

## Synthesis of 4*H*-imidazole-5-carbaldoxime 3-oxides and 4*H*-imidazole-5-carbonitrile 3-oxides

I. A. Kirilyuk,<sup>a\*</sup> D. A. Morozov,<sup>a,b</sup> Yu. S. Tabatchikova,<sup>a</sup> V. S. Medvedev,<sup>a,b</sup> A. V. Lebedev,<sup>a</sup> G. V. Romanenko,<sup>c</sup>  
T. V. Rybalova,<sup>a</sup> and I. A. Grigor'ev<sup>a,b</sup>

<sup>a</sup>N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences,  
9 prosp. Akad. Lavrent'eva, 630090 Novosibirsk, Russian Federation.

Fax: +7 (383) 330 9752. E-mail: kirilyuk@nioch.nsc.ru

<sup>b</sup>Novosibirsk State University,

2 ul. Pirogova, 630090 Novosibirsk, Russian Federation.

Fax: +7 (383) 330 2237. E-mail: m\_falcon@nioch.nsc.ru

<sup>c</sup>International Tomography Center, Siberian Branch of the Russian Academy of Sciences,  
3a ul. Institutskaya, 630090 Novosibirsk, Russian Federation.

Fax: +7 (383) 330 9752

The condensation of 3-hydroxyamino-3-methylbutan-2-one or 3-ethyl-3-hydroxyamino-pentan-2-one with aldehydes and ammonia afforded a series of new 1-hydroxy-4-methyl-2,5-dihydroimidazoles, whose oxidation gave rise to the corresponding 5-methyl-4*H*-imidazole 3-oxides. The latter, like 1-hydroxy-4-methyl-2,5-dihydroimidazoles, react with Pr<sup>IV</sup>ONO in the presence of bases to form 4*H*-imidazole-5-carbaldoxime 3-oxides, which are transformed into 4*H*-imidazole-5-carbonitrile 3-oxides in the reaction with TsCl in the presence of Et<sub>3</sub>N. The by-products produced in different steps of the synthesis were isolated and characterized.

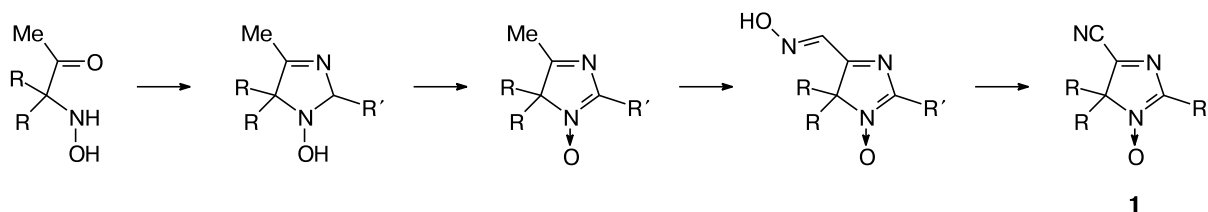
**Key words:** α-hydroxyamino ketones, 4*H*-imidazole 3-oxides, nitrosation, nitrones, 2,5-dihydroimidazoles.

The reactivity of 4*H*-imidazole *N*-oxides imposes limitations on the reaction conditions and the nature of the reagents for the synthesis of functional derivatives of this series. In particular, these compounds readily react with nucleophilic reagents both in acidic<sup>1,2</sup> and alkaline<sup>3</sup> media and can easily undergo one-electron oxidation.<sup>4,5</sup> Recently, we have developed convenient methods for nitrosation of 5-methyl-4*H*-imidazole 3-oxides at the methyl group, which allowed the synthesis of the previously inaccessible derivatives of this series, for example, of 4*H*-imidazole-5-carbonitrile 3-oxides **1**. These compounds readily react with amines, resulting in the replacement of the cyano group. These transformations made it possible to prepare vari-

ous promising pH-sensitive spin probes for biophysical and biomedical studies.<sup>6–9</sup> At the same time, the ease of replacement of the cyano group in compounds **1** offers great possibilities for the synthesis of various functional derivatives, including fungicidally active 3,5-dihydroimidazol-4-ones,<sup>10,11</sup> as well as other potentially biologically active derivatives. In the present study, we considered the characteristic features of the synthesis of the previously unknown 4*H*-imidazole-5-carbonitrile 3-oxides **1** serving as key compounds in the synthesis of functional derivatives of 4*H*-imidazole 3-oxide.

New 4*H*-imidazole-5-carbonitrile 3-oxides **1a–l** were synthesized by analogy with the methods described

Scheme 1



in our earlier study.<sup>6</sup> The general approach is presented in Scheme 1.

1-Hydroxy-2,5-dihydroimidazoles **2a–j** were synthesized by condensation of  $\alpha$ -hydroxyamino ketones **3a,b** with aldehydes in ethanol in the presence of a 25% aqueous ammonia solution (see the Experimental section, method *A*) or an ammonium acetate solution (method *B*) or, alternatively, in a saturated ammonia solution in methanol (method *C*) (Scheme 2, Table 1).

In all cases, the condensation of  $\alpha$ -hydroxyamino ketones **3a,b** with aldehydes and ammonia according to the method *A* affords 1-hydroxy-2,5-dihydroimidazoles **2**; however, the yields of the target compounds in the reactions with aldehydes containing electron-donating substituents  $R'$  are low. In some cases, the use of the method *B* results in an increase in the yield of compounds **2**; however, the yields of the products prepared by condensation with thiophene-2-carbaldehyde and furfural remain low. It should be noted that we succeeded in isolating nitrone **4** from the reaction mixture. Earlier,<sup>12</sup> we have reported that the condensation of 2-hydroxyamino-2-methyl-1-phenylpropan-1-one with thiophene-2-carbaldehyde and ammonia affords exclusively 2-methyl-1-phenyl-2-(thiophen-2-ylmethyleneamino)propan-2-one *N*-oxide (**6**). Attempts to transform the latter compound into the corresponding 1-hydroxy-2,5-dihydroimidazole failed. Unlike compound **6**, ketonitronone **4** can undergo cyclization in the presence of a saturated ammonia solution in methanol to give 1-hydroxy-2,5-dihydroimidazole **2a**; however, several weeks are required to achieve a high conversion in this reaction (*cf.* Ref. 13). The condensation of  $\alpha$ -hydroxyamino ketone **3a** with aldehydes according to the method *C* made it possible to substantially increase the yield of the target compounds **2a,b**.

It should be noted that the best yield of 1-hydroxy-4,5,5-trimethyl-2,5-dihydroimidazole (**2h**) in the condensation of 3-hydroxyamino-3-methylbutan-2-one oxime (**3a**) with formaldehyde and ammonia is achieved within 3 h after mixing of the reagents (method *A*). An increase in the reaction time leads to a substantial decrease in the yield of the target product.

**Table 1.** Methods of synthesis and the yields of compounds **2a–l**

Compound	R	R'	Method	Yield (%)
<b>2a</b>	Me	2-Thienyl	<i>A</i>	30
			<i>B</i>	40
			<i>C</i>	75
<b>2b</b>	Me	2-Furyl	<i>A</i>	25
			<i>C</i>	72
<b>2c</b>	Me	4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	<i>A</i>	85
<b>2d</b>	Me	4-MeOC <sub>6</sub> H <sub>4</sub>	<i>A</i>	35
			<i>B</i>	75
<b>2e</b>	Et	Ph	<i>B</i>	80
<b>2f</b>	Me	2-HOC <sub>6</sub> H <sub>4</sub>	<i>A</i>	35
			<i>B</i>	80
<b>2g</b>	Me	4-(NCCH <sub>2</sub> O)C <sub>6</sub> H <sub>4</sub>	<i>B</i>	70
<b>2h</b>	Me	H	<i>A</i>	80
<b>2i</b>	Me	Me	<i>A</i>	75
<b>2j</b>	Et	CH <sub>2</sub> CH <sub>2</sub> C(Me) <sub>2</sub> NO <sub>2</sub>	<i>A</i>	70
<b>2k</b>	Me	3-Pyridyl	<i>A</i>	85*
<b>2l</b>	Me	2,3,4-(MeO) <sub>3</sub> C <sub>6</sub> H <sub>2</sub>	<i>A</i>	50*

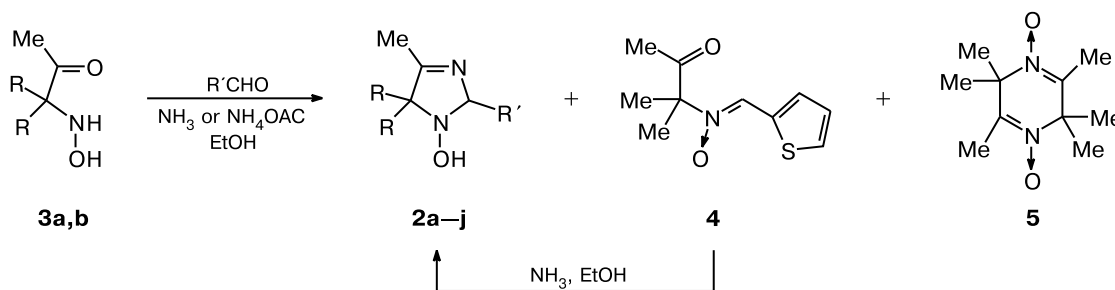
\* The yield of the corresponding 4*H*-imidazole 3-oxide, which was prepared by oxidation of 1-hydroxy-2,5-dihydroimidazole without isolation of the latter.

The synthesis of compounds **2** is also accompanied by the formation of 2,2,3,5,5,6-hexamethyl-2,5-dihydropyrazine 1,4-dioxide (**5**) as a by-product.<sup>14</sup> For example, the reaction of compound **3a** with acetaldehyde and ammonia produces **5** in 15% yield.

The spectroscopic characteristics of 2,5-dihydroimidazoles **2a–j** are consistent with those of the related compounds described earlier<sup>6–8,12</sup> (Tables 2–4).

The oxidation of hydroxylamines **2a–g** with lead dioxide in chloroform smoothly affords stable crystalline 4*H*-imidazole 3-oxides **7a–g** (Scheme 3). It is not necessary to isolate the corresponding 1-hydroxy-2,5-dihydroimidazoles **2** in the free state for the synthesis of 4*H*-imidazole 3-oxides **7**. In some cases, for example, in the case of condensation of  $\alpha$ -hydroxyamino ketone **3a** with 3-pyridinecarbaldehyde, 2,3,4-trimethoxybenzal-

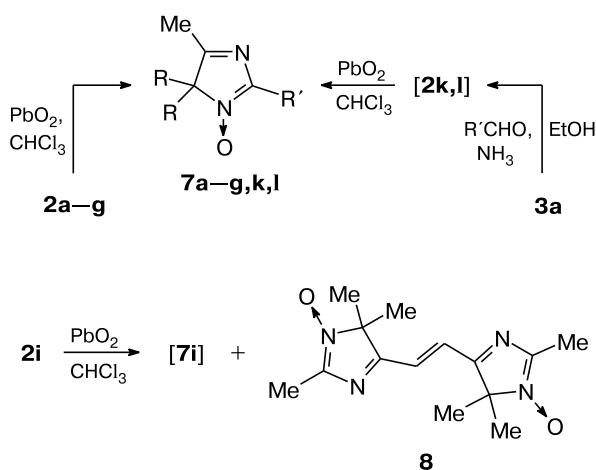
**Scheme 2**



**3:** R = Me (**a**), Et (**b**)

dehyde, and ammonia, the resulting mixture of compounds was oxidized in chloroform without separation (see Scheme 3). 4*H*-Imidazole 3-oxides **7k,l** were isolated by chromatography. The spectroscopic characteristics of the reaction products are given in Tables 2, 5, and 6 and are in good agreement with those of the known derivatives of this series.<sup>6–8,15</sup>

