

## An Efficient One-Pot Four-Component Synthesis of Functionalized Imidazo[1,2-*a*]pyridines

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An efficient one-pot four-component protocol for the synthesis of imidazo[1,2-*a*]pyridines was developed by condensing ethane-1,2-diamine (**2**), 1,1-bis(methylthio)-2-nitroethene (**1**), aldehydes **3**, and activated methylene compounds in EtOH under reflux conditions (*Tables 1–3*). The features of this procedure are operational simplicity, good yields of products, *in situ* preparation of heterocyclic ketene amins (HKA), and catalyst-free conditions.

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**Introduction.** – Multicomponent reactions (MCRs) are of increasing importance in organic and medicinal chemistry [1]. They have distinct advantages over a linear stepwise process, including the removal of the need to purify after each chemical transformation, the ability to produce a large number of derivatives around a common scaffold by varying each of the components involved in the reaction, and high atom economy [2].

Heterocyclic ketene amins (HKAs) are powerful and versatile intermediates in heterocyclic synthesis [3]. Reactions of HKAs with a variety of bis-electrophilic reagents have so far been applied to make five- and six-membered and fused heterocycles during the past years [4]. HKAs have been frequently found as pharmacophores and could play important roles in drug discovery. Recently, Alizadeh and co-workers, have reported new MCRs *via in situ* formation of nitroketene aminal for the synthesis of various heterocycles [5]. In this context, imidazo[1,2-*a*]pyridine derivatives show interesting features that make them attractive for use in HKA-based MCRs. HKAs are one of the main intermediates used to synthesize of imidazo[1,2-*a*]pyridines [6].

Imidazo[1,2-*a*]pyridines are becoming more and more important in medicinal and organic chemistry. They have displayed a broad spectrum of pharmacological and biological activities, such as antitumoral [7], antiviral [8], anti-inflammatory [9], antibacterial [10], antifungal [11], anti-ulcer [12], antiprotozoal [13], and antiretroviral activities [14]. They are contained in marketed drugs such as the clinical anti-ulcer compound soraprazan, alpidem (a nonsedative anxiolytic), the PDE 3 inhibitor olprinone, and the sedative zolpidem (*Fig.*) [15]. Bicyclic pyridin motifs **I** are of general interest within medicinal chemistry with therapeutic properties, and a series of substituted variants of **I** ( $n = 1$  or  $2$ ) have been reported as a basis for analgesics and anti-inflammatory agents (*Fig.*) [16].

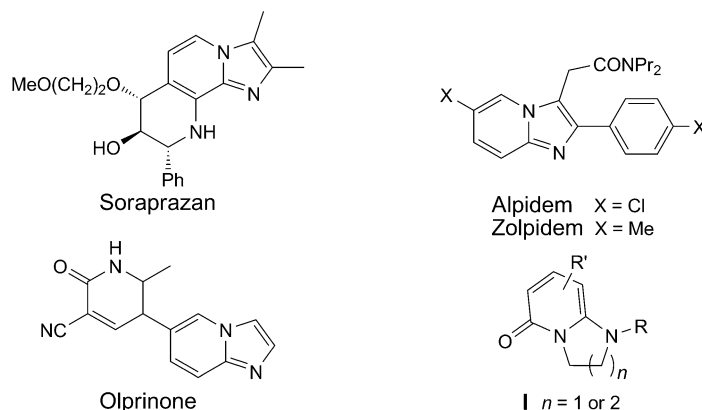


Figure. Representatives of medicinally important imidazopyridines

As a part of our current studies on the MCRs to synthesize novel heterocycles [17], we describe herein an efficient four-component synthesis of imidazo[1,2-*a*]pyridines *via in situ* preparation of a nitroketene amination.

**Results and Discussion.** – In the initial stage, the reaction of ethane-1,2-diamine (**1**), 1,1-bis(methylthio)-2-nitroethene (**2**), aldehyde **3**, and 3-oxo-3-phenylpropanenitrile (**4**) in EtOH under reflux conditions in the absence of any catalysts led to the formation of imidazo[1,2-*a*]pyridine-6-carbonitriles **5a–5d** in good yields after 8 h (Table 1). It was interesting that the desired products **6** or **7** were not detected at all. The structures of the products **5a–5d** were fully characterized by IR and <sup>1</sup>H- and <sup>13</sup>C-NMR spectra, and elemental analysis. The <sup>1</sup>H-NMR spectrum of **5a** exhibited two *d* at δ(H) 4.27 and

