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STRUCTURES OF THE PYRAZOLINES OBTAINED FROM TIGLIC ALDEHYDE AND METHYLHYDRAZINE

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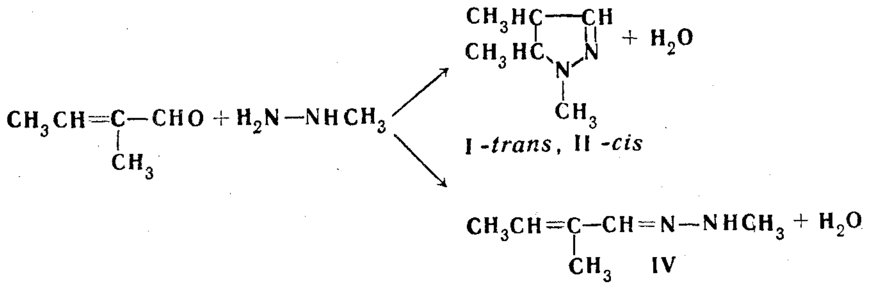
Using gas-liquid chromatography and PMR spectra, it is shown that condensation of tiglic aldehyde and methylhydrazine gives, in addition to the corresponding methylhydrazone, a mixture of stereoisomeric, 1, 4, 5-trimethyl-Δ^2-pyrazolines and 1, 3, 4-trimethyl-Δ^2-pyrazoline. Thus the reaction of formation of pyrazolines from unsaturated carbonyl compounds and hydrazines is not stereospecific and may involve hitherto unknown rearrangements.

In elucidating the mechanism of pyrazoline ring closure when unsaturated carbonyl compounds react with hydrazines, the question of the configurations of the resultant pyrazolines is quite important. Among other things, there is a general absence of data about the stereoisomerism of the simplest dialkyl-Δ^2-pyrazolines, and papers which have appeared of recent years [1, 2] consider only application of PMR to study of the geometrical isomerism of phenyl-substituted Δ^2-pyrazolones.

The simplest cis-trans isomers in the Δ^2-pyrazoline series should be found in the so far unknown 4, 5-dimethyl derivative, but study of that pyrazoline could be complicated by double bond migration.

Actually, its isomer suffers the conversion $\Delta^2 \rightarrow \Delta^{1,3}$ even on distillation, and according to the data at our disposal, this can apparently occur with all pyrazolines unsubstituted at the nitrogen. Under more drastic conditions such pyrazolines can be caused to undergo prototropic isomerization with double bond shift, to the fifth carbon atom [4, 5]. Such complications were excluded with the hitherto unknown 1, 4, 5-trimethyl-Δ^2-pyrazoline, which was also chosen as the subject of the research.

Condensation of triglic aldehyde with methylhydrazine gives both a pyrazoline and the corresponding unsaturated hydrazone.



The pyrazoline: hydrazone ratio varies appreciably, depending on the reaction conditions, probably because of the comparatively facile cyclization of the hydrazone to pyrazoline. Gas chromatographic investigation showed that the pyrazoline fractions $C_6H_{12}N_2$ contain not two, but 3 major components (Fig. 1), and differ only in respect of the ratios of these components, depending on the boiling range. The IR spectra lacked H–N valence vibration bands (3200–3300 cm^{-1}), but had bands for the Me–N group (2785 cm^{-1}), as well as bands at 3050 and 1584 cm^{-1}, characteristic of Δ^2-pyrazolones with unsaturation at position 3. Thus the reaction products were N-methyl substituted Δ^2-pyrazolines. The PMR spectra of the pyrazoline fraction support this conclusion (Fig. 2); they have two signals τ = 3.43 and 3.53 ppm, lying in the region typical of the H–C^3 protons of Δ^2-pyrazolines [6], and an intense singlet of the Me–N groups (7.34 ppm*). As the PMR spectra lack signals for groups HC–N=N (5.4–5.8 ppm [3, 8]), H–C=C (4–6 ppm), and H–N–N=C (4.1–5.8 ppm [6, 9]), the possibility of formation of any Δ^1, Δ^3, and Δ^4-pyrazolines is excluded, and so is the possibility of formation of Δ^2-pyrazolines not substituted at the nitrogen.

The absence of multiplet absorption in the 7.7–8.7 ppm region, characteristic of the C–CH$_2$–Me group, excludes all heterocyclic rings with the Et–C group. As formation of N-ethyl, N-propyl, and N-isopropylpyrazoline rings is improbable here, the remaining possibility to be considered is that the preparations under investigation contain only six 1, x, y-trimethyl-Δ^2-pyrazolones (including cis-trans isomers).

