Stereospecific Synthesis of (Z)-1,3-Oxazolobenzimidazoles from Imidazoleand Benzene-Ring-Substituted Benzimidazoles and α , β -Acetylenic γ -Hydroxynitriles

Ludmila V. Andriyankova, Kseniya V. Belyaeva, Lina P. Nikitina, Anastasiya G. Mal'kina, Andrei V. Afonin, Boris A. Trofimov*

A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch, Russian Academy of Sciences, 1 Favorsky Str., 664033 Irkutsk, Russian Federation

Fax +7(3952)419346; E-mail: boris_trofimov@irioch.irk.ru Received 16 April 2010; revised 26 April 2010

Abstract: A stereospecific, facile synthesis of (*Z*)-1,3-oxazolobenzimidazoles from imidazole- and benzene-ring-substituted benzimidazoles and α , β -acetylenic γ -hydroxynitriles has been elaborated. The reaction proceeds smoothly in acetonitrile without catalyst (room temperature, 3–5 days or 35–40 °C, 20–72 h) to afford the target compounds in 33–90% yields. The annulation involves an intermediate vinyl carbanion with zwitterionic character, which, after transformation into an O-centered zwitterion, is further inserted into the aromatic system of the imidazole ring. The synthesis contributes to the basic benzimidazole and acetylene chemistry and drug design.

Key words: substituted benzimidazoles, α , β -acetylenic γ -hydroxynitriles, zwitterion intermediates, annulations, 1,3-oxazolodihydrobenzimidazoles

The benzimidazole unit is known to be an important pharmacophore and privileged structure in medicinal chemistry. This scaffold is a frequent structural motif for expressing chemical functionality in biologically active molecules.¹ Optimization of benzimidazole-based structures is important in marketed medicines such as Vitamin B_{12} ,² the antiulcer agent Omeprazole,^{1,3} Lansoprazol and (s)-Rabeprazol,⁴ amongst others. Several functionalized benzimidazoles possess antithrombic,⁵ antiproliferative,⁶ antibacterial^{7,8} and antifungal⁸ activity, and they can act as hair-growth stimulating agents.9 The antiviral activity of a series of substituted benzimidazole, B-L- and B-D-2'-deoxyribonucleosides against selected RNA and DNA viruses including HIV-1 and human RSV was evaluated.10 Among the condensed benzimidazoles, imidazobenzimidazoles in particular were mentioned as antioxidants and radioprotectors and some were shown to possess antiarhythmic, spasmolytic and antisecretory properties.¹¹ A number of these compounds have also been shown to restrict the transport of calcium ions through membranes and to reduce blood pressure.¹¹

Consequently, functionalization of benzimidazole, in particular to produce new condensed derivatives, remains an important task of organic synthesis. Of special interest are functionalized condensed derivatives of benzimidazole

SYNTHESIS 2010, No. 16, pp 2828–2834 Advanced online publication: 07.07.2010 DOI: 10.1055/s-0030-1258152; Art ID: Z09710SS © Georg Thieme Verlag Stuttgart · New York containing a 1,3-oxazolidine moiety, which are practically unknown.

Recently, we have briefly reported on the annulation of 1substituted benzimidazoles with α , β -acetylenic γ -hydroxynitriles to furnish the first representatives of benzimidazoles condensed with 1,3-oxazolidine cycles with exclusively the Z-configuration.¹² However, the reaction was exemplified by only a limited number of benzimidazoles having substituents in the 1-position of the imidazole ring and, therefore, the real scope and synthetic importance of this synthesis remained obscure. In particular, it was unclear whether the benzene-ring-substituted benzimidazoles could be employed in this synthesis.

The aim of this work was to evaluate the true generality of this promising reaction. Thus, we have systematically studied the reaction of benzimidazoles **1a–f** substituted both at the imidazole and on the benzene rings with α , β -acetylenic γ -hydroxynitriles **2a** and **2b**.

The experiments have shown that benzimidazoles 1a-f substituted at the benzene ring do obey the general reaction scheme, i.e., they react exactly in the same manner as the previously described¹² benzimidazoles substituted at the 1-position of the imidazole ring. However, to reach reasonable preparative yields, a number of modifications had to be applied to the reaction conditions. Namely, in this case, the reaction was better conducted in solution (unlike the former reported protocol), and the most appropriate solvent appeared to be acetonitrile. Additionally, it proved to be useful to apply slight heating (35–40 °C) to significantly shorten the reaction time (from 3-5 days to 20–72 h) and improve the product yields (by ca. 30%). Finally, a new family (12 compounds) of functionalized benzimidazoles 3a-l condensed with oxazolidines possessing a substituent in the benzene moiety has been synthesized in up to 90% yields (Table 1).