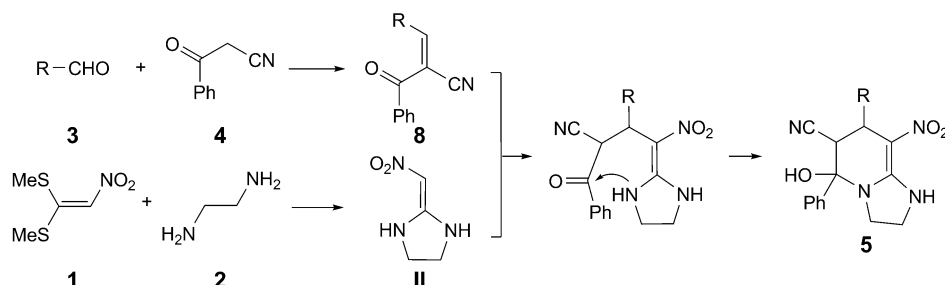
Table 1. Synthesis of [1,2-*a*]Pyridine-6-carbonitriles **5**

| Product <b>5</b> | RCHO ( <b>3</b> )                   | Yield [%] |
|------------------|-------------------------------------|-----------|
| <b>5a</b>        | Benzaldehyde                        | 61        |
| <b>5b</b>        | 1 <i>H</i> -Indole-3-carboxaldehyde | 55        |
| <b>5c</b>        | 4-Fluorobenzaldehyde                | 85        |
| <b>5d</b>        | 3-Nitrobenzaldehyde                 | 91        |

3.52 with  $^3J = 11.5$  Hz for the CH groups that confirmed non-dehydration of product **5** and indicated *trans*-configuration of the two vicinal H-atoms.

The formation of products **5** can be rationalized by the initial formation of intermediate **8** via *Knoevenagel* condensation of **3** and **4**. Subsequent addition of HKA **II** (formed *in situ* by reaction of **1** with **2**) to the intermediate **8** followed by cyclization afforded products **5** (*Scheme*).

Scheme. Proposed Mechanism of the Formation of Product **5**



To further explore the potential of this protocol for the imidazo[1,2-*a*]pyridine synthesis, the 3-oxo-3-(piperidin-1-yl)propanenitrile (**9**) was selected as an activated-methylene compound in the four-component reaction (*Table 2*). It was interesting that the 5-aminoimidazo[1,2-*a*]pyridin **11** was not detected at all, while imidazo[1,2-*a*]pyridines **10** were obtained in good yields. All the products were characterized by IR, mass, and NMR spectra and elemental analysis.

Table 2. Synthesis of Imidazo[1,2-*a*]pyridines **10**

| Product <b>10</b> | RCHO ( <b>3</b> )         | Yield [%] |
|-------------------|---------------------------|-----------|
| <b>10a</b>        | Benzaldehyde              | 65        |
| <b>10b</b>        | 3-Nitrobenzaldehyde       | 83        |
| <b>10c</b>        | Pyridine-2-carboxaldehyde | 79        |
| <b>10d</b>        | 2-Nitrobenzaldehyde       | 75        |

When *Meldrum's acid* (**12**) and dimedone (**14**) were selected as active  $\beta$ -dicarbonyl compounds in the four-component reaction, the desired imidazo[1,2-*a*]pyridines **13** and **15** were obtained in good yields (Table 3).

Table 3. *Synthesis of Compounds 13 and 15*

| Product    | RCHO ( <b>3</b> )                   | Yield [%] |
|------------|-------------------------------------|-----------|
| <b>13a</b> | Benzaldehyde                        | 57        |
| <b>13b</b> | 2,4-Dichlorobenzaldehyde            | 71        |
| <b>13c</b> | 3-Nitrobenzaldehyde                 | 74        |
| <b>13d</b> | 4-Methoxybenzaldehyde               | 67        |
| <b>13e</b> | Pyridine-2-carboxaldehyde           | 70        |
| <b>15a</b> | Benzaldehyde                        | 51        |
| <b>15b</b> | Pyridine-2-carboxaldehyde           | 68        |
| <b>15c</b> | 1 <i>H</i> -Indole-3-carboxaldehyde | 45        |
| <b>15d</b> | 3-Nitrobenzaldehyde                 | 83        |
| <b>15e</b> | 4-Methoxybenzaldehyde               | 54        |

In conclusion, we achieved the new one-pot, four-component, and catalyst-free synthesis of highly functionalized imidazo[1,2-*a*]pyridines. The catalyst-free reactions carried out in EtOH are considerably safer, nontoxic, environmentally friendly, and inexpensive. The absence of a catalyst for the reaction avoids the use of moisture sensitive and heavy metal such as *Lewis* acids. This method is applicable to the synthesis of different types of imidazo[1,2-*a*]pyridines.

