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Reaction of 2-Amino-5,5-bis(hydroxymethyl)-1-methyl-1,5-dihydro-4*H*-imidazol-4-one with Aromatic Aldehydes

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Abstract—The reaction of 5,5-bis(hydroxymethyl)creatinine with aromatic aldehydes in the boron trifluoride etherate results in 2-aryl derivatives of 2'-amino-3'-methyl-(1,3-dioxane)-5-spiro-4'-imidazolidin-5'-one.

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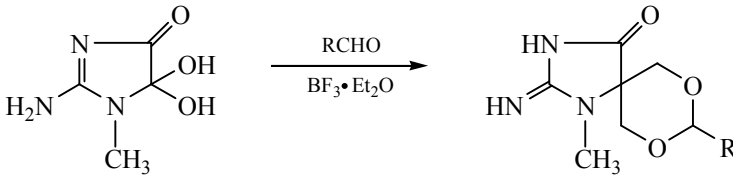
We have previously shown [1] that the acid-catalyzed reaction of 2-amino-5,'5-bis(hydroxymethyl)-4-tiazol-4(5*H*)one [5,5-bis(hydroxymethyl)pseudothiohydantoin] with aromatic aldehydes in concentrated sulfuric acid or boron trifluoride etherate afforded the corresponding cyclic acetals of spirane structure, (1,3-dioxane)-5-spiro-5'-(1,3-thiazolidine) derivatives. It was interesting to find out how the aza-analog of 2-amino-5,5-bis(hydroxymethyl)-4-tiazolinone, 2-amino-5,5-bis(hydroxymethyl)-1-methyl-1,5-dihydro-4*H*-imidazol-4-one [5,5-bis(hydroxymethyl)creatinine] **I** would behave in such reactions [2].

Unlike 2-amino-5,5-bis(hydroxymethyl)-4-tiazolinone, compound **I** does not react with either *p*-dimethylamino- or *p*-nitrobenzaldehyde in sulfuric acid, but the reaction with benzaldehyde, *p*-nitro-, and *p*-chlorobenzaldehyde in the boron trifluoride etherate medium as described in [1] results in spirane products **IIa–IIc** as hydrotetrafluoroborates in the first two cases, and as the free base in the latter case. The formation of salts **IIa**·HBF_4 and **IIb**·HBF_4 may be due to the presence of moisture in the reaction mixture from the source compound **I** dihydrate and, as a consequence, by the partial hydrolysis of BF_3. We failed to obtain the cyclic acetals with *p*-methoxy- and *p*-dimethylaminobenzaldehyde under these conditions, although in the case of the latter aldehyde in the spectrum of the precipitate isolated from the reaction mixture the signals corresponding to the spirane were found.



R = C_6H_5 (**a**), *p*-$NO_2C_6H_4$ (**b**), *p*-ClC_6H_4 (**c**).

We failed to isolate the free base by neutralizing salts **IIa**·HBF_4 and **IIb**·HBF_4 with sodium carbonate. Probably the imidazolidine ring opening occurs as a result of the neutralization corresponding to the well-known creatinine → creatine transformation in alkaline medium [3]. The separation of the water-soluble derivatives of creatine from inorganic salts failed.

The structure of compounds **IIa**·HBF_4, **IIb**·HBF_4 and **IIc** was confirmed by the ^{1}H NMR spectra. Note that integral intensity of the NH group protons in the ^{1}H NMR spectra was less than expected by unknown reasons. The coincidence with the calculated values in the mass spectra of the molecular weights, as well as the characteristic isotope distributions of the molecular

ions confirms elemental composition of the compounds obtained.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker AM-400 (400 MHz) instrument in DMSO-d_6. The IR spectra were registered on a Shimadzu FTIR-8400S spectrophotometer from KBr pellets. The elemental analysis was performed on a Leco CHNS (O) 942 analyzer. TLC was carried out on Silufol UV-254 plates, eluent alcohol–chloroform, 1:4 (**I**, **IIa**·HBF_4 and **IIb**·HBF_4), 1:7 (**IIc**). The mass spectra were recorded on a Bruker micrOTOF 10,223 mass spectrometer by ESI (ElectroSpray Ionization) method in acetonitrile (cation and anion of **IIa**, anion of **IIc**), acetonitrile–formic acid (cation and anion of **IIa**), methanol (cation and anion of **IIb**), and methanol–formic acid (cation of **IIc**).

