Brief Communications

Synthesis of (difluoroamino)tetrazoles and [(difluoroamino)alkyl]tetrazoles

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(Difluoroamino)tetrazoles were obtained by direct fluorination of 5-aminotetrazoles with gaseous fluorine. Reactions of 2-(oxoalkyl)- and 2-(hydroxyalkyl)tetrazoles with difluoroamine yielded [(difluoroamino)alkyl]tetrazoles.

Key words: fluorine, difluoroamine, (difluoroamino)tetrazoles.

The synthesis of difluoroamino compounds with the use of various difluoroaminating reagents has been extensively studied.[1] However, most of the relevant papers are devoted to the preparation of aliphatic and alicyclic difluoroamino derivatives. For heteroaromatic compounds, there are few examples of such reactions. Among them, the synthesis of 2,4,6-tris(difluoroamino)triazine,[2] 6-(difluoroamino)pyrimidines,[3] and 5-(difluoroamino)-dinitromethyltetrazole derivatives,[4] as well as the fluorination of aminofurazans into the corresponding (difluoroamino)furazans are worth mentioning.[5]

In continuation of these investigations, we studied some methods for the synthesis of (difluoroamino)-tetrazoles containing an NF_2 group directly bound to the heterocycle and those for the preparation of alkyltetrazole derivatives with a difluoroamino group in the aliphatic radical.

In the former case, the fluorination of an amino group in the series of *N*-alkyl-5-aminotetrazoles (**1a—d**) was studied. 1-Methyl- (**1a**) and 2-methyl-5-aminotetrazoles (**1b**) were isolated in the individual form to compare their behavior during fluorination. 1,2-Bis-(5-aminotetrazolyl)ethane (**1c**) and 1,3-bis(5-aminotetrazolyl)-2-hydroxypropane (**1d**) were fluorinated as mixtures of isomers with an alkylene fragment bridging the tetrazole rings in positions 1 and 2 (three isomers in which the bridge connects positions 1 and 1′; 1 and 2′; and 2 and 2′; their ratio was not determined). To carry out the reaction, gaseous fluorine diluted with helium to 30 vol % was passed at a decreased temperature through a solution of tetrazole in acetonitrile in the presence of NaF.

It was found that, under these conditions, the fluorination of the amino group of compounds **1a—c** occurs selectively to give the corresponding 5-(difluoroamino) derivatives **2a—c** (Scheme 1).

In the case of **1d**, the expected difluoroamino derivatives were not isolated, probably, because of the instability of the hydroxy group under these conditions (this group is known to be oxidizable when exposed to fluorine).[6]

Thus, like the furazan ring,[5] the tetrazole ring proved to be rather fluorine-resistant. As can be judged from the yields of difluoroamino derivatives **2a,b**, 1- and

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[†] Deceased

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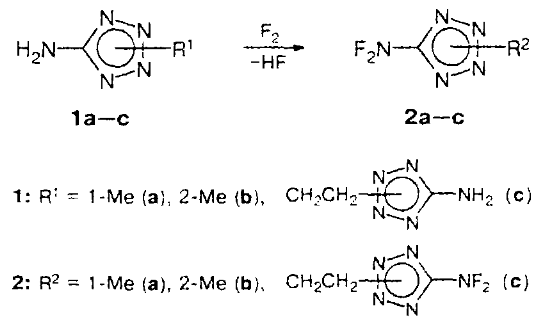
Scheme 1

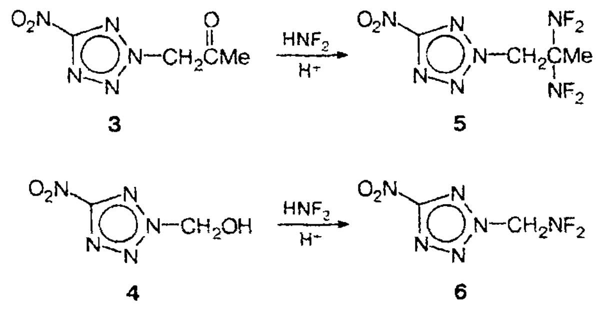


2-alkyl-5-aminotetrazoles show similar behavior in the fluorination.

5-(Difluoroamino)tetrazoles are quite stable under normal conditions. However, the partial decomposition observed in the distillation of compounds **2a,b** suggests their relatively low thermal stability. Isomers **2a,b** have close physicochemical characteristics (b.p., n_D^{20}, and d_4^{20}). In the ^{19}F NMR spectrum of **2a**, the signal from the NF_2 group is slightly shifted downfield.

To study whether a difluoroamino group can be introduced into the alkyl radical of substituted tetrazoles, we carried out reactions of 2-(2-oxopropyl)- (**3**) and 2-hydroxymethyl-5-nitrotetrazoles (**4**) with difluoroamine. Such transformations require a strong protonating catalyst, and 15—20% oleum was used for this purpose. Under these conditions, the carbonyl group of compound **3** is rather smoothly transformed into a bis(difluoroamino)methylene group, while the CH_2OH group of compound **4** is transformed into a (difluoroamino)methyl group (Scheme 2). At the same time, the yield of the target 2-[2,2-bis(difluoroamino)propyl]-5-nitrotetrazole (**5**) from ketone **3** is >90%, whereas 2-[(difluoroamino)methyl]-5-nitrotetrazole (**6**) is formed from alcohol **4** in much lower yields. Thus, the difluoroamination of alcohol **4** is less efficient than that of ketone **3**, which is consistent with the literature data.[1] The prior acylation of compound **4** with acetyl chloride insignificantly increased the yield of product **6**.

