REACTIONS OF HYDRAZINE DERIVATIVES

# XLV. The Transformation of 3, 4-Tetramethylene-5, 5-pentamethylenepyrazoline under the Action of Sulfur*

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On the basis of a combined study of chemical properties and UV, IR, PMR, and mass spectra, it has been shown that the product of the transformation of 3, 4-tetramethylene-5, 5-pentamethylenepyrazoline under the action of sulfur has the structure of 3-pentyl-4, 5, 6, 7-tetrahydroindazole.

We have previously reported that 3, 4-tetramethylene-5, 5-pentamethylenepyrazoline (I), which can easily be obtained by the cyclization of the azine of

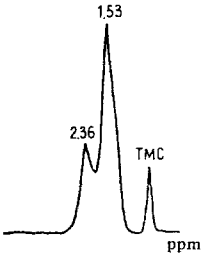



Fig. 1. PMR spectrum of cyclohexanone azine.

cyclohexanone [3], loses two atoms of hydrogen on being heated with sulfur and is converted into a base $C_{12}H_{18}N_2$ (II) in good yield. The process apparently takes place with some isomerization, since we have had to reject several probable structures (including some obtained specially by independent synthesis) as erroneous [2]. Some anomaly in chemical properties has been found for this pyrazoline on reduction [4] and therefore we have specially purified the starting material and subjected it to additional study to confirm its structure.

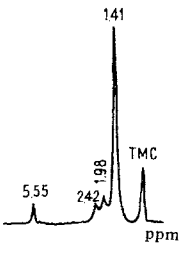



Fig. 2. PMR spectrum of 3, 4-tetramethylene-5, 5-pentamethylenepyrazoline (I).

The PMR spectrum of cyclohexanone azine (Fig. 1) has two peaks with an intensity ratio of 2 : 3 in the 2.36 and 1.53 ppm region, which correspond to eight protons in the $\alpha$-position to the C=N group and 12 protons in the $\beta$- and $\gamma$-positions. According to the literature [5], in the azines additional splitting of the peaks of $\alpha$-$CH_2$ groups takes place because of non-coplanarity (one $\begin{matrix}-CH_2\\-CH_2\end{matrix}$C=N– group lies in a plane perpendicular to the other similar group), but in our case we did not observe this splitting. When the azine is converted to the pyrazoline I, a peak appears in the 5.55 ppm region and the group of peaks in the 1.41, 1.98, and 2.42 ppm regions is retained (Fig. 2). It may be assumed that the peak in the 2.42 ppm region is connected with the proton of the CH group in position 4 of the pyrazoline ring but the complex nature of the interaction of the protons and the inadequate splitting make an accurate assignment difficult.

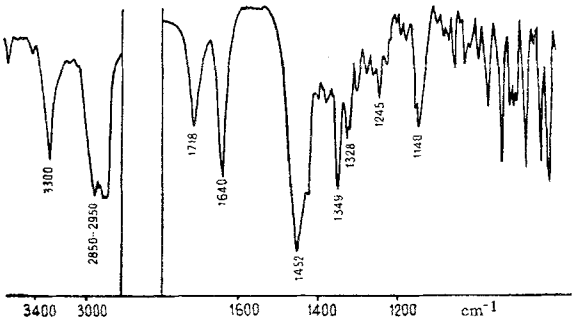


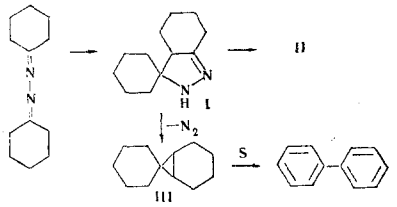

Fig. 3. IR spectrum of 3, 4-tetramethylene-5, 5-pentamethylenepyrazoline (I).