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* All chemical shifts are given on the τ scale (for tetramethylsilane).

The singlet signal at 8.18 ppm which our results disclose (as also do recently published spectra [9]), must belong to protons of the position 3 methyl group in the pyrazoline ring, this methyl group being present in only two possible isomers, viz. 1,3,4- and 1,3,5-trimethyl-Δ^2-pyrazolines. We specially synthesized both of these isomers, and by chromatographing them on three different columns, showed that the third peak on the chromatograms of the preparations, prepared from tiglic aldehyde, belongs to 1,3,4-trimethyl-Δ^2-pyrazoline (III). Despite the reaction product's low content of III (9%), its formation is of great interest, since it points to the possibility of hitherto unknown rearrangements when hydrazines react with unsaturated carbonyl compounds. It is intended to carry out special research on the mechanism of formation of structural isomers in these reactions.

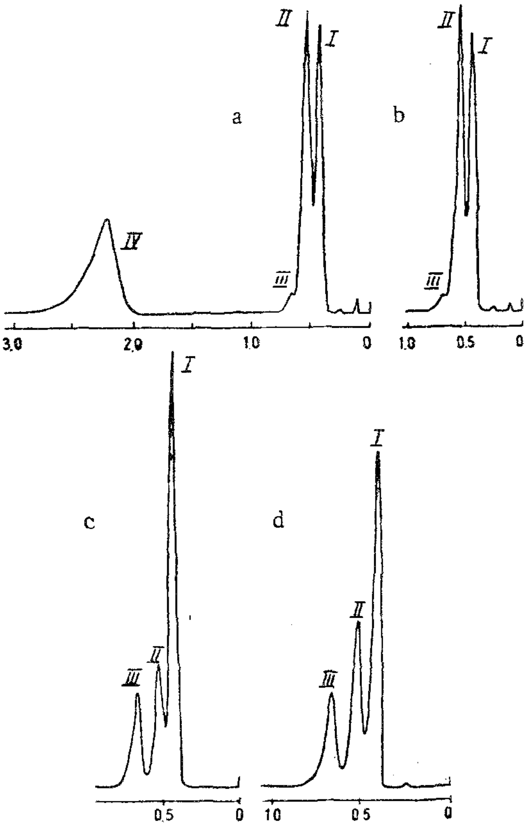

Fig. 1. Chromatograms of products of reaction of tiglic aldehyde with methylhydrazine: a) Reaction products before distilling (experiment b), b) pyrazoline fraction (experiment b), bp 52-57° C (40 mm), c) pyrazoline fraction (experiment a) bp 135.2-137.2° C (758 mm), d) pyrazoline obtained by isomerizing tiglic aldehyde. On the horizontal axes are the retention volumes for n-heptanol.

The main components corresponding to peaks I and II on the chromatograms, cannot be either 1,4,4- or 1,5,5-trimethyl-Δ^2-pyrazolines, for then the signal of the six protons of the gem-dimethyl groups, in the 8.8-9 ppm region, would be strongest in the PMR spectra. Hence, of the six possible isomeric trimethyl-Δ^2-pyrazolines, the main components of the pyrazoline fractions can be only cis- and trans-isomers of 1,4,5-trimethyl-Δ^2-pyrazoline.

For chromatogram peak assignment to the cis- and trans forms, respectively, it was not possible to use the rules given in [2] regarding τ values and J doublets of $H-C^5$ Φ, since here the $H-C^5$ Φ signal was overlapped by $H-C^4$ and CH_3-N signals. The problem was solved by comparing signals of CH_3-C^4 and CH_3-C^5, giving peaks in the 8.7-9.2 ppm region (two doublets from each stereoisomer). Assignment of 8 peaks to 4 doublets was effected by comparing the 40 Mc spectrum (Fig. 2, a) with the spectrum of the same fraction at 60 Mc. The 1,2-doublet (Fig. 2) must be assigned to the CH_3-C^4 group of the cis-isomer, as having the maximum chemical shift value (9.15 ppm), due to the large screening by the adjacent CH_3-C^5group in the cis position. The intensity of the 1,2 doublet in the spectra of different fractions changes similarly to the second peak in the chromatograms (compare Fig. 1, b and c with Fig. 2, a and b). Hence the second peak in the chromatograms must be ascribed to cis-1,4,5-trimethyl-Δ^2-pyrazoline (II), and the second one to the trans isomer (I).

