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SYNTHESIS OF NOVEL HETEROCYCLIC SYSTEM – IMIDAZO[5,1-*b*][1,3]BENZOXAZINE

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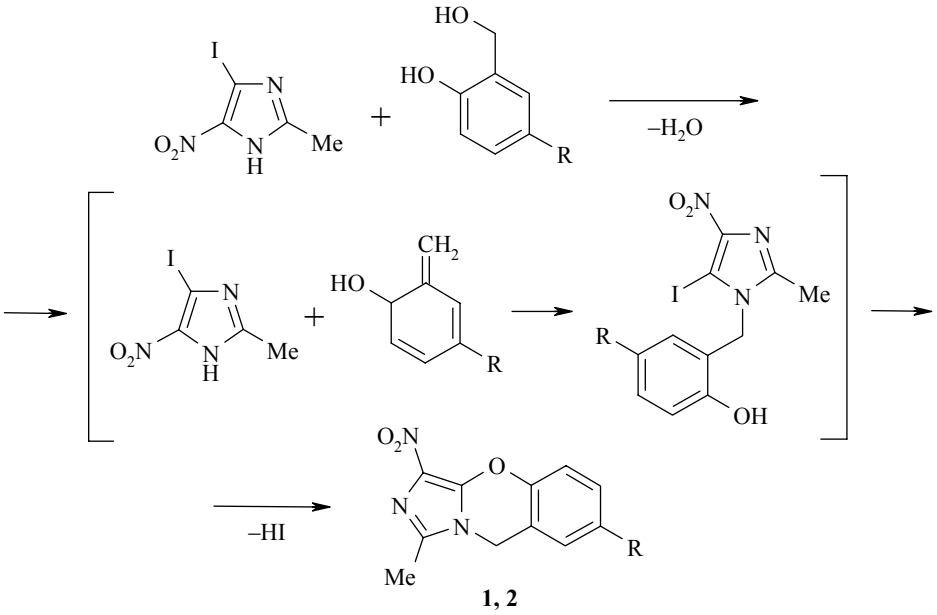
There is no information in the literature about the synthesis of compounds containing the condensed imidazo[5,1-*b*][1,3]benzoxazine system. At the same time, the high biological activity of many imidazole and benzoxazine derivatives serves as a stimulus to synthesize condensed heterocycles containing both of these fragments simultaneously [1-3].

We propose a simple, one stage method for preparing the substituted imidazo[5,1-*b*][1,3]benzoxazines **1, 2** consisting of the reaction of 4-iodo-2-methyl-5-nitroimidazole with substituted 2-hydroxymethylphenols through refluxing in DMF.



1, 2

1 R = Br; **2** R = NO_2

The reaction takes place *via* the intermediate stage of forming an *o*-methylenequinone (*o*-quinonemethide) [4] which attacks the imidazole molecule to form a substituted 2-(1H-imidazol-1-ylmethyl)phenol and then undergoes an intramolecular cyclization with release of an HI molecule.

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IR spectra were recorded on a Shimadzu FTIR-8400S spectrophotometer using KBr tablets. ^{1}H NMR spectra were taken on a Bruker AM 300 spectrometer (300 MHz) using DMSO-d_6 and with TMS as internal standard. Mass spectra were recorded on a Finnigan Trance DSQ chromatographic mass spectrometer with direct introduction of the sample into the ion source.

7-Bromo-1-methyl-3-nitro-9H-imidazo[5,1-*b*][1,3]benzoxazine (1). A mixture of 4-iodo-2-methyl-5-nitroimidazole (1.0 g, 4 mmol) and 4-bromo-2-hydroxymethylphenol (0.84 g, 4.14 mmol) in DMF (10 ml) was heated at 125-130°C for 3 h and than at reflux for 3 h. The mixture was cooled, poured into water, the precipitate filtered off, and crystallized from DMF to give compound **1** (0.81 g, 66%) as colorless crystals with mp 275-277°C. IR spectrum, ν, cm^{-1}: 3047 (CH_{arom}), 2924, 2854 (CH_3), 1620, 1597, 1578 (C=C/C=N), 1477, 1377, 1350, 1269, 1234, 1173, 1115, 1088 (C–O–C). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.36 (3H, s, CH_3); 5.26 (2H, s, CH_2); 7.33 (1H, d, *J* = 8.8, H-5); 7.60 (1H, d, *J* = 8.8, H-6); 7.67 (1H, s, H-8). Mass spectrum, (EI, 70 eV, for ^{79}Br isotope), *m/z* (I_{rel}, %): 309 $[M]^+$ (98); 263 $[M\text{-}NO_2]^+$ (5), 238 (11), 210 (31), 184 $[C_7H_5BrO]^+$ (12), 156 $[C_6H_5Br]^+$ (14), 77 $[C_6H_5]^+$ (32), 51 (15), 43 $[HNCO]^+$ (78). Found %: C 42.71; H 2.54; N 13.22. $C_{11}H_8BrN_3O_3$. Calculated, %: C 42.58; H 2.58; N 13.55.

1-Methyl-3,7-dinitro-9H-imidazo[5,1-*b*][1,3]benzoxazine (2) was prepared similarly to compound **1** from 4-iodo-2-methyl-5-nitroimidazole (1.14 g, 4.5 mmol) and 2-hydroxymethyl-4-nitrophenol (0.81 g, 4.8 mmol) as pink crystals with mp 302-303°C (with decomp.) (from DMF) in 0.63 g (51%) yield. IR Spectrum, ν, cm^{-1}: 3040 (CH_{arom}), 2928, 2858 (CH_3), 1601, 1578 (C=C/C=N), 1531 (NO_2), 1477, 1389, 1342 (NO_2), 1281, 1258, 1227, 1184, 1088 (C–O–C). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.40 (3H, s, CH_3); 5.44 (2H, s, CH_2); 7.38 (1H, d, *J* = 9.1 H-5); 7.87 (1H, d, *J* = 9.1, H-6); 8.01 (1H, s, H-8). Mass spectrum, (EI, 70 eV), *m/z* (I_{rel}, %): 276 $[M]^+$ (65), 230 $[M\text{-}NO_2]^+$ (5), 204 (8), 184 $[M\text{-}2\ NO_2]^+$ (3), 177 (15), 151 $[C_7H_5NO_3]^+$ (4), 77 $[C_6H_5]^+$ (12), 43 $[HNCO]^+$ (100). Found, %: C 47.97; H 2.85; N 19.80. $C_{11}H_8N_4O_5$. Calculated, %: C 47.83; H 2.90; N 20.29.

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