Scheme 3

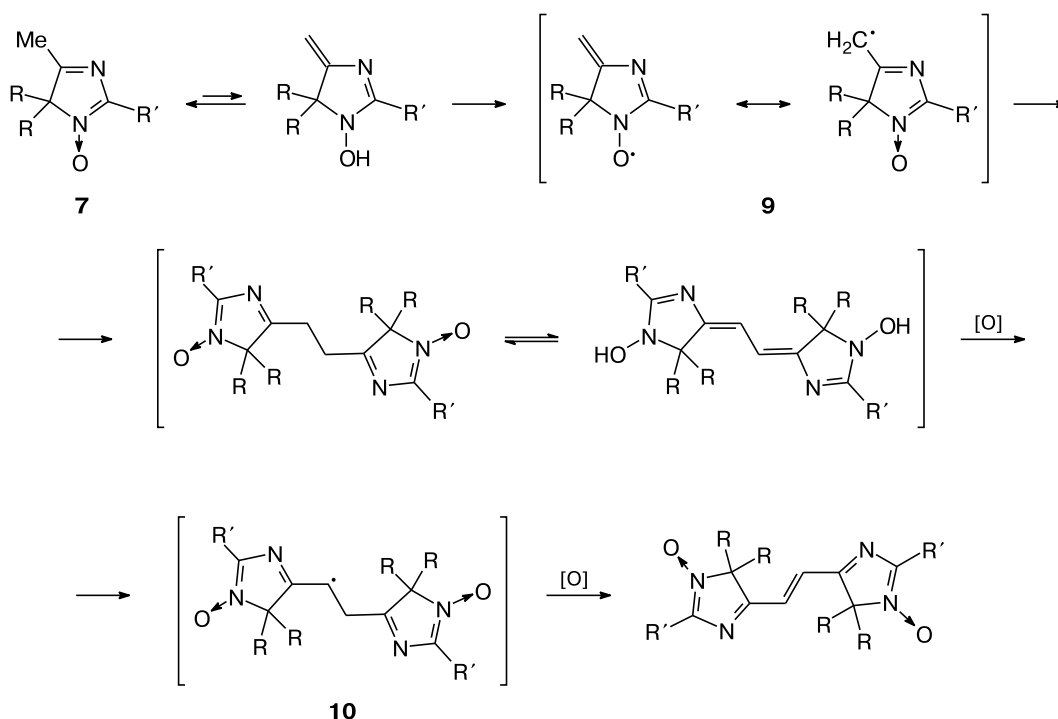


**7**: R = Me (**a–d, f, g, i, k, l**), Et (**e**); R' = 2-thienyl (**a**), 2-furyl (**b**), 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub> (**c**), 4-MeOC<sub>6</sub>H<sub>4</sub> (**d**), Ph (**e**), 2-HOC<sub>6</sub>H<sub>4</sub> (**f**), 4-(NCCH<sub>2</sub>O)C<sub>6</sub>H<sub>4</sub> (**g**), Me (**i**), 3-pyridyl (**k**), 2,3,4-(MeO)<sub>3</sub>C<sub>6</sub>H<sub>2</sub> (**l**)

It should be noted that samples of compounds **7** synthesized according to this method can have a bright color (orange, crimson, or brown) due to the formation of inseparable impurities. The intensity of the color increases in the presence of a large excess of an oxidizing agent.

Unlike compounds **2a–g** containing an aromatic or heteroaromatic substituent at position 2 of the heterocycle, imidazoline **2h** is oxidized with lead or manganese dioxides to give a complex mixture of colored products, among which compound **7h** was not detected. The slow portionwise addition of an oxidizing agent to a solution of compound **2i** resulted in the formation of the reaction mixture containing the corresponding 4*H*-imidazole 3-oxide **7i**. The <sup>1</sup>H NMR spectroscopic data for compound **7i** are given in Table 5. However, **7i** is unstable and attempts to isolate this compound in the pure state failed. In the presence of a larger excess of the oxidizing agent, 4*H*-imidazole 3-oxide **7i** is not accumulated in the reaction mixture, and 1,2-bis(2,4,4-trimethyl-4*H*-imidazol-5-yl 3-oxide)ethylene (**8**) is formed as the major reaction product (see Scheme 3). The UV spectrum of compound **8** has long-wavelength absorption maxima at 459 and 301 nm close to those observed in the spectrum of the structurally similar dimer synthesized earlier.<sup>16</sup> In the <sup>1</sup>H NMR spectrum, the signals of the geminal methyl groups and the methylnitron group are shifted downfield by ~0.1 ppm compared to those in the spectrum of compound **7i**. In addition, the singlet at δ 7.11 corresponding

Scheme 4



**Table 2.** Melting points, elemental analysis data, and the IR and UV spectroscopic data

Com- pound	M.p./°C (solvent)	Found (%)			Molecular formula	IR, $\nu/\text{cm}^{-1}$	UV, $\lambda_{\text{max}}/\text{nm}$ (loge)
		Calculated	C	H			
<b>1a</b>	133–138 (hexane)	<u>54.95</u> 54.78	<u>4.02</u> 4.14	<u>18.98</u> 19.16	$\text{C}_{10}\text{H}_9\text{N}_3\text{OS}$	2223 (C≡N); 1555, 1518 (C=N, C=C)	413 (3.40), 296 (4.17)
<b>1b</b>	105–110 (hexane)	<u>58.80</u> 59.11	<u>4.43</u> 4.46	<u>20.37</u> 20.68	$\text{C}_{10}\text{H}_9\text{N}_3\text{O}_2$	2224 (C≡N); 1596, 1551, 1527, 1501 (C=N, C=C)	410 (3.48), 292 (4.25)
<b>1c</b>	198–202 (hexane)	<u>55.86</u> 55.81	<u>3.95</u> 3.90	<u>21.93</u> 21.70	$\text{C}_{12}\text{H}_{10}\text{N}_4\text{O}_3$	2229 (C≡N); 1596 (C=N); 1517, 1344 (NO <sub>2</sub> )	382 (3.89), 266 (4.19)
<b>1d</b>	117–120 (hexane)	<u>64.32</u> 64.19	<u>5.49</u> 5.39	<u>17.35</u> 17.27	$\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}_2$	2224 (C≡N); 1606, 1577, 1536, 1517 (C=N, C=C)	410 (2.93), 295 (3.92)
<b>1e</b>	57–59 (hexane)	<u>69.74</u> 69.69	<u>6.29</u> 6.27	<u>17.45</u> 17.41	$\text{C}_{14}\text{H}_{15}\text{N}_3\text{O}$	2221 (C≡N); 1527, 1511 (C=N, C=C)	396 (3.78), 275 (3.87)
<b>1f</b>	65–68 (hexane)	<u>62.95</u> 62.87	<u>4.91</u> 4.84	<u>18.34</u> 18.33	$\text{C}_{12}\text{H}_{11}\text{N}_3\text{O}_2$	2231 (C≡N); 1613, 1578, 1555, 1520 (C=N, C=C)	312 (3.78), 246 (4.20)
<b>1g</b>	112–115 (hexane— AcOEt, 1 : 1)	<u>61.77</u> 62.00	<u>6.10</u> 5.81	<u>12.40</u> 12.76	$\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_4$	2221 (C≡N); 1759, 1725 (C=O); 1604, 1574, 1519 (C=N, C=C)	407 (3.32), 294 (4.18)
<b>1h</b>	89–91 (hexane)	<u>52.27</u> 52.55	<u>5.10</u> 5.14	<u>30.23</u> 30.64	$\text{C}_6\text{H}_7\text{N}_3\text{O}$	2227 (C≡N); 1524 (C=N)	353 (3.90), 240 (3.07)
<b>1i</b>	25–29 (hexane)	<u>55.89</u> 55.62	<u>6.38</u> 6.00	<u>27.67</u> 27.80	$\text{C}_7\text{H}_9\text{N}_3\text{O}$	2217 (C≡N); 1597, 1542 (C=N)	367 (3.35), 306 (3.44)
<b>1j</b>	Oil	<u>55.36</u> 55.70	<u>7.34</u> 7.19	<u>19.74</u> 19.99	$\text{C}_{13}\text{H}_{20}\text{N}_4\text{O}_3$	2218 (C≡N); 1540, 1375 (NO <sub>2</sub> )	373 (3.79)
<b>1k</b>	126–128 (hexane)	<u>61.81</u> 61.67	<u>4.78</u> 4.71	<u>26.21</u> 26.15	$\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}$	2229 (C≡N); 1588, 1570, 1528, 1509 (C=C, C=N)	380 (3.67), 290 (3.94)
<b>1l</b>	128–130 (hexane)	<u>59.24</u> 59.40	<u>5.69</u> 5.65	<u>13.44</u> 13.85	$\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_4$	2216 (C≡N); 1597, 1529, 1503 (C=C, C=N)	392 (3.37), 294 (3.93)
<b>2a</b>	177–178 (EtOH)	<u>57.03</u> 57.11	<u>6.76</u> 6.71	<u>13.24</u> 13.32	$\text{C}_{10}\text{H}_{14}\text{N}_2\text{OS}$	1640 (C=N)	—
<b>2b</b>	154–157 (AcOEt)	<u>61.88</u> 61.84	<u>7.30</u> 7.27	<u>14.40</u> 14.42	$\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_2$	1647 (C=N)	—
<b>2c</b>	192–194 (AcOEt)	<u>57.64</u> 57.82	<u>6.29</u> 6.07	<u>17.01</u> 16.86	$\text{C}_{12}\text{H}_{15}\text{N}_3\text{O}_3$	1638 (C=N); 1522, 1349 (NO <sub>2</sub> )	268 (4.02)
<b>2d</b>	146–148 (AcOEt)	<u>66.70</u> 66.64	<u>7.94</u> 7.74	<u>11.70</u> 11.96	$\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_2$	1632 (C=N)	281 (3.06), 274 (3.12)
<b>2e</b>	143–147 (AcOEt)	<u>72.11</u> 72.38	<u>8.72</u> 8.68	<u>11.92</u> 12.06	$\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}$	1643 (C=N)	252 (2.73), 257 (2.70)
<b>2f</b>	188–191 (AcOEt)	<u>64.34</u> 64.12	<u>7.46</u> 7.40	<u>12.38</u> 12.46	$\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}_2 \cdot$ $\cdot 0.25\text{H}_2\text{O}$	1641 (C=N)	278 (3.44)
<b>2g</b>	153–155 (EtOH)	<u>64.79</u> 64.85	<u>6.83</u> 6.61	<u>16.10</u> 16.20	$\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}_2$	1638 (C=N); 2090 (C≡N)	271 (3.07), 278 (3.01)
<b>2h</b>	82–84 (hexane)	<u>56.00</u> 56.22	<u>9.54</u> 9.44	<u>22.06</u> 21.86	$\text{C}_6\text{H}_{12}\text{N}_2\text{O}$	1650 (C=N)	—

(to be continued)

Table 2 (continued)