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### Experimental Part

*General.* The chemicals used in this work were obtained from *Fluka* and *Merck* and were applied without further purification. M.p.: *Electrothermal-9100* apparatus; uncorrected. IR Spectra: *BOMEM-MB-series* FT-IR apparatus;  $\tilde{\nu}$  in  $\text{cm}^{-1}$ .  $^1\text{H}$ - and  $^{13}\text{C}$ - Spectra: *Bruker-DRX-300-Avance* spectrometer; at 300.13 and 75.47 MHz, resp.; in ( $\text{D}_6$ )DMSO;  $\delta$  in ppm rel. to  $\text{Me}_4\text{Si}$  as internal standard, *J* in Hz. EI-MS

(70 eV); Shimadzu-GCMS-QP1100EX mass spectrometer; in  $m/z$ . VarioEL-CHNS apparatus Elemental analyses: (Elementar Analysensysteme GmbH).

**Compounds 5a–5d. General Procedure.** A soln. of ethane-1,2-diamine (**1**; 1 mmol) and 1,1-bis(methylthio)-2-nitroethene (**2**; 1 mmol) in EtOH (5 ml) was magnetically stirred for 3 h under reflux. Then a soln. of aldehyde **3** (1 mmol) and 3-oxo-3-phenylpropanenitrile (**4**; 1 mmol) in EtOH (3 ml) was added to the mixture and refluxed for 5 h. The mixture was cooled to r.t. and the precipitated product collected by filtration and washed with AcOEt ( $2 \times 3$  ml): **5**.

**1,2,3,5,6,7-Hexahydro-5-hydroxy-8-nitro-5,7-diphenylimidazo[1,2-a]pyridine-6-carbonitrile (5a):** Yield 61%. White solid. M.p. 205–208°. IR (KBr): 3362, 2903, 2251, 1601.  $^1\text{H-NMR}$ : 3.29–3.39 ( $m$ ,  $\text{CH}_2$ ); 3.52 ( $d$ ,  $J = 11.5$ ,  $\text{CH}$ ); 3.62–3.64 ( $m$ ,  $\text{CH}_2$ ), 4.26 ( $d$ ,  $J = 11.5$ ,  $\text{CH}$ ); 7.20–7.67 ( $m$ , 10 arom. H); 9.35 (br.  $s$ , NH).  $^{13}\text{C-NMR}$ : 42.8; 43.1; 45.1; 50.5; 83.7; 105.8; 118.2; 126.9; 127.1; 127.9; 128.6; 129.4; 139.3; 141.7; 157.4. MS: 362 ( $M^+$ ). Anal. calc. for  $\text{C}_{20}\text{H}_{18}\text{N}_4\text{O}_3$  (362.38): C 66.29, H 5.01, N 15.46; found: C 66.32, H 5.06, N 15.43.

**1,2,3,5,6,7-Hexahydro-5-hydroxy-7-(1H-indol-3-yl)-8-nitro-5-phenylimidazo[1,2-a]pyridine-6-carbonitrile (5b):** Yield 55%. White solid. M.p. 198–200°. IR (KBr): 3333, 2923, 2251, 1620.  $^1\text{H-NMR}$ : 3.40–3.47 ( $m$ ,  $\text{CH}_2$ ); 3.52–3.62 ( $m$ ,  $\text{CH}_2$ ); 4.46 ( $d$ ,  $J = 6.9$ ,  $\text{CH}$ ); 4.83 ( $d$ ,  $J = 6.9$ ,  $\text{CH}$ ); 7.41–7.95 ( $m$ , 9 arom. H); 8.57 ( $s$ , 1 arom. H); 9.38 (br.  $s$ , NH); 10.11 (br.  $s$ , NH).  $^{13}\text{C-NMR}$ : 19.0; 42.5; 44.3; 56.5; 82.9; 105.0; 117.1; 123.8; 127.1; 127.2; 127.4; 129.0; 129.4; 138.5; 139.9; 147.9; 155.7; 157.5. MS: 401 ( $M^+$ ). Anal. calc. for  $\text{C}_{22}\text{H}_{19}\text{N}_5\text{O}_3$  (401.42): C 66.83, H 4.77, N 17.45; found: C 66.80, H 4.71, N 17.45.

