Chemistry

B. V. Ioffe, D. D. Tsitovich

1964

SovietRxiv

Abstract

Full Text

Chemistry

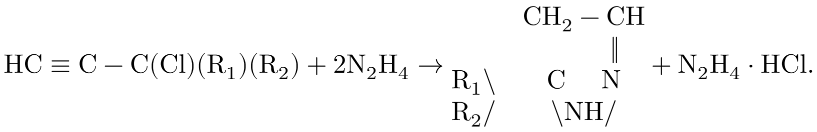
B. V. Ioffe, D. D. Tsitovich

A New Method for the Synthesis of Pyrazolines

Condensation of Tertiary Acetylenic Chlorides with Hydrazine

(Presented by Academician A. N. Nesmeyanov, October 14, 1963)

In studying the possibility of synthesizing unknown hydrazines of the acetylene series, we carried out the reaction of tertiary acetylenic chlorides with anhydrous hydrazine. In the case of dimethylacetylenylchloromethane this reaction begins already at room temperature, while with its homologs it proceeds on heating to 40-50° and then continues with evolution of heat, formation of hydrazine hydrochloride, and liquid nitrogenous compounds of the general formula $C_{nH_{2n}}N_2$. The composition of these substances corresponds to the normal products of alkynylation—acetylenic hydrazines; however, negative reactions with Fehling' s solution, cold ammoniacal silver nitrate solution, and Ilosvay' s reagent indicate that they are not hydrazines or hydrazones and do not contain acetylenic hydrogen. Refractometric data also exclude the possibility of assigning to the compounds obtained the structure of acyclic unsaturated hydrazine derivatives, making a pyrazoline structure very probable. The IR spectra contain the characteristic frequencies typical of Δ^2-pyrazolines (see the experimental part), and from the totality of the data obtained it follows that the products of condensation of tertiary acetylenic chlorides with hydrazine are the previously unknown 5,5-dialkyl-Δ^2-pyrazolines:

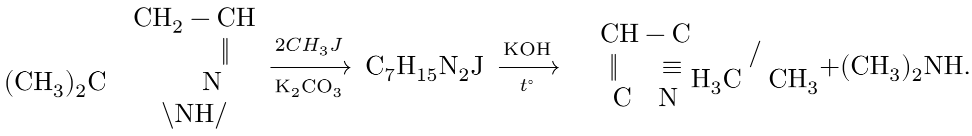


$$\mathrm{HC \equiv C - C(Cl)(R_1)(R_2) + 2N_2H_4 \rightarrow} \begin{array}{ccc} & \mathrm{CH_2 - CH} & \\ & \qquad \quad \| & \\ \mathrm{R_1 \backslash} & \mathrm{C \quad N} & \\ \mathrm{R_2 /} & \mathrm{\backslash NH /} & \end{array} \mathrm{+ N_2H_4 \cdot HCl.}$$

$$(R_1 = CH_3,\ C_2H_5; \quad R_2 = CH_3,\ C_2H_5,\ C_4H_9)$$

The four simplest 5,5-dialkylpyrazolines described in detail for the first time (Table 1) are colorless liquids, rapidly turning yellow in air but stable in a nitrogen atmosphere, with a characteristic odor reminiscent of pyridine.* The yields of pyrazolines were 43-63%; thus the new reaction has preparative value, especially since the prospects for using known methods for the synthesis of 5,5-dialkylpyrazolines are limited (an attempt to obtain 5,5-dimethylpyrazoline by condensation of β,β-dimethylacrolein with hydrazine hydrate was unsuccessful).

The structure of the carbon skeleton of the pyrazolines was confirmed, using the 5,5-dimethyl derivative as an example, by exhaustive methylation and ammonitrile cleavage (^{2}) to β,β-dimethylacrylonitrile and dimethylamine:



$$(CH_3)_2C\begin{matrix}CH_2-CH\\ \|\\ N\\ \backslash NH/\end{matrix}\xrightarrow[K_2CO_3]{2CH_3J}C_7H_{15}N_2J\xrightarrow[t^\circ]{KOH}\begin{matrix}CH-C\\ \|\qquad\equiv\\ C\qquad N\end{matrix}H_3C\,/\,CH_3+(CH_3)_2NH.$$

---

* In a recently published brief note (^{1}), 5,5-dimethylpyrazoline is mentioned as a by-product of the interaction of isoprene with sodium hydrazide and hydrazine, but no data confirming its structure are reported.

The structure of the synthesized 5,5-dialkyl-Δ^2-pyrazolines is also confirmed by NMR spectra, which will be published and discussed in a separate communication.

The formation of Δ^2-pyrazolines from tertiary acetylenic chlorides and hydrazine apparently results from isomerization of some initial products (possibly acetylenic hydrazines). In this connection it was of interest to determine whether the synthesized Δ^2-pyrazolines contain admixtures of isomers. Gas-liquid chromatograms of the products obtained* showed the presence of impurities with shorter retention times in amounts from 2.5 to 10.5% (Table 1). In the case of dimethylacetylene chloromethane, by lowering the condensation temperature and distilling the reaction mixture very slowly at atmospheric pressure, it was possible to increase significantly the content of the low-boiling product, to which, on the basis of NMR and IR spectroscopic data, the structure of the hitherto unknown 5,5-dimethyl-Δ^1-pyrazoline should be assigned.

