 3H), 4.72 (br d, J = 1.5 Hz, 1H), 7.78 (d, J = 1.5 Hz, 1H); ^13C NMR: δ 34.55, 120.19, 136.61, 148.00. Anal. Calcd for C₄H₅N₃O₂: C, 37.80; H, 3.97; N, 33.06. Found C, 38.16; H, 3.83; N, 32.86.

1,2-Dimethyl-4-nitro-1H-imidazole (19a). White needles (53 %), mp 182.0–184.0 ºC (lit.50 mp 184 ºC). ^1H NMR: δ 2.39 (s, 3H), 2.47 (s, 3H), 8.54 (s, 1H), 8.87 (s, 1H); ^13C NMR: δ 12.85, 33.74, 120.71, 146.10, 145.07.

1,2-Dimethyl-5-nitro-1H-imidazole (19b). White prisms (18 %), mp 134.0–135.0 ºC (lit.66 mp 134.0-135.0 oC). ^1H NMR: δ 2.39 (s, 3H), 2.47 (s, 3H), 8.54 (s, 1H), 8.87 (s, 1H); ^13C NMR: δ. 13.70, 32.90, 131.89, 149.98.

4-Nitroisoxazole (21a). Yellow prisms (73 %), mp 45.0–46.0 ºC (lit.57 mp 46.0–47.0 ºC). ^1H NMR: δ 8.85 (s, 1H), 9.32 (s, 1H); ^13C NMR: δ 144.44, 157.84. Anal. Calcd for C₃H₂N₂O₃ (114.06): C, 31.59; H, 1.77; N, 24.56. Found C, 31.63; H, 1.55; N, 24.31.

5-Methyl-4-nitroisoxazole (21b). Yellow oil (64 %), (lit.57 bp 88.0–90.0 / 18 Torr). ^1H NMR: δ 2.87 (d, J = 0.7 Hz, 3H), 8.76 (q, J = 0.7 Hz, 1H); ^13C NMR: δ 12.97, 131.08, 145.88, 170.66.

3,5-Dimethyl-4-nitroisoxazole (21c). Yellowish prisms (72 %), mp 63.0-64.0 ºC (lit. 55 mp 63.0-64.0 ºC). ¹H NMR: δ 2.56 (s, 3H), 2.82 (s, 3H); ¹³C NMR: δ 11.49, 13.81, 130.14, 155.50, 171.89.

2,5-Dimethyl-4-nitro-1,3-thiazole (23). Brownish prisms (67 %), mp 55.5–56.5 ºC (lit. 60 mp 56.5 ºC). ¹H NMR: δ 2.71 (s, 3H), 2.79 (s, 3H); ¹³C NMR: δ 13.10, 19.08, 138.36, 150.84, 161.29. Anal. Calcd for C₅H₆N₂O₂S (158.18): C, 37.97; H, 3.82; N, 17.71. Found C, 38.08; H, 3.74; N, 17.54.

References and Notes