**7-(4-Fluorophenyl)-1,2,3,5,6,7-hexahydro-5-hydroxy-8-nitro-5-phenylimidazo[1,2-a]pyridine-6-carbonitrile (5c):** Yield 85%. White solid. M.p. 209–212°. IR (KBr): 3283, 2879, 2257, 1617.  $^1\text{H-NMR}$ : 3.32–3.35 ( $m$ ,  $\text{CH}_2$ ); 3.54–3.63 ( $m$ ,  $\text{CH}$ ,  $\text{CH}_2$ ); 4.26 ( $d$ ,  $J = 11.4$ ,  $\text{CH}$ ); 7.05–7.65 ( $m$ , 9 arom. H); 9.34 (br.  $s$ , NH).  $^{13}\text{C-NMR}$ : 42.0; 43.1; 45.5; 50.1; 83.6; 105.6; 115.0; 118.1; 127.3; 128.9; 129.4; 129.8; 129.9; 139.2; 139.9; 157.3. MS: 380 ( $M^+$ ). Anal. calc. for  $\text{C}_{20}\text{H}_{17}\text{FN}_4\text{O}_3$  (380.37): C 63.15, H 4.50, N 14.73; found: C 63.20, H 4.52, N 14.71.

**1,2,3,5,6,7-Hexahydro-5-hydroxy-8-nitro-7-(3-nitrophenyl)-5-phenylimidazo[1,2-a]pyridine-6-carbonitrile (5d):** Yield 91%. White solid. M.p. 224–256°. IR (KBr): 3300, 3097, 2965, 2905, 2247, 1613.  $^1\text{H-NMR}$ : 3.12–3.20 ( $m$ ,  $\text{CH}_2$ ); 3.66–3.88 ( $m$ ,  $\text{CH}$ ,  $\text{CH}_2$ ); 4.24–4.47 ( $d$ ,  $J = 11.3$ ,  $\text{CH}$ ); 6.79–7.04 ( $m$ , 9 arom. H); 9.37 (br.  $s$ , NH).  $^{13}\text{C-NMR}$ : 43.0; 43.8; 55.4; 83.6; 104.8; 117.9; 122.2; 127.2; 127.3; 128.9; 129.5; 129.9; 135.6; 139.1; 139.8; 143.8; 157.3. MS: 407 ( $M^+$ ). Anal. calc. for  $\text{C}_{20}\text{H}_{17}\text{N}_5\text{O}_5$  (407.38): C 58.97, H 4.21, N 17.19; found: C 59.02, H 4.25, N 17.15.

**Compounds 10a–10d. General Procedure.** As described for **5a–5d**, with ethane-1,2-diamine (**1**; 1 mmol), 1,1-bis(methylthio)-2-nitroethene (**2**; 1 mmol), EtOH (5 ml), aldehyde **3** (1 mmol), and 3-oxo-3-(piperidin-1-yl)propanenitrile (**9**; 1 mmol) in EtOH (3 ml): **10**.

**1,2,3,7-Tetrahydro-5-hydroxy-8-nitro-7-phenylimidazo[1,2-a]pyridine-6-carbonitrile (10a):** Yield 65%. Yellow solid. M.p. 260–265° (dec.). IR (KBr): 3395, 3288, 2887, 1641, 1614.  $^1\text{H-NMR}$ : 3.68–3.74 ( $m$ ,  $\text{CH}_2$ ); 3.88–3.94 ( $m$ ,  $\text{CH}_2$ ); 4.97 ( $s$ ,  $\text{CH}$ ); 7.08–7.17 ( $m$ , 3 arom. H); 7.28–7.30 ( $m$ , 2 arom. H); 8.30 (br.  $s$ , OH); 9.21 (br.  $s$ , NH).  $^{13}\text{C-NMR}$ : 43.2; 43.5; 43.8; 74.7; 108.3; 126.2; 127.7; 128.1; 146.4; 153.8; 162.6. MS: 284 ( $M^+$ ). Anal. calc. for  $\text{C}_{14}\text{H}_{12}\text{N}_4\text{O}_3$  (284.27): C 59.15, H 4.25, N 19.71; found: C 59.19, H 4.20, N 19.75.