In all the cases, the annulation remained strictly stereospecific, and delivered the products with *Z*-configuration only. However, special care should be taken to avoid traces of water in the reaction mixture because, otherwise, the reaction becomes a three-component one involving water as a third component that follows a multi-position rearrangement pathway to give furanylformamides.¹³





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Table 1 Synthesis of 1,3-Oxazolobenzimidazoles 3a-l from Benzimidazoles 1a-f and Nitriles 2a and 2b (continued)



^a Isolated yield. The reaction conditions are given in the experimental details.

^b Yields are given taking into account the conversion.

Cycloadducts **3a–l** were formed as either powders or oils, and were soluble in chloroform, ethanol and dimethylsulfoxide (DMSO). The structures of 1,3-oxazolobenzimidazoles **3a–l** were proved by ¹H and ¹³C NMR analysis, IR spectroscopy and by 2D NOESY techniques.

In the ¹H NMR spectra of 1,3-oxazolobenzimidazoles **3a**– **I**, a characteristic olefin proton singlet (H-10) at $\delta = 4.17$ – 5.65 ppm can be seen that is indicative of the formation of only one isomer. The Z-configurational assignment of the isomers follows from the fact that in the 2D NOESY spectrum of 1,3-oxazolobenzimidazole **3b**, a cross-peak between signals of the olefin proton H-10, the H-9a proton



Figure 1 Cross-peaks in the 2D NOESY spectrum of 1,3-oxazolobenzimidazole **3b**.

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and the *ortho*-protons of the cyclohexyl moiety is observed. The spectrum also contains cross-peaks between the H-8 proton and the protons of the methyl substituent (Figure 1).

The structure of 1,3-oxazolobenzimidazoles **3** was also confirmed by the fact that in the ¹H and ¹³C NMR spectra, the signals corresponding to H-9a and C-9a are high-field shifted by \sim 2 ppm and \sim 40 ppm, respectively, as compared to signals arising from H-2 and C-2 in the starting benzimidazoles **1**.

The IR spectra show absorption bands in the region of $2205-2217 \text{ cm}^{-1}$, which can be assigned to the cyano group at the double bond, as well as bands in the region of $1029-1149 \text{ cm}^{-1}$, which are typical for the C–O–C bonds.

The reaction is assumed to be triggered by the nucleophilic addition of benzimidazoles **1a–f**, as neutral nucleophiles, to the triple bond of acetylenes **2a** or **2b**, generating reversible zwitterionic vinyl carbanion **A**, which is further transformed into the oxygen-centered zwitterion **B** via hydrogen transfer from the hydroxy group to the carbanionic center. The $\mathbf{A} \rightarrow \mathbf{B}$ transformation is likely to proceed in a concerted mode, in accordance with the *trans*-nucleophilic addition rule to



Scheme 1 Tentative mechanism for the formation of the 1,3-oxazolobenzimidazoles 3a-l.

acetylenes,¹⁴ thus securing the observed Z-stereospecificity. Afterwards, intramolecular insertion of the anionic moiety of intermediate **B** into the imidazole aromatic system at the positively charged C2-position takes place to form the end products 3a-l (Scheme 1).

Although the effect of the substituents on the product yields is not explicitly expressed, the low conversion (15-34%) and longer reaction times (at 35–40 °C the reaction requires 72 h instead of 20–24 h for other imidazoles) for 5-nitro-substituted benzimidazoles **1e** and **1f** is consistent with Scheme 1, which implies that the reaction rate is retarded (slower nucleophilic addition to the triple bond) for the less electron-donating benzimidazoles.

