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## Abstract

## Full Text

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# CLEAVAGE OF THE PYRAZOLINE RING DURING ACYLATION

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Pyrazolines that have no substituent at the nitrogen atom can, under the action of acid anhydrides or acid chlorides, be converted into the corresponding N-acylpyrazolines ([1,2]). However, it was observed that acylation of pyrazolines sometimes proceeds anomalously. Thus, Freideberg and Stolz ([3]), on benzoylating 5-methyl-3-phenylpyrazoline, obtained, instead of 1-benzoyl-5-methyl-3-phenylpyrazoline, a substance with m.p. 214°, the structure of which they did not investigate. In benzoylating 3,5,5-trimethylpyrazoline (I) by the Schotten-Baumann method, we isolated two substances. One of them (A) had m.p. 236° and dissolved in aqueous alkali, while the other (B) had m.p. 93° and did not dissolve in alkalis.

In 1894, Curtius and Wirsing ([4]), and later Frey and Hofmann ([5]), on the action of benzoyl chloride on this pyrazoline (I), obtained substance A, which they described as 1-benzoyl-3,5,5-trimethylpyrazoline (II). In 1928, Lochte and co-workers ([6]) reported that benzoylpyrazoline (II), having m.p. 236°, is formed during the cyclization of acetone azine (III) under the action of benzoyl chloride. However, substance A (m.p. 236°), taken by the above-mentioned authors to be benzoylpyrazoline (II), is in fact N,N′-dibenzoylhydrazine (IV), as proved in our experiments, which were confirmed by an independent synthesis and by comparison of absorption spectra. Substance B (m.p. 93°), not isolated by the previous authors, is the desired benzoylpyrazoline (II).

It turned out that the reaction between benzoyl chloride and pyrazoline (I), depending on its conditions, can be directed either toward complete cleavage of the pyrazoline ring with formation of dibenzoylhydrazine (IV), or only toward normal benzoylation. If pyrazoline is introduced into an excess of benzoyl chloride in the presence of aqueous alkali, only dibenzoylhydrazine (IV) is obtained. With the reverse order of mixing of the components, or in the complete absence of moisture, only benzoylpyrazoline (II) is formed. It is interesting that with acetone azine (III) the reaction proceeds analogously, giving in anhydrous media only benzoylpyrazoline (II), whereas in the presence of moisture and an excess of benzoyl chloride the azine is cleaved with formation of dibenzoylhydrazine (IV).

(scheme)
(I), (II), (III), (IV)

During cleavage of acetone azine (III), in addition to dibenzoylhydrazine (IV), acetone is formed, identified as the semicarbazone, and from pyrazoline (I), the oxide of mesityl was similarly obtained, and was also converted into the semicarbazone.

The capacity for comparatively easy cleavage of the C—N bond in pyrazolines is similar to the analogous properties of their structural analogs—$\beta$-aminoketones, the mechanism of elimination of the amino group from which has been systematically studied ($^7$). In the presence of a constant excess of free pyrazoline, or under anhydrous conditions, hydrogen chloride is eliminated and acylation occurs; under the action of hydroxyl ions (in an aqueous-alkaline medium) and with an excess of benzoyl chloride, a proton is eliminated from position 4, followed by opening of the ring.

$$\text{(I)} \xrightarrow{C_6H_5COCl} \text{protonated benzoyl derivative} \xrightarrow{-H^+} \text{(II)}$$

$$\text{protonated benzoyl derivative} \xrightarrow{-H^+} CH_3{-}C(=N{-}NHCOC_6H_5){-}CH=C(CH_3)_2$$

$$CH_3{-}C(=N{-}NHCOC_6H_5){-}CH=C(CH_3)_2 \longrightarrow \underset{\text{(IV)}}{C_6H_5CONHNHCOC_6H_5} + CH_3COCH=C(CH_3)_2$$

The formation of dibenzoylhydrazine (IV) was also observed by us in the benzoylation of 4-ethyl-5-propylpyrazoline. This action of benzoyl chloride is not specific to this acylating