Unusual reaction of iodofurazans with nucleophilic reagents

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Nucleophilic reagents cause detachment of the iodine atom from 3-iodo-4-R-furazans and opening of the furazan ring to give salts of the corresponding α-hydroxyiminoacetonitriles.

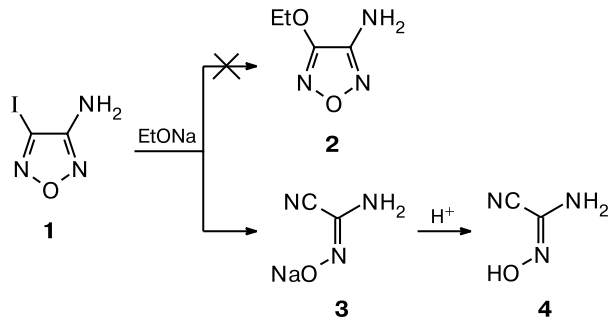
Key words: furazans, iodofurazans, nucleophilic substitution, α-hydroxyiminoacetonitriles, ring opening.

Nucleophilic displacement of a nitro group bound to the furazan ring has been thoroughly studied and is widely used for the synthesis of various furazan derivatives.[1] However, information on the involvement of halofurazans in these reactions is very scarce.[2] It was shown[3,4] that the nitro group at the furazan ring is more mobile than the chlorine atom. Literature data on reactions of iodofurazans with nucleophilic reagents are lacking.

Recently, we have developed the first general method for the synthesis of iodofurazans through nonaqueous diazotization—iodination of aminofurazans.[5] The present study is devoted to some reactions of these previously inaccessible iodo derivatives.

We found that iodofurazans react with nucleophilic reagents differently from other halo- and nitrofurazans. For instance, treatment of 3-amino-4-iodofurazan (**1**) with sodium ethoxide at room temperature did not yield the expected ethoxy derivative **2**.[6] According to elemental analysis and spectroscopic data, the resulting insoluble precipitate is a sodium salt of α-amino-α-hydroxyiminoacetonitrile (**3**) (Scheme 1). The same salt was obtained in 70—80% yield in the reactions of compound **1** with sodium methoxide and isopropoxide and with a solution of NaOH in glyme. Acidification of salt **3** gave cyano oxime **4**.

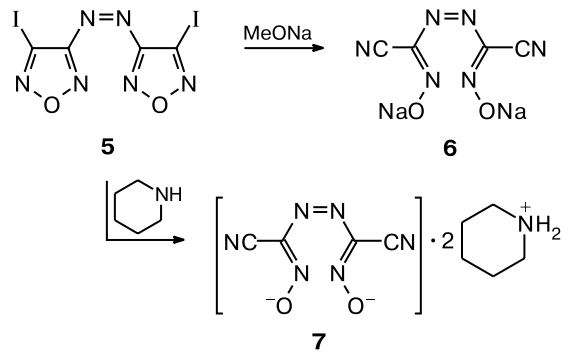
Scheme 1



Compound **1** does not react with piperidine at room temperature; on heating, iodine is liberated. No individual compounds were identified in the resulting dark mixture.

More reactive diiodoazofurazan **5** [5] easily reacts with both sodium alkoxides and piperidine. However, in both cases, the furazan ring also undergoes opening to give the corresponding salts **6** and **7** (Scheme 2).

Scheme 2



The structures of salts **3**, **6**, and **7** were confirmed by spectroscopic and elemental analysis data. The IR spectra of these compounds contain a characteristic low-intensity band at 2170—2220 cm^{-1} for ν(C≡N) stretching vibrations. In their ^{13}C NMR spectra, the signal for the nitrile C atom appears at δ 106—112.

Usually, the furazan ring is fairly stable. However, some furazan derivatives are well known as being prone to ring opening.[2] For instance, base-catalyzed opening of monosubstituted furazans occurs easily, with 1,3-migration of the proton and cleavage of the N—O bond. The migration of the radical center formed as a result of the decomposition of furazandiazonium salts[7] or iodosylbenzene furazancarboxylates[8] also leads to acyclic products. In this case, the key step is the transfer of the reactive center in the ring from the C atom to the O atom.

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Apparently, the formation of acyclic products in the reactions of iodofurazans with nucleophiles follows a similar fashion. The bulky iodine atom (as the leaving group) does not stabilize the transition state. One can assume that the radical anion center formed at the C atom upon the detachment of iodine rapidly moves to the O atom, thus favoring the ring opening.

Hence, the presented data extend the range of possible ways of opening the furazan ring. It should be noted that the synthesis of compounds combining different substituents (like that obtained through the transformations described above) is a difficult problem.[9—12] For this reason, this reaction can be of both theoretical and practical interest.

