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ISOMERIZATION OF 5,5-DIMETHYLPYRAZOLINES. PREPARATION AND PROPERTIES OF 5,5-DIMETHYL-Δ^1-PYRAZOLINE AND 3,4-DIMETHYL-Δ^2-PYRAZOLINE

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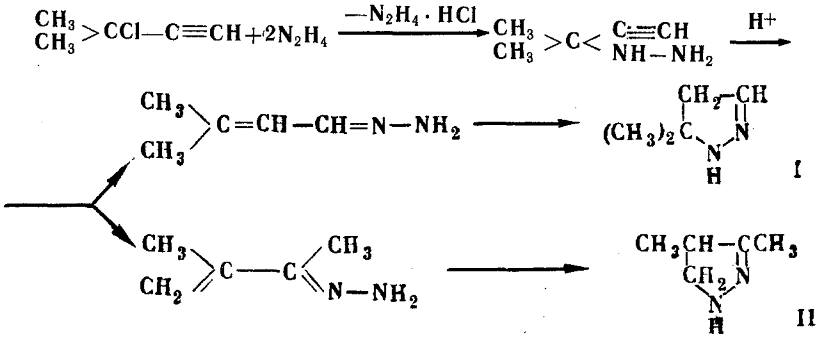
Slow distillation of 5, 5, -dimethyl-Δ^2-pyrazoline isomerizes it to 5, 5-dimethyl-Δ^1-pyrazoline, and heating the latter with hydrazine hydrochloride reconverts it to the Δ^2 isomer. This is the first experimental evidence that the Δ^2 double bond in a pyrazoline can move to the Δ^1 position, i.e., in a direction the reverse of that previously known. The 5, 5-dimethyl-Δ^1-pyrazoline described is the simplest Δ^1 pyrazoline hitherto isolated.

When characterizing 5, 5-dialkyl-Δ^2-pyrazolines prepared by condensing tertiary acetylenic chlorides with hydrazine, the present authors [1] stated that gas chromatography results indicate the presence of a small percent of impurity after storing for a short time. Since elementary analyses and molecular weights agree well with those of pyrazolines, the impurities were apparently isomers. Distillation of a product through a column at atmospheric pressure (and not under reduced pressure, as previously described) gave dimethylpyrazoline preparations of considerably lower refractive index and density than pure 5, 5-dimethyl-Δ^2-pyrazoline (I), and containing considerably more (up to 43%) of the more volatile component. Starting from the working hypothesis that acetylenic hydrazines are formed in the reaction under consideration, and that they undergo subsequent isomerization, the side product to be expected was 3, 4-dimethyl-Δ^2-pyrazoline. Actually the authors have observed [2] that when tertiary acetylenic chlorides react with hydrazines, rearrangements giving rise to unsaturated hydrazones can occur, similar to the rearrangements undergone by tertiary acetylenic alcohols to unsaturated carbonyl compounds (Meyer-Schuster and Rupe rearrangements). In the present case such rearrangements could lead to formation of mixtures of two isomeric Δ^2 pyrazolines



3, 4-Dimethylpyrazoline (II) is not described in the literature, and a reverse synthesis was effected from methyl isopropenyl ketone and hydrazine, to throw light on the question of its presence in the reaction products. However, it was found that II has not smaller values of the boiling point, density, and refractive index than I, but greater ones. The chromatograph peak corresponding to II (Fig. 1) comes after the peak of I, but where there were previously no peaks in the chromatograms of the reaction products. Hence there was no support for the assumption that the isomer formed at the same time as I is 3, 4-dimethyl-Δ^2-pyrazoline.

Comparison of IR spectra of 5, 5-dimethyl-Δ^2-pyrazoline and of a preparation enriched in the isomeric impurity (Fig. 2) showed that as the content of the more volatile component increases, the valence vibration bands of the groups C = N (1586 cm^{-1}), H–C = N (3045 cm^{-1}) [3], and H–N (3290 cm^{-1}), characteristic of Δ^2-pyrazolines, get weaker, and at the same time a second band (1552 cm^{-1}) appears in the region of characteristic frequencies of double bond valence vibrations*. Hence it follows that the impurity does not contain a NH group, and is not a Δ^2-pyrazoline, differing from the latter in the position of the double bond.

