CHLORINATION OF 1,5-DIMETHYLPYRAZOLE

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UDC 547.772.1

The chlorination of 1,5-dimethylpyrazole by gaseous chlorine in acetic acid in the presence of sodium acetate affords 1-methyl-3,4-dichloro-5-(dichloromethyl)pyrazole, which is subsequently converted to the 5-(trichloromethyl) derivative.

Previously [1] we studied the chlorination of 1,5- and 1,3-dimethylpyrazoles I and II by gaseous chlorine in carbon tetrachloride [1]. Under these conditions, 1,3-dimethylpyrazole II is converted to 1,3-dimethyl-4-chloropyrazole (III), and 1-methyl-4-chloro-5-(dichloromethyl)pyrazole (IV) is obtained from compound I. Because of the formation of CCl_4-insoluble hydrochlorides of compounds III and IV, they do not undergo further chlorination. During binding of hydrogen chloride in the chlorination of compound II in acetic acid in the presence of sodium acetate, 1,3-dimethyl-4,4-dichloro-5-pyrazolone was obtained [2].

In the present paper, we studied the chlorination of compound I under analogous conditions. The reaction is characterized by low selectivity, as a result of which several compounds are formed. Because it is complicated to recover them in pure form, the reaction mixtures were analyzed with data of chromatography–mass spectrometry and PMR spectra (Table 1).

In the chlorination of compound I for 1 h at 100°C the main product was 1,5-dimethyl-4-chloropyrazole (V), together with which products of more intensive chlorination were formed. The product, containing two chlorine atoms in the molecule, was 1-methyl-4-chloro-5-(chloromethyl)pyrazole (VI), which was confirmed by the fact that the PMR spectrum of the mixture of the chlorination products contained the signal of the chloromethyl group at 4.55 ppm [3] and also by the fact that the mass spectrum of the chromatographic fraction containing this compound contained no peak of the ion with m/z $(M - 1)^+$, characteristic of the spectra of compounds I [4] and V, which favors the structure of compound VI and not of 1,5-dimethyl-3,4-dichloropyrazole, which has the same molecular weight.

Further chlorination of compound VI afforded 5-(dichloromethyl)pyrazole IV [1].

A compound with four chlorine atoms in the molecule accumulated in the reaction material with increasing chlorination time (Table 1). It was recovered in pure form by distillation after chlorination of compound I for 10 h. Combined analysis of the ^1H and ^{13}C NMR spectra of 1-methyl-4-chloro-5-(dichloromethyl)pyrazole and the obtained compound (Tables 1 and 2) made it possible to consider the latter to be 1-methyl-3,4-dichloro-5-(dichloromethyl)pyrazole (VII) and not 1-methyl-4-chloro-5-(trichloromethyl)pyrazole (VIII) having the same molecular weight and also identified among the chlorination products (Table 1). Thus, compound IV was chlorinated both at the dichloromethyl group and in the 3 position, with the latter occurring at a higher rate.

In the case of chlorination at 100°C for 8 h, we also observed in the reaction material a product of exhaustive chlorination of compound I, 1-methyl-3,4-dichloro-5-(trichloromethyl)-pyrazole (IX), the only signal in the PMR spectrum of which was somewhat shifted to a strong field with respect to the singlet of protons of the N-methyl group in the spectrum of compound IV (Table 1).

In the chlorination of dimethylpyrazole I at 100°C, a compound was also formed in whose mass spectrum the heaviest ion was an ion with m/z 246 containing one chlorine atom. This

D. I. Mendeleev Moscow Chemicotechnological Institute, Moscow 125820. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 352-354, March, 1990. Original article submitted July 11, 1988.

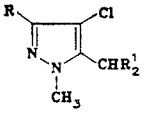
0009-3122/90/2603-0301 $12.50

TABLE 1. Chlorination of 1,5-Dimethylpyrazole

Product	Ratio*1 of chlorination products, %, after holding for			PMR spectrum, ppm (singlets)			$M^{+\cdot}$ (^{35}Cl) in mass spectrum
	1 h	2 h	8 h*2	1-CH_3	3-H	5-R	
V	78	48	—	3,65	7,23	2,13	130
VI	5	5	—	3,82	—*3	4,55	164
IV	12	18	—	4,08	7,32	7,02	198
VII	5	18	60	4,03	—	6,98	232
VIII	—	Traces	15	4,15	7,35	—	232
IX	—	—	25	4,12	—	—	266
X	Traces	11	Traces	3,90*4	7,27	7,70	246