Experimental Part

Tertiary acetylenic chlorides were obtained from alcohols by the action of concentrated hydrochloric acid in the presence of copper and cuprous chloride (^{3}). The constants and yields of the compounds introduced into the reaction with hydrazine are given in Table 2.

Reaction of acetylenic chlorides with hydrazine. Into a 200-ml round-bottom flask equipped with a reflux condenser, dropping funnel, thermometer, and stirrer were placed 33.4 g

* The separation was carried out on a UKh-1 chromatograph with a two-meter column (13% tricyanoethoxypropane on INZ-600 support) in a helium atmosphere.

Table 1

5,5-Dialkylpyrazolines synthesized from tertiary acetylenic chlorides

Name	Empirical formula	B.p., °C (mm)	d_4^{20}	n_D^{20}	n_C^{20}	ΔT_C^{20}	$\omega F C D$	MR_D^*, found	MR_D^*, calculated	EM_D	M^{**}, found	M^{**}, calculated	$N, \%$, found	$N, \%$, calculated	$C, \%$, found	$C, \%$, calculated	$H, \%$, found	$H, \%$, calculated	Yield, %	Content of main component, %
5,5-Dimethylpyrazoline	$C_5H_{10}N_2$	67.0 (40)	0.9214	1.4591	1.4563	136.2	23.08	29.03	29.35	−0.32	97.8; 99.9	98.15	28.94; 28.69	28.56	60.96; 61.06	61.18	10.41; 10.34	10.27	64.5	95.1
5-Ethyl-5-methylpyrazoline	$C_6H_{12}N_2$	85.1 (40)	0.9260	1.4641	1.4614	103.2	22.23	33.45	33.93	−0.48	115.2; 117.6	112.2	25.47; 25.37	24.98	64.46; 64.47	64.18	10.61; 10.90	10.78	63.0	96.4
5,5-Diethylpyrazoline	$C_7H_{14}N_2$	93.2 (28)	0.9298	1.4695	1.4660	101.4	21.63	37.93	38.51	−0.58	128.5; 127.6	126.2	22.18; 22.40	22.20	66.66; 66.70	66.61	11.35; 11.15	11.18	55.5	97.5
5-Methyl-5-*n*-butylpyrazoline	$C_8H_{16}N_2$	69.0 (2)	0.9032	1.4624	1.4597	96.3	21.14	42.70	43.09	−0.39	139.7; 140.8	140.2	20.24; 20.49	19.98	68.46; 68.37	68.51	11.56; 11.64	11.50	43.5	89.4

* By refraction of the ordinary ray.
** Cryoscopic in benzene.

Table 2

Tertiary acetylenic chlorides used for the synthesis of pyrazolines

Formula	B.p., °C (pressure, mm)	n_D^{20}	Yield, %	Literature data: b.p., °C	Literature data: n_D^{20}
$HC \equiv C-C(Cl)(CH_3)-CH_3$	73.5−74.5 (740)	1.4191	49−53	73−76$^{(3)}$	1.4156$^{(3)}$
$HC \equiv C-C(Cl)(CH_3)-C_2H_5$	103.5−105.5 (756)	1.4320	50−53	53−56$^{(3)}$ (128)	1.4302$^{(3)}$
$HC \equiv C-C(Cl)(C_2H_5)-C_2H_5$	72.0−73.0 (99)	1.4428	70	70−72$^{(3)}$ (100); 73−76 (100)$^{(8)}$	1.4389$^{(3)}$; 1.4437$^{(8)}$ (18.5°)
$HC \equiv C-C(Cl)(CH_3)-CH_2CH_2C_2H_5$	47.0−48.0 (14)	1.4394	83	−*	−

* Not described in the literature. Found, %: C 66.65, 66.52; H 9.12, 9.16. $C_8H_{13}Cl$. Calculated, %: C 66.43; H 9.06.

(1 mole) of 96% hydrazine is heated on a water bath to 40–50°* and, with vigorous stirring, 0.5 mole of the tertiary acetylenic chloride is added at such a rate that the mixture boils not too strongly and the reaction does not get out of control. This usually takes about half an hour. Then, without interrupting the stirring, the mixture is heated for two hours at 140–150°. On cooling, the lower layer of the reaction mixture crystallizes completely. The crystals have m.p. 94° (after recrystallization from methyl alcohol) and are hydrazine monochlorohydrate, obtained in almost theoretical amount (about 32 g).

Found, %: Cl 51.48, 51.52 (by Volhard)
$N_2H_4 \cdot HCl$. Calculated, %: Cl 51.75

The yellowed upper layer is decanted from the crystals and distilled in vacuum on a 12-plate column. The characteristics of the principal fractions are given in Table 1. Compounds of composition $C_{nH_{2n}}N_2$ may, generally speaking, belong to one of three types: 1) saturated bicyclic, 2) monocyclic with one double bond (C=C, C=N, N=N), 3) acyclic with one triple or two double bonds.