**1,2,3,7-Tetrahydro-5-hydroxy-8-nitro-7-(3-nitrophenyl)imidazo[1,2-a]pyridine-6-carbonitrile (10b):** Yield 83%. Yellow solid. M.p. 256–258° (dec.). IR (KBr): 3340, 3321, 2879, 1640, 1638.  $^1\text{H-NMR}$ : 3.73–3.81 ( $m$ ,  $\text{CH}_2$ ); 3.90–3.97 ( $m$ ,  $\text{CH}_2$ ); 5.15 ( $s$ ,  $\text{CH}$ ); 7.30 ( $s$ , 1 arom. H); 7.47–7.52 ( $m$ , 1 arom. H); 7.71–7.64 ( $m$ , 1 arom. H); 7.97–7.99 ( $m$ , 1 arom. H); 8.36 (br.  $s$ , OH); 9.16 (br.  $s$ , NH).  $^{13}\text{C-NMR}$ : 43.2; 43.5; 43.8; 73.8; 107.4; 121.5; 122.5; 129.7; 134.5; 147.5; 148.5; 153.6; 152.4; 162.8. MS: 329 ( $M^+$ ). Anal. calc. for  $\text{C}_{14}\text{H}_{11}\text{N}_5\text{O}_5$  (329.27): C 51.07, H 3.37, N 21.27; found: C 51.19, H 3.20, N 21.21.

**1,2,3,7-Tetrahydro-5-hydroxy-8-nitro-7-(pyridin-2-yl)imidazo[1,2-a]pyridine-6-carbonitrile (10c):** Yield 79%. Yellow solid. M.p. 264–268° (dec.). IR (KBr): 3385, 3288, 2885, 1643, 1630.  $^1\text{H-NMR}$ : 3.73–3.92 ( $m$ , 2  $\text{CH}_2$ ); 5.03 ( $s$ ,  $\text{CH}$ ); 7.13 ( $s$ , 1 arom. H); 7.26–7.28 ( $m$ , 1 arom. H); 7.45 ( $s$ , 1 arom. H); 7.60–7.63 ( $m$ , 1 arom. H); 8.36 (br.  $s$ , OH), 9.28 (br.  $s$ , NH).  $^{13}\text{C-NMR}$ : 43.2; 43.5; 43.9; 73.8; 106.3; 121.3; 121.8; 136.9; 148.9; 154.1; 162.1; 163.3; 164.4. MS: 285 ( $M^+$ ). Anal. calc. for  $\text{C}_{13}\text{H}_{11}\text{N}_5\text{O}_3$  (285.26): C 54.74, H 3.89, N 24.55; found: C 54.75, H 3.89, N 24.56.

**1,2,3,7-Tetrahydro-5-hydroxy-8-nitro-7-(2-nitrophenyl)imidazo[1,2-a]pyridine-6-carbonitrile (10d).** Yield 75%. Yellow solid. M.p. 236–238°. IR (KBr): 3517, 3391, 2941, 2864, 1644, 1530. <sup>1</sup>H-NMR: 3.61–3.66 (*m*, CH<sub>2</sub>); 4.11–4.14 (*m*, CH<sub>2</sub>); 4.74 (*s*, CH); 7.21–7.23 (*m*, 1 arom. H); 7.50–7.53 (*m*, 1 arom. H); 7.61–7.64 (*m*, 1 arom. H); 7.93–7.95 (*m*, 1 arom. H); 8.75 (*br s*, OH), 9.59 (*br s*, NH). <sup>13</sup>C-NMR: 43.3; 43.6; 45.1; 74.6; 106.3; 124.8; 128.8; 128.9; 134.3; 136.8; 149.3; 166.4. MS: 329 (*M*<sup>+</sup>). Anal. calc. for C<sub>14</sub>H<sub>11</sub>N<sub>5</sub>O<sub>5</sub> (329.27): C 51.07, H 3.37, N 21.27; found: C 51.10, H 3.39, N 21.25.

**Compounds 13a–13e. General Procedure.** As described for **5a–5d**, with ethane-1,2-diamine (**1**; 1 mmol), 1,1-bis(methylthio)-2-nitroethene (**2**; 1 mmol), EtOH (5 ml), aldehyde **3** (1 mmol), and Meldrum's acid (= 2,2-dimethyl-1,3-dioxane-4,6-dione; **12**; 1 mmol) in EtOH (3 ml): **13**.

