

RECYCLIZATION REACTIONS

OF HETEROCYCLES.

XIX.* REACTION OF 2,5-DIMETHYL-1,3,4-OXA-
AND - 1,3,4-THIADIAZOLES WITH HYDRAZINES

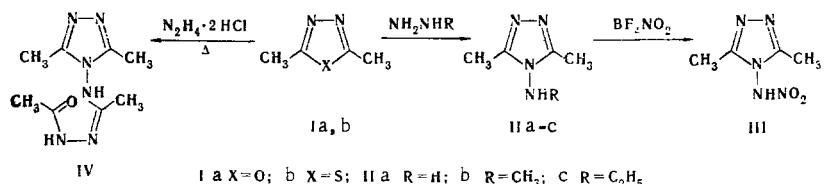
O. P. Shvaika, N. I. Korotkikh,
G. F. Tereshchenko, and N. A. Kovach

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2,5-Dimethyl-1,3,4-oxa- and - 1,3,4-thiadiazoles are recyclized to 2,5-dimethyl-4-amino-1,2,4-triazole on reaction with hydrazine. Recyclization occurs with greater difficulty and only with oxadiazole in the case of alkylhydrazines. Nitration of 2,5-dimethyl-4-amino-1,2,4-triazole gives its N-nitroamino derivative.

2,5-Di(perfluoroalkyl)-1,3,4-oxadiazoles react with hydrazine [2] and 2-aryl- and 2-aryl-5-alkyl-1,3,4-oxadiazoles react with benzoylhydrazine (on heating) [3] to give hydrazidines, which can be converted in acidic media to N-amino-sym-triazoles.

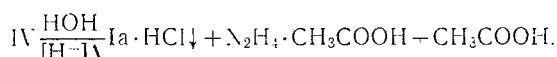
We have shown that 2,5-dimethyl-1,3,4-oxa- and - 1,3,4-thiadiazoles I are recyclized directly to N-amino-triazole IIa under the influence of hydrazine or hydrazine hydrate; the intermediates cannot be isolated.



It should be noted that oxadiazole Ia undergoes recyclization considerably more rapidly than thiadiazole Ib.

The reaction of nitronium tetrafluoroborate with N-aminotriazole IIa gave its N-nitroamino derivative (III).

Compound IV is formed with oxadiazole Ia is heated with hydrazine hydrochloride. Like the IR spectra of I, the IR spectrum of IV contains a band at 193 nm. The frequencies of the aminotriazole system that are peculiar to other triazoles I (also see [4]) and the amide bands that characterize the side chain of the molecule are observed in the IR spectrum (see the experimental section). Compound IV is hydrolyzed to fragments that confirm the structure assigned to it when it is refluxed in hydrochloric acid:



The recyclization of oxadiazole Ia with alkylhydrazines proceeds with appreciably greater difficulty to give N-alkylamino-sym-triazoles IIb, c, whereas thiadiazole Ib does not undergo recyclization. 2,5-Diphenyl-1,3,4-oxadiazole is not recyclized under the influence of hydrazine and alkylhydrazines (at least when the mixture is heated for 1 h).

* See [1] for communication XVIII.

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For comparison, we note that the reaction of 1,3,4-oxadiazolium salts is more complex [5], and 1,3,4-thiadiazolium salts are recyclized to dihydro-sym-tetrazines [6].

EXPERIMENTAL

The molecular weight was determined by the Zinger-Clark method [7]. Thin-layer chromatography (TLC) was carried out under standard conditions [8] on activity IV (Brockmann classification) aluminum oxide with elution by methanol-chloroform (1:4) and development by iodine vapors. The UV spectra of aqueous solutions (10^{-4} M) of the compounds were recorded with a Specord spectrophotometer. The IR spectra of KBr pellets were recorded with a UR-20 spectrometer.

3,5-Dimethyl-4-amino-1,2,4-triazole (IIa). A) A 0.32-ml (10 mmole) sample of hydrazine was added to 0.98 g (10 mmole) of 2,5-dimethyl-1,3,4-oxadiazole Ia, and the mixture was allowed to stand for 0.5 h. It was then filtered to give 1.01 g (90%) of white crystals with mp 196-198° (from alcohol-dioxane; mp 198° [9, 10]).

B) A mixture of 1.14 g (10 mmole) of 2,5-dimethyl-1,3,4-thiadiazole Ib and 0.32 g (10 mmole) of hydrazine was heated at 110° for 1.5 h until hydrogen sulfide evolution ceased. The solidified mass was treated with diethyl ether, the mixture was filtered, and the solid material was vacuum dried at 60-70° to give 0.7 g of product. Another 0.1 g of the same compound and 0.2 g of starting thiadiazole Ib were isolated from the filtrate. The overall yield of 4-aminotriazole IIa, with mp 197-198° [alcohol-dioxane (1:5)], was 0.8 g (71%).