The IR spectrum of the pyrazoline I has absorption maxima (Fig. 3) corresponding to C–H stretching vibrations (2850–2950 $cm^{-1}$) and deformation vibrations (1452 $cm^{-1}$) of $CH_2$ groups, N–H stretching vibrations (3300 $cm^{-1}$) and C=N stretching vibrations (1640 $cm^{-1}$), which correspond to the ascribed structure and to the chemical properties of the substance [2]. The mass spectrum of the pyrazoline is given in the table.

On being heated with sulfur, a small amount (about 10%) of the pyrazoline undergoes Kishner decomposition with the evolution of nitrogen and the formation of 1, 1-pentamethylenedicyclo[o, 1, 4]heptane (cf. [3]). The IR spectrum of this hydrocarbon III (Fig. 4) is typical for this type of compounds (strong absorption in the 1438, 1480, 2805, and 2888 $cm^{-1}$ regions). The PMR spectrum (Fig. 5) has signals from protons of three types, namely in the 0.41 ppm region (two protons attached to a cyclopropane ring), the 1.19 ppm region (eight protons of $\alpha$-$CH_2$ groups), and the 1.40 ppm region (ten protons of the other $CH_2$ groups),

*For part XLIV, see [1].

which completely confirms its structure and, at the same time, the structure of the pyrazoline I. In dehydrogenation, part of the hydrocarbon III is converted into biphenyl, which it was possible to isolate and identify. Thus, the structure of the initial pyrazoline is not a matter of doubt.



Substance II obtained on dehydrogenation, which we described as $C_{12}H_{18}N_2$, was contaminated with the initial pyrazoline and substances containing sulfur. However, two distillations in vacuum using Raney nickel to destroy the sulfur compounds led to a chromatographically pure substance stable on storage.

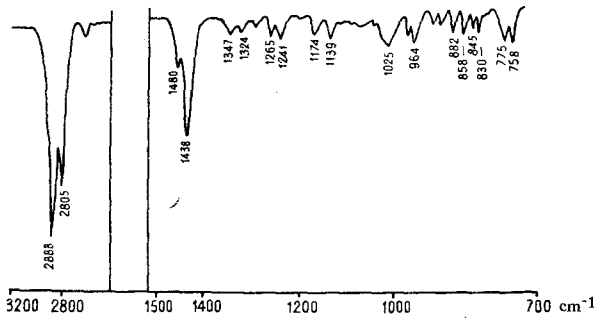
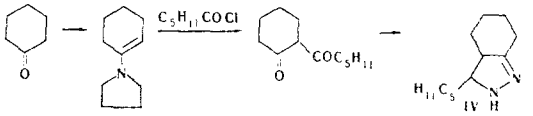
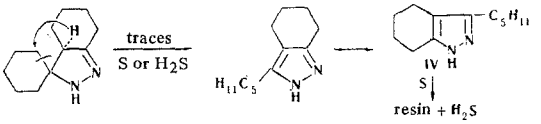



Fig. 4. IR spectrum of 1, 1-pentamethylene-bicyclo[0, 1, 4]heptane.

Since the properties of the compound II obtained indicate that it belongs to the class of pyrazoles, to compare their properties we carried out a special synthesis of 3-pentyltetrahydroindazole (IV) in the following way:



After both substances had been carefully purified, their physicochemical characteristics proved to be practically identical. However, the dehydrogenation of I gave a yield of the base II of about 75% of theoretical and almost the theoretical amount of hydrogen sulfide was evolved. Thus, the base II must have lost two hydrogen atoms and have the composition $C_{12}H_{18}N_2$, while the pyrazole IV has the composition $C_{12}H_{20}N_2$. On studying the behavior of the pyrazole IV when it was heated with sulfur, we found that the molecule of the pyrazole may yield up to 4 moles of hydrogen sulfide (with a sufficient amount of sulfur), with the formation of a complex mixture of unidentifiable products. The fortuitous coincidence of the results of elementary analysis and the volume of $H_2S$ liberated led us into error. Substance II proved to be the indazole IV. The route for the conversion of the pyrazoline I into 3-pentyltetrahydroindazole (IV) is obviously the following:



The pyrazoline rearranges under the action of catalytic amounts of sulfur or hydrogen sulfide into 3-pentyltetrahydroindazole IV, part of which liberates hydrogen

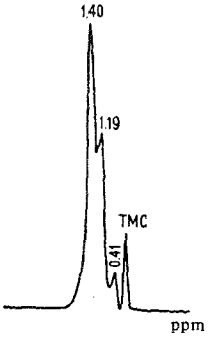
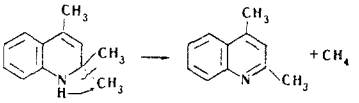



Fig. 5. PMR spectrum of 1, 1-pentamethylene-bicyclo[0, 1, 4]heptane (III).

sulfide on heating with sulfur. The process is similar to the aromatization of acetone anil which takes place with the liberation of a molecule of methane and the formation of 2, 4-dimethylquinoline



## EXPERIMENTAL

**Treatment of 3, 4-tetramethylene-5, 5-pentamethylenepyrazoline (I) with sulfur.** The pyrazoline I with bp 167° C (15 mm), mp 60° C, was obtained from 65 g (~0.34 mole) of pure cyclohexanone azine (mp 34° C), by the action of 33 g (~0.37 mole) of oxalic acid in 200 ml of benzene.

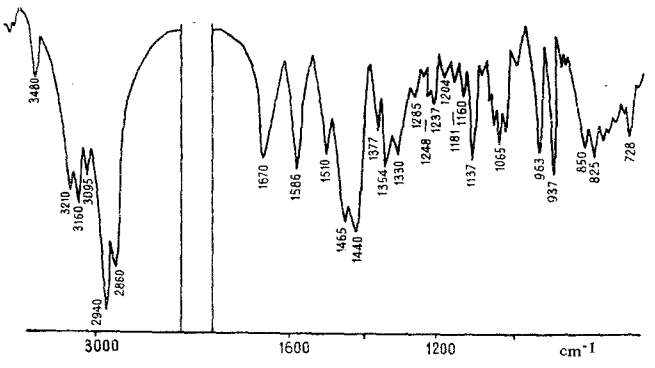



Fig. 6. IR spectrum of 3-pentyl-4, 5, 6, 7-tetrahydroindazole (IV).

A mixture of 30 g (~0.16 mole) of the pyrazoline, 1.5 g (~0.16 g-at) of powdered sulfur, and 20 ml of benzene was heated in a Würtz flask for 1 hr 30 min at a gradually increasing temperature. At 80° C (boiling point of the benzene) the evolution of hydrogen sulfide began. At the end of the experiment, when the evolution of $H_2S$ had ceased, the temperature in the mixture reached 200° C. Distillation yielded 2.7 g of a bicycloheptane [3], bp 100–120° C

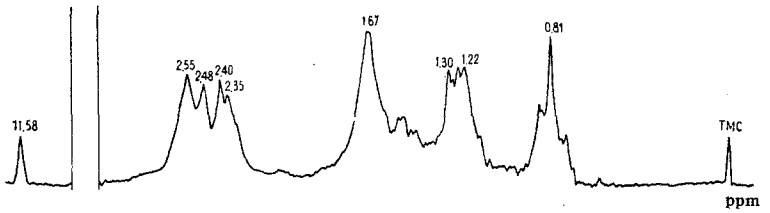



Fig. 7. PMR spectrum of 3-pentyl-4, 5, 6, 7-tetrahydroindazole (IV).

(7 mm) and a main fraction with bp 165–168° C (7 mm). From the undistillable residue (~15% by weight) chromatography in benzene on Florisil with subsequent elution by means of chloroform and methanol yielded only highly colored resinous substances darkening in the light. The small forerun (about 1 g) with bp 140–165° C (7 mm) was dissolved in benzene and passed through a column of alumina (Woelm, neutral, activity I). Elution with petroleum ether gave colored impurities, after which elution with benzene yielded biphenyl, which was identified by its mp and its UV and IR spectra.