The PMR spectrum of the mixture of isomers (Fig. 3 and Table 1) differs from that of I in the intensities of its four signals [(H–C = N, H–N, H_2C[4], and (Me_2C)], and by the appearance of signals from three new varieties of protons, two triplets from adjacent CH_2 groups with mutual spin-spin interaction, and of an intense signal with a somewhat lower chemical shift than that of the gem-methylene groups of the Δ^2 isomer, obviously belonging to a Me_2C group adjacent

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*More precisely, is greatly intensified.

to the double bond. These PMR spectrum peculiarities indicate that the second component of the mixture is the hitherto unknown 5, 5-dimethyl-Δ^1-pyrazoline (III).

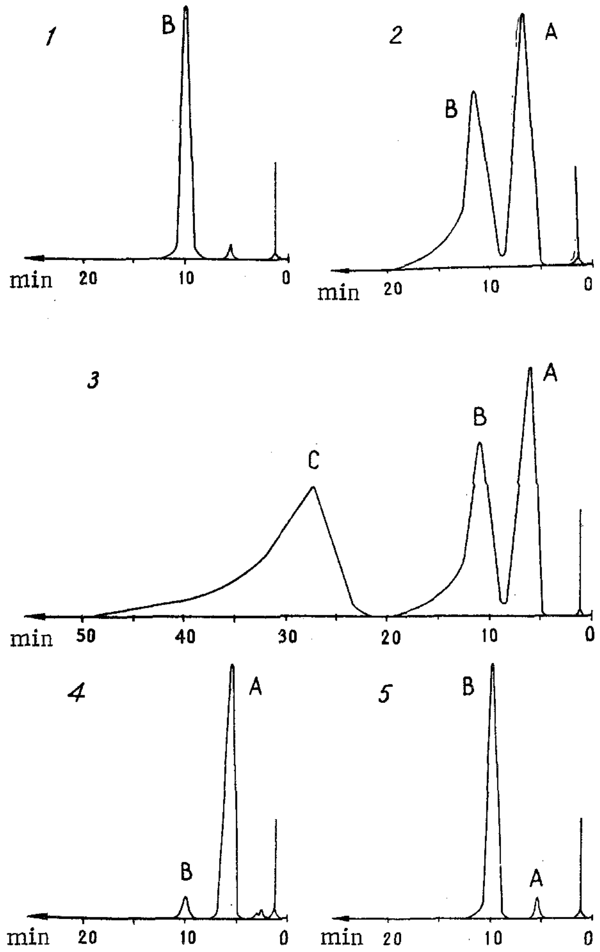

Fig. 1. Gas-liquid chromatograms of mixtures of isomeric pyrazolines: 1) 96.9% 5, 5-dimethyl-Δ^2-pyrazoline; 2) Dimethylpyrazoline preparation obtained by distilling at atmospheric pressure; 3) Mixture of the preceding preparation with 3, 4-dimethyl-Δ^2-pyrazoline; 4) 93.8% 5, 5-dimethyl-Δ^1-pyrazoline; 5) Δ^1-pyrazoline isomerization product. A, B, and C are respectively the peaks of 5, 5-dimethyl-Δ^1-pyrazoline, 5, 5-dimethyl-Δ^2-pyrazoline, and 3, 4-dimethyl-Δ^2-pyrazoline. Ukh-1 chromatograph, column (2-meter) with 25% tricyanoethoxypropane on Cellite 545, temperature 120°, carrier gas helium (70 ml/min)

By multiple repetition of the reaction between dimethylacetylenylchloromethane with hydrazine, it was found that product composition depends on the conditions under which the reaction products are distilled. Vacuum distillation gave preparations consisting of almost pure Δ^2-isomer bp 66.5-67.3° (40 mm), while distillation at atmospheric pressure gave preparations boiling at various temperatures between 137 and 145°, the amount of low boiling isomer being greater, the more slowly the distillation was carried out. The impression formed was that III was formed from I during actual distillation at an elevated temperature. Actually distillation of I in a more effective column (about 20 theoretical plates), at a rate of 2-3 ml/hr, and reflux ratio 60-100 gave 73% of the reaction product with a significantly greater refractive index (n_D^{20} 1.4376), and the GLC data showed that it contained only 12.5% I. Purification by distilling through a vacuum column gave a preparation containing 93.8% 5, 5-dimethyl-Δ^1-pyrazoline, a colorless liquid with a pyridinecamphor odor, which turned yellow in air, but which was stable when stored in a sealed tube. Like the Δ^2-isomer, it does not reduce Fehlings solution, but unlike the latter it does not react with phenyl isocyanate, and forms an adduct with CuCl. Comparison of the physical constants shows (Table 2) that the Δ^1-isomer is characterized by rather lower boiling point, density, refractive index, and dispersion that the Δ^2-isomer. The same relationship between the properties was found for the isomeric esters of Δ^1- and Δ^2-pyrazoline carboxylic acids [4].