Compound	M.p./°C (solvent)	Found (%)			Molecular formula	IR, $\nu/\text{cm}^{-1}$	UV, $\lambda_{\text{max}}/\text{nm}$ (log $\epsilon$ )
		Calculated	C	H			
<b>2i</b>	69–71 (hexane)	<u>59.50</u> 59.12	<u>10.02</u> 9.92	<u>19.71</u> 19.70	$\text{C}_7\text{H}_{14}\text{N}_2\text{O}$	1645 (C=N)	—
<b>2j</b>	127–129 (hexane)	<u>57.34</u> 57.54	<u>9.56</u> 9.29	<u>15.25</u> 15.49	$\text{C}_{13}\text{H}_{25}\text{N}_3\text{O}_3$	1650 (C=N); 1538, 1374 ( $\text{NO}_2$ )	—
<b>4</b>	—	<u>56.70</u> 56.85	<u>6.20</u> 6.20	<u>6.56</u> 6.63	$\text{C}_{10}\text{H}_{13}\text{NO}_2\text{S}$	1723 (C=O); 1573, 1502 (C=N, C=C); 3145, 3080, 3074 (H—C=)	318 (4.13)
<b>7a</b>	90–94 (hexane)	<u>57.93</u> 57.67	<u>6.02</u> 5.81	<u>13.70</u> 13.45	$\text{C}_{10}\text{H}_{12}\text{N}_2\text{OS}$	1587, 1558 (C=N, C=C)	345 (3.78), 263 (4.24)
<b>7b</b>	87–89 (hexane)	<u>62.20</u> 62.49	<u>6.39</u> 6.29	<u>14.59</u> 14.57	$\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_2$	1576, 1555, 1522 (C=N, C=C)	342 (3.92), 263 (4.32)
<b>7c</b>	144–147 (AcOEt)	<u>58.17</u> 58.29	<u>5.73</u> 5.30	<u>16.65</u> 16.99	$\text{C}_{12}\text{H}_{13}\text{N}_3\text{O}_3$	1596, 1570 (C=N, C=C); 1516, 1344 ( $\text{NO}_2$ )	367 (3.96), 263 (4.11)
<b>7d</b>	65–68 (hexane)	<u>67.24</u> 67.22	<u>7.12</u> 6.94	<u>11.98</u> 12.06	$\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}_2$	1604, 1587, 1540 (C=N, C=C)	340 (3.96), 268 (4.37)
<b>7e</b>	103–105 (hexane)	<u>73.22</u> 73.01	<u>7.99</u> 7.88	<u>12.17</u> 12.16	$\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}$	1588, 1570, 1527 (C=N, C=C)	332 (3.79), 246 (4.26)
<b>7f</b>	125–126 (hexane)	<u>66.32</u> 66.04	<u>6.53</u> 6.47	<u>12.75</u> 12.84	$\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_2$	1610, 1589, 1553 (C=N, C=C)	314 (3.33), 247 (3.83)
<b>7g</b>	176–178 (AcOEt)	<u>65.54</u> 65.35	<u>5.98</u> 5.88	<u>16.20</u> 16.33	$\text{C}_{14}\text{H}_{15}\text{N}_3\text{O}_2$	1605, 1587, 1567, 1543 (C=N, C=C); 2070 (C≡N)	335 (3.90), 262 (4.36)
<b>7k</b>	96–99 (hexane)	<u>64.77</u> 65.01	<u>6.38</u> 6.45	<u>16.26</u> 16.08	$\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}$	1584, 1560, 1520 (C=N, C=C)	332 (3.90), 241 (4.28)
<b>7l</b>	153–156 (AcOEt)	<u>61.53</u> 61.63	<u>9.65</u> 9.58	<u>7.01</u> 6.90	$\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_4$	1595, 1585, 1532 (C=N, C=C)	329 (3.73), 261 (4.11)
<b>8</b>	220–222 (hexane)	<u>60.95</u> 60.85	<u>7.32</u> 7.30	<u>20.05</u> 20.28	$\text{C}_{14}\text{H}_{20}\text{N}_4\text{O}_2$	1536 (C=N, C=C)	459 (4.31), 301 (3.58)
<b>11a</b>	225–235 (AcOEt)	<u>48.48</u> 48.77	<u>4.59</u> 4.91	<u>16.72</u> 17.06	$\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}_2\text{S} \cdot$ $\cdot 0.5\text{H}_2\text{O}$	1563, 1539 (C=N, C=C)	382 (3.58), 288 (4.48)
<b>11b</b>	205–211 (AcOEt)	<u>54.25</u> 54.29	<u>5.18</u> 5.01	<u>18.90</u> 19.00	$\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}_3$	1592, 1537 (C=N, C=C)	389 (3.64), 283 (4.51)
<b>11c</b>	234–237 (AcOEt)	<u>51.87</u> 52.17	<u>4.30</u> 4.38	<u>20.25</u> 20.28	$\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_4$	1571, 1506 (C=N, C=C); 1516, 1336 ( $\text{NO}_2$ )	371 (4.06), 279 (4.26)
<b>11d</b>	230–234 (EtOH)	<u>59.74</u> 59.76	<u>6.03</u> 5.79	<u>15.74</u> 16.08	$\text{C}_{13}\text{H}_{15}\text{N}_3\text{O}_3$	1603, 1572, 1541 (C=N, C=C)	381 (3.55), 290 (4.50)
<b>11e</b>	196–200 (AcOEt)	<u>63.51</u> 63.38	<u>6.87</u> 6.71	<u>15.41</u> 15.84	$\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}_2 \cdot$ $\cdot 1/3\text{H}_2\text{O}$	1579, 1539 (C=N, C=C)	378 (3.67), 269 (4.52)
<b>11f</b>	211–216 (AcOEt)	<u>58.33</u> 58.29	<u>5.40</u> 5.30	<u>17.04</u> 16.99	$\text{C}_{12}\text{H}_{13}\text{N}_3\text{O}_3$	1608, 1551, 1530 (C=N, C=C)	334 (3.32), 270 (3.90)
<b>11g</b>	186–189 (AcOEt)	<u>58.71</u> 58.78	<u>6.07</u> 6.09	<u>12.17</u> 12.10	$\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}_5$	1759 (C=O); 1606, 1576, 1543 (C=N, C=C)	382 (3.61), 287 (4.53)
<b>11h</b>	170 (decomp.) (EtOH)	<u>46.53</u> 46.45	<u>6.03</u> 5.85	<u>26.82</u> 27.08	$\text{C}_6\text{H}_9\text{N}_3\text{O}_2$	1542, 1505 (C=N, C=C); 3161 (C—H, nitron)	353 (3.88), 229 (3.93)

(to be continued)

**Table 2** (continued)

Compound	M.p./°C (solvent)	Found Calculated (%)			Molecular formula	IR, v/cm <sup>-1</sup>	UV, λ <sub>max</sub> /nm (logε)
		C	H	N			
<b>11i</b>	205–210 (AcOEt)	<u>49.87</u> 49.70	<u>6.77</u> 6.55	<u>25.09</u> 24.84	C <sub>7</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	1566, 1521 (C=N, C=C)	361 (3.97), 259 (4.01)
<b>11j</b>	167–169 (AcOEt)	<u>52.07</u> 52.34	<u>7.61</u> 7.43	<u>18.76</u> 18.78	C <sub>13</sub> H <sub>22</sub> N <sub>4</sub> O <sub>4</sub>	1562 (C=N, C=C); 1535, 1374 (NO <sub>2</sub> )	367 (3.85), 277 (3.45)
<b>11k</b>	210–214 (AcOEt)	<u>56.85</u> 56.89	<u>5.53</u> 5.21	<u>23.96</u> 24.12	C <sub>11</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub>	1596, 1574, 1534 (C=N, C=C)	377 (3.55), 286 (4.16)
<b>11l</b>	155–157 (AcOEt)	<u>56.33</u> 56.07	<u>6.05</u> 5.96	<u>12.96</u> 13.08	C <sub>15</sub> H <sub>19</sub> N <sub>3</sub> O <sub>5</sub>	1601, 1546, 1532 (C=N, C=C)	377 (3.55), 286 (4.16)
<b>12</b>	217–221 (AcOEt)	<u>70.28</u> 70.66	<u>6.57</u> 6.64	<u>13.43</u> 13.73	C <sub>42</sub> H <sub>47</sub> N <sub>7</sub> O <sub>4</sub>	1524 br (C=N, C=C)	519 (4.30), 491 (4.33), 379 (4.05), 361 (4.04) (CHCl <sub>3</sub> )
<b>13</b>	230–234 (AcOEt)	<u>70.33</u> 70.02	<u>7.29</u> 6.92	<u>12.76</u> 12.70	C <sub>43</sub> H <sub>49</sub> N <sub>7</sub> O <sub>4</sub> · ·0.5AcOEt	1521 br (C=N, C=C)	482 (4.28), 370 (4.05), 352 (4.03), 280 (4.67)
<b>18</b>	180–184 (AcOEt)	<u>52.61</u> 52.34	<u>7.69</u> 7.43	<u>18.91</u> 18.78	C <sub>13</sub> H <sub>22</sub> N <sub>4</sub> O <sub>4</sub>	1566 (C=N, C=C); 1545, 1344 (NO <sub>2</sub> )	329 (3.72), 243 (4.05)
<b>19</b>	201–203 (AcOEt)	<u>47.77</u> 47.70	<u>6.57</u> 6.47	<u>21.28</u> 21.39	C <sub>13</sub> H <sub>21</sub> N <sub>5</sub> O <sub>5</sub>	1530, 1507 (C=N, C=C); 1536, 1348 (NO <sub>2</sub> )	369 (3.70), 261 (4.30)

*Note.* The elemental analysis data for S, found/calculated (%): 14.30/14.62 (**1a**), 15.00/15.25 (**2a**), 15.06/15.18 (**4**), 15.40/15.40 (**7a**), 13.00/13.02 (**11a**).

to the proton of the ethylene fragment is observed instead of the singlet for the protons of the methyl group at position 5 of the heterocycle.

It is known<sup>16</sup> that the oxidation of 4*H*-imidazole 3-oxides containing the ethoxycarbonylmethyl or benzoylmethyl fragment at position 5 of the heterocycle and existing in equilibrium with the ene hydroxylamine tautomeric form can afford vinyl imino nitroxide radicals, which are transformed into ethane- or ethylene-type dimers. Apparently, the oxidation of compounds **7** can also be accompanied by these transformations (Scheme 4).

The successive conjugation of the imino and nitron groups in 5-methyl-4*H*-imidazole 3-oxides **7** leads to an increase in the acidity of the methyl group at position 5 of the heterocycle and is responsible for the ease of enolization and reactions with electrophilic reagents. 4*H*-Imidazole 3-oxides **7a–f, k, l** were nitrosated with isopropyl nitrite in the presence of bases (Scheme 5). In most cases, the best yield and the satisfactory reaction rate were achieved in the reactions with the use of sodium isopropoxide in propan-2-ol as the base. Poorly soluble compound **7c** was nitrosated with a solution of sodium methoxide in methanol. The nitrosation of compound **7f**

was performed in the presence of triethylamine. Oximes **11** are yellow, brown, or orange crystalline compounds.

The nitrosation of compound **7g** in the presence of sodium isopropoxide is accompanied by the attachment of propan-2-ol at the nitrile group. As a result, isopropyl ester of the corresponding carboxylic acid **11g** was isolated after the treatment of the reaction mixture (see Scheme 5).

The reaction of compound **7e** with isopropyl nitrite in the presence of sodium isopropoxide produced a mixture, from which bright-red crystalline compound **12** was isolated in 15% yield along with oxime **11e** (Scheme 6). The <sup>1</sup>H and <sup>13</sup>C NMR spectra of compound **12** have a triple set of signals of the 5,5-diethyl-2-phenyl-4*H*-imidazole 3-oxide fragment. In addition, the NMR spectra have signals of the ketoxime group and the trisubstituted ethylene fragment. The UV spectrum has long-wavelength absorption maxima at 519 and 491 nm corresponding to the bathochromic shift by 120–140 nm compared to the spectrum of oxime **11e**. These maxima are indicative of the presence of an extended conjugated system. Based on these data and the results of elemental analysis, we assigned the structure of 1,2,3-tris(4,4-diethyl-2-phenyl-4*H*-imidazol-5-yl 3-oxide)propanone oxime to com-

Table 3. <sup>1</sup>H NMR spectroscopic data for 1-hydroxy-4-methyl-2,5-dihydroimidazoles **2a–j**

Com- pound	Solvent	$\delta$ (J/Hz)						
		H(2) (1 H)	4-Me (3 H)	5-R	2-R'			OH (s, 1 H)
					C(2)H (H <sub>o</sub> )	C(3)H (H <sub>m</sub> )	C(4)H (H <sub>p</sub> )	Other H
<b>2a</b>	CD <sub>3</sub> OD— CDCl <sub>3</sub>	5.66 (q, J = 2)	2.04 (d, J = 2)	1.24, 1.32 (both s, 3 H each)	7.19 (m, 1 H)	7.01 (m, 1 H)	7.33 (m, 1 H)	—
<b>2b</b>	(CD <sub>3</sub> ) <sub>2</sub> CO	5.36 (q, J = 2.5)	1.93 (d, J = 2.5)	1.15, 1.20 (both s, 3 H each)	6.31 (m, 1 H)	6.34 (m, 1 H)	7.46 (m, 1 H)	7.31
<b>2c</b>	CDCl <sub>3</sub> — (CD <sub>3</sub> ) <sub>2</sub> SO	5.38 (s)	1.97 (s)	1.15, 1.21 (both s, 3 H each)	7.67, 8.16 (AA'BB' system, J = 7.5)	—	—	7.83
<b>2d</b>	(CD <sub>3</sub> ) <sub>2</sub> CO	5.27 (q, J = 2)	1.95 (d, J = 2)	1.18, 1.22 (both s, 3 H each)	7.33, 6.88 (AA'BB' system, J = 8.5)	—	—	7.01
<b>2e</b>	CDCl <sub>3</sub>	5.58 (q, J = 2)	1.87 (d, J = 2)	0.85, 0.94 (both t, 3 H each, J = 7.5); 1.45, 2.00 (both m, 3 H each)	7.27–7.39 (m, 5 H)	—	—	5.31
<b>2f</b>	(CD <sub>3</sub> ) <sub>2</sub> SO	5.55 (br.s)	1.92 (br.s)	1.11, 1.22 (both s, 3 H each)	7.26 (m, 1 H)	6.77 (m, 2 H)	7.12 (m, 1 H)	—
<b>2g</b>	(CD <sub>3</sub> ) <sub>2</sub> SO	5.22 (q, J = 2)	1.94 (d, J = 2)	1.10, 1.18 (both s, 3 H each)	7.38, 7.05 (AA'BB' system, J = 8.7)	—	—	7.73
<b>2h</b>	CDCl <sub>3</sub>	4.69 (q, J = 2)	1.93 (t, J = 2)	1.15 (s, 6 H)	—	—	—	8.10
<b>2i</b>	CDCl <sub>3</sub>	4.56 (m)	1.92 (d, J = 2)	1.10, 1.23 (both s, 3 H each)	—	—	—	—
<b>2j</b>	CDCl <sub>3</sub>	4.63 (m)	1.87 (d, J = 2)	0.78, 0.84, (both t, 3 H each, J = 7.2); 1.35 (q, 1 H, CH <sub>2</sub> (Et), J = 7.2); 1.97 (AB system, 1 H, CH <sub>2</sub> (Et), J = 14.5); 1.49 (m, 2 H, CH <sub>2</sub> (Et))	1.53, 1.67 (both m, 1 H each, CH <sub>2</sub> CH <sub>2</sub> CNO <sub>2</sub> ); 2.00, 2.16 (both m, 1 H each, CH <sub>2</sub> CNO <sub>2</sub> )	—	—	5.15

Note. The NMR spectra were recorded on Bruker AC 200 (compounds **2a, b, e, h**), Bruker AV 300 (compounds **2c, d, f, g, i**), and Bruker AM 400 (compound **2j**) instruments.

