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ONCE AGAIN THE QUESTION OF CYCLIZATION OF PYRAZOLONES-5 UNSUBSTITUTED AT THE NITROGEN INTO TRIPYRAZOLYLENES

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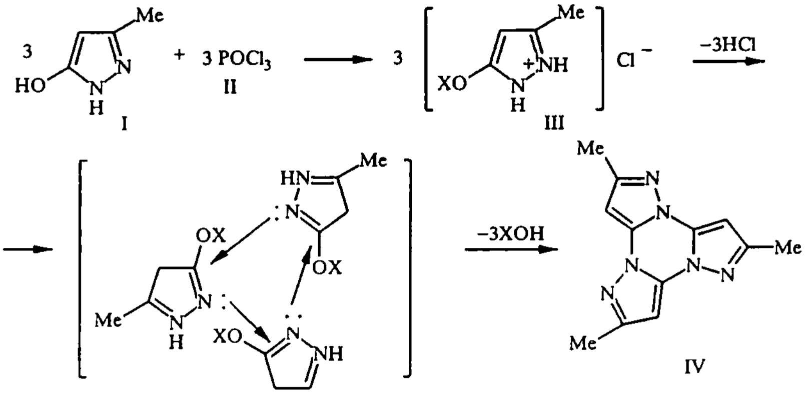
The experimental data were refined and the yields were improved significantly in cyclization of pyrazolones-5 into tripyrazolylenes-1,5 with phosphorus oxychloride.

In 1994, we published an article on cyclization of pyrazolones-5 unsubstituted at the nitrogen atom of the nucleus into tripyrazolylenes-1,5 [1], but we later found a brief communication from Swedish chemists [2] in which this cyclization was described in 1967 on the example of 3-methylpyrazolone-5 with a yield of 67%, while we were able to obtain a yield of only 29%. In further attempts to obtain 3-methyl(tripyrazolylene-1,5), we naturally attempted to use the method proposed in [2]. However, all attempts led to a zero yield. We then conducted a more detailed study of the cyclization process (see also [1]).



When pyrazolone is mixed with phosphorus oxychloride, an exothermic reaction takes place with liberation of HCl and formation of compound III. When 0.5 mole of compound I is mixed with 0.55 mole of reagent II, the temperature increases to ~70°C, then begins to fall. On heating again in an open vessel with evaporation of the excess oxychloride II, the temperature slowly increases to 175°C (HCl continues to evolve intensively), and an exothermic reaction begins with rapid elevation of the temperature of the mixture to 210°C. For a higher yield, the mixture was held at 190°C for another 3 h. If a second exothermic reaction (probably conversion of III into IV) does not begin, the yield of tripyrazolylene IV is equal to zero. Heating of a mixture of compound I and an excess of reagent II in xylene in a reflux condenser for 12 h and then heating of the residue (after vacuum distillation of the solvents) with repeated addition of oxychloride II. However, in this case, the mixture is certainly heated below 130°C and it is not understood how the second stage of the process can take place. It is hypothesized that in vacuum distillation of the solvents after the first stage, the mixture was heated above 170°C, but this in no way follows from the reported experiment. By slightly altering separation of the tripyrazolylenes, we were able to markedly increase their yields (see Experimental section) in comparison to what was reported in [1].

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With initial components of less than 0.1 mole, the jump in the temperature in the exothermic stage at 175°C is not always marked, but heating to 190°C is necessary to obtain tripyrazolylenes. We previously [3] described synthesis of 3,4-trimethylenepyrazolone-5 in standard conditions in boiling 2-carboethoxycyclopentanone with hydrazine hydrate in alcohol with acetic acid with a high yield. However, in attempts to reproduce this synthesis, we obtained very low yields of pyrazolone (< 10%). The same result was obtained in the reaction without addition of acetic acid in boiling in alcohol. After repeated attempts to change the conditions, we were able to obtain stable yields of pyrazolone (up to 80%) in mixing equimolar quantities of 2-carboethoxycyclopentanone and 85% hydrazine hydrate with subsequent heating to 160°C in the mixture with evaporation of water and alcohol in an open vessel.

EXPERIMENTAL

Tri[3-methylpyrazolylene-1,5]. In a 250-ml round-bottomed flask placed in a metal bath, 0.5 mole (49 g) of 3-methylpyrazolone-5 was scattered, 0.1 ml of water was added, and 0.55 mole (52 ml) of phosphorus oxychloride was poured in by parts over 8-10 min. Everything had to be done under a hood, since hydrogen chloride evolved very intensively. The temperature of the reaction mixture increased to ~70°C. The mixture was then slowly heated to 100°C for 1 h, intensive evolution of HCl continued, and a thick melt was formed. Some of the excess $POCl_3$ was distilled off. After the temperature in the reaction flask attained 130°C, the intensity of evolution of HCl decreased and the mixture began to turn violet. An exothermic reaction began at 175°C (at this time, the flask had to be taken out of the bath) and the temperature spontaneously increased rapidly to 210°C. At the same time, the mixture solidified and sublimation of tripyrazolylene and 3-methyl-5-chloropyrazole, always present as an impurity, began. The flask was again placed in the bath and held at 190°C for another 3 h. After cooling, 120 ml of water was added and boiled for 30 min. The mixture was then transferred to a 1-liter beaker, another 300 ml of water was added, it was neutralized with soda and boiled again in a vacuum cabinet with evaporation of the water and 3-methyl-5-chloropyrazole to a volume of ~250 ml. The mixture was cooled, the tripyrazolylene was filtered off, ground in a mortar, and washed with hot 5% solutions of caustic soda, sulfuric acid, and water. The crystals were carefully dried and boiled with 60 ml of hexane—benzene mixture 6:1 for 1 h with a reflux condenser. After cooling, the residue was filtered off, washed with hexane (30 ml), and dried, yielding 16 g (40%) of tripyrazolylene with mp = 199-202°C. The substance was pure enough for further studies. Published data: mp = 194-196°C, yield of 29% [1]; mp = 205-207°C [2].

Tri[3,4-dimethylpyrazolylene-1,5] was obtained similarly with a yield of 54%, mp = 212-214°C (from acetic acid). Published data: yield of 26%, mp = 210-212°C [1].

Tri[3,4-trimethylenepyrazolylene-1,5] was prepared similarly in heating for 2 h at 180°C with a yield of 69% (before sublimation). Mp = 335-337°C (purification by sublimation). Published data: yield of 30%, mp = 334-336°C [3].

3,4-Trimethylenepyrazolone-5. Here, 15.6 g (0.1 mole) of 2-carboethoxycyclopentanone was mixed with 6.3 g (0.105 mole) of 85% hydrazine hydrate in a 100-ml round-bottomed flask (the mixture was heated to ~50°C), and the flask was placed in a metal bath and slowly heated to 165°C. At 100°C, the water and alcohol began to boil energetically, and the mixture gradually solidified. The mixture was held at 165°C in the bath for 2 h, cooled, boiled with a reflux condenser with 20 ml of methanol for 1 h, cooled to 5-10°C, and the crystals of pyrazolone were filtered off, yielding 9.8 g (79%), mp = 267-268°C [3].

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