The only Δ^1-pyrazoline without functional groups, known, is 3, 5-diphenyl-Δ^1-pyrazoline, synthesized only in 1962 [5]. Hitherto Δ^1-pyrazolines containing alkyl substituents have not been known, so that the 5, 5-dimethyl-Δ^1-pyrazoline described here is the simplest representative of the class of Δ^1-pyrazolines which has been studied.

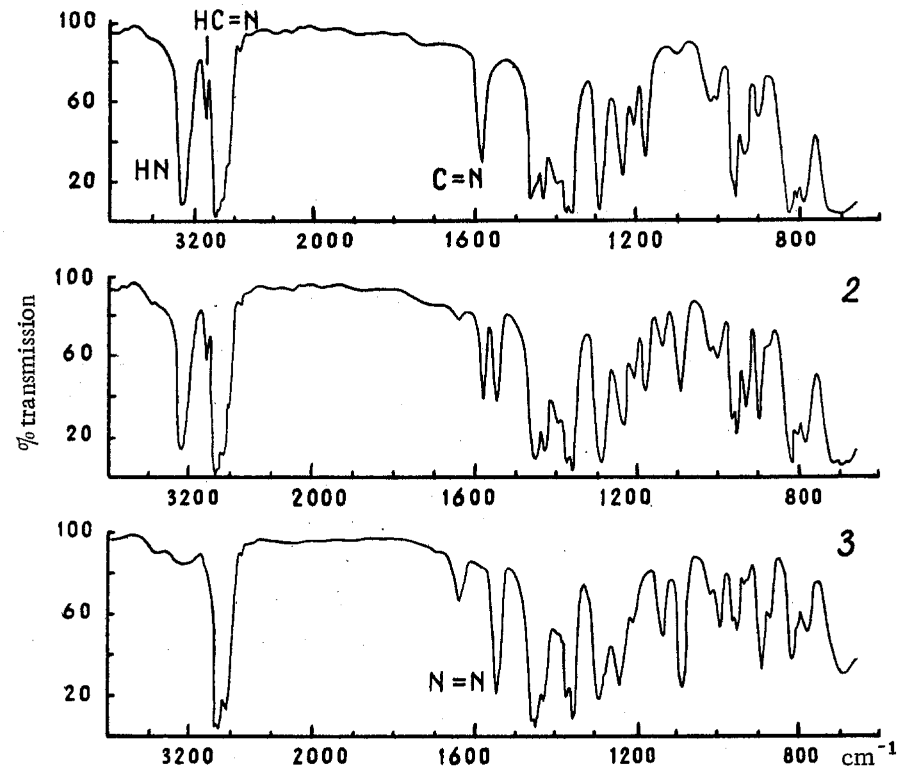

Fig. 2. IR spectra:
1) 5, 5-Dimethyl-Δ^2-pyrazoline; 2) Mixed dimethylpyrazolines, with 43% of the more volatile isomer; 3) 5, 5-Dimethyl-Δ^1-pyrazoline (Nippon-Bunko DS 301 spectrometer, NaCl cell, 25 μ thick).