2-Amino-1-methyl-8-phenyl-7,9-dioxa-1,3-diazaspiro[4.5]decan-4-one hydrotetrafluoroborate (IIa·HBF_4). A mixture of 0.50 g (2.39 mmol) of 5,5-bis-hydroxymethylcreatinine dihydrate **I** and 0.47 g (0.45 ml, 4.43 mmol) of benzaldehyde in 2.5 ml of the freshly distilled boron trifluoride etherate was stirred at room temperature for 2 h. The complete dissolution was not observed. After storing the suspension for 3 days a precipitate formed. The reaction mixture was stirred again at room temperature. After 1.5 h 2.0 ml of diethyl ether was added. The mixture was stirred for 5 h and then left to stand overnight. On the next day the resulting precipitate was filtered off, washed with diethyl ether, and dried in a vacuum desiccator for 5 h. Yield 0.59 g (70.7%). Recrystallization from ethanol (2.3 ml of ethanol per 0.1 g) and drying in a vacuum desiccator for 5 h yielded 40–50% of the target product. Mp 217–219°C. IR spectrum (KBr), ν, cm^{-1}: 3404 (NH), 3361 (NH), 3297 (NH), 3217 (NH), 1776 (C=O), 1705 (C=N). ^{1}H NMR spectrum (400 MHz), δ, ppm (*J*, Hz): 8.97 br.s (2H, NH), 7.40 m (5H, C_6H_5), 5.77 s (1H, C^8H), 4.53 d (2H, C^6H_A, $C^{10}H_A$, J_{AB}^{gem} 11.8), 4.27 d (2H, C^6H_B, $C^{10}H_B$, J_{AB}^{gem} 11.8), 3.42 s (3H, NCH_3). Mass spectrum, *m*/*z*: 262.1191 $[C_{13}H_{15}N_3O_3 + H]^+$ (calculated 260.1041), 260.1036 $[C_{13}H_{15}N_3O_3 - H]^-$ (calculated 262.1186), 87.0030 $[BF_4]^-$ (calculated 87.0035). Found, %: C 45.05; H 4.75; N 12.00. $C_{13}H_{16}BF_4N_3O_3$. Calculated, %: C 44.73; H 4.62; N 12.04.