Table 4. <sup>13</sup>C NMR spectroscopic data ( $\delta$ ) for 1-hydroxy-4-methyl-2,5-dihydroimidazoles **2a–j**

Com- pound	Solvent	5-R					2-R'				
		C(4)	C(5)	4-Me	Me	CH <sub>2</sub>	C(1) (C <sub>i</sub> )	C(2) (C <sub>o</sub> )	C(3) (C <sub>m</sub> )	C(4) (C <sub>p</sub> )	Other C
<b>2a</b>	CD <sub>3</sub> OD— (CD <sub>3</sub> ) <sub>2</sub> SO	86.99	180.07	15.70	15.82, 24.07	—	145.44	126.73	125.56	125.41	—
<b>2b</b>	(CD <sub>3</sub> ) <sub>2</sub> CO	87.02	179.70	16.15	16.73, 23.85	—	152.27	108.56	110.17	142.59	—
<b>2c</b>	CDCl <sub>3</sub> — (CD <sub>3</sub> ) <sub>2</sub> SO	89.84	179.93	16.54	16.16, 24.38	—	148.80	123.21	129.07	147.41	—

(to be continued)

Table 4 (continued)

Com- pound	Solvent	C(2)	C(4)	C(5)	4-Me	5-R		2-R'				
						Me	CH <sub>2</sub>	C(1)(C <sub>i</sub> )	C(2)(C <sub>o</sub> )	C(3)(C <sub>m</sub> )	C(4)(C <sub>p</sub> )	Other C
<b>2d</b>	—	90.89	178.94	71.60	16.09	15.76, 23.53	—	131.99	129.09	113.48	159.43	55.20
<b>2e</b>	CDCl <sub>3</sub>	92.97	178.26	78.50	16.63	8.52, 9.47	25.75, 29.10	141.15	128.04	127.52	127.81	—
<b>2f</b>	(CD <sub>3</sub> ) <sub>2</sub> SO	88.19	178.46	71.14	16.15	15.86, 24.12	—	124.81	156.66, 129.58	119.13, 116.06	129.08	—
<b>2g</b>	(CD <sub>3</sub> ) <sub>2</sub> SO	89.49	178.19	70.80	16.06	15.56, 24.10	—	135.39	129.11	114.23	155.75	53.49 (CH <sub>2</sub> ); 116 (CN)
<b>2h</b>	CDCl <sub>3</sub>	83.20	176.20	73.80	14.90	20.10	—	—	—	—	—	—
<b>2i</b>	CDCl <sub>3</sub>	85.40	177.11	71.65	16.18	15.64, 23.69	—	—	—	—	—	19.06
<b>2j</b>	CDCl <sub>3</sub>	91.30	176.52	78.84	17.04	8.55, 9.54	25.86, 29.84	29.47 (CH <sub>2</sub> ); 36.15 (CH <sub>2</sub> CNO <sub>2</sub> ); 25.67, 25.88 (CH <sub>3</sub> ); 88.18 (CNO <sub>2</sub> )	—	—	—	—

Note. The NMR spectra were recorded on Bruker AV 300 (compounds **2a–i**) and Bruker AM 400 (compound **2j**) instruments operating at 75 and 100 MHz, respectively.

Table 5. Yields and the <sup>1</sup>H NMR spectroscopic data for 4*H*-imidazole 3-oxides

Com- pound	Yield (%)	Solvent	δ (J/Hz)					
			5-R (s)	4-R	2-R'		Other H	
<b>1a</b>	90	CDCl <sub>3</sub> <sup>a</sup>	—	1.62 (s, 6 H)	8.05 (m, 1 H)	7.22 (m, 1 H)	7.60 (m, 1 H)	—
<b>1b</b>	90	CDCl <sub>3</sub> <sup>a</sup>	—	1.60 (s, 6 H)	7.62 (m, 1 H)	6.63 (m, 1 H)	7.65 (m, 1 H)	—
<b>1c</b>	80	CDCl <sub>3</sub> <sup>b</sup>	—	1.65 (s, 6 H)	8.68, 8.30 (AA'BB' system, <i>J</i> = 9)	—	—	—
<b>1d</b>	85	(CD <sub>3</sub> ) <sub>2</sub> CO <sup>a</sup>	—	1.62 (s, 6 H)	8.51, 7.10 (AA'BB' system, <i>J</i> = 9)	—	—	3.89 (s, 3 H, OMe)
<b>1e</b>	90	CDCl <sub>3</sub> <sup>c</sup>	—	0.70 (t, 6 H, 2 CH <sub>3</sub> , <i>J</i> = 7.3); 2.12 (q, 4 H, 2 CH <sub>2</sub> , <i>J</i> = 7.3)	8.60 (m, 2 H)	7.51 (m, 3 H)	7.48 (m, 1 H)	10.72 (s, 1 H)
<b>1f</b>	80	CDCl <sub>3</sub> <sup>c</sup>	—	1.70 (s, 6 H)	7.90 (m, 1 H)	6.99 (m, 2 H)	7.48 (m, 1 H)	4.80 (s, 2 H, CH <sub>2</sub> ); 5.06 (sept, 1 H, CH); 1.23 (d, CH <sub>3</sub> , <i>J</i> = 6.2)
<b>1g</b>	80	(CD <sub>3</sub> ) <sub>2</sub> CO <sup>b</sup>	—	1.62 (s, 6 H)	8.51, 7.10 (AA'BB' system, <i>J</i> = 9)	—	—	—

(to be continued)



Table 5 (continued)

Com- pound	Yield (%)	Solvent	$\delta$ (J/Hz)					
			5-R (s)	4-R	2-R'			
					C(2)H (H <sub>o</sub> )	C(3)H (H <sub>m</sub> )	C(4)H (H <sub>p</sub> )	Other H
<b>1h</b>	70	CDCl <sub>3</sub> <sup>c</sup>	—	1.53 (s, 6 H)	—	—	—	7.88 (s, 1 H)
<b>1i</b>	80	CDCl <sub>3</sub> <sup>c</sup>	—	1.52 (s, 6 H)	—	—	—	2.40 (s, 3 H)
<b>1j</b>	80	CDCl <sub>3</sub> <sup>c</sup>	—	0.56 (t, 6 H, 2 CH <sub>3</sub> , <i>J</i> = 7.3); 1.91 (q, 2 H, CH <sub>2</sub> , <i>J</i> = 7.3); 1.97 (AB system, 2 H, CH <sub>2</sub> , <i>J</i> <sub>AB</sub> = 14.5)	—	2.22, 2.70 (both m, 2 H each, CH <sub>2</sub> CH <sub>2</sub> ); 1.56 (s, 6 H, 2 CH <sub>3</sub> )	—	—
<b>1k</b>	90	(CD <sub>3</sub> ) <sub>2</sub> CO <sup>a</sup>	—	1.68 (s, 6 H)	—	9.61, 8.84 (both m, 1 H)	7.56 (m, 1 H)	8.71 (m, 1 H)
<b>1l</b>	90	CDCl <sub>3</sub> <sup>a</sup>	—	1.60 (s, 6 H)	—	7.87 (d, 1 H, <i>J</i> = 9)	6.77 (d, 1 H, <i>J</i> = 9)	—
<b>7a</b>	90	CDCl <sub>3</sub> <sup>a</sup>	2.32 (3 H)	1.47 (s, 6 H)	—	8.02 (m, 1 H)	7.17 (m, 1 H)	7.52 (m, 1 H)
<b>7b</b>	90	(CD <sub>3</sub> ) <sub>2</sub> CO <sup>a</sup>	2.31 (3 H)	1.42 (s, 6 H)	—	7.67 (m, 1 H)	6.68 (m, 1 H)	7.75 (m, 1 H)
<b>7c</b>	95	CDCl <sub>3</sub> <sup>c</sup>	2.34 (3 H)	1.49 (s, 6 H)	—	8.79, 8.25 (AA'BB' system, <i>J</i> = 9)	—	—
<b>7d</b>	90	(CD <sub>3</sub> ) <sub>2</sub> CO <sup>a</sup>	2.32 (3 H)	1.42 (s, 6 H)	—	8.68, 7.05 (AA'BB' system, <i>J</i> = 9)	—	3.86 (s, 3 H, OMe)
<b>7e</b>	90	CDCl <sub>3</sub> <sup>b</sup>	2.23 (3 H)	0.55 (t, 6 H, 2 CH <sub>3</sub> , <i>J</i> = 7); 1.77 (q, 2 H, CH <sub>2</sub> , <i>J</i> = 7.2); 2.08 (AB system, 2 H, CH <sub>2</sub> , <i>J</i> <sub>AB</sub> = 14.5)	—	8.68 (m, 2 H)	7.44 (m, 3 H)	—
<b>7f</b>	95	CDCl <sub>3</sub> <sup>c</sup>	2.31 (3 H)	1.47 (s, 6 H)	—	7.92 (m, 1 H)	6.91 (m, 2 H)	7.38 (m, 1 H)
<b>7g</b>	85	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>c</sup>	2.38 (3 H)	1.51 (s, 6 H)	—	8.69, 7.15 (AA'BB' system, <i>J</i> = 10)	—	12.26 (s, 1 H, OH)
<b>7i</b>	—	CDCl <sub>3</sub> <sup>c</sup>	2.28 (3 H)	1.41 (s, 6 H)	—	—	—	4.98 (s, 2 H, CH <sub>2</sub> )
<b>7k</b>	85	(CD <sub>3</sub> ) <sub>2</sub> CO <sup>a</sup>	2.36 (3 H)	1.47 (s, 6 H)	—	9.72, 8.98 (both m, 1 H each)	7.49 (m, 1 H)	8.63 (m, 1 H)
<b>7l</b>	50	CDCl <sub>3</sub> <sup>a</sup>	2.31 (3 H)	1.46 (s, 6 H)	—	8.04 (d, 1 H, <i>J</i> = 9)	6.73 (d, 1 H, <i>J</i> = 9)	—
<b>8</b>	32	CDCl <sub>3</sub> <sup>c</sup>	7.11 (1 H)	1.56 (s, 6 H)	—	—	—	—
<b>11a</b>	80	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>b</sup>	8.03 (1 H, CH)	1.70 (s, 6 H)	—	8.15 (m, 1 H)	7.29 (m, 1 H)	7.77 (m, 1 H)
<b>11b</b>	70	(CD <sub>3</sub> ) <sub>2</sub> CO <sup>a</sup>	7.99 (1 H, CH); 11.70 (1 H, OH)	1.57 (s, 6 H)	—	7.67 (m, 1 H)	6.71 (m, 1 H)	7.79 (m, 1 H)
<b>11c</b>	70	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>a</sup>	8.07 (1 H, CH)	1.61 (s, 6 H)	—	8.76, 8.40 (AA'BB' system, <i>J</i> = 9)	—	—
<b>11d</b>	70	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>b</sup>	7.96 (1 H, CH); 12.70 (1 H, OH)	1.51 (s, 6 H)	—	8.49, 7.05 (AA'BB' system, <i>J</i> = 9)	—	3.79 (s, 3 H, OMe)