In conclusion, benzimidazoles that are substituted both at the N-1 atom and on the benzene ring, are annulated regio- and stereospecifically with α , β -acetylenic γ -hydroxynitriles under mild conditions to furnish new functional heterocyclic systems, (Z)-1,3-oxazolobenzimidazoles, in moderate to high yields. The reaction proceeds by nucleophilic addition of benzimidazoles through their most nucleophilic N3-atom to the triple bond via the zwitterionic vinyl carbanion, which is further transformed into the Ocentered anion; the latter species is finally inserted into the aromatic imidazole ring at the positively charged C2position. Thus, a conceptionally new general methodology for the functionalization of the benzimidazole core has been developed. The novel representatives of condensed functionalized benzimidazoles are potential candidates of medicinal value and are promising precursors for drug design.

¹H and ¹³C NMR spectra were recorded with a Bruker DPX-400 spectrometer operating at 400.13 MHz (¹H) or 100.62 MHz (¹³C) by using CDCl₃ as a solvent (HMDS as an internal standard); the atom numbering for the assignment of the peaks in the NMR spectra is that shown in Table 1. IR spectra were recorded with a Bruker IFS-25 instrument (KBr or film). All melting points were determined with a Kofler micro hot stage apparatus. Elemental analyses were performed with a FLASH EA 1112 Series instrument. MeCN solvent was dried by standard methods. The α , β -acetylenic γ -hydroxynitriles **2a** and **2b** were prepared by the procedure described in the literature.¹⁵ Benzimidazoles **1a–f** were prepared by alkylation according to the literature protocol.¹⁶ The reaction was monitored by examining the disappearance of the IR absorption bands for the starting nitriles **2a** and **2b** in the reaction mixtures.

(Z)-2-{2,2,6,7,9-Pentamethyl-9,9a-dihydro[1,3]oxazolo[3,2a]benzimidazol-3(2H)-yliden}acetonitrile (3a); Typical Procedure

A mixture of 1,5,6-trimethylbenzimidazole (**1a**; 0.160 g, 1 mmol) and nitrile **2a** (0.109 g, 1 mmol) in anhydrous MeCN (1.0 mL) was

stirred at 35–40 °C for 20 h then cooled to r.t. After removal of the solvent, the residue was washed with anhydrous Et_2O (5 × 0.3 mL) to give **3a**.

Yield: 0.161 g (60%); orange powder; mp 146-148 °C.

IR (KBr): 432, 594, 612, 639, 730, 741, 760, 824, 847, 865, 911, 962, 990, 1004, 1045, 1076, 1149, 1178, 1191, 1208, 1224, 1259, 1291, 1372, 1392, 1432, 1459, 1479, 1504, 1627, 2217, 2874, 2941, 2984, 3075 cm⁻¹.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.37, 1.60 (2 × s, 6 H, 2 × CH₃-2), 2.28 (s, 3 H, CH₃-6), 2.30 (s, 3 H, CH₃-7), 3.41 (s, 3 H, N-CH₃), 4.17 (s, 1 H, H-10), 6.05 (s, 1 H, H-9a), 6.67 (s, 1 H, H-8), 6.82 (s, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 20.2 (CH₃-7), 20.3 (CH₃-6), 27.7, 29.1 (2 × CH₃-2), 33.4 (N-CH₃), 68.6 (C-10), 84.2 (C-2), 109.9 (C-9a), 110.5 (C-8), 117.8 (C-5), 119.2 (CN), 128.8 (C-6), 131.6 (C-7), 132.9 (C-4a), 139.6 (C-8a), 168.3 (C-3).

Anal. Calcd for $C_{16}H_{19}N_3O$: C, 71.35; H, 7.11; N, 15.60. Found: C, 71.42; H, 6.93; N, 15.12.

(Z)-Spiro-1,3-oxazolobenzimidazole 3b

Prepared from 1,5,6-trimethylbenzimidazole (**1a**; 0.160 g, 1 mmol) and nitrile **2b** (0.149 g, 1 mmol) after 22 h.

Yield: 0.173 g (56%); flesh-colored powder; mp 194–195 °C.