**2,3,6,7-Tetrahydro-8-nitro-7-phenylimidazo[1,2-a]pyridin-5(1H)-one (13a).** Yield 57%. White solid. M.p. 252–256°. IR (KBr): 3224, 3007, 2917, 1699. <sup>1</sup>H-NMR: 2.55–2.60 (*m*, CH); 3.16–3.24 (*m*, CH); 3.75–3.97 (*m*, 2 CH<sub>2</sub>); 4.52–4.55 (*m*, CH); 7.13–7.18 (*m*, 2 arom. H); 7.20–7.32 (*m*, 3 arom. H); 9.71 (*br s*, NH). <sup>13</sup>C-NMR: 37.6; 40.6; 43.05; 43.9; 106.7; 126.8; 127.3; 129.1; 142.9; 153.1; 167.8. MS: 259 (*M*<sup>+</sup>). Anal. calc. for C<sub>13</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub> (259.26): C 60.22, H 5.05, N 16.21; found: C 60.25, H 5.08, N 16.13.

**7-(2,4-Dichlorophenyl)-2,3,6,7-tetrahydro-8-nitroimidazo[1,2-a]pyridin-5(1H)-one (13b):** Yield 71%. White solid. M.p. 246–247°. IR (KBr): 3294, 3073, 2923, 1709. <sup>1</sup>H-NMR: 2.46–2.50 (*m*, CH); 3.25–3.31 (*m*, CH); 3.81–3.91 (*m*, 2 CH<sub>2</sub>); 4.83–4.86 (*m*, CH); 7.10 (*d*, *J* = 8.18, 1 arom. H); 7.30 (*d*, *J* = 8.18, 1 arom. H); 7.64 (*s*, 1 arom. H); 9.82 (*br s*, NH). <sup>13</sup>C-NMR (75 MHz, (D<sub>6</sub>)DMSO): 35.5; 37.7; 43.2; 44.1; 104.9; 128.2; 128.7; 129.8; 132.8; 133.8; 138.8; 153.4; 166.9. MS: 328 (*M*<sup>+</sup>). Anal. calc. for C<sub>13</sub>H<sub>11</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>3</sub> (328.15): C 47.58, H 3.38, N 12.81; found: C 47.60, H 3.31, N 12.85.

**2,3,6,7-Tetrahydro-8-Nitro-7-(3-nitrophenyl)imidazo[1,2-a]pyridin-5(1H)-one (13c).** Yield 74%. White solid. M.p. 236–240°. IR (KBr): 3378, 3058, 2917, 1713. <sup>1</sup>H-NMR: 2.64–2.69 (*m*, CH); 3.22–3.30 (*m*, CH); 3.79–3.93 (*m*, 2 CH<sub>2</sub>); 4.70–4.73 (*m*, CH); 7.58–7.60 (*m*, 2 arom. H); 8.01–8.04 (*m*, 1 arom. H); 8.06 (*s*, 1 arom. H); 9.75 (*br s*, NH). <sup>13</sup>C-NMR: 37.3; 37.7; 39.9; 44.0; 105.9; 121.9; 122.4; 130.7; 133.4; 145.2; 148.4; 153.1; 167.4. MS: 304 (*M*<sup>+</sup>). Anal. calc. for C<sub>13</sub>H<sub>12</sub>N<sub>4</sub>O<sub>5</sub> (304.26): C 51.32, H 3.98, N 18.41; found: C 51.36, H 4.02, N 18.40.

**2,3,6,7-Tetrahydro-7-(4-methoxyphenyl)-8-nitroimidazo[1,2-a]pyridin-5(1H)-one (13d):** Yield 67%. White solid. M.p. 237–241° (dec.). IR (KBr): 3224, 3000, 2911, 1699. <sup>1</sup>H-NMR (300 MHz, (D<sub>6</sub>)DMSO): 2.55–2.57 (*m*, CH); 3.11–3.17 (*m*, CH); 3.68 (*s*, Me); 3.77–3.92 (*m*, 2 CH<sub>2</sub>); 4.45–4.47 (*m*, CH); 6.82 (*d*, *J* = 6.4, 2 arom. H); 7.04 (*d*, *J* = 6.4, 2 arom. H); 9.75 (*br s*, NH). <sup>13</sup>C-NMR: 36.7; 43.0; 43.9; 55.5; 107.0; 114.4; 127.8; 134.7; 153.0; 158.2; 167.9. MS: 289 (*M*<sup>+</sup>). Anal. calc. for C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>O<sub>4</sub> (289.29): C 58.13, H 5.23, N 14.53; found: C 58.15, H 5.25, N 14.55.