(to be continued)

Table 5 (continued)

Com- pound	Yield (%)	Solvent	5-R (s)	δ (J/Hz)				
				4-R	C(2)H (H <sub>o</sub> )	C(3)H (H <sub>m</sub> )	2-R'	Other H
<b>11e</b>	55	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>c</sup>	8.03 (1 H, CH)	0.55 (t, 6 H, 2 CH <sub>3</sub> , <i>J</i> = 7.3); 2.11 (q, 2 H, CH <sub>2</sub> , <i>J</i> = 7.3); 2.23 (AB system, 2 H, CH <sub>2</sub> , <i>J</i> <sub>AB</sub> = 14.6)	8.63 (m, 2 H)	7.50 (m, 3 H)	—	—
<b>11f</b>	70	(CD <sub>3</sub> ) <sub>2</sub> CO <sup>a</sup>	8.07 (1 H, CH); 11.93 (1 H, OH)	1.68 (s, 6 H)	7.97 (m, 1 H)	6.92 (m, 2 H)	7.45 (m, 1 H)	11.94 (s, 1 H, OH)
<b>11g</b>	50	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>a</sup>	7.99 (1 H, CH)	1.66 (s, 6 H)	8.63, 7.04 (AA'BB' system, <i>J</i> = 9)	—	—	4.69 (s, 2 H, CH <sub>2</sub> ); 5.13 (sept, 1 H, CH); 1.28 (d, CH <sub>3</sub> , <i>J</i> = 6.2)
<b>11h</b>	75	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>a</sup>	8.05 (1 H, CH)	1.62 (s, 6 H)	—	—	—	7.92 (s, 1 H, CH)
<b>11i</b>	65	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>a</sup>	7.89 (1 H, CH)	1.59 (s, 6 H)	—	—	—	2.39 (s, 3 H)
<b>11j</b>	50	CDCl <sub>3</sub> <sup>b</sup>	7.82 (1 H, CH); 11.93 (1 H, OH)	0.40 (t, 6 H, 2 CH <sub>3</sub> , <i>J</i> = 7.2); 1.96 (q, 2 H, CH <sub>2</sub> , <i>J</i> = 7.2); 2.06 (AB system, 2 H, CH <sub>2</sub> , <i>J</i> <sub>AB</sub> = 14.4)	2.23, 2.69 (both m, 2 H each, CH <sub>2</sub> CH <sub>2</sub> ); 1.55 (s, 6 H, 2 CH <sub>3</sub> )	—	—	—
<b>11k</b>	80	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>a</sup>	8.05 (1 H, CH); 12.73 (1 H, OH)	1.55 (s, 6 H)	9.62, 8.85 (both m, 1 H each)	7.58 (m, 1 H)	8.68 (m, 1 H)	—
<b>11l</b>	65	CDCl <sub>3</sub> <sup>a</sup>	8.05 (1 H, CH); 12.73 (1 H, OH)	1.74 (s, 6 H)	7.95 (d, 1 H, <i>J</i> = 9)	6.77 (d, 1 H, <i>J</i> = 9)	—	3.87, 3.91, 3.96 (all s, 3 H each)
<b>12</b>	13	CDCl <sub>3</sub> <sup>c</sup>	6.99 (1 H, CH); 12.76 (1 H, OH)	0.15 (br.t, 3 H, Me); 0.54 (t, 3 H, Me, <i>J</i> = 7.1); 0.63, 0.94 (both m, 6 H each, Me); 1.94, 2.20 (both m, 3 H each, CH <sub>2</sub> ); 2.42 (m, 2 H, CH <sub>2</sub> ); 2.55 (m, 1 H, CH <sub>2</sub> ); 2.74 (br.m, 2 H, CH <sub>2</sub> ); 2.94 (br.m, 1 H, CH <sub>2</sub> )	8.45, 8.59, 8.63 (all m, 2 H each)	7.07 (br.m, 2 H); 7.37 (br.m, 1 H); 7.45 (m, 4 H); 7.53 (br.m, 2 H)	—	—
<b>13</b>	60	CDCl <sub>3</sub> <sup>c</sup>	4.14 (3 H, OMe); 6.93 (1 H, CH)	0.22, 0.51, 0.65, 0.94 (all t, 3 H each, Me, <i>J</i> = 7.3); 0.87 (t, 6 H, Me, <i>J</i> = 7.3); 1.94, 2.13 (both m, 3 H each, CH <sub>2</sub> ); 2.25 (m, 2 H, CH <sub>2</sub> ); 2.52 (m, 4 H, CH <sub>2</sub> )	8.47 (m, 2 H); 8.56 (m, 4 H)	7.34, 7.43, 7.48 (all m, 3 H each)	—	—
<b>18</b>	15	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>b</sup>	2.26 (3 H, Me)	0.59 (t, 6 H, 2 CH <sub>3</sub> , <i>J</i> = 7.3); 1.86 (q, 2 H, CH <sub>2</sub> , <i>J</i> = 7.3); 2.03 (AB system, 2 H, CH <sub>2</sub> , <i>J</i> <sub>AB</sub> = 14.5)	1.65 (s, 6 H, 2 CH <sub>3</sub> ); 3.73 (s, 2 H, CH <sub>2</sub> )	—	—	—
<b>19</b>	7	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>b</sup>	7.94 (1 H, CH)	0.57 (t, 6 H, 2 CH <sub>3</sub> , <i>J</i> = 7.3); 2.05 (q, 2 H, CH <sub>2</sub> , <i>J</i> = 7.3); 2.22 (AB system, 2 H, CH <sub>2</sub> , <i>J</i> <sub>AB</sub> = 14.5)	1.65 (s, 6 H, 2 CH <sub>3</sub> ); 3.70 (s, 2 H, CH <sub>2</sub> )	—	—	—

<sup>a</sup> The spectra were recorded on a Bruker AC 200 instrument.<sup>b</sup> The spectra were recorded on a Bruker AM 400 instrument.<sup>c</sup> The spectra were recorded on a Bruker AV 300 instrument.

Table 6. <sup>13</sup>C NMR spectroscopic data (δ) for 4*H*-imidazole 3-oxides

Com- pound	Solvent	C(2)	C(4)	C(5)	5-R	4-R		2-R				
						Me	CH <sub>2</sub>	C(1) (C <sub>1</sub> )	C(2) (C <sub>2</sub> )	C(3) (C <sub>3</sub> )	C(4) (C <sub>4</sub> )	Other C
<b>1a</b>	CDCl <sub>3</sub> <sup>a</sup>	144.91	82.14	151.00	111.19	21.42	—	127.14	127.48	129.88	129.99	—
<b>1b</b>	CDCl <sub>3</sub> <sup>a</sup>	141.22	82.56	150.56	111.21	21.46	—	141.09	112.53	115.56	144.87	—
<b>1c</b>	CDCl <sub>3</sub> <sup>b</sup>	145.48	84.99	150.13	111.08	21.75	—	131.17	123.81	127.61	148.48	—
<b>1d</b>	CDCl <sub>3</sub> <sup>a</sup>	146.75	83.14	150.09	111.53	21.59	—	118.83	129.06	114.00	161.75	55.31
<b>1e</b>	CDCl <sub>3</sub> <sup>a</sup>	148.40	92.82	149.26	111.74	7.28	29.18	125.73	127.13	128.77	131.53	—
<b>1f</b>	CDCl <sub>3</sub> <sup>b</sup>	151.13	83.44	159.04	110.59	21.41	—	118.40	155.58,	119.76,	134.74	—
									130.50	119.94		
<b>1g</b>	CDCl <sub>3</sub> <sup>a</sup>	146.32	82.98	149.78	111.14	21.29	—	119.43	128.76	114.31	159.58	64.93 (CH <sub>2</sub> ); 167.33 (C=O); 69.01 (CH); 21.29 (CH <sub>3</sub> )
<b>1h</b>	CDCl <sub>3</sub> <sup>a</sup>	136.91	82.3	150.01	111.25	21.11	—	—	—	—	—	—
<b>1i</b>	CDCl <sub>3</sub> <sup>a</sup>	149.28	81.86	149.87	111.49	21.37	—	12.06	—	—	—	—
<b>1j</b>	CDCl <sub>3</sub> <sup>b</sup>	147.77	86.97	152.80	111.39	6.86	28.45	20.49	34.98	91.12	25.41	—
<b>1k</b>	CDCl <sub>3</sub> <sup>a</sup>	145.20	84.24	150.37	111.31	21.75	—	122.52	147.79,	133.65	151.58	—
									123.46			
<b>1l</b>	CDCl <sub>3</sub> <sup>a</sup>	145.97	81.91	152.94	111.64	21.62	—	112.77	124.53,	107.08,	156.23	56.03, 60.73, 61.60
									149.62	142.69		
<b>7a</b>	CDCl <sub>3</sub> <sup>a</sup>	143.34	79.85	182.17	16.57	21.46	—	128.24	127.00	129.04	129.09	—
<b>7b</b>	CDCl <sub>3</sub> <sup>a</sup>	139.86	80.41	182.32	16.80	21.56	—	142.25	112.35	115.03	144.02	—
<b>7c</b>	CDCl <sub>3</sub> <sup>a</sup>	144.01	82.94	181.41	16.86	21.93	—	132.60	128.10	123.65	147.94	—
<b>7d</b>	CDCl <sub>3</sub> <sup>a</sup>	145.11	80.98	181.22	16.61	21.63	—	120.07	129.51	113.64	161.04	55.16
<b>7e</b>	CDCl <sub>3</sub> <sup>b</sup>	147.37	90.12	178.60	17.14	7.08	28.45	126.73	127.47	128.26	130.34	—
<b>7f</b>	CDCl <sub>3</sub> <sup>a</sup>	150.94	81.11	186.61	16.85	21.62	—	114.08	150.94,	119.10,	131.03	—
									134.14	119.77		
<b>7g</b>	CDCl <sub>3</sub> <sup>a</sup>	144.84	81.46	181.73	16.65	21.62	—	122.17	129.76	114.47	157.65	53.19 (CH <sub>2</sub> ); 114.70 (C≡N)
<b>7k</b>	CDCl <sub>3</sub> <sup>a</sup>	143.37	81.89	181.40	16.77	21.75	—	123.56	123.15,	134.00	150.60	—
									148.84			
<b>7l</b>	CDCl <sub>3</sub> <sup>a</sup>	144.11	79.60	180.70	16.69	21.65	—	114.21	152.93,	142.51,	155.42	55.90, 60.70, 61.47
									124.95	106.92		
<b>8</b>	CDCl <sub>3</sub> <sup>a</sup>	149.94	78.42	174.03	125.01	22.94	—	11.99	—	—	—	—
<b>11a</b>	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>a,c</sup>	144.13	79.57	176.16	143.47	24.43	—	128.45	127.87	129.36	129.90	—
<b>11b</b>	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>a</sup>	140.47	80.20	173.11	145.14	23.73	—	142.08	112.81	114.67	144.02	—
<b>11c</b>	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>d</sup>	144.22	82.27	171.81	143.62	23.78	—	132.35	127.47	123.94	147.56	—
<b>11d</b>	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>b</sup>	145.60	80.56	172.69	143.94	23.84	—	119.94	129.18	114.32	161.23	55.63
<b>11e</b>	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>b</sup>	149.81	90.99	172.27	143.84	7.08	30.53	126.09	127.78	128.43	131.24	—