IR (KBr): 429, 511, 560, 603, 695, 734, 768, 846, 961, 1046, 1097, 1147, 1218, 1275, 1395, 1448, 1505, 1617, 1649, 2211, 2937, 2862, 3065 cm⁻¹.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.27–1.96 (m, 10 H, cycl), 2.21 (s, 3 H, CH₃-6), 2.23 (s, 3 H, CH₃-7), 2.89 (s, 3 H, N-CH₃), 4.33 (s, 1 H, H-10), 6.22 (s, 1 H, H-9a), 6.36 (s, 1 H, H-8), 7.65 (s, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 19.9 (CH₃-6), 20.3 (CH₃-7), 21.6, 21.9, 24.5 (3 × CH₂, cycl), 33.5 (N-CH₃), 35.3, 36.6 (2 × CH₂, cycl), 67.4 (C-10), 87.3 (C-2), 109.7 (C-9a), 110.8 (C-8), 118.0 (C-5), 119.7 (CN), 127.7 (C-6), 132.7 (C-7), 133.6 (C-4a), 140.9 (C-8a), 168.0 (C-3).

Anal. Calcd for $C_{19}H_{23}N_3O$: C, 73.76; H, 7.49; N, 13.58. Found: C, 73.24; H, 7.23; N, 13.07.

(Z)-2-{9-Benzyl-2,2,6,7-tetramethyl-9,9a-dihydro[1,3]oxazo-lo[3,2-*a*]benzimidazol-3(2*H*)-yliden}acetonitrile (3c)

Prepared from 1-benzyl-5,6-dimethylbenzimidazole (**1b**; 0.236 g, 1 mmol) and nitrile **2a** (0.109 g, 1 mmol) after 24 h.

Yield: 0.273 g (79%); white powder; mp 121–124 °C.

IR (KBr): 429, 518, 563, 597, 628, 676, 697, 721, 734, 749, 829, 843, 864, 908, 954, 975, 990, 1012, 1025, 1074, 1085, 1143, 1157, 1193, 1223, 1254, 1278, 1287, 1317, 1360, 1410, 1422, 1441, 1456, 1469, 1502, 1612, 1645, 2206, 2855, 2900, 2925, 2970, 3031, 3070, 3087 cm⁻¹.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.42, 1.44 (2 × s, 6 H, 2 × CH₃-2), 2.10 (s, 3 H, CH₃-6), 2.19 (s, 3 H, CH₃-7), 4.40 (s, 1 H, H-10), 4.37, 4.46 (2 × d, ²*J*_{H-H} = 16.4 Hz, 2 H, CH₂ from *N*-benzyl), 6.23

(s, 1 H, H-9a), 6.39 (s, 1 H, H-8), 7.20–7.30 (m, 5 H, Ph from *N*-benzyl), 7.56 (s, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 19.6 (CH₃-6), 19.9 (CH₃-7), 27.0, 28.6 (2×CH₃-2), 50.7 (CH₂ from *N*-benzyl), 68.3 (C-10), 84.1 (C-2), 108.3 (C-9a), 109.1 (C-8), 117.6 (C-5), 119.0 (CN), 127.4 (*p*-C, Ph from *N*-benzyl), 127.0 (*o*-C, Ph from *N*-benzyl), 128.7 (*m*-C, Ph from *N*-benzyl), 129.0 (C-6), 132.7 (C-4a), 137.4 (*i*-C, Ph from *N*-benzyl), 140.1 (C-7), 142.5 (C-8a), 168.3 (C-3).

Anal. Calcd for $C_{22}H_{23}N_3O$: C, 76.49; H, 6.71; N, 12.16. Found: C, 76.82; H, 6.73; N, 12.40.

(Z)-Spiro-1,3-oxazolobenzimidazole 3d

Prepared from 1-benzyl-5,6-dimethylbenzimidazole (**1b**; 0.236 g, 1 mmol) and nitrile **2b** (0.149 g, 1 mmol) after 24 h.

Yield: 0.259 g (67%); brown oil.

IR (film): 429, 586, 699, 727, 738, 845, 908, 930, 954, 990, 1028, 1077, 1101, 1134, 1160, 1173, 1221, 1259, 1272, 1354, 1389, 1400, 1450, 1500, 1578, 1614, 1652, 2208, 2857, 2933, 3006, 3032, 3064, 3086 cm⁻¹.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.20–1.90 (m, 10 H, cycl), 2.11 (s, 3 H, CH₃-6), 2.19 (s, 3 H, CH₃-7), 4.42 (s, 1 H, H-10), 4.38–4.45 (m, 2 H, CH₂ from N-benzyl), 6.25 (s, 1 H, H-9a), 6.37 (s, 1 H, H-8), 7.20–7.30 (m, 5 H, Ph from *N*-benzyl), 7.58 (s, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 19.5 (CH₃-6), 19.8 (CH₃-7), 21.4, 21.6, 24.6, 35.2, 36.8 (5 × CH₂, cycl), 50.6 (CH₂ from *N*-benzyl), 69.0 (C-10), 85.6 (C-2), 108.4 (C-9a), 109.0 (C-8), 117.5 (C-5), 120.1 (CN), 127.3 (*p*-C, Ph from *N*-benzyl), 127.5 (*o*-C, Ph from *N*-benzyl), 128.6 (*m*-C, Ph from *N*-benzyl), 132.7 (C-7), 134.0 (C-4a), 137.4 (*i*-C, Ph from *N*-benzyl), 142.4 (C-8a), 168.5 (C-3).