No melting-point depression was observed for a mixture of samples of 4-aminotriazole IIa obtained by methods A and B with a sample synthesized by the method in [9, 10]. The product had R_f 0.84. UV spectrum: λ_{max} 192 nm (ϵ $5.9 \cdot 10^3$). IR spectrum, cm^{-1} : ν_{NH} 3260 s, 3160 s; ν_{CH_3} 3050 m, 2940 m; $\nu_{\text{C}=\text{N}}$ 1670 m; δ_{NH_2} 1545 m, 1260 m; δ_{CH_3} 1430 s, 1400 m, 1360 w; aminotriazole system: 1100 s, 1050 w, 1000 s, and 990 m. The hydrochloride of IIa had mp 232° (from alcohol; 232° [9, 10]).

3,5-Dimethyl-4-methylamino-1,2,4-triazole (IIb, R = CH_3). A solution of 1.96 g (20 mmole) of oxadiazole Ia and 0.92 g (20 mmole) of methylhydrazine was refluxed for 3 h, after which the unchanged components were removed by distillation, and the residue was vacuum distilled. The resulting viscous yellow liquid crystallized when it was cooled, and the crystals were squeezed dry on the filter to give 0.25 g (9%) of a product with mp 107-110° (after sublimation). Found: N 44.5%. $\text{C}_5\text{H}_{10}\text{N}_4$. Calculated: N 44.4%.

3,5-Dimethyl-4-ethylamino-1,2,4-triazole (IIc, R = C_2H_5). This compound was obtained by the method in the preceding experiment from 0.98 g (10 mmole) of oxadiazole Ia and 0.6 g (10 mmole) of ethylhydrazine after refluxing for 5 h. The yield of product with mp 134-135° (after sublimation) and R_f 0.86, was 0.15 g (11%). UV spectrum: λ_{max} 192 nm (ϵ $5.9 \cdot 10^3$). IR spectrum, cm^{-1} : ν_{NH} 3190 m, 3050 s; ν_{CH_3} 2700-2900 br; $\nu_{\text{C}=\text{N}}$ 1610 m; δ_{NH} 1530 m, 1300 m; δ_{Alk} 1450 m, 1420 m, 1390 m, and 1370 w; N-aminotriazole system: 1070 s, 1110 w, and 990 w. Found: N 39.8%. $\text{C}_6\text{H}_{12}\text{N}_4$. Calculated: N 40.0%.

Triazoles IIb, c were obtained as colorless crystals that were soluble in water, alcohols, and hot benzene but insoluble in hexane.

3,5-Dimethyl-4-nitroamino-1,2,4-triazole (III). A 3.07-g (23.1 mmole) sample of nitronium tetrafluoroborate was dissolved in anhydrous acetonitrile at 0.10°, after which 2.27 g (23.1 mmole) of anhydrous potassium acetate was added, and 2.07 g (18.5 mmole) of aminotriazole IIa was added gradually at 0-5°. The mixture was then allowed to stand at 0-5° for 1.5 h, after which the solvent was removed by vacuum distillation at room temperature. A small amount of alcohol was added to the residue, and the mixture was worked up to give 2 g (69%) of a white crystalline substance with mp 185° (dec., from alcohol). Found: C 30.8; H 4.3; N 44.3%. $\text{C}_4\text{H}_7\text{N}_4\text{O}_2$. Calculated: C 30.6; H 4.5; N 44.6%.

1-(3,5-Dimethyl-1,2,4-triazol-4-yl)-2-methyl-1,3,4-triazahex-2-en-5-one (IV). A mixture of 3 g (30.6 mmole) of oxadiazole Ia and 0.69 g (6.7 mmole) of hydrazine hydrochloride was refluxed for 30 min, after which it was cooled, and the vitreous mass was dissolved in alcohol. The alcohol solution was treated with sodium bicarbonate and filtered, the alcohol was removed from the filtrate by distillation, and the residue was dissolved in n-butanol and precipitated by the addition of ether to give 0.8 g (30%) of a product with mp 162-163° (from n-butanol) and R_f 0.71. UV spectrum: λ_{max} 193 nm (ϵ $1.15 \cdot 10^4$). IR spectrum, cm^{-1} : ν_{NHass} 3100 s; ν_{CH_3} 2750-2900 s; amide I 1710 s; $\nu_{\text{C}=\text{N}}$ 1670 m; 1640 m; amide II and δ_{NH} 1560 s, 1540 s, and 1530 s; δ_{CH_3} 1450 s, 1430 s 1300 m, and 1370 s; amide III 1290 s, 1260 s; N-aminotriazole system: 1110 w, 1070 m, 1050 m, 1030 m, 1010 s, and 990 m. Found: C 45.6; H 6.7; N 40.1%; M 225. $\text{C}_8\text{H}_{16}\text{N}_6\text{O}_2$. Calculated: C 45.7; H 6.7; N 40.0%; M 210.

Hydrolysis of IV. A 0.17-ml (1.48 mmole) sample of concentrated HCl was added to 0.3 g (1.43 mmole) of triazole IV, and the mixture was heated. The resulting solution was refluxed for 30 min, cooled, and filtered

to give white acicular crystals. The crystals were dried to give 0.14 g (66%) of a product with mp 230-232° that was identical to the above-obtained sample of IIa · HCl with respect to its investigated properties. The strong odor of acetic acid was observed when the mother liquor was acidified. Benzalazine, with mp 92°, precipitated when benzaldehyde was added to the mother liquor; no melting-point depression was observed for a mixture of this product with an authentic sample.

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