2-Imino-1-methyl-8-(4-nitrophenyl)-7,9-dioxa-1,3-diazaspiro[4.5]decan-4-one hydrotetrafluoroborate (IIb·HBF_4). A mixture of 2.00 g (11.54 mmol) of 5,5-bis-hydroxymethylcreatinine dihydrate **I** and 1.81 g (11.98 mmol) of *p*-nitrobenzaldehyde in 20 ml of the freshly distilled boron trifluoride etherate was stirred for 0.5 h at room temperature and then for 3 h at 50–60°C. The complete dissolution was not observed, the finely dispersed precipitate subsequently formed. To the reaction mixture cooled to room temperature was added 6.0 ml of diethyl ether. The mixture was stirred for 2 h, the precipitate was filtered off, washed with diethyl ether, and dried in a vacuum desiccator for 4 h. Yield of the crude product was 2.86 g (62.9%). Recrystallization from ethanol (4–5 ml of ethanol per 0.1 g of the substance) and drying in a vacuum desiccator for 4 h gave 6–10% yield, mp 212–215°C. IR spectrum (KBr), ν, cm^{-1}: 3436 (NH), 3346 (NH), 3296 (NH), 3232 (NH), 3122 (NH),1780.2 (C=O), 1713 (C=N). ^{1}H NMR spectrum (400 MHz), δ, ppm (*J*, Hz): 9.06 br.s (2H, NH), 8.25 d ($2H_{Ar}$, *J* 7.9), 7.73 d ($2H_{Ar}$, *J* 7.9), 5.97 s (1H, C^8H), 4.60 d (2H, C^6H_A, $C^{10}H_A$, J_{AB}^{gem} 11.8), 4.32 d (2H, C^6H_B, $C^{10}H_B$, J_{AB}^{gem} 11.8), 3.38 s (3H, NCH_3). Found, %: C 39.66; H 4.09; N 14.34. $C_{13}H_{15}BF_4N_4O_5$. Calculated, %: C 39.62; H 3.84; N 14.22. Mass spectrum, *m*/*z*: 307.1019 $[C_{13}H_{14}N_4O_5 + H]^+$ (calculated 307.1037), 305.0918 $[C_{13}H_{14}N_4O_5 - H]^-$ (calculated 305.0891), 87.0064 $[BF_4]^-$ (calculated 87.0035).

2-Imino-1-methyl-8-(4-chlorophenyl)-7,9-dioxa-1,3-diazaspiro[4.5]decan-4-one (IIc). To a stirred suspension of 1.03 g (4.92 mmol) of 5,5-bis-hydroxymethylcreatinine dihydrate **I** and 6 ml of the freshly distilled boron trifluoride etherate was added 0.71 g (5.04 mmol) of *p*-chlorobenzaldehyde. The reaction mixture was stirred at room temperature for 10 min and then at 50–60°C for 2 h. Yellow finely dispersed precipitate was formed. The suspension was kept overnight, thereafter the pale yellow mass was stirred with 6.0 ml of diethyl ether at room temperature for 2 h. The precipitate was filtered off, washed with diethyl ether, and dried in a vacuum desiccator for 5 h. Yield of the crude product was 1.20 g (63.6%). Recrystallization from ethanol (4–5 ml of ethanol per 0.1 g) and drying in a vacuum desiccator for 4 h gave 4–8% yield, mp 275–277°C. IR spectrum (KBr), ν, cm^{-1}: 3332 (NH), 1709 (C=O), 1661 (C=N). ^{1}H NMR

spectrum (400 MHz), δ, ppm (*J*, Hz): 7.92 br.s (1H, NH), 7.46 d ($2H_{Ar}$, *J* 8.9), 7.41 d ($2H_{Ar}$, *J* 8.9), 5.72 s (1H, C^8H), 4.21 d (2H, C^6H_A, $C^{10}H_A$, J_{AB}^{gem} 11.8), 4.12 d (2H, C^6H_B, $C^{10}H_B$, J_{AB}^{gem} 11.8), 3.30 s (3H, NCH_3). Found, %: C 52.08; H 4.77; N 13.83. $C_{13}H_{14}ClN_3O_3$. Calculated, %: C 52.80; H 4.77; N 14.21. Mass spectrum, *m*/*z*: 296.0780 $[C_{13}H_{14}ClN_3O_3 + H]^+$ (calculated 296.0796), 294.0769 $[C_{13}H_{14}ClN_3O_3 - H]^-$ (calculated 294.0651).

REFERENCES

1. Ramsh, S.M., Ivanenko, A.G., Shpilevyi, V.A., Medvedskii, N.L., and Kushakova, P.M., *Khim. Geterotsikl. Soedin.,* 2004, no. 7, p. 1068.
2. Ramsh, S.M., Zheltonog, N.G., Khrabrova, E.S., and Golovanova, E.A., *Khim. Geterotsikl. Soedin.,* 1991, no. 6, p. 767.
3. Lempert, C., *Chem. Revs*., 1959, vol. 59, no. 4, p. 667.