Since repeated distillation led to concentration of the trans isomer in the low-boiling fractions, and of the cis isomer in the high-boiling ones, boiling temperature and retention time sequences for the isomers were the same.

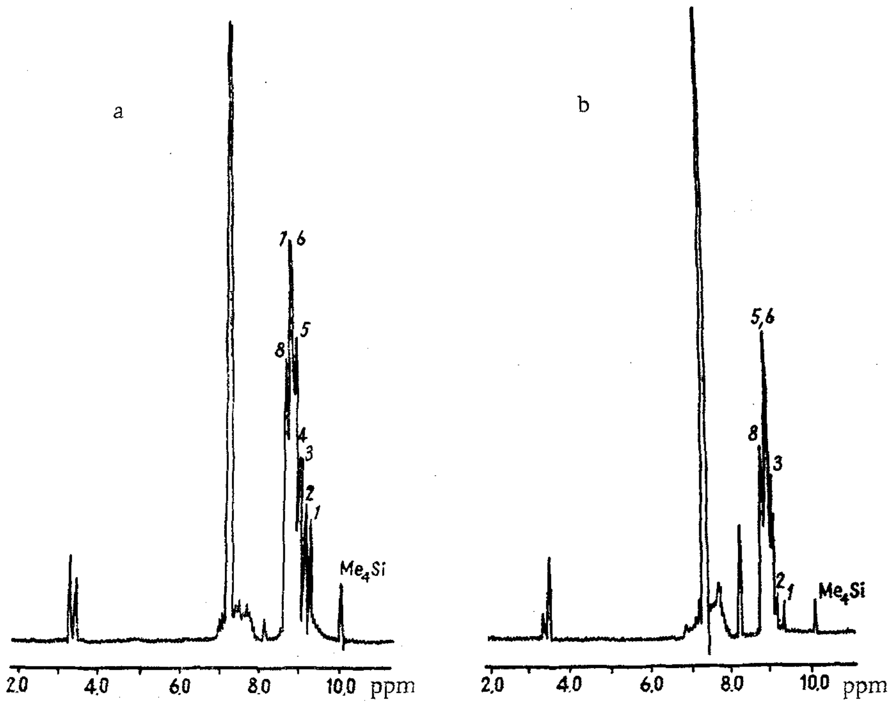

Fig. 2. PMR spectra of pyrazolines obtained from tiglic alcehyde and methylhydrazine: a) Fraction bp 52–57° C (40 mm), b) fraction bp 135.2–137.2° C (758 mm) (JNM-3 spectrometer 40 Mc; internal standard tetramethylsilane).

The simultaneous formation of cis-and trans forms in comparable amounts indicates that the condensation of tiglic aldehyde with methylhydrazine is non-stereospecific. It is of interest that the trans isomer predominates in the products of cyclizing tiglic aldehyde methylhydrazone (Fig. 1d).

Retention Times as Compared with n-Heptanol

Compound	Stationary liquid phase		
	Cyano-ethylated mannitol	Apiezon L	Silicone elastomer
Trans-1,4,5-trimethyl-Δ^2-pyrazoline	0.41	0.30	0.37
Cis-1,4,5-trimethyl-Δ^2-pyrazoline	0.52	0.36	0.44
1,3,4-Trimethyl-Δ^2-pyrazoline	0.65	0.41	0.56
1,3,5-Trimethyl-Δ^2-pyrazoline	0.58	0.36	0.31

Experimental*

Reaction of methylhydrazine with tiglic aldehyde. a) Using the conditions previously employed to synthesize N-alkylpyrazolines [7], 42 g (0.5 mole) tiglic aldehyde [10] [bp 116.3°–119° (758 mm), n_D^{20} 1.4470, GLC showed it to contain 2.8% impurities] was dropped into a stirred mixture of 23 g (0.5 mole) methylhydrazine [bp 87.3°–88° (775 mm), n_D^{20} 1.4332], 78 g $NaH_2PO_4 \cdot 2H_2O$ and 150 ml water, which was cooled in ice. Distillation through a column of 37.7 g of the resultant mixture of organic compounds gave the following cuts: 1) 48°–52° (40 mm), n_D^{20} 1.4493, 0.9 g; 2) 52°–56° (40 mm), n_D^{20} 1.4500, 5.7 g (16.1%); 3) 56° (40 mm)–65° (9 mm), n_D^{20} 1.4747, 3.2 g; 4) 65°–67° (9 mm), n_D^{20} 1.5240, 22.3 g (43.4%); residue 3.2 g resin.

