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Abstract

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HOFMANN CLEAVAGE OF THE PYRAZOLINE RING

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Numerous studies on the Hofmann degradation of hydrogenated nitrogen-containing heterocycles have been devoted mainly to the study of pyrrolidine and piperidine derivatives, including those with condensed nuclei (1,2). From transformations of exhaustive methylation products it was established that, for such compounds, stereospecific trans-β-elimination with ring opening usually occurs, as a rule at temperatures not below 100°. Only in a few cases—in derivatives of tetrahydroquinoline and dihydroisoindole—is methyl alcohol eliminated without opening of the ring. For iodomethylates of N-alkylpiperidines it was shown (3) that, when an ethyl radical is present at the nitrogen atom, the elimination of ethylene rather than ring cleavage becomes predominant; when the ethyl radical is replaced by heavier normal radicals—propyl, butyl, hexyl, and octyl—olefins always accompany the main product, 5-dialkylamino-1-pentene. No information was available in the literature on the Hofmann cleavage of heterocycles with two nitrogen atoms, including pyrazolines.

Meanwhile, the question of the possibility of Hofmann cleavage of the pyrazoline ring is of special interest, since it is now known (4—6) that the pyrazoline ring in quaternary salts unsubstituted in position 3 is readily cleaved by the action of alkali, but at the nitrogen—nitrogen bond, and not at the nitrogen—carbon bond:

$$\text{[[structural formula]]} \xrightarrow{\text{OH}^-} \mathrm{H_2O + J^- + R_4R_3N{-}CH(R_2){-}CH(R_1){-}C{\equiv}N} \quad (1)$$

\end{equation}

This transformation, analogous to Hofmann cleavage, is a general property of such pyrazolinium salts. In none of the cases we studied were products of the Hofmann course of the reaction (elimination of hydrogen in position 4 with cleavage of the C^5—N^+ bond) detected.

It was of great interest to determine whether cleavage of the pyrazoline ring with rupture of the C—N bond and preservation of the less stable N—N bond is at all possible. For this purpose it was necessary to study quaternary pyrazolinium salts substituted in position 3, in which the aminonitrile rearrangement (1) is excluded.

As objects of investigation we chose the iodomethylates and iodoethylates of 1,3-dimethylpyrazoline and 1,3,4-trimethylpyrazoline. It turned out that all four quaternary pyrazolinium iodides decompose unambiguously with ring cleavage at the nitrogen—carbon bond and formation of unsaturated N,N-dialkylhydrazones:

$$\text{[[structural formula]]} \xrightarrow{\text{KOH}} \mathrm{KJ} + \mathrm{H_2O} + \mathrm{CH_2{=}C(R_1){-}C(CH_3){=}N{-}N(CH_3)R} \qquad (2)$$

\end{equation}

$$(R = \mathrm{CH_3} \text{ or } \mathrm{C_2H_5}, \quad R_1 = \mathrm{H} \text{ or } \mathrm{CH_3})$$

The reaction proceeds on heating with solid caustic potash to 130—160°. The yields of hydrazones were 49—75%. Products of decomposition at the bond

nitrogen—no nitrogen was detected. As was to be expected, reaction (2) proceeds at a considerably higher temperature than the aminonitrile rearrangement. However, these conditions do not differ from those of the Hofmann cleavage of other heterocycles. As can be seen, the iodomethylates of 1,3-dimethylpyrazolines behave in the same way as the iodomethylates of most other heterocyclic systems, i.e., they undergo β-elimination with ring opening. Attention should be drawn to the fact that the iodoethylates decompose not with elimination of ethylene, but likewise according to scheme (2), i.e., contrary to Hofmann' s rule.

The transformation of quaternary pyrazoline salts that we have studied may serve as a convenient method for the synthesis of N,N-dialkylhydrazones of unsaturated ketones. In the direct condensation of the simplest dialkylhydrazines and vinyl ketones, hydrazones are either not obtained at all (because of cyclization into pyrazoline salts) or their yields are low (7). The constants of four previously unknown unsaturated dialkylhydrazones synthesized by us from pyrazolines are given in Table 1. For comparison, the table also gives the constants of the diethylhydrazone of methyl isopropenyl ketone (also not described in the literature and obtained by condensation of diethylhydrazine with the ketone).

Experimental Part

Iodomethylates of 1,3- and 1,3,4-trimethylpyrazolines are formed in quantitative yield upon addition

Table 1

N,N-Dialkylhydrazones of α,β-unsaturated ketones

Starting substance	N,N-Dialkylhydrazone	Empirical formula	Yield, %	b.p., °C (1, mm Hg)	d_4^{20}	n_D^{20}	n_C^{20}	$\Delta F C$	$\Phi C D$	MR_D, found	MR_D, calc.*	Exaltation, EM_D	Exaltation, $E\Sigma_D$	C, %, found	C, %, calc.	H, %, found	H, %, calc.	N, %, found	N, %, calc.
1,1,3-Trimethylpyrazoline iodide + KOH	Dimethylhydrazone of methyl vinyl ketone	$C_6H_{12}N_2$	75	47.0 – 48.0 (51)	0.8389	1.4715	1.4661	197.8	44.93	37.40	35.75	1.65	1.47	64.58; 64.64	64.25	10.93; 10.99	10.77	24.72; 25.12	24.98
1,1,3,5-Tetramethylpyrazoline iodide + KOH	Dimethylhydrazone of methyl isopropenyl ketone	$C_7H_{14}N_2$	49	59.0 – 60.0 (43)	0.8357	1.4678	1.4635	157.6	35.82	41.97	40.40	1.57	1.24	66.91; 66.80	66.62	11.67; 11.66	11.18	22.59; 22.17	22.20
1,1,3,4-Tetramethylpyrazoline iodide + KOH	Dimethylhydrazone of methyl isopropenyl ketone	$C_7H_{14}N_2$	53	60.5 – 61.5 (43)	0.8404	1.4704	1.4656	177.6	37.76	41.93	40.40	1.53	1.21	66.85; 67.32	66.62	11.19; 11.36	11.18	22.04; 22.05	22.20
1-Ethyl-1,3,4-trimethylpyrazolinium iodide	Methylethylhydrazone of methyl isopropenyl ketone	$C_8H_{16}N_2$	57	71.5 – 72.5 (40)	0.8354	1.4648	1.4606	155.2	33.39	46.36	45.03	1.33	0.95	68.06; 68.47	68.52	11.49; 11.69	11.50	19.68; 19.71	19.98
Methyl isopropenyl ketone + diethylhydrazine	Diethylhydrazone of methyl isopropenyl ketone	$C_9H_{18}N_2$	18	60.0 – 61.0 (15)	0.8336	1.4636	1.4591	155.6	33.56	51.02	49.71	1.31	0.84	69.96; 70.16	70.08	11.85; 12.10	11.76	18.05; 18.23	18.17