**2,3,6,7-Tetrahydro-8-nitro-7-(pyridin-2-yl)imidazo[1,2-a]pyridin-5(1H)-one (13e).** Yield 70%. White solid. M.p. 242–244°. IR (KBr): 3204, 3013, 2930, 1699, 1636, 1588. <sup>1</sup>H-NMR: 2.63–2.69 (*m*, CH); 3.08–3.13 (*m*, CH); 3.77–3.94 (*m*, 2 CH<sub>2</sub>); 4.44–4.46 (*m*, CH); 7.21–7.29 (*m*, 2 arom. H); 7.68–7.70 (*m*, 1 arom. H); 8.39–8.41 (*m*, 1 arom. H); 9.64 (*br s*, NH). <sup>13</sup>C-NMR: 37.2; 42.9; 43.7; 106.5; 122.4; 122.8; 137.2; 149.7; 153.3; 161.5; 167.9. MS: 260 (*M*<sup>+</sup>). Anal. calc. for C<sub>12</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub> (260.25): C 55.38, H 4.65, N 21.53; found: C 55.40, H 4.68, N 21.50.

**Compounds 15a–15e. General Procedure.** As described for **5a–5d**, with ethane-1,2-diamine (**1**; 1 mmol), and 1,1-bis(methylthio)-2-nitroethene (**2**; 1 mmol), EtOH (5 ml), aldehyde **3** (1 mmol), and dimedone (= 5,5-dimethylcyclohexane-1,3-dione; **14**; 1 mmol) in EtOH (3 ml): **15**.

**2,3,5,7,8,9-Hexahydro-8,8-dimethyl-4-nitro-5-phenylimidazo[1,2-a]quinolin-6(1H)-one (15a):** Yield 51%. Yellow solid. M.p. 264–267°. IR (KBr): 3338, 2960, 2929, 2863, 1722, 1637. <sup>1</sup>H-NMR: 0.83 (*s*, Me); 1.03 (*s*, Me); 2.08 (*ABq*, *J* = 15.5, CH<sub>2</sub>); 2.49–2.57 (*m*, CH<sub>2</sub>); 3.56–3.82 (*m*, CH<sub>2</sub>); 4.06 (*m*, CH<sub>2</sub>); 5.07 (*s*, CH); 7.09–7.20 (*m*, 5 arom. H); 9.41 (*br s*, NH). <sup>13</sup>C-NMR: 26.5; 29.8; 32.2; 38.7; 43.8; 45.2; 49.9; 107.8; 114.1; 126.5; 128.1; 128.3; 144.7; 149.5; 152.1; 193.7. MS: 339 (*M*<sup>+</sup>). Anal. calc. for C<sub>19</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub> (339.39): C 67.24, H 6.26, N 12.38; found: C 67.20, H 6.29, N 12.35.

**2,3,5,7,8,9-Hexahydro-8,8-dimethyl-4-nitro-5-(pyridin-2-yl)imidazo[1,2-a]quinolin-6(1H)-one (15b):** Yield 68%. Yellow solid. M.p. 280–285° (dec.). IR (KBr): 3340, 2949, 2901, 1667. <sup>1</sup>H-NMR: 0.78 (*s*, Me); 1.01 (*s*, Me); 2.06 (*ABq*, *J* = 15.9, CH<sub>2</sub>); 2.42–2.59 (*m*, CH<sub>2</sub>); 3.80–3.86 (*m*, CH<sub>2</sub>); 3.98–4.15 (*m*, CH<sub>2</sub>); 5.07 (*s*, CH); 7.06–7.09 (*m*, 1 arom. H); 7.37–7.39 (*m*, 1 arom. H); 7.57–7.61 (*m*, 1 arom. H); 8.30–8.33 (*m*, 1 arom. H); 9.44 (*br s*, NH). <sup>13</sup>C-NMR: 26.2; 29.9; 32.2; 38.7; 40.3; 43.7; 45.1; 49.8; 107.3; 113.1; 121.9;

124.5; 135.7; 149.2; 150.1; 152.5; 162.15; 193.8. MS: 340 ( $M^+$ ). Anal. calc. for  $C_{18}H_{20}N_4O_3$  (340.38): C 63.52, H 5.92, N 16.46; found: C 63.56, H 5.95, N 16.47.