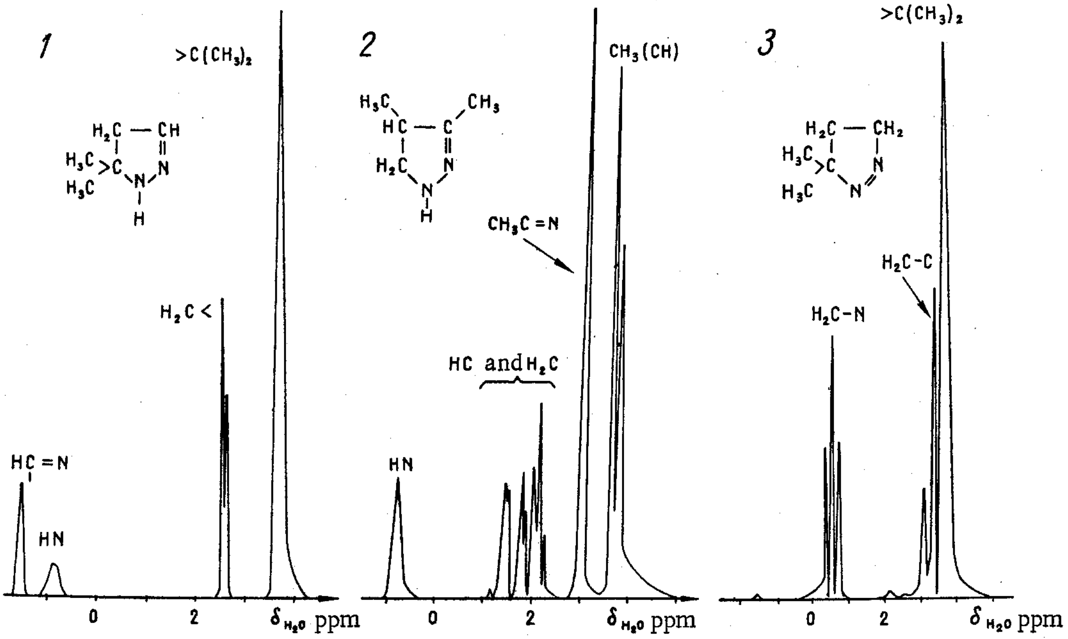

Fig. 3. PMR spectra (INM-3 spectrometer)

The current view [6] regarding the instability of Δ^1-pyrazolines compared with the Δ^2-isomers must be considered incorrect. Unlike many Δ^2-pyrazolines, 5, 5-dimethyl-Δ^1-pyrazoline does not give off nitrogen when stored, and is quite stable when distilled. Heated with hydrazine hydrochloride III isomerizes with shift of the double bond to the Δ^2 position. Such transformation of Δ^1-pyrazoline derivatives to the Δ^2 isomers, as well as the transformation of aliphatic azo compounds to hydrazones, have long been known. However examples of the reverse reaction, $\Delta^2 \rightarrow \Delta^1$ were previously unknown, though such an isomerization was proposed for the intermediate stage of the thermal decomposition of Δ^2-pyrazolines [7].

Table 1

Proton Magnetic Resonance Spectra of 5, 5-Dimethylpyrazolines

Δ^2-isomer				Mixture of 83% Δ^1-isomer and 17% Δ^2-isomer			
Chemical shift δ H_2O	Signal form and spin-spin interaction constant cps	Signal relative intensity**	Signal assignment	Chemical shift δ H_2O	Signal form and spin-spin interaction constant cps	Signal relative intensity*	Signal assignment
3.78	Singlet	6	$(CH_3)_2C^5$	3.80	Singlet	—	$(CH_3)_2C^5$ of Δ^2-isomer present
				3.60	Singlet	3	$(CH_3)_2C^5$
				3.41	Two lines of triplet 7.6****	~1	H_2C^4
2.40	Doublet	2	H_2C^4	2.43	Doublet	—	H_2C^4 of Δ^2-isomer present
				0.57	Triplet	(1)	H_2C^3
−1.10	Wide singlet	1	H—N	−1.66	Singlet***	0,12	HC^3 of Δ^2-isomer present
−1.70	Singlet***	(1)	HC^3				

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*Relative to the field of signal of HC [3].