Scheme 2



Experimental

^{1}H and ^{19}F NMR spectra were recorded on a Hitachi Perkin—Elmer R-20 spectrometer (60.0 and 56.45 MHz, respectively). The ^{1}H chemical shifts are given with respect to hexamethyldisiloxane (internal standard); the ^{19}F chemical shifts are referenced to trifluoroacetic acid (external standard). The purity of the products was checked by TLC on Silufol UV-254 plates. The starting compounds **1a,b** were prepared according to the known procedures;[7,8] bis(tetrazolyl)alkanes **1c,d** were obtained by the general procedure for the alkylation of aminotetrazole with alkyl halides[9]. Compounds **3** and **4** were synthesized from 5-nitrotetrazole.[10—12]

Caution! Manipulations involving difluoroamino derivatives, especially difluoroamine, can result in an explosion.

5-(Difluoroamino)-1-methyltetrazole (2a). A mixture of fluorine (30 vol %) and helium (70 vol %) was bubbled at a rate of 2 L h^{-1} with stirring through a solution of aminotetrazole **1a** (3.5 g, 0.035 mol) and NaF (4.0 g, 0.095 mol) in 30 mL of MeCN at −10 °C for 4 h. Then, the reaction vessel was purged with nitrogen, the precipitate was separated, and the filtrate was treated with water (400 mL). The organic layer was separated, and the aqueous layer was extracted with ether (100 mL). The combined extracts were washed with water (4×150 mL), dried over $MgSO_4$, and concentrated *in vacuo*, and the residue was fractionated to give product **2a** (1.7 g, 37%), b.p. 68—70 °C (6 Torr), n_D^{20} 1.4205, d_4^{20} 1.382. Found (%): C, 16.19; H, 2.03; F, 27.45; N, 52.02. $C_2H_3F_2N_5$. Calculated (%): C, 17.78; H, 2.22; F, 28.15; N, 51.85. ^{19}F NMR, δ: −137.7 (s, NF_2). ^{1}H NMR, δ: 3.60 (s, CH_3).

5-Difluoroamino-2-methyltetrazole (2b). Under the above conditions, aminotetrazole **1b** (3 g, 0.03 mol) in the presence of NaF (6 g, 0.142 mol) was fluorinated in a mixture of Freon-113 (25 mL) and MeCN (60 mL) to give product **2b** (0.93 g, 23.7%), b.p. 61 °C (15 Torr), n_D^{20} 1.4210, d_4^{20} 1.380. Found (%): C, 18.38; H, 1.96; F, 27.17; N, 50.93. $C_2H_3F_2N_5$. Calculated (%): C, 17.78; H, 2.22; F, 28.15; N, 50.85. ^{19}F NMR, δ: −140.4 (s, NF_2). ^{1}H NMR, δ: 3.80 (s, CH_3).

A mixture of isomeric bis[5-(difluoroamino)tetrazolyl]ethanes (2c). A mixture of aminotetrazoles **1c** (5 g, 0.026 mol) in the presence of NaF (10 g, 0.238 mol) in 50 mL of MeCN was fluorinated as described for tetrazole **1a**. Product **2c** (2.26 g, 29%) is a mixture of three isomers (their ratio was not determined), m.p. 37—38 °C (from heptane). Found (%): C, 17.12; H, 1.45; F, 26.19; N, 51.95. $C_4H_4F_4N_{10}$. Calculated (%): C, 17.92; H, 1.50; F, 28.36; N, 52.24. ^{19}F NMR, δ: −138.1 (br.s, NF_2). ^{1}H NMR, δ: 4.1 (s, 2 CH_2).

2-[2,2-Bis(difluoroamino)propyl]-5-nitrotetrazole (5). To a solution of compound **3** (1.0 g, 6 mmol) in 15 mL of dry CH_2Cl_2 20% oleum (4 mL) was added. Difluoroamine (2 mL, 56 mmol) obtained from triphenyl(difluoroamino)methane (30 g)[1] was condensed in the reaction vessel through a bubbling tube with stirring at 0—5 °C. The reaction mixture was stirred at 0 °C for 2 h until the difluoroamine ceased to condense in the reflux condenser, then at −20 °C for 3 h, and poured onto crushed ice with water. Products were extracted with CH_2Cl_2 (2×15 mL). The organic layer was separated, dried with $MgSO_4$, and concentrated to give tetrazole **5** (1.4 g, 91.6%), m.p. 94 °C (from aqueous ethanol), R_f 0.48 ($CHCl_3$ as an eluent). Found (%): C, 18.36; H, 2.40; F, 28.69; N, 37.73. $C_4H_5F_4N_7O_2$. Calculated (%): C, 18.54; H, 1.94; F, 29.33; N, 37.84. ^{19}F NMR, δ: −108.1 (s, NF_2). ^{1}H NMR, δ: 1.82 (s, CH_3); 5.57 (s, CH_2).

2-[(Difluoroamino)methyl]-5-nitrotetrazole (6). Under similar conditions, product **6** (1.2 g, 22%) was obtained from compound **4** (4.4 g, 0.03 mol) as a difficultly crystallizable solid; R_f 0.42, CH_2Cl_2 as an eluent. Found (%): C, 12.52; H, 0.97; F, 22.58; N, 47.82. $C_2H_2F_2N_6O_2$. Calculated (%): C, 13.34; H, 1.12; F, 21.10; N, 46.67. ^{19}F NMR, δ: −110.0 (br.s, NF_2). ^1H NMR, δ: 2.32 (t, CH_2, J_{H-F} = 2.5 Hz).

Recrystallization of the product from an aqueous—ethanol solution gave monosolvate **6** (with one molecule of ethanol), m.p. 91—92 °C. Found (%): C, 21.86; H, 3.64; F, 16.56; N, 37.08. $C_2H_2F_2N_6O_2 \cdot C_2H_6O$. Calculated (%): C, 21.24; H, 3.57; F, 16.80; N, 37.16.

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