The **molecular refractions** of the compounds obtained make it possible to exclude any acyclic structures. Thus, for example, the compound $C_5H_{10}N_2$ obtained from dimethylacetylenylchloromethane has MR_D 29.03, whereas calculation gives, for acetylenic hydrazines and amino nitriles of this composition, MR_D 30.3 and 28.5, respectively (from Fogel bond refractions). The latter of these numbers approaches the experimental value, but for amino nitriles one would expect considerably lower refractive indices (n_D 1.42–1.43) and smaller dispersions (ω_{FCD} 19–20)—cf. (4). The additive value of the molecular the refraction of acetylenic hydrazines (30.3) considerably exceeds the experimental value, and for compounds with two double bonds the additive values are still larger, so that the possibility of formation of unsaturated hydrazines and hydrazones is excluded. The experimental values of MR_D are close to those calculated for Δ^1- and Δ^2-pyrazolines (29.20 and 29.35, respectively), but differ considerably from the refraction of Δ^3-pyrazolines (30.12). A depression on the order of 0.3-0.5 is apparently associated with the presence of a quaternary carbon atom in the pyrazoline ring, as has already been noted by Auwers(5). Molecular refractions, however, do not exclude the possibility of unknown bicyclic structures, for which MR_D values close to the refraction of pyrazolines may be expected, and definitive confirmation of the pyrazoline structure is provided by IR spectroscopy.

The IR spectra of the compounds obtained* contain strong absorption bands at 1590 cm^{-1}, corresponding to the stretching vibrations of C = N, bands of the stretching vibrations of hydrogen in the HC = N groups of pyrazolines at 3040–

* In the case of the simplest acetylenic tertiary chloride (dimethylacetylenylchloromethane), heating is not required.

3050 cm^{-1} (6), and strong bands at 3270-3290 cm^{-1}, which should be assigned to NH stretching vibrations. Bands of acetylenic, allenic, and nitrile groups in the region 1900-2300 cm^{-1} are absent. The totality of these data corresponds to the structure of Δ^2-pyrazolines.

Iodomethylation of 5,5-dimethyl-Δ^2-pyrazoline. To a mixture of 24 g (0.245 mole) of pyrazoline, 34 g of potassium hydroxide, and 8 ml of water, 19.5 g (0.49 mole) of methyl iodide was slowly added dropwise, and warming began immediately. After heating for one hour on a boiling water bath, the reaction mixture was transferred to a dish, dried in a vacuum desiccator over sulfuric acid to constant weight, and extracted for 20 h with chloroform in a Soxhlet extractor. The dark chloroform solution was evaporated, and the residue was recrystallized from a mixture of methanol and ethyl acetate (1:1). Yield: 14.5 g (23.3%) of light-yellow crystals, mp 162° (decomp.).

Found, %: I 50.41, 50.19
$C_7H_{15}N_2J$. Calculated, %: I 49.94

Decomposition of the iodide with alkali. To a solution of 13 g (0.05 mole) of the salt in 10 ml of water was added a one-and-a-half-fold excess of 50% KOH solution. The organic layer was salted out with potassium hydroxide and distilled from a flask with a dephlegmator. The gas evolved on heating was collected in a water trap. The heterogeneous distillate was dried with potassium hydroxide and distilled. Obtained: 3.6 g (78%) of β,β-dimethylacrylonitrile—a colorless liquid with bp 141-142° at 762 mm, d_4^{20} 0.8421, n_D^{20} 1.4390. MR_D found 25.33. $C_4H_7C\equiv N$. Calculated 24.61. EM_D 0.72.

The aqueous solution from the trap was neutralized with hydrochloric acid and evaporated. The precipitated salt, after recrystallization from methanol, had mp 170.5°. Literature data for dimethylamine hydrochloride (7): mp 171°.

Leningrad State University
named after A. A. Zhdanov

Received
10 X 1963

REFERENCES

[1] Th. Kaufmann, H. Müller, Ch. Kosel, *Angew. Chem.*, **74**, 248 (1962).
[2] B. V. Ioffe, K. N. Zelenin, DAN, **144**, 1303 (1962).
[3] G. F. Hennion, A. P. Boiselle, *J. Org. Chem.*, **26**, 725 (1961).
[4] B. V. Ioffe, K. N. Zelenin, ZhOKh, **33**, No. 10 (1963).
[5] K. Auwers, H. Heimke, *Ann. Chem.*, **458**, 175 (1927).
[6] B. V. Ioffe, K. N. Zelenin, ZhOKh, **33**, 3575 (1963).
[7] H. A. Bruson, T. W. Reiner, *J. Am. Chem. Soc.*, **65**, 18 (1943).
[8] I. Heilbron, G. M. Bunbury, *Dictionary of Organic Compounds*, 1, 1949, p. 886.
[9] T. A. Favorskaya, I. A. Favorskaya, ZhOKh, **10**, 451 (1940).

* Recorded on a Nippon Bunko DS-301 double-beam spectrophotometer in cells of constant thickness 25 μ.