Anal. Calcd for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N, 10.90. Found: C, 77.35; H, 7.17; N, 10.58.

(Z)-2-{7-Methoxy-2,2,9-trimethyl-9,9a-dihydro[1,3]oxazo-lo[3,2-*a*]benzimidazol-3(2*H*)-yliden}acetonitrile (3e)

Prepared from 1-methyl-6-methoxybenzimidazole (1c; 0.162 g, 1 mmol) and nitrile 2a (0.109 g, 1 mmol) after 20 h.

Yield: 0.119 g (44%); yellow oil.

IR (film): 495, 617, 730, 779, 817, 986, 1035, 1091, 1125, 1176, 1215, 1290, 1325, 1349, 1465, 1509, 1585, 1620, 1649, 2208, 2875, 2933, 2977, 3070 cm⁻¹.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.44, 1.46 (2 × s, 6 H, 2 × CH₃-2), 2.87 (s, 3 H, *N*-CH₃), 3.69 (s, 3 H, *O*-CH₃-7), 4.36 (s, 1 H, H-10), 6.01 (s, 1 H, H-8), 6.25 (d, ³*J*_{H5-H6} = 6.8 Hz, 1 H, H-6), 6.44 (s, 1 H, H-9a), 7.69 (d, ³*J*_{H5-H6} = 6.8 Hz, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 27.2, 28.6 (2 × CH₃-2), 32.2 (*N*-CH₃), 55.6 (*O*-CH₃-7), 67.5 (C-10), 84.9 (C-2), 96.0 (C-8), 101.9 (C-9a), 108.6 (C-6), 117.0 (C-5), 118.9 (CN), 128.4 (C-4a), 143.8 (C-8a), 158.3 (C-7), 168.2 (C-3).

Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.85; H, 6.17; N, 15.80.

(Z)-Spiro-1,3-oxazolobenzimidazole 3f

Prepared from 1-methyl-6-methoxybenzimidazole (1c; 0.162 g, 1 mmol) and nitrile 2b (0.149 g, 1 mmol) after 20 h.

Yield: 0.103 g (33%); white powder; mp 130-134 °C.

IR (KBr): 516, 585, 594, 654, 694, 718, 792, 865, 933, 977, 1029, 1064, 1077, 1104, 1126, 1176, 1222, 1259, 1327, 1352, 1380, 1406, 1434, 1455, 1487, 1616, 1640, 2205, 2836, 2866, 2974, 3000, 3065 cm⁻¹.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.24–1.95 (m, 10 H, cycl), 2.85 (s, 3 H, *N*-CH₃), 3.75 (s, 3 H, *O*-CH₃-7), 4.27 (s, 1 H, H-10), 6.09

(s, 1 H, H-8), 6.23 (s, 1 H, H-9a), 6.27 (d, ${}^{3}J_{\text{HS}-\text{H6}} = 6.8$ Hz, 1 H, H-6), 7.71 (d, ${}^{3}J_{\text{HS}-\text{H6}} = 6.8$ Hz, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): $\delta = 22.0, 22.3, 25.0 (3 \times CH_2, cycl), 32.3 ($ *N*-CH₃), 36.0, 37.1 (2 × CH₂, cycl), 55.7 (*O*-CH₃-7), 66.7 (C-10), 87.5 (C-2), 95.8 (C-8), 101.9 (C-9a), 110.5 (C-6), 117.9 (C-5), 119.3 (CN), 128.0 (C-4a), 144.7 (C-8a), 158.5 (C-7), 168.0 (C-3).

Anal. Calcd for $C_{18}H_{21}N_3O_2$: C, 69.43; H, 6.08; N, 13.49. Found: C, 69.00; H, 6.07; N, 13.24.