Repeated distillation of second cuts from several runs gave a pyrazoline cut bp 135.2°–137.2° (758 mm), d_4^{20} 0.8737; n_D^{20} 1.4475, n_C^{20} 1.4434, Δ_{FC} 112.7, ω_{FCD} 25.18, MR_D 114.4, 111.5; N 24.81, 25.19%. Calculated for $C_6H_{12}N_2$:

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* With the assistance of N. N. Klyueva and Yu. Ya. Dumpis.

N 24.97%, MR_D 34.19*, M 112.1. It did not reduce Fehling's solution in the hot. From the chromatogram peak areas (Fig. 1c) it contains 61% I, 20% II, and 19% III.

Two distillations of the fourth cuts gave tiglic aldehyde methylhydrazone, bp 65°–67°(9 mm), d_4^{20} 0.8936, n_D^{20} 1.5228, n_C^{20} 1.5162, Δ_{FC} 224.1, ω_{FCD} 46.70, MR_D 38.34, EM_D 2.77, $E\Sigma_D$ 2.47. Found: N 24.74, 24.86%. Calculated for $C_6H_{12}N_2$: N 24.97%; MR_D 35.57. It was a yellow liquid with a spicy odor, which reduced Fehling's solution in the hot. Boiling with sulfuric acid (1 : 5) hydrolyzed it to tiglic aldehyde, identified as its 2,4-dinitrophenylhydrazone, mp 218°–219° C (ex EtOAc), undepressed mixed mp with an authentic specimen (the literature gives [11] mp 222° C). The structure of the unsaturated hydrazone is also confirmed by its high relative dispersion and exaltation. The IR spectrum shows frequencies of 1575 and 1622 cm^{-1}, characteristic of the C=C–C=N system [13], and of 3350 cm^{-1} (N – H valence vibrations), and 2787 cm^{-1} (CH_3-N).

b) The synthesis was also repeated without addition of NaH_2PO_4, when the yield of pyrazoline fraction was 21%, bp 135.5°–136.6°, d_4^{20} 0.8766, n_D^{20} 1.4470, and it contained 36% I, 49% II, and 15% III. The yield of tiglic aldehyde methylhydrazone was 48%, bp 65.8°–68° (10 mm), d_4^{20} 0.8981, n_D^{20} 1.5228.

In a special run all cuts were analyzed chromatographically. The products from 0.6 moles of reactants contained 27% I, 33% II, 7% III, and 33% IV. Distillation of 65 g of the mixture gave 1) 30°–52° (40 mm), n_D^{20} 1.4237, 2.5 g (55% I and 45% II), 2) 52–57° (40 mm), n_D^{25} 1.4458, 24.6 g (41% I, 53% II, 6% III), 3) 57° (40 mm)–67.5° (10 mm), n_D^{25} 1.4784, 5.0 g (55% I + II + III and 45% IV), 4) 67.5°–69° (10 mm), n_D^{25} 1.5070, 22.5 g (13% I + II + III and 87% IV).

Isomerization of tiglic aldehyde methylhydrazone. A mixture of 12 g tiglic aldehyde methylhydrazone and 1 g methylhydrazine hydrochloride (catalyst) was distilled from a flask through a rod and disc column, when it gave 10.2 g distillate bp 80–135° C. Repeated distillation led to the isolation of 5.9 g (50%) of a pyrazoline fraction bp 135–137° (747 mm), d_4^{20} 0.8655, n_D^{20} 1.4484, n_C^{20} 1.4570, Δ_{FC} 118.8, ω_{FCD} 26.49. GLC showed (Fig. 1d) it to contain 49% I, 31% II, and 20% III.

In another experiment, IV was boiled for 2 hr 30 min with 20% of its weight in glacial AcOH. Chromatography of the reaction products showed that there was 88% isomerization, with formation of a mixture of pyrazolines I (46%), II (27%), and III (27%).

Boiling IV for 2 hr 30 min with alkali left its refractive index almost unchanged, but on keeping in a sealed tube for 3 months, n_D^{20} fell from 1.5240 to 1.4890.