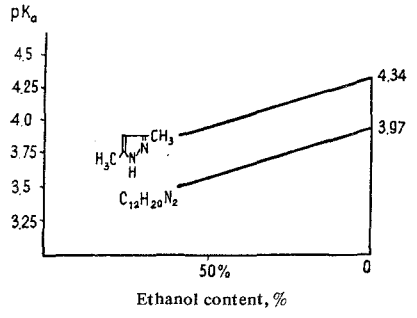



Fig. 8. Extrapolation curves of $pK_a$.

The main reaction product, bp 165–168° C (7 mm), resinified to a considerable extent when hydrogen chloride was passed into a benzene solution, and became colored on standing in sunlight. The picrate deposited in the form of an oil difficult to crystallize.

Attempts to free it from impurities by chromatography on a column of alumina (neutral, Woelm, solvent benzene, gradient elution with benzene, chloroform, and methanol) did not give adequate purification. In view of this, the substance was twice redistilled in vacuum with a short column, first over zinc dust and then over Raney nickel. Yellowish oil, bp 198–199° C (10 mm); $d_4^{20}$ 0.9903; $n_D^{20}$ 1.5118. The substance purified in this way was stable to the action of light and was chromatographically homogeneous. Found, %: C 81.54, 81.51; H 7.67, 7.54. Calculated for $C_{18}H_{20}N_2$, %: C 81.73; H 7.67. On chromatography in a thin layer of alumina (Brockmann grade II, benzene–chloroform (1:1), $R_f$ 0.14. Ascending chromatography on Whatman paper No. 1 gave $R_f$ 0.83 (80% ethanol) and 0.89 (benzene–chloroform (1:1)). The spots were revealed with iodine vapor. For procedure, see previous papers [7–9]. The pH of hydrolysis of the sulfate (for procedure, see [10]) was 2.17.

**3-Pentyl-4, 5, 6, 7-tetrahydroindazole (IV).** With vigorous stirring at 35° C, a mixture of 44.4 g (~0.33 mole) of caproyl chloride and 150 ml of dry chloroform was added dropwise to a solution of 50 g (~0.33 mole) of N-(1-cyclohexenyl)-pyrrolidine and 36.2 g (~0.36 mole) of anhydrous triethylamine in 400 ml of absolute chloroform. After being stirred for an hour at 40° C, the mixture was left for a day. Then 85 ml of 20% hydrochloric acid was added and it was boiled for 5 hr. The chloroform layer was separated off, washed with water, and distilled in vacuum to give 42 g (70%) of α-caproylcyclohexanone, bp 149–153° C (11 mm); $n_D^{20}$ 1.4912. Found, %: C 80.94, 80.97; H 7.49, 7.38. Calculated for $C_{18}H_{20}O_2$, %: C 80.61; H 7.50. A mixture of 20 g of α-caproylcyclohexanone and 5 ml of hydrazine hydrate was heated in the water bath for one hr and was distilled in vacuum. This gave 18.6 g (94%) of substance IV, bp 194–195° C (9 mm); $d_4^{20}$ 0.9896; $n_D^{20}$ 1.5113. Found, %: C 81.47, 81.43; H 7.63, 7.60. Calculated for $C_{18}H_{20}N_2$, %: C 81.73; H 7.67.