(Z)-2-{9-Benzyl-7-methoxy-2,2-dimethyl-9,9a-dihydro[1,3]oxazolo[3,2-*a*]benzimidazol-3(2*H*)-yliden}acetonitrile (3g)

Prepared from 1-benzyl-6-methoxybenzimidazole (1d; 0.238 g, 1 mmol) and nitrile 2a (0.109 g, 1 mmol) after 20 h.

Yield: 0.312 g (90%); white powder; mp 99-100 °C.

IR (KBr): 460, 520, 577, 608, 681, 699, 732, 745, 764, 791, 842, 913, 952, 969, 1030, 1080, 1091, 1117, 1147, 1166, 1197, 1213, 1245, 1268, 1278, 1321, 1354, 1366, 1423, 1455, 1497, 1602, 1615, 1644, 2208, 2854, 2931, 2962, 2984, 3009, 3026, 3062 cm⁻¹.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.45, 1.47 (2 × s, 6 H, 2 × CH₃-2), 3.68 (s, 3 H, O-CH₃-7), 4.35, 4.38 (2 × d, ²J_{H-H} = 16.4 Hz, 2 H, CH₂ from *N*-benzyl), 4.36 (s, 1 H, H-10), 6.02 (s, 1 H, H-8), 6.26 (d, ³J_{H5-H6} = 6.8 Hz, 1 H, H-6), 6.45 (s, 1 H, H-9a), 7.20–7.30 (m, 5 H, Ph from *N*-benzyl), 7.70 (d, ³J_{H5-H6} = 6.8 Hz, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 27.2, 28.7 (2 × CH₃-2), 50.2 (CH₂ from *N*-benzyl), 55.6 (*O*-CH₃-7), 67.5 (C-10), 84.9 (C-2), 96.0 (C-8), 101.9 (C-9a), 108.6 (C-6), 117.1 (C-5), 119.1 (CN), 127.5 (*o*-C, Ph from *N*-benzyl), 127.6 (*p*-C, Ph from *N*-benzyl), 128.4 (C-4a), 128.8 (*m*-C, Ph from *N*-benzyl), 136.9 (*i*-C, Ph from *N*-benzyl), 143.6 (C-8a), 158.2 (C-7), 168.4 (C-3).

Anal. Calcd for $C_{21}H_{21}N_3O_2$: C, 72.60; H, 6.09; N, 12.10. Found: C, 72.22; H, 6.14; N, 11.77.

(Z)-Spiro-1,3-oxazolobenzimidazole 3h

Prepared from 1-benzyl-6-methoxybenzimidazole (1d; 0.238 g, 1 mmol) and nitrile 2b (0.149 g, 1 mmol) after 22 h.

Yield: 0.283 g (73%); yellow oil.

IR (film): 435, 445, 504, 589, 639, 704, 739, 825, 943, 1033, 1078, 1171, 1213, 1273, 1324, 1359, 1404, 1450, 1498, 1613, 1650, 2206, 2861, 2937, 3034, 3065 cm⁻¹.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.20–2.10 (m, 10 H, cycl), 3.72 (s, 3 H, O-CH₃-7), 4.39 (s, 1 H, H-10), 4.41, 4.50 (2 × d, ²*J*_{H-H} = 16.4 Hz, 2 H, CH₂ from *N*-benzyl), 6.05 (s, 1 H, H-8), 6.27 (d, ³*J*_{H5-H6} = 6.8 Hz, 1 H, H-6), 6.46 (s, 1 H, H-9a), 7.20–7.30 (m, 5 H, Ph from *N*-benzyl), 7.71 (d, ³*J*_{H5-H6} = 6.8 Hz, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 21.8, 22.2, 24.8, 35.8, 35.9 (5 × CH₂, cycl), 50.3 (CH₂ from *N*-benzyl), 55.6 (*O*-CH₃-7), 68.3 (C-10), 86.5 (C-2), 95.9 (C-8), 101.8 (C-9a), 108.8 (C-6), 117.1 (C-5), 119.2 (CN), 127.6 (*o*,*p*-C, Ph from *N*-benzyl), 128.8 (*m*-C, Ph from *N*-benzyl), C-4a), 137.0 (*i*-C, Ph from *N*-benzyl), 143.3 (C-8a), 158.1 (C-7), 168.7 (C-3).