1,3,5-Trimethyl-Δ^2-pyrazoline was obtained in 65% yield from 0.5 mole methylpropenylketone [12] (bp 122°–123°, n_D^{20} 1.4350) and 0.5 mole methylhydrazine, bp 55.7°–57.5° (40 mm), d_4^{20} 0.8738, n_D^{20} 1.4490, n_C^{20} 1.4458, ω_{FCD} 25.41, MR_D 34.43. Found: N 25.13, 25.21%. Calculated for $C_6H_{12}N_2$: N 24.97%, MR_D 34.19. GLC showed the material to contain 97.1% basic compound.

PMR spectrum: CH_3-C^5 doublet 8.81 ppm (J 5.2 cps), CH_3-C^3 singlet 8.16 ppm, CH_3-N singlet 7.42 ppm, H-C^4 and H–C^5 multiplets in the 7.0–7.6 ppm region.

1,3,4-Trimethyl-Δ^2-pyrazoline. A 99.2% material (ex methylhydrazine and methylisopropenylketone [7]) had bp 56.3°–56.5° (38 mm), d_4^{20} 0.8781, n_D^{20} 1.4510.

PMR spectrum (CJ-60 spectrometer): CH_3-C^4 doublet 8.90 ppm (J 6.4 cps), CH_3-C^3 singlet 8.18 ppm, CH_3-N singlet 7.40 ppm, H–C^4 and H–C^5 multiplets 6.72–7.80 ppm.

Gas-liquid chromatography has been but little used in the study of organic derivatives of hydrazine. There are only papers about separating mixtures of hydrazine methylhydrazine and dimethylhydrazine [14], and some pyrazolines [3]. There are great difficulties in connection with chromatographing alkylhydrazines, unsaturated hydrazones, and some pyrazolines, due to their instability, especially in contact with metal surfaces, and metal column and syringes were precluded. A Tsvet-1 chromatograph was fitted with glass columns, a special device for introducing the sample, and teflon connections. Samples were introduced with a magnetic glass capillary pipet, and there was no contact with metal along the entire path to the flameionization detector. In every case the temperature was held at the minimum for stable working of the detector (70° C). A number of stationary liquid phases was tested for separating the pyrazolines, resulting in choice of a column 1.2 m long, with 10% cyanoethylated mannitol on cellite 545 (60–70 mesh); a sectional 3-meter column was also used. Further, in identifying pyrazoline III, another three columns (1.2 m) were used, with liquid phases of different polarities: 10% Apiezon L on silanated chromosorb W (60–80 mesh), 10% E301 silicone elastomer on the same carrier, and 15% polyethylene glycol (M-400) plus triethanolamine (1 : 1) on INZ-600 brick (0.25–0.50 mm). The carrier gas was N_2 or He. The table gives the relative retention times for the four pyrazolines investigated.

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* For Δ^2-pyrazoline.

REFERENCES

1. A. Hassner and M. J. Michelson, J. Org. Chem., **27**, 298, 1962.
2. A. Hassner and M. J. Michelson, J. Org. Chem., **27**, 3974, 1962.
3. B. V. Ioffe and D. D. Tsitovich, KhGS [Chemistry of Heterocyclic Compounds], 559, 1965.
4. I. I. Grandberg and A. N. Kost, ZhOKh, **32**, 1906, 1962.
5. J. Elguero and R. Jaquier, Bull. Soc. Chim., 769, 1965.
6. V. S. Stopskii, V. B. Lebedev, B. V. Ioffe, and A. A. Petrov, DAN, **166**, 399, 1966.
7. B. V. Ioffe and K. N. Zelenin, ZhOKh, **33**, 3589, 1963.
8. R. J. Crouford, R. J. Dummel, and A. Hishra, J. Am. Chem. Soc., **87**, 3023, 3768, 1965.
9. G. L. Closs and H. Heyn, Tetrah., **22**, 463, 1966.
10. B. V. Ioffe, Z. I. Sergeeva, V. V. Tsibul'skii, and N. I. Klyueva, ZhOrKh, **2**, no. 12, 1966.
11. J. Doeuvre, Bull. Soc. Chim., 204, 1934.
12. General Laboratory Manual of Organic Chemistry [in Russian], Mir, Moscow, 1965.
13. B. V. Ioffe and K N. Zelenin, DAN, **141**, 1369, 1961.
14. C. Bighi and G. Saglietto, J. Chromatogr., **18**, 291, 1965.

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