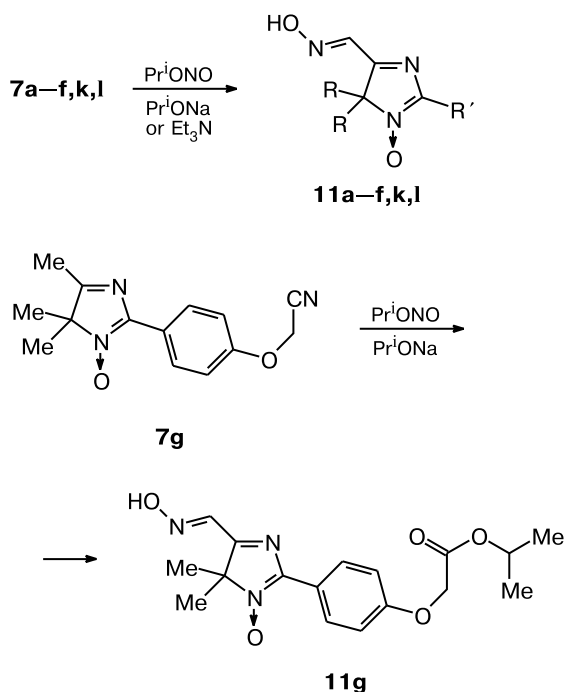
(to be continued)

Table 6 (continued)

Com- pound	Solvent	4-R			5-R			2-R'			Other C
		Me	CH <sub>2</sub>	C(4)	C(5)	C(2)	C(1)(C <sub>i</sub> )	C(2)(C <sub>o</sub> )	C(3)(C <sub>m</sub> )	C(4)(C <sub>p</sub> )	
<b>11f</b>	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>a</sup>	23.74	—	81.10	178.07	143.89	114.05	159.08, 134.59	119.63, 119.64	131.18	—
<b>11g</b>	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>b</sup>	23.08	—	81.07	174.48	143.28	120.11	129.67	114.15	159.50	64.87 (CH <sub>2</sub> ); 168.00 (C=O); 69.26 (CH); 21.11 (CH <sub>3</sub> )
<b>11h</b>	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>d</sup>	23.20	—	82.30	172.50	142.5	—	—	—	—	—
<b>11i</b>	CDCl <sub>3</sub> <sup>a</sup>	22.52	—	79.16	175.85	142.65	11.18	—	—	—	—
<b>11j</b>	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>b</sup>	6.92	30.04	87.12	173.02	143.61	20.51	35.02	89.20	25.26	—
<b>11k</b>	(CD <sub>3</sub> ) <sub>2</sub> SO <sup>b</sup>	23.91	—	81.86	172.90	143.95	123.60	147.79, 124.09	134.00	151.03	—
<b>11l</b>	CDCl <sub>3</sub> <sup>a</sup>	23.65	—	79.87	174.58	144.06	113.35	125.30, 153.25	107.07, 142.57	156.26	56.04, 60.81, 61.61
<b>12</b>	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>a</sup>	7.28, 7.34, 7.39, 7.8, 8.4	29.4, 29.6, 31.3, 31.5, 33.2, 33.4	90.0, 90.4, 91.7	169.7, 170.0, 172.4	120.58 (CH); 133.5 (C=C); 148.7 (C=N)	126.2, 126.31, 126.35	127.8, 128.0	128.2, 128.5, 128.6	131.4, 131.5	—
<b>13</b>	CDCl <sub>3</sub> <sup>b</sup>	7.04, 7.12, 7.17, 7.51, 7.55, 7.98	29.22, 29.48, 31.52, 31.55, 32.78, 33.25	89.97, 90.26, 91.30	168.98, 169.07, 169.20	119.95 (=CH); 132.54 (C=CH); 148.28 (C=NO); 63.88 (OMe)	126.33, 126.53, 126.60	126.91, 127.40, 127.5	128.15, 128.24, 130.33, 130.83, 130.89	—	—
<b>18</b>	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>a</sup>	6.80	28.47	87.14	180.62	16.90	144.53	34.11	91.21	26.01	—
<b>19</b>	CD <sub>3</sub> OD— CDCl <sub>3</sub> <sup>a</sup>	7.10	26.08	87.17	171.21	143.75	144.67	34.28	91.85	26.08	—

<sup>a</sup>The spectra were recorded on a Bruker AV 300 instrument.<sup>b</sup>The spectra were recorded on a Bruker AM 400 instrument.<sup>c</sup>The spectrum was recorded in the presence of a 1.5-fold excess of Bu<sub>4</sub>OK to increase the solubility.<sup>d</sup>The spectra were recorded on a Bruker AC 200 instrument.

Scheme 5

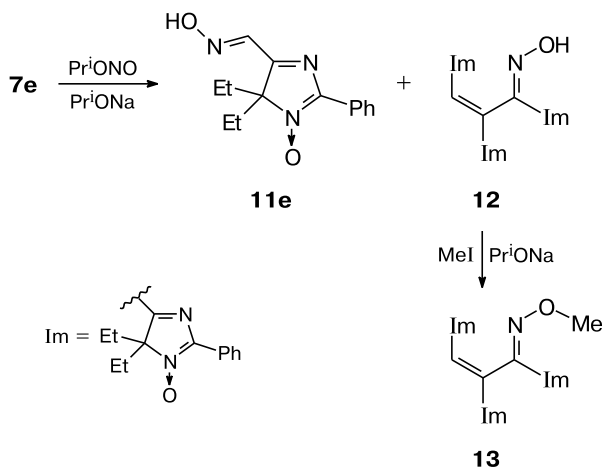


**11:** R = Me (**a–d, f, k, l**), Et (**e**); R' = 2-thienyl (**a**), 2-furyl (**b**), 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub> (**c**), 4-MeOC<sub>6</sub>H<sub>4</sub> (**d**), Ph (**e**), 2-HOC<sub>6</sub>H<sub>4</sub> (**f**), 3-pyridyl (**k**), 2,3,4-(MeO)<sub>3</sub>C<sub>6</sub>H<sub>2</sub> (**l**)

compound **12**. The structure of compound **12** was confirmed by the X-ray diffraction data for compound **13** (Fig. 1). The latter was prepared by alkylation of oxime **12** with methyl iodide (see Scheme 6). It should be noted that the X-ray diffraction data are of low quality. They confirmed the molecular structure but did not allow us to discuss the geometric details.

The formation of compound **12** can be represented by Scheme 7.

Scheme 6

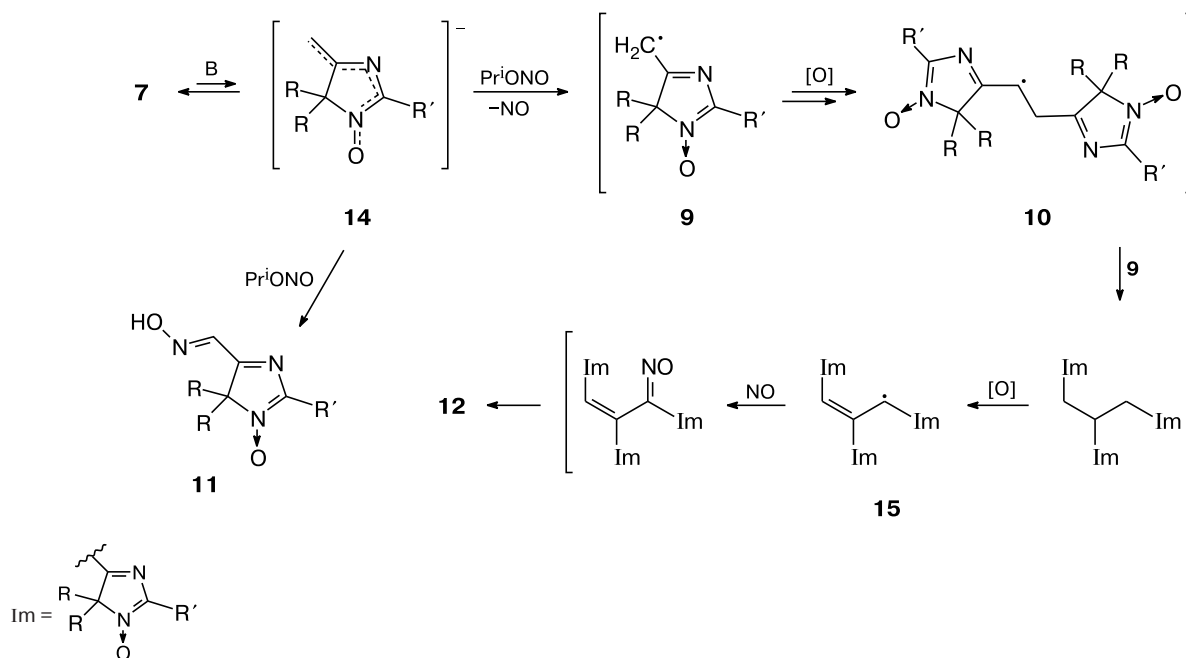


Under the conditions of nitrosation, both the nucleophilic attack of carbanion **14** on the nitrogen atom of isopropyl nitrite giving rise to oxime **11** and the one-electron oxidation of carbanion **14** with isopropyl nitrite resulting in the formation of radical **9** and evolution of nitrogen oxide NO would be expected to proceed. Further transformations of this radical can afford trimeric radical **15** stabilized by delocalization of the unpaired electron in the common conjugated system of the allylic fragment and the 4*H*-imidazole 3-oxide moieties (see Scheme 7). The formation of compound **12** is apparently attributed to the reaction of this radical with a NO molecule.

Since compounds **7h** (R = Me, R' = H) and **7i** (R = R' = Me) were not isolated in the pure form, the corresponding oximes were synthesized according to another procedure. The synthesis of 4,4-dimethyl-4*H*-imidazole-5-carbaldoxime 3-oxide (**11h**) by the reaction of 1-hydroxy-5,5-dimethyl-2,5-dihydroimidazole 3-oxide (**16**) with amyl nitrite in liquid ammonia in the presence of sodium amide was documented.<sup>17</sup> We failed to reproduce this procedure (which is apparently erroneous); under these conditions, compound **2h** is transformed into oxime **11h** in high yield. Further investigations showed that it is not necessary to use strong bases, such as sodium amide, for this transformation. The reaction proceeds in the presence of sodium ethoxide or triethylamine. In the latter case, the reaction can be performed at room temperature, and it is convenient to use isopropyl nitrite as the nitrosating agent. The treatment of compounds **2h–j** with a three- to fourfold excess of isopropyl nitrite in the presence of a catalytic amount of triethylamine by analogy with the synthesis of 2-ethyl-5-methyl-4*H*-imidazole 3-oxides<sup>6,7</sup> gives rise to the corresponding oximes **11h–j** (Scheme 8). Isopropyl nitrite acts as a mild oxidizing agent and a nitrosating agent. Initially, the reaction produces nitroxide radical **17**, which undergoes disproportionation characteristic of nitroxide radicals containing the β-hydrogen atoms, resulting in accumulation of 4*H*-imidazole 3-oxides **7h–j** in the reaction mixture (see Scheme 8). The oxidation of compounds **2h–j** to the corresponding 4*H*-imidazole 3-oxides is accompanied by vigorous evolution of nitrogen oxide and warming of the reaction mixture, the reagent (isopropyl nitrite) being partially removed with the gas that is evolved. To decrease losses of the reagent, isopropyl nitrite was initially added portionwise, and 1 equiv. of isopropyl nitrite was added after evolution of NO ceased.