**Properties of the base II and of 3-pentyltetrahydroindazole (IV) obtained by independent synthesis.** Both compounds II and IV consisted of viscous oils which did not crystallize on cooling to −80° C. They were almost insoluble in water and petroleum ether but readily soluble in the usual organic solvents. They withstood heating in sealed tubes with concentrated hydrochloric acid to 200° C for 6 hr without change and did not liberate ammonia on being heated with anhydrous zinc chloride to 250° C. On being heated with anhydrous alkalis or sodium amide, they gave stable salts readily hydrolyzed by water. They were stable to the action of weak oxidizing agents and to reduction even under severe conditions (Raney nickel, 160° C, 150 atm). They did not undergo dehydrogenation on being heated with 15% of palladium on carbon at 200–220° C. The UV spectra of compounds II and IV were identical (in methanol, $\lambda_{max}$ 223 nm, log ε 3.8), and their IR and PMR spectra (Figs. 6, 7) were also identical. The PMR spectrum clearly showed the triplet of a $CH_3$ group (0.81 ppm), a diffuse 4-proton peak of two $CH_2$ group adjacent to the $CH_3$ group in a pentyl radical (1.22–1.30 ppm), a 6-proton peak of three $CH_2$ groups in the β-position with respect to an aromatic nucleus (1.67 ppm), and two unresolved quartets of two $CH_2$ groups (positions 3 and 5 of the nucleus–2.55–2.48 ppm) and of a $CH_2$ group in position 4 (2.40–2.35 ppm). The signal from the NH group was in the 11.58 ppm region. The spectrum agrees with the usual characteristics for pyrazoles [6].

Many of the other constants were very similar, including their chromatographic mobilities and, which is particularly important, their $pK_a$ values (3.97 for II and 3.96 for IV).

The IR spectra* were recorded on a UR-10 instrument in a thin layer with an NaCl prism in the 700–2000 $cm^{-1}$ region and an LiF prism in the 2500–3500 $cm^{-1}$ region.

The PMR spectra of 20% solutions in $CCl_4$ with tetramethylsilane as internal standard were taken on a INM-3 instrument with a frequency of 40 MHz. The PMR spectrum of 3-pentyltetrahydroindazole (IV) was recorded on a INMH-100 instrument with a frequency of 100 MHz under the same conditions.

The mass spectra of compounds I, II, and IV were obtained on a MKh-1303 mass spectrometer with a modified recording device [10] under the following operating conditions. Temperature of the ion source and inlet system 250° C, ionizing voltage 50 V, emission current 1.5 mA, accelerating voltage 2 kV. In considering the mass spectra (table), the peaks of ions the relative intensities of which were ≥ 1% were taken into consideration. A comparison of the mass spectra of compounds II and IV, having molecular ions with m/e 192, showed their complete identity. The presence of a chain of five carbon atoms leads to β-cleavage with respect to the aromatic nucleus with the transfer of a hydrogen atom. The fragmentary ion so formed with mass 136 gives the maximum peak, the intensity of which is 24.3% of the total ionic current.

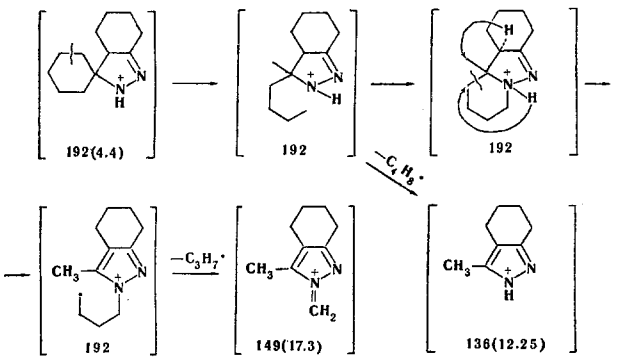
The decomposition of the pyrazoline I took place in a far more complex fashion; its mass spectrum showed the formation of the maximum peak of an ion with mass 149 (17.3% of the total ionic current). Isotopic peaks in the mass spectra of compounds II, IV, and I show the presence in the fragmentary ions with m/e 136 of two

* For recording the IR spectra, we express our thanks to L. S. Leont'eva (All-Union Scientific-Research Chemical and Pharmaceutical Institute).