Anal. Calcd for C₂₄H₂₅N₃O₂: C, 74.39; H, 6.50; N, 10.84. Found: C, 74.72; H, 6.42; N, 10.43.

(Z)-2-{2,2,9-Trimethyl-6-nitro-9,9a-dihydro[1,3]oxazolo[3,2*a*]benzimidazol-3(2*H*)-yliden}acetonitrile (3i)

Prepared from 1-methyl-5-nitrobenzimidazole (1e; 0.177 g, 1 mmol) and nitrile 2a (0.109 g, 1 mmol) after 24 h.

Yield: 0.226 g (79%); red oil.

IR (film): 497, 536, 578, 607, 621, 647, 683, 712, 749, 786, 796, 809, 874, 894, 976, 1005, 1056, 1085, 1107, 1139, 1169, 1187,

1244, 1278, 1337, 1384, 1398, 1504, 1516, 1605, 1651, 2208, 2877, 2931, 2980, 3023, 3062, 3097 $\rm cm^{-1}.$

¹H NMR (400.13 MHz, CDCl₃): δ = 1.36, 1.50 (2 × s, 6 H, 2 × CH₃-2), 3.07 (s, 3 H, *N*-CH₃), 5.54 (s, 1 H, H-10), 6.65 (s, 1 H, H-9a), 6.76 (d, ³*J*_{H7-H8} = 6.8 Hz, 1 H, H-8), 7.98 (d, ³*J*_{H7-H8} = 6.8 Hz, 1 H, H-7), 8.01 (s, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 26.4, 28.1 (2 × CH₃-2), 30.5 (*N*-CH₃), 74.6 (C-10), 83.2 (C-2), 104.8 (C-9a), 106.7 (C-8), 108.1 (C-5), 118.9 (CN), 123.5 (C-7), 135.5 (C-4a), 138.9 (C-6), 147.6 (C-8a), 168.6 (C-3).

Anal. Calcd for $C_{14}H_{14}N_4O_3$: C, 58.74; H, 4.93; N, 19.57. Found: C, 58.29; H, 4.70; N, 19.22.

(Z)-Spiro-1,3-oxazolobenzimidazole 3j

Prepared from 1-methyl-5-nitrobenzimidazole (1e; 0.177 g, 1 mmol) and nitrile 2b (0.149 g, 1 mmol) after 72 h.

Yield: 0.140 g (43%, conversion of 1e was 34%); brown powder; mp 66–69 °C.

IR (KBr): 499, 562, 616, 633, 742, 795, 822, 901, 947, 977, 1053, 1088, 1131, 1168, 1291, 1393, 1446, 1514, 1604, 1648, 2216, 2862, 2938, 3095 cm⁻¹.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.20–2.00 (m, 10 H, cycl), 3.06 (s, 3 H, *N*-CH₃), 4.68 (s, 1 H, H-10), 6.36 (d, ³J_{H7-H8} = 6.8 Hz, 1 H, H-8), 6.51 (s, 1 H, H-9a), 7.78 (d, ³J_{H7-H8} = 6.8 Hz, 1 H, H-7), 8.40 (s, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): $\delta = 21.8$, 22.2, 24.6 (3 × CH₂, cycl), 30.3 (*N*-CH₃), 34.9, 36.9 (2 × CH₂, cycl), 75.3 (C-10), 84.4 (C-2), 104.4 (C-9a), 106.1 (C-8), 109.8 (C-5), 118.9 (CN), 123.0 (C-7), 135.3 (C-4a), 140.1 (C-6), 146.9 (C-8a), 168.4 (C-3).

Anal. Calcd for $C_{17}H_{18}N_4O_3$: C, 62.57; H, 5.56; N, 17.17. Found: C, 62.13; H, 5.35; N, 17.63.

(Z)-2-{9-Benzyl-6-nitro-2,2-dimethyl-9,9a-dihydro[1,3]oxazo-lo[3,2-*a*]benzimidazol-3(2*H*)-yliden}acetonitrile (3k)

Prepared from 1-benzyl-5-nitrobenzimidazole (**1f**; 0.253 g, 1 mmol) and nitrile **2a** (0.109 g, 1 mmol) after 24 h.

Yield: 0.196 g (54%); yellow powder; mp 207–208 °C.