Earlier,<sup>6</sup> we have reported that the reaction of isopropyl nitrite in the presence of triethylamine is not accompanied by nitrosation of the methylene fragment of the ethyl group at position 2 of the imidazole ring. The synthesis of compound **11i** is also not accompanied by the formation of large amounts of by-products. On the con-

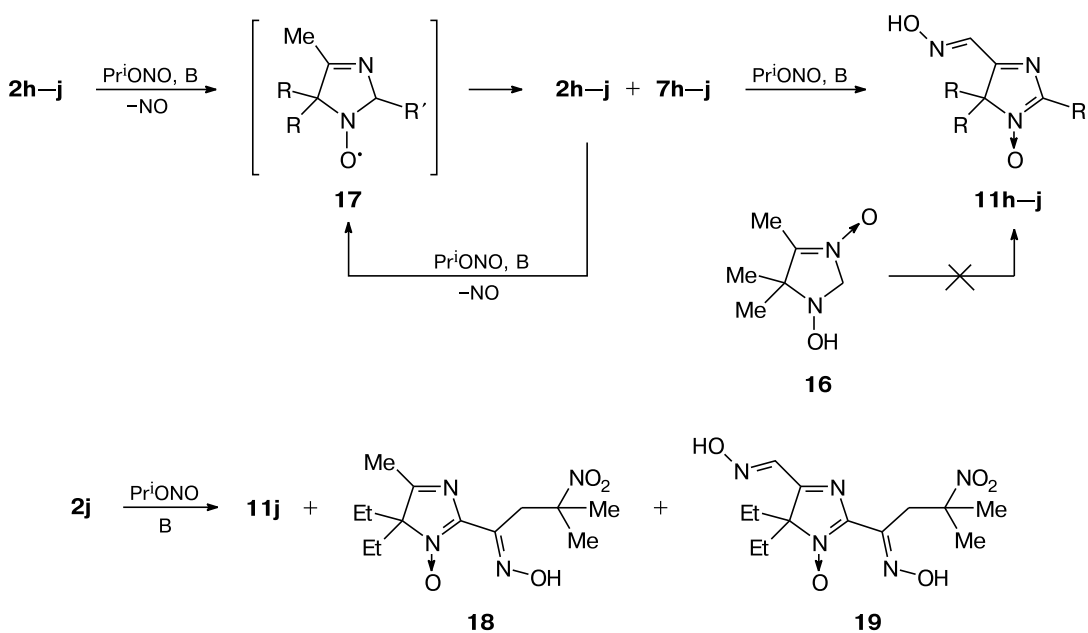
Scheme 7



trary, the treatment of imidazoline **2j** with isopropyl nitrite in the presence of triethylamine affords a mixture of oximes **11j**, **18**, and **19**. The presence of the oxime group in the alkyl chain at position 2 of the heterocycle in compounds **18** and **19** was confirmed by  $^{13}\text{C}$  NMR spec-

troscopic data (see Table 6). It is known<sup>18,19</sup> that an increase in the electron-withdrawing character of the substituent at the carbon atom of the nitron group causes the upfield shift of the signal of this atom. Actually, the signal for the carbon atom of the nitron group in the

Scheme 8



B is a base

**11**: R = Me (**h**, **i**), Et (**j**); R' = H (**h**), Me (**i**),  $\text{CH}_2\text{CH}_2\text{C}(\text{Me})_2\text{NO}_2$  (**j**)

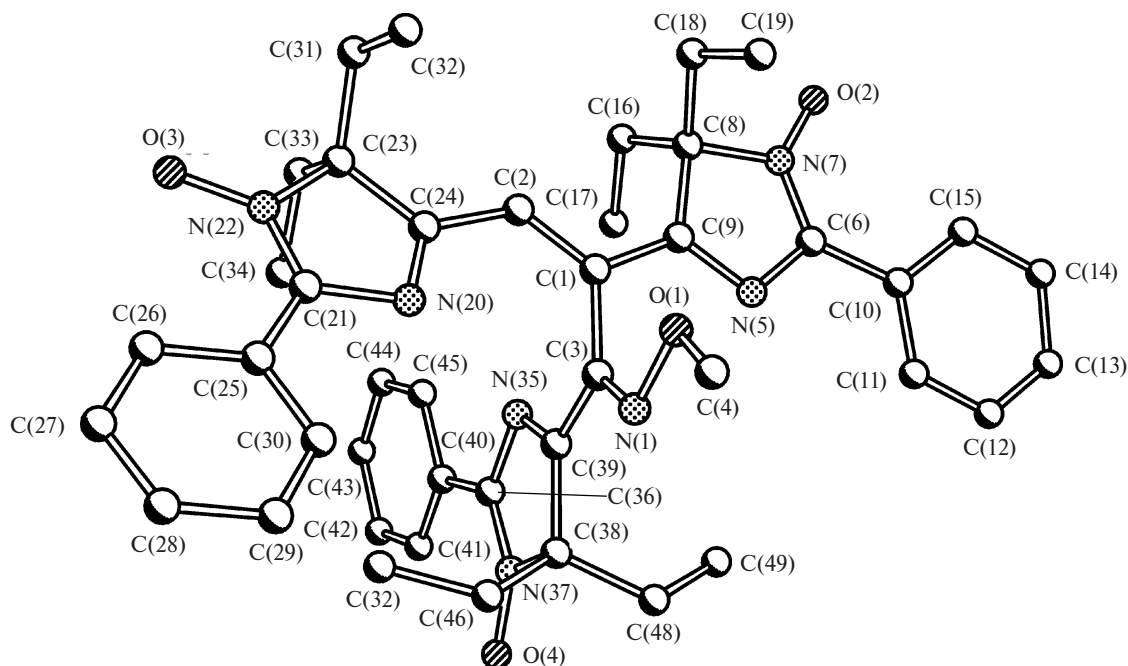
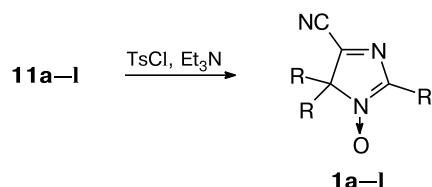


Fig. 1. X-ray diffraction structure of compound 13.

spectra of compounds **18** and **19** is shifted upfield by 9–10 ppm compared to the spectra of compound **11j** and 2-ethyl-4,4-dimethyl-4*H*-imidazole-5-carbald-oxime 3-oxide<sup>6</sup> ( $\delta$  155.19) containing the methylene fragment at the  $\alpha$ -carbon atom of the nitron group. The signal for the tertiary carbon atom at the nitro group in compounds **18** and **19** undergoes only a slight downfield shift (by 1–1.7 ppm compared to the corresponding signal in the spectrum of compound **11j**). It should be noted that the yield of oxime **11j** increases to 50%, whereas the yields of compounds **18** and **19** decrease with decreasing temperature of the reaction mixture from 30 to 10 °C. The difference in the reactivity of the methylene fragments in 2-ethyl- and 2-(3-methyl-3-nitrobutyl)-4*H*-imidazole 3-oxides is apparently attributed to the electronic effect of the nitro group.

The treatment of oximes **11a–l** with *p*-toluenesulfonyl chloride in the presence of triethylamine readily affords nitriles **1a–l** (Scheme 9). Interestingly, the presence of the 2-hydroxyphenyl substituent in compound **11f** does not complicate this transformation, and the reaction proceeds only at the oxime group. Nitriles **1** are stable yellowish (**1a–e,g–l**) or red (**1f**) crystalline compounds. The spectroscopic feature of compounds **1** (compared to other derivatives of 4*H*-imidazole 3-oxide) is that the signal for the imine carbon atom C(5) in the <sup>13</sup>C NMR spectra is substantially shifted upfield (see Table 6). Earlier,<sup>15</sup> we have observed the corresponding influence of electron-withdrawing substituents in the series of 4*H*-imidazole 3-oxide derivatives.

Scheme 9



**1**: R = Me (**a–d, f–i, k, l**), Et (**e, j**); R' = 2-thienyl (**a**), 2-furyl (**b**), 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub> (**c**), 4-MeOC<sub>6</sub>H<sub>4</sub> (**d**), Ph (**e**), 2-HOC<sub>6</sub>H<sub>4</sub> (**f**), 4-(NCCH<sub>2</sub>O)C<sub>6</sub>H<sub>4</sub> (**g**), H (**h**), Me (**i**), CH<sub>2</sub>CH<sub>2</sub>C(Me)<sub>2</sub>NO<sub>2</sub> (**j**), 3-pyridyl (**k**), 2,3,4-(MeO)<sub>3</sub>C<sub>6</sub>H<sub>2</sub> (**l**)

To summarize, we synthesized new 4*H*-imidazole 3-oxide derivatives and developed procedures for the synthesis of 4*H*-imidazole-5-carbonitrile 3-oxides containing various substituents at positions 2 and 4 of the heterocycle. The by-products that are formed in the different steps of the synthesis were isolated for the first time.

## Experimental

The IR spectra were measured on a Bruker Vector 22 FT-IR spectrometer in KBr pellets at a concentration of 1 : 150 or in a thin layer. The UV spectra were recorded on an HP Agilent 8453 instrument in EtOH (10<sup>-4</sup> M solutions). The <sup>1</sup>H NMR spectra were measured on Bruker AC 200 (200.132 MHz), Bruker AV 300 (300.132 MHz), and Bruker AM 400 (400.132 MHz) spectrometers in 5–10% CDCl<sub>3</sub>, DMSO-*d*<sub>6</sub>, and CD<sub>3</sub>OD solutions using the signal of the solvent as the standard. The assignment of the signals for the protons of compound **11j** was made based on the spectra measured with partial spin decoupling. The <sup>13</sup>C NMR spectra were

recorded on Bruker AM 400 (100.614 MHz), Bruker AV 300 (75.476 MHz), and Bruker AC 200 (50.323 MHz) spectrometers at 300 K. The assignment of the signals was made based on the known data.<sup>6–8,15,18</sup>

The melting points were determined on a Kofler hot-stage microscope. The course of the reactions was monitored by TLC on Sorbfil UV-254 plates. The chromatographic purification was carried out by column chromatography using Kieselgel 60 silica gel (Merck).  $\alpha$ -Hydroxyamino ketones **3a** (see Ref. 20) and **3b** (see Ref. 7) were synthesized according to known procedures. 2,3,4-Trimethoxybenzaldehyde was provided by V. M. Tormyshev (N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences); 4-methyl-4-nitropentanal, by V. A. Reznikov (the same Institute). The melting points and spectroscopic characteristics of all compounds are given in Tables 2–6.

**1-Hydroxy-4,5,5-trimethyl-2,5-dihydroimidazoles 2a–d,f,j (general procedure A).** A 25% aqueous ammonia solution (2.5 mL) and aldehyde (100 mmol) were added with stirring to a solution of  $\alpha$ -hydroxyamino ketone hydrochloride **3a,b** (100 mmol) in methanol (10 mL). The resulting suspension was stirred for 5 h. Then the reaction mixture was kept in a refrigerator (0 °C) for 10–12 h. The precipitate of compounds **2a–d,f,j** that formed was filtered off, washed with water and 50% methanol, and recrystallized.

To isolate **3-methyl-3-[(2-thienylmethylene)amino]butan-2-one *N*-oxide (4)**, which was prepared by condensation of compound **3a** with 2-thiophenecarbaldehyde, the precipitate of **2a** was separated, the filtrate was concentrated, the residue was triturated with diethyl ether, and the precipitate was filtered off, washed with diethyl ether, and recrystallized from a 1 : 1 AcOEt–hexane mixture. The yield was 15%, colorless crystals, m.p. 98–102 °C (from hexane). <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD–CDCl<sub>3</sub>),  $\delta$ : 1.69 (s, 6 H, CMe<sub>2</sub>); 2.15 (s, 3 H, Me); 7.16, 7.47, and 7.51 (all m, 1 H each, thienyl); 8.07 (s, 1 H, HC=N). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD–CDCl<sub>3</sub>),  $\delta$ : 22.6 (CMe<sub>2</sub>); 23.6 (Me); 78.9 (CMe<sub>2</sub>); 127.4 (HC=N); 203.7 (C=O); 126.6 (C(2)); 129.4 (C(3)); 132.2 (C<sub>7</sub>); 130.2 (C(4)).

**General procedure B.** Ammonium acetate (3 g) and aldehyde (100 mmol) were added with stirring to a solution of  $\alpha$ -hydroxyamino ketone hydrochloride **3a,b** (100 mmol) in methanol (10 mL). After 5–7 h, the reaction mixture was twice diluted with water and kept in a refrigerator for 10–12 h. The precipitate that formed was filtered off and recrystallized.

**General procedure C.** A solution of  $\alpha$ -hydroxyamino ketone hydrochloride **3a** (100 mmol) in methanol (5 mL) was saturated with gaseous ammonia. A solution of aldehyde (100 mmol) in methanol (5 mL) was saturated with ammonia separately. The solutions were mixed, and ammonia continued to be passed for 15 min. After 3 h, the precipitate that formed was filtered off, washed with water and 50% methanol, and recrystallized from ethanol.

**1-Hydroxy-4,5,5-trimethyl-2,5-dihydroimidazole (2h).** A 38% aqueous formaldehyde solution (10 mL, 130 mmol) and a 25% aqueous ammonia solution (15 mL) were added with stirring and cooling to a solution of  $\alpha$ -hydroxyamino ketone **3a** (10 g, 65 mmol) in methanol (20 mL) cooled to 10 °C (the reaction mixture warmed up). After cooling to ~20 °C, the mixture was allowed to stand for 2.5 h and then concentrated under reduced pressure. The viscous residue was triturated with propan-2-ol (50 mL), the precipitate was filtered off, and the solution was concentrated under reduced pressure. These steps were repeated 2–3 times. Then the mixture was kept *in vacuo* to remove residual water and the solvent and dissolved in ethyl acetate. The solution was dried with MgSO<sub>4</sub> and

concentrated under reduced pressure. The residue was recrystallized from hexane.