2,3,5,7,8,9-Hexahydro-5-(1H-indol-3-yl)-8,8-dimethyl-4-nitro-imidazo[1,2-a]quinolin-6(1H)-one (**15c**): Yield 45%. Yellow solid. M.p. 275–277° (dec.). IR (KBr): 3359, 3321, 2955, 2879, 1655.  $^1H$ -NMR: 0.77 (s, Me); 1.01 (s, Me); 2.05 (ABq,  $J = 15.8$ ,  $CH_2$ ); 2.51–2.59 (m,  $CH_2$ ); 3.80–3.87 (m,  $CH_2$ ); 4.02–4.21 (m,  $CH_2$ ); 5.04 (s, CH); 6.90–7.96 (m, 5 arom. H); 9.32 (br. s, NH); 10.76 (br. s, NH).  $^{13}C$ -NMR: 26.6; 29.1; 29.9; 32.1; 38.6; 43.8; 45.3; 49.9; 107.9; 111.6; 114.3; 117.8; 118.7; 119.7; 120.7; 124.0; 126.2; 136.4; 148.5; 152.1; 193.8. MS: 378 ( $M^+$ ). Anal. calc. for  $C_{21}H_{22}N_4O_3$  (378.42): C 66.65, H 5.86, N 14.81; found: C 66.60, H 5.85, N 14.80.

2,3,5,7,8,9-Hexahydro-8,8-dimethyl-4-nitro-5-(3-nitrophenyl)-imidazo[1,2-a]quinolin-6(1H)-one (**15d**). Yield 83%. Yellow solid. M.p. 285–287° (dec.). IR (KBr): 3359, 3071, 2943, 2935, 1661.  $^1H$ -NMR: 0.83 (s, Me); 1.04 (s, Me); 2.08 (ABq,  $J = 16.0$ ,  $CH_2$ ); 2.56–2.65 (m,  $CH_2$ ); 3.82–3.88 (m,  $CH_2$ ); 3.98–4.23 (m,  $CH_2$ ); 5.14 (s, CH); 7.48–7.54 (m, 1 arom. H); 7.68–7.70 (m, 1 arom. H); 7.98–8.04 (m, 2 arom. H); 9.5 (br. s, NH).  $^{13}C$ -NMR: 26.4; 29.8; 32.3; 38.2; 38.7; 43.9; 45.3; 49.6; 107.0; 112.8; 121.7; 123.0; 129.7; 135.0; 146.9; 147.6; 150.3; 151.8; 193.8. MS: 384 ( $M^+$ ). Anal. calc. for  $C_{19}H_{20}N_4O_5$  (384.39): C 59.37, H 5.24, N 14.58; found: C 59.30, H 5.29, N 14.52.

2,3,5,7,8,9-Hexahydro-5-(4-methoxyphenyl)-8,8-dimethyl-4-nitro-imidazo[1,2-a]quinolin-6(1H)-one (**15e**): Yield 54%. Yellow solid. M.p. 286–289° (dec.). IR (KBr): 3346, 3007, 2962, 2898, 1656.  $^1H$ -NMR: 0.85 (s, Me); 1.04 (s, Me); 2.08 (ABq,  $J = 16.0$ ,  $CH_2$ ); 2.45–2.61 (m,  $CH_2$ ); 3.67 (s, Me); 3.82–3.86 (m,  $CH_2$ ); 3.98–4.18 (m,  $CH_2$ ); 5.03 (s, CH); 6.73 (d,  $J = 7.8$ , 2 arom. H); 7.11 (d,  $J = 7.4$ , 2 arom. H); 9.33 (br. s, NH).  $^{13}C$ -NMR: 26.5; 29.9; 32.2; 38.7; 38.6; 43.8; 45.2; 49.9; 55.3; 108.0; 113.4; 114.4; 129.2; 136.9; 149.1; 152.0; 157.9; 193.7. MS: 369 ( $M^+$ ). Anal. calc. for  $C_{20}H_{23}N_3O_4$  (369.41): C 65.03, H 6.28, N 11.37; found: C 65.08, H 6.30, N 11.35.

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