* The refractive indices are referred to hydrogen (in tubes with a silver permanganate heater).

** Satisfactory microanalyses for carbon and hydrogen (in tubes with the product of decomposition of potassium permanganate) are obtained with a large current—usually after 6-8 combustions.

methyl iodide (0.3 mole) to a benzene solution of the corresponding pyrazoline (0.25 mole in 400 ml), in the form of colorless crystalline substances.

IR spectra of N,N-dialkylhydrazones of ketones

Fig. 1. IR spectra of N,N-dialkylhydrazones of ketones (recorded on double-beam UR-10 and DS-301 spectrophotometers; layer thickness 25-35 μ). **I**—dimethylhydrazone of methyl vinyl ketone; **II**—methylethylhydrazone of methyl vinyl ketone; **III**—dimethylhydrazone of methyl isopropenyl ketone; **IV**—methylethylhydrazone of methyl isopropenyl ketone; **V**—diethylhydrazone of methyl isopropenyl ketone.

The iodomethylate of 1,3-dimethylpyrazoline melts at 169-170°.

Found, %: J 52.26, 52.57 (by titration according to Volhard)
$C_6H_{13}N_2J$. Calculated, %: J 52.85

The iodomethylate of 1,3,4-trimethylpyrazoline has m.p. 176°.

Found, %: J 50.48, 50.58
$C_7H_{15}N_2J$. Calculated, %: J 49.94

Iodoethylates of pyrazolines were synthesized under more severe conditions—by boiling with a reflux condenser equivalent amounts (0.3 mole) of ethyl iodide and pyrazoline in 100 ml of benzene for one and a half hours. The yields of the substances were 90-95%.

1-Ethyl-1,3-dimethylpyrazolinium iodide is a yellow viscous oil. It was used for the reaction in the unpurified state.

1-Ethyl-1,3,4-dimethylpyrazolinium iodide melts at 84-86°.

Found, %: I 47.08, 46.97
$C_8H_{17}N_2J$. Calculated, %: I 47.32

Hofmann cleavage of 1,1,3-trialkylpyrazolinium iodides. A mixture of 0.25 mole of pyrazoline iodoalkylate and 0.5 mole of powdered caustic potash was placed in a Wurtz flask with a thermometer immersed in the reaction mass and heated on a flask heater. At 110-120° decomposition of the iodoalkylate begins, proceeding smoothly at 130-160°, with formation of a yellow heterogeneous distillate with a pungent lachrymatory odor. Heating was continued until distillation of the distillate ceased. The yield of the organic layer (after drying and drying over alkali) in different experiments was 95-100%, calculated for formation of the product with elimination of a molecule of water.

The distillate was distilled on a vacuum column with an efficiency of 12 theoretical plates. In all distillations the principal fractions were the corresponding N,N-dialkylhydrazones of unsaturated ketones—yellow lachrymatory liquids, titrated with aqueous 0.1 *N* HCl in the presence of bromophenol blue without a distinct transition point and readily hydrolyzed at the C=N bond upon heating with aqueous acid solutions. In order to obtain pure preparations, the principal fractions were distilled once more (methylethylhydrazone of methyl isopropenyl ketone—three times) and after this were characterized by physicochemical constants, analyses (see Table 1), and IR spectra.

The hydrolysis products of the preparations with 6*N* sulfuric acid were distilled off and identified with the aid of semicarbazones, which for derivatives of methyl vinyl ketone melted at 139-140°, and for methyl isopropenyl ketone derivatives at 173-174° (no depression in all cases upon fusion with specially prepared semicarbazones). According to the literature, semicarbazone of methyl vinyl ketone melts at 141° (^{8}), and that of methyl isopropenyl ketone at 172.6-173.5° (^{9}).

IR spectra of unsaturated hydrazones (Fig. 1), like those described by us earlier (^{7}), contain intense absorption bands of stretching vibrations of the C=C double bonds in the region 1620-1630 cm^{-1} and C=N at 1580-1959 cm^{-1}. The intense maxima in the interval 2765-2790 cm^{-1}, characteristic of the spectra of all the preparations (except diethylhydrazone of methyl isopropenyl ketone), have been assigned by us to absorption of the N—CH_3 group (^{10}). The frequencies at 3075, 3050, 994-996, 917-918, 1830-1855, 1415-1421, 1287-1293 cm^{-1}, found in the spectra of methyl vinyl ketone derivatives, correspond to absorption of the vinyl group. The spectra of the hydrazones of methyl isopropenyl ketone contain frequencies at 3075-3095, 896-908, 1796-1800, 1430-1435 cm^{-1}, which corresponds to absorption of the CH_2=C group (^{11}).

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