IR (KBr): 455, 519, 562, 591, 644, 665, 695, 728, 737, 785, 806, 815, 839, 865, 950, 992, 1070, 1091, 1133, 1158, 1191, 1282, 1299, 1318, 1363, 1398, 1417, 1442, 1454, 1503, 1519, 1600, 1653, 2213, 2876, 2916, 2976, 3033, 3065 cm^{-1}.

¹H NMR (400.13 MHz, CDCl₃): δ = 1.37, 1.50 (2 × s, 6 H, 2 × CH₃-2), 4.70, 4.83 (2 × d, ²J_{H-H} = 16.4 Hz, 2 H, CH₂ from *N*-benzyl), 5.65 (s, 1 H, H-10), 6.70 (d, ³J_{H7-H8} = 6.8 Hz, 1 H, H-8), 6.82 (s, 1 H, H-9a), 7.30–7.40 (m, 5 H, Ph from *N*-benzyl), 7.98 (d, ³J_{H7-H8} = 6.8 Hz, 1 H, H-7), 8.28 (s, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 26.5, 28.2 (2 × CH₃-2), 48.1 (CH₂ from *N*-benzyl), 75.5 (C-10), 82.9 (C-2), 105.5 (C-9a), 106.0 (C-8), 108.9 (C-5), 119.0 (CN), 123.4 (C-7), 127.9 (*o*-C, Ph from *N*-benzyl), 128.1 (*p*-C, Ph from *N*-benzyl), 129.1 (*m*-C, Ph from *N*-benzyl), 136.0 (C-4a), 136.6 (*i*-C, Ph from *N*-benzyl), 139.5 (C-6), 146.8 (C-8a), 168.7 (C-3).

Anal. Calcd for $C_{20}H_{18}N_4O_3$: C, 66.29; H, 5.01; N, 15.46. Found: C, 66.02; H, 4.98; N, 15.54.

(Z)-Spiro-1,3-oxazolobenzimidazole 3l

Prepared from 1-benzyl-5-nitrobenzimidazole (**1f**; 0.253 g, 1 mmol) and nitrile **2b** (0.149 g, 1 mmol) after 72 h.

Yield: 0.218 g (54%, conversion of 1f was 15%); yellow powder; mp 138–141 °C.

IR (KBr): 424, 465, 543, 596, 634, 699, 731, 741, 749, 796, 819, 887, 938, 959, 1060, 1077, 1097, 1107, 1133, 1202, 1221, 1281,

1308, 1322, 1335, 1349, 1356, 1393, 1445, 1472, 1495, 1600, 1654, 2214, 2857, 2937, 3008, 3045, 3070, 3084 $\rm cm^{-1}.$

¹H NMR (400.13 MHz, CDCl₃): δ = 1.20–2.00 (m, 10 H, cycl), 4.61, 4.69 (2 × d, ${}^{2}J_{H-H}$ = 16.4 Hz, 2 H, CH₂ from *N*-benzyl), 4.75 (s, 1 H, H-10), 6.37 (d, ${}^{3}J_{H7-H8}$ = 6.8 Hz, 1 H, H-8), 6.52 (s, 1 H, H-9a), 7.20–7.30 (m, 5 H, Ph from *N*-benzyl), 7.88 (d, ${}^{3}J_{H7-H8}$ = 6.8 Hz, 1 H, H-7), 8.41 (s, 1 H, H-5).

¹³C NMR (100.62 MHz, CDCl₃): δ = 21.7, 22.2, 24.6, 35.0, 36.9 (5 × CH₂, cycl), 48.5 (CH₂ from *N*-benzyl), 75.3 (C-10), 84.5 (C-2), 104.3 (C-9a), 106.0 (C-8), 110.1 (C-5), 118.8 (CN), 122.7 (C-7), 128.1 (*o*-C, Ph from *N*-benzyl), 128.7 (*p*-C, Ph from *N*-benzyl), 129.3 (*m*-C, Ph from *N*-benzyl), 135.2 (C-4a), 135.7 (*i*-C, Ph from *N*-benzyl), 140.2 (C-6), 146.7 (C-8a), 168.2 (C-3).

Anal. Calcd for $C_{23}H_{22}N_4O_3$: C, 68.64; H, 5.51; N, 13.92. Found: C, 68.14; H, 5.31; N, 13.68.

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