Mass Spectra of the 3-Pentyltetrahydroindazoles II and IV and of 3, 4-Tetramethylene-5, 5-pentamethylenepyrazoline (I)

| m/e | II, IV | I | m/e | II, IV | I | m/e | II, IV | I |
|---|---|---|---|---|---|---|---|---|
| 26 | 0.7 | 1.35 | 80 | 3.45 | 8.45 | 132 | 1.35 | 1.05 |
| 27 | 4.1 | 6.2 | 82 | 2.55 | 6.4 | 133 | 2.7 | 2.2 |
| 28 | 3.15 | 5.8 | 83 | 0.95 | 3.1 | 134 | 3.55 | 2.4 |
| 29 | 4.25 | 4.6 | 91 | 3.15 | 5.8 | 135 | 37.7 | 29.9 |
| 30 | 1.1 | 1.65 | 92 | 1.9 | 2.2 | 136 | 100.0 | 59.25 |
| 39 | 4.35 | 8.45 | 93 | 2.05 | 4.15 | 137 | 9.5 | 5.8 |
| 40 | 1.35 | 2.05 | 94 | 6.9 | 8.9 | 146 | — | 1.3 |
| 41 | 10.25 | 17.2 | 95 | 9.25 | 9.05 | 147 | 1.1 | 6.95 |
| 42 | 3.1 | 5.8 | 96 | 1.9 | 8.75 | 148 | 0.8 | 2.05 |
| 43 | 2.9 | 2.4 | 97 | 0.9 | 3.1 | 149 | 31.55 | 100.0 |
| 44 | 2.3 | 2.8 | 98 | — | 4.3 | 150 | 12.55 | 19.25 |
| 51 | 1.3 | 1.65 | 105 | 1.15 | 2.4 | 151 | 1.3 | 1.8 |
| 52 | 1.85 | 1.65 | 106 | 1.4 | 1.8 | 161 | — | 1.9 |
| 53 | 4.4 | 5.95 | 107 | 11.55 | 14.65 | 162 | — | 2.95 |
| 54 | 3.3 | 10.5 | 108 | 9.75 | 8.0 | 163 | 9.25 | 9.2 |
| 55 | 3.25 | 12.15 | 109 | 2.25 | 3.4 | 164 | 7.8 | 8.9 |
| 56 | 0.9 | 1.95 | 110 | — | 7.1 | 165 | 0.9 | 1.05 |
| 57 | 0.95 | 1.05 | 111 | — | 1.3 | 174 | — | 1.35 |
| 65 | 2.85 | 3.85 | 117 | — | 1.2 | 175 | — | 2.7 |
| 66 | 2.1 | 2.5 | 118 | 1.0 | 1.05 | 177 | 1.65 | — |
| 67 | 5.9 | 10.95 | 119 | 2.3 | 3.55 | 178 | — | 1.05 |
| 68 | 1.85 | 4.3 | 120 | 1.65 | 2.05 | 189 | — | 2.8 |
| 69 | 1.6 | 6.4 | 121 | 13.7 | 12.3 | 190 | — | 3.4 |
| 70 | — | 1.2 | 122 | 4.85 | 4.15 | 191 | 3.7 | 4.15 |
| 77 | 1.05 | 5.8 | 123 | 1.7 | 3.25 | 192 | 24.25 | 25.3 |
| 78 | 1.65 | 2.05 | 124 | 1.3 | 5.05 | 193 | 3.45 | 3.7 |
| 79 | 3.4 | 8.75 | 131 | 1.05 | 0.9 | | | |

nitrogen atoms and the retention of the pyrazole nucleus. The decomposition of the pyrazoline I under the action of electron impact can be represented by the following scheme: *




The $pK_a$ values were determined by potentiometric titration of the bases in aqueous ethanolic solutions with subsequent extrapolation [7] to zero concentration of ethanol (Fig. 8). The electrophoretic mobilities for compounds II and IV were zero (400 V, 50% HCOOH buffer, 8 hr, spots revealed with iodine vapor).

* Here the figures under the formulas denote the mass numbers and the figures in parentheses the intensities of the peaks of the corresponding ions in % of the total ionic current.

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