**Relative to the field of signal of H_2C [3].

***On raising the splitting capacity, triplet (I = 1.6).

****A third of the line overlaps with the preceding singlet.

Table 2

Properties of Δ^1- and Δ^2-5, 5-Dimethylpyrazolines

Constants	Δ^1-pyrazoline	Δ^2-pyrazoline
Boiling point °C (40 mm)	54.5-55.0	67.5-68.5
Density d_4^{20}	0.8945	0.9251
Refractive index n_D^{20}	1.4351	1.4596
Refractive index n_D^{20}	1.4326	1.4566
Mean dispersion Δ_{FC}	88.4	107.2
Relative dispersion ω_{FCD}	20.32	23.32
Molecular refraction MR_D	28.64	29.04
" " " (calculated	(29.20)	(29.35)
% Δ-isomer impurity present (by GLC)	6.2	3.1

Experimental

3, 4-Dimethyl-Δ^2-pyrazoline (II). 42 g (0.5 mole) methyl isopropenyl ketone (bp 98-99°, n_D^{20} 1.4230) was added in 30 min to a 50% aqueous solution of hydrazine cooled in ice. Next day the product was salted out with solid potassium hydroxide, dried, and vacuum distilled through a column (12 theoretical plates). The main cut 23 g (47%) bp 63-65° (14 mm) after redistilling had bp 82.9-83.1° (41.5 mm); d_4^{20} 0.9405; n_D^{20} 1.4728; n_C^{20} 1.4696; Δ_{FC}^{20} 114.9; ω_{FCD} 24.30. Found: C 61.23, 61.31; H 10.07, 1020; N 28.71, 28.99%; M 93.6, 95.7; MR_D 29.75. Calculated for $C_5H_{10}N_2$: C 61.19; H 10.27; N 28.54%; M 98.15; MR_D 29.35.

3, 4-Dimethyl-Δ^2-pyrazoline is a colorless mobile liquid with an odor reminiscent of pyridine, which slowly turns yellow in air, but which is stable in a nitrogen atmosphere. It does not reduce Fehling's solution. Its structure is fully confirmed by its PMR spectrum (Fig. 3).

Conversion of 5, 5-dimethyl-Δ^2-pyrazoline (I) to 5, 5-dimethyl-Δ^1-pyrazoline (III). 86 g I, bp 67.5-68.5° (40 mm) d_4^{20} 0.9251; n_D^{20} 1.4596 (96.9% according to GLC data) was distilled through an approximately 20 theoretical plate column, at a take-off rate of 2-3 ml/hr, and reflux ratio 1 : 60 to 1 : 100. The following cuts were taken (756 mm):

1) Up to 134.5°, 2.3 g, not investigated; 2) 134.5-135.0°, 34.8 g, d_4^{20} 0.8870, n_D^{20} 1.4413; 3) 135.0-135.5°, 28.0 g, d_4^{20} 0.8835, n_D^{20} 1.4376. The residue (19.4 g) was tar and column hold-up.

Chromatographic analysis of the fraction gave a 60% total yield of III (on the converted Δ^2-isomer). For further purification, 61 g product bp 135-135.5° was vacuum distilled in the same column, when it gave 26.3 g (43%) III with the physical constants given in Table 2. Found: C 61.37, 61.17; H 9.95, 10.03; N 28.66, 28.57%; M 99.8, 98.8. Calculated for $C_5H_{10}N_2$: C 61.19; H 10.27; N 28.54%; M 98.15. With a hydrochloric acid solution of CuCl it gave a red precipitate of adduct, characteristic of an azo structure [8] (this reaction is not given by a Δ^2-pyrazoline).

Isomerization of 5, 5-dimethyl-Δ^1-pyrazoline to Δ^2-pyrazoline. 60 g 75% preparation of III was refluxed and stirred for 5 hr at 145° with 68 g hydrazine hydrochloride. On cooling the liquid layer was poured off from the solid salt and vacuum distilled. The following cuts were taken (40 mm): 1) 55-57°, 21.3 g; 2) 57-67°, 9 g, n_D^{20} 1.4489, intermediate; 3) 67-68°, 24 g d_4^{20} 0.9248; n_D^{20} 1.4601. GLC data showed that the first fraction corresponded to the starting preparation of III. The third fraction (yield 41%), was 95.5% Δ^2-isomer.

1-(Phenylcarbamide)-5, 5-dimethyl-Δ^2-pyrazoline. About 1 g phenyl isocyanate was added dropwise to 1 g of fraction 3 placed in a test tube. There was immediate evolution of heat, and after some time colorless crystals separated. After two recrystallizations from carbon tetrachloride, they had mp 109°. Found: C 66.54, 66.46; H 7.03, 6.91; N 19.30, 19.41%. Calculated for $C_{12}H_{15}N_3O$: C 66.34; H 6.96; N 19.34%.

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