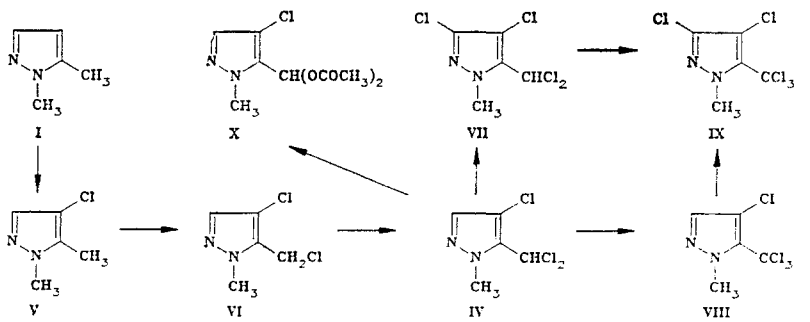
*1 Determined according to data of PMR spectra of corresponding mixtures.
*2 Composition of fraction after separation of precipitate of compound X.
*3 Signal overlaps in the spectrum of the mixture with the signal of the 3-H proton of compound V.
*4 Signals of protons of acetoxy group at 2.08 ppm.

TABLE 2. Carbon-13 NMR Spectra of Chlorination Products of 1,5-Dimethylpyrazole in DMSO-D_6



Compound	R	R'	Chemical shift, ppm						
			1-CH_3	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	CH	CH_3 (Ac)	CO (Ac)
IV	H	Cl	36,8	134,8	106,3	133,4	57,7	—	—
VII	Cl	Cl	37,1	135,0	104,6	133,4	57,1	—	—
X	H	OAc	38.5	136.5	109.5	132.5	81.0	20.0	168.5

compound was recovered in pure form and identified according to data of IR and ^1H and ^{13}C NMR spectra (Tables 1 and 2) as 1-methyl-5-[bis(acetoxy)methyl]-4-chloropyrazole (X), which was formed in the reaction of compound IV with sodium acetate.



Thus, the sharp difference in the reactivity of positions 3 and 5 during electrophilic halogenation [1] and of the methyl groups located at these positions during radical halogenation [5] is responsible for the low selectivity of chlorination of 1,5-dimethylpyrazole in contrast to its isomer II.

EXPERIMENTAL

The IR spectrum was recorded with a Specord M-80 spectrophotometer in carbon tetrachloride. The PMR spectra were measured with a Tesla BS-467 instrument (60 MHz), the ^{13}C

NMR spectra were measured with a Brucker CXP-100 instrument (100 MHz) in DMSO-D_6, and the internal standard was HMDS. Chromatography–mass spectrometry of the reaction mixtures was carried out with a Hewlett-Packard 5985 chromatograph–mass spectrometer with an ionization energy of 70 eV. The GLC conditions were a capillary column with ℓ = 25 m, the solid phase was a chemically bound silicone elastomer, the carrier gas was helium at 2 ml/min, and the injector temperature was 250°C.

The data of elemental analysis of compounds VII and X for C, H, and N correspond to the calculated data.

Chlorination of 1,5-Dimethylpyrazole I. A. A solution of 25 g (0.26 mole) of pyrazole I in 150 ml of acetic acid was heated to 100°C, 67 g of sodium acetate was added, and gaseous chlorine was passed through the solution (3-4 liters/h was consumed). Samples were withdrawn (with respect to 50 ml of the reaction solution) after 1, 2, and 8 h after the beginning of the reaction, acetic acid was driven off in vacuo, and the residue was dissolved in CCl_4 and analyzed by chromatography–mass spectrometry. From a sample obtained after holding for 8 h, crystals precipitated during standing (48 h), and they were separated from the liquid phase and recrystallized from CCl_4. We obtained 3.4 g (12%) of compound X ($C_9H_{11}ClN_2O_4$), mp 80-82°C. IR spectrum: 1690 cm^{-1} (C=O).

B. To a solution of 19.2 g (0.2 mole) of compound I in 100 ml of acetic acid was added 44 g of sodium acetate, and chlorine was passed for 10 h at 70°C, the precipitate was filtered, acetic acid was driven off from the filtrate, and the residue was distilled in vacuo (1 mm). The following fractions were obtained: 0.8 g (bp 45-50°C), 18.6 g (50-57°C), and 4.1 g (57-70°C). During prolonged standing (7 days), the second fraction partially crystallized. The crystals were separated from the liquid phase and recrystallized from hexane. We obtained 5.1 g (11%) of compound VII ($C_5H_4ClN_2$), mp 62-63°C.

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