**1-Hydroxy-2,4,5,5-tetramethyl-2,5-dihydroimidazole (2i)** was synthesized analogously with the use of a solution of an equimolar amount of acetaldehyde, which was prepared by purging gaseous acetaldehyde through methanol (10 mL). Within 3 h after mixing of the reagents, methanol was evaporated under reduced pressure. Compound **2i** was extracted with chloroform, and the extract was dried with MgSO<sub>4</sub>. Chloroform was evaporated under reduced pressure, and the residue was recrystallized from hexane.

To isolate **2,2,3,5,5,6-hexamethyl-2,5-dihydropyrazine 1,4-dioxide (5)**, an aqueous solution, which was obtained after extraction of compound **2i**, was concentrated to dryness under reduced pressure, the residue was triturated with a 10 : 1 chloroform–methanol mixture, and the precipitate was filtered off. The solution was dried with MgSO<sub>4</sub> and concentrated under reduced pressure. The residue was recrystallized from chloroform. The spectroscopic characteristics of compound **5** are identical to those of the authentic sample.<sup>14</sup>

**5-Methyl-4*H*-imidazole 3-oxides 7a–g (general procedure).** Lead oxide PbO<sub>2</sub> (9.5 g, 40 mmol) was added portionwise with magnetic stirring to solutions or suspensions of the corresponding imidazolines **2a–g** (10 mmol) in chloroform (30 mL) until the starting compound was completely consumed (TLC data; diethyl ether as the eluent) for 0.5–5 h. The oxidizing agent was filtered off, the solvent was evaporated under reduced pressure, and compounds **7a–g** were recrystallized.

**4,4,5-Trimethyl-4*H*-imidazole 3-oxides 7k,l.** The reaction mixture, which was prepared by condensation of  $\alpha$ -hydroxyamino ketone **3a** with 3-pyridinecarbaldehyde or 2,3,4-trimethoxybenzaldehyde according to the method A, was concentrated to dryness under reduced pressure, and the residue was oxidized with PbO<sub>2</sub> in chloroform as described above. Compounds **7k,l** were isolated by silica gel column chromatography using chloroform as the eluent.

**1,2-Bis(2,4,4-trimethyl-4*H*-imidazol-5-yl 3-oxide)ethylene (8).** Lead oxide PbO<sub>2</sub> (10 g, 42 mmol) was added to a solution of compound **2i** (1 g, 7 mmol) in chloroform (15 mL), and the reaction mixture was stirred for 5 h. The oxidizing agent was filtered off and washed with chloroform. The solution was concentrated under reduced pressure. The residue was triturated with diethyl ether. The precipitate was filtered off and chromatographed on a silica gel column using chloroform as the eluent. The yield was 0.32 g (32%), red crystals having a metallic luster.

**4,4-Dimethyl-4*H*-imidazole-5-carbaldoxime 3-oxides 11a,b,d,g,k,l (general procedure).** Sodium metal (1 g, 43 mmol) was added to propan-2-ol (30 mL). The reaction mixture was carefully heated with stirring until sodium was completely dissolved. The solution was cooled to 5 °C. Then isopropyl nitrite (3.5 mL, 39 mmol) and a solution of compound **7** (16 mmol) in isopropanol (20 mL) were added with stirring to a suspension of sodium isopropoxide. The reaction mixture was allowed to stand for 1–8 h. The course of the reaction was monitored by TLC using ethyl acetate as the eluent, samples of the reaction mixture being neutralized with acetic acid before the analysis. After the consumption of the starting compound, the reaction mixture was neutralized with acetic acid to pH 5–6, and propan-2-ol was distilled off under reduced pressure. A saturated NaCl solution (30 mL) was added to the residue, and the precipitate was filtered off, dried in air, and recrystallized.

Under the same conditions, the nitrosation of compound **7e** afforded a mixture of compounds **11e** and **12**, which were separated by silica gel column chromatography using chloroform as the eluent.



**4,4-Dimethyl-2-(4-nitrophenyl)-4H-imidazole-5-carbaldoxime 3-oxide (11c).** Isopropyl nitrite (8 mL, 76.4 mmol) was added with stirring to a cold solution of compound **7c** (6.22 g, 25.2 mmol) in a 0.1 M sodium methoxide solution in methanol (500 mL). The reaction mixture was allowed to stand for 4 h. The course of the reaction was monitored by TLC using ethyl acetate as the eluent, samples of the reaction mixture being neutralized with acetic acid before the analysis. After the consumption of the starting compound, the reaction mixture was neutralized with acetic acid to pH 5–6, and methanol was distilled off under reduced pressure. A saturated NaCl solution (30 mL) was added to the residue, and the precipitate of oxime **11c** was filtered off and dried in air.

**2-(2-Hydroxyphenyl)-4,4-dimethyl-4H-imidazole-5-carbaldoxime 3-oxide (11f).** Triethylamine (2 mL, 15 mmol) and isopropyl nitrite (3 mL, 34 mmol) were successively added to a solution of compound **7f** (2.2 g, 9 mmol) in dichloromethane (5 mL). The reaction mixture was kept at 22 °C for 24 h. The precipitate that formed was filtered off, washed with a small amount of a 2 : 1 mixture of *tert*-butylmethyl ether and propan-2-ol, and dried.

**1,2,3-Tris(4,4-diethyl-2-phenyl-4H-imidazol-5-yl 3-oxide)-propanone oxime O-methyl ether (13).** Methyl iodide (0.15 mL, 1.6 mmol) was added with stirring to a solution of compound **12** (0.3 g, 0.42 mmol) in a 0.1 M sodium isopropoxide solution in propan-2-ol (10 mL). The reaction mixture was allowed to stand for 24 h and then acidified with acetic acid to pH 6. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column using chloroform as the eluent. Compound **13** was recrystallized from ethyl acetate.

**4,4-Dimethyl-4H-imidazole-5-carbaldoxime 3-oxide (11h).** *A.* Imidazoline **2h** (2 g, 16 mmol) was added to a solution of sodium amide in liquid ammonia, which was prepared from sodium (0.54 g, 23 mmol) and liquid ammonia (100 mL). The reaction mixture was cooled to –60 °C, and isopropyl nitrite (4 mL, 40 mmol) was added dropwise. The resulting brick-red mixture was stirred for 1 h, and ammonia was evaporated. The residue was dissolved in methanol (20 mL) and acidified with acetic acid to pH 6. Methanol was evaporated under reduced pressure and triturated with H<sub>2</sub>O (20 mL). The precipitate that formed was filtered off and recrystallized from ethanol. The yield was 0.68 g (29%).

*B.* Isopropyl nitrite (20 mL, 195 mmol) was added dropwise to a solution of imidazoline **2h** (10 g, 78 mmol) in a 1.3 M sodium methoxide solution (90 mL) cooled to –25 °C. The reaction mixture was stirred for 1 h, the temperature being gradually raised to ~20 °C. Then the mixture was neutralized by adding a solution of AcOH (6.7 mL) in propan-2-ol (20 mL), which was accompanied by a change in the color of the solution from black-green to orange-red. The precipitate of sodium acetate was filtered off, and the solution was concentrated to dryness under reduced pressure. Water (50 mL) was added to the residue, and the mixture was heated to 80 °C (until complete dissolution). The resulting solution was kept in a refrigerator for 24 h, and the precipitate of oxime **11h** was filtered off and recrystallized from ethanol. The yield was 2.85 g (23%).

*C.* Triethylamine (0.1 mL) was added to a solution of compound **2h** (1.0 g, 7.8 mmol) in THF (3.5 mL); or in a minimum amount of a 1 : 1 CHCl<sub>3</sub>–CCl<sub>4</sub> mixture). To prevent nitric acid, which was formed on the walls of the vessel as a result of oxidation of NO that was evolved in air, from being passed to the reaction mixture, the reaction vessel was sealed with a cap. Isopropyl nitrite (3 mL, 28.7 mmol) was added portionwise to the reaction solution so as to prevent warming-up, vigorous evolution of NO, and boiling-up of the reaction mixture (if necessary, the mixture was cooled with cold

water). After completion of evolution of NO, isopropyl nitrite (1 mL, 9.55 mmol) was added to the reaction mixture. After 24 h, the precipitate of oxime **11h** was filtered off and washed with *tert*-butylmethyl ether. The yield was 0.9 g (75%).

**2,4,4-Trimethyl-4H-imidazole-5-carbaldoxime 3-oxide (11i)** was synthesized analogously by nitrosation of compound **2i**. The course of the reaction was monitored by TLC using ethyl acetate as the eluent. After completion of the reaction, the solvent was evaporated under reduced pressure. Water and *tert*-butylmethyl ether were added to the residue, and the reaction mixture was shaken until complete dissolution. The organic phase was extracted with water. The combined aqueous solutions were saturated with NaCl and extracted with chloroform. The extract was dried with MgSO<sub>4</sub>, chloroform was evaporated under reduced pressure, the residue was triturated with ethyl acetate, and the precipitate of oxime **11i** was filtered off.

Under the same conditions, the nitrosation of imidazoline **2j** afforded a mixture of compounds **11j**, **18**, and **19**, which were separated by silica gel column chromatography using chloroform as the eluent. The yields were 34% (**11j**), 15% (**18**), and 7% (**19**). The nitrosation at 5–10 °C afforded compounds **11j**, **18**, and **19** in 50, 3, and 7% yields, respectively.

**4,4-Dimethyl-4H-imidazole-5-carbonitrile 3-oxides 1a–g;–l (general procedure).** Triethylamine (16 mL, 110 mmol) was added to a suspension of the corresponding oxime **11a–l** (50 mmol) in chloroform (75 mL). The reaction mixture was stirred until complete dissolution. Then *p*-toluenesulfonyl chloride (9.5 g, 50 mmol) was added portionwise. The course of the reaction was monitored by TLC using chloroform as the eluent. After the starting compound was completely consumed, the reaction mixture was washed with a saturated aqueous NaCl solution and dried with MgSO<sub>4</sub>. The drying agent was filtered off, and the solvent was evaporated under reduced pressure. The residue was chromatographed on a silica gel column using chloroform as the eluent.

**4,4-Dimethyl-4H-imidazole-5-carbonitrile 3-oxide (1h)** was prepared analogously, but after the completion of the reaction, chloroform was evaporated under reduced pressure, the residue was triturated with diethyl ether, the precipitate of triethylammonium salts was filtered off, diethyl ether was evaporated, and the residue was sublimed *in vacuo* (4 Torr) at 100 °C.

**X-ray diffraction study of compound 13** was carried out on a Smart APEX diffractometer (Bruker AXS) according to a standard procedure (Mo-K $\alpha$  radiation,  $2\theta < 47^\circ$ ). The crystals were of low quality. Hence, the X-ray diffraction data confirmed the molecular structure, but the details of the geometry cannot be discussed. The structure was solved by direct methods using the SIR2002 program and refined by the least-squares method with anisotropic displacement parameters for all nonhydrogen atoms (with isotropic displacement parameters for H atoms) with the use of the SHELXL-97 program package. The hydrogen atoms were positioned geometrically and refined using a riding model. The ethanol solvent molecule is disordered over two positions with equal occupancies. The crystallographic data are as follows: C<sub>43</sub>H<sub>49</sub>N<sub>7</sub>O<sub>4</sub>·0.5(C<sub>2</sub>H<sub>6</sub>O), M = 750.93, monoclinic system, space group C2/c, *a* = 38.767(8) Å, *b* = 11.339(2) Å, *c* = 19.805(4) Å,  $\beta$  = 90.164(5)°, *V* = 8706(3) Å<sup>3</sup>, *Z* = 8, *d*<sub>calc</sub> = 1.167 g cm<sup>-3</sup>,  $\mu$  = 0.077 mm<sup>-1</sup>, *R* = 0.1558 for 2989 reflections with *I* > 2 $\sigma$ (*I*), 545 refined parameters, *wR*<sub>2</sub> = 0.3311, GOF = 1.191 for all 6333 independent reflections.

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