Experimental

Melting points were determined on a Gallenkamp melting unit and are uncorrected. IR spectra were recorded on a Specord IR75 spectrometer (KBr pellets). Mass spectra were recorded on a Varian MAT CH-111 instrument (70 eV). Natural-isotope ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 and 75.7 MHz, respectively). The starting iodofurazans **1** and **5** were prepared according to a previously developed procedure.[5]

α-Amino-α-hydroxyiminoacetonitrile, sodium salt (3). Compound **1** (0.42 g, 2 mmol) was added in small portions at 0 °C to a solution of EtONa prepared from sodium (0.096 g, 4.2 mmol) and EtOH (5 mL). The resulting mixture was stirred at ~20 °C for 1.5 h, diluted with ether, and left in a refrigerator for ~12 h. The precipitate was filtered off and reprecipitated from EtOH with ether to give product **3** (0.17 g, 79.8%) as a white amorphous powder, m.p. 113 °C (decomp.). Found (%): C, 22.41; H, 1.90; N, 39.21; Na, 21.92. $C_2H_2N_3NaO$. Calculated (%): C, 22.44; H, 1.88; N, 39.25; Na, 21.88. IR, ν/cm^{-1}: 3224, 3164, 3120, 2172, 1612, 1536, 1444, 1404, 1244, 1224, 1036, 1000. ^{1}H NMR (DMSO-d_6), δ: 4.5—5.0 (br., NH_2). ^{13}C NMR (DMSO-d_6), δ: 106.1 (C≡N); 145.6 (C—CN).

α-Amino-α-hydroxyiminoacetonitrile (4). 20% Hydrochloric acid (20 mL) was added dropwise at 5—10 °C to a vigorously stirred suspension of salt **3** (1.07 g, 10 mmol) in 50 mL of ether. After the whole of the acid was added, the reaction mixture was allowed to warm to 20 °C. Then the ethereal layer was separated, and the product was extracted from the acid layer with ether (20 mL). The combined ethereal extracts were dried with $MgSO_4$ and concentrated and the residue was reprecipitated from CH_2Cl_2 with carbon tetrachloride to give product **4** (0.49 g, 58%) as a light cream-colored amorphous powder, m.p. 79—81 °C. Found (%): C, 28.20; H, 3.52; N, 49.41. $C_2H_3N_3O$. Calculated (%): C, 28.24; H, 3.55; N, 49.40. IR, ν/cm^{-1}: 3438, 3320, 3160, 2860, 2825, 2160, 1660, 1640, 1590, 1440, 1375, 1238, 980, 885. ^{1}H NMR (DMSO-d_6), δ: 6.52 (2 H, NH_2); 10.90 (1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 113.7 (C≡N); 151.2 (C—CN).

Azobis-*N*,*N*′-(α-hydroxyiminoacetonitrile), disodium salt (6). A solution of sodium (0.096 g, 4.2 mmol) in 2 mL of MeOH was added dropwise at 0 °C to a solution of compound **5** (0.418 g, 1 mmol) in 1 mL of MeOH. The precipitate that formed was filtered off and washed with an acetone—ether mixture (2 : 3, v/v) to give salt **6** (0.2 g, 95%), m.p. 327—327.5 °C. Found (%): C, 22.83; N, 39.96; Na, 21.86. $C_4N_6Na_2O_2$. Calculated (%): C, 22.87; N, 40.01; Na, 21.89. IR, ν/cm^{-1}: 2220, 1652, 1616, 1420, 1216. ^{13}C NMR (DMSO-d_6), δ: 112.0 (C≡N); 150.5 (C—CN).

Azobis-*N*,*N*′-(α-hydroxyiminoacetonitrile), dipiperidinium salt (7). Piperidine (0.38 g, 4.4 mmol) was added to a solution of compound **5** (0.4 g, 0.95 mmol) in 5 mL of CH_2Cl_2. The reaction mixture was stirred at ~20 °C for 0.5 h. The precipitate that formed was filtered off and washed with CH_2Cl_2 (25 mL) and ether (25 mL) to give product **7** (0.22 g, 68%) as a light brown amorphous powder, m.p. 169—172 °C. Found (%): C, 50.08; H, 7.24; N, 33.25. $C_{14}H_{24}N_8O_2$. Calculated (%): C, 49.99; H, 7.19; N, 33.31. MS, *m/z*: 337 [M$^+$], 97, 85. IR, ν/cm^{-1}: 3016, 2960, 2872, 2652, 2528, 2364, 2212, 1632, 1424, 1408, 1380, 1264, 1184, 1164, 1140, 1116, 1080, 1032, 952. ^{1}H NMR (DMSO-d_6), δ: 1.56 (m, 6 H); 5.61 (m, 4 H). ^{13}C NMR (DMSO-d_6), δ: 22.3, 23.1, 44.3 (CH_2N); 110.3 (C≡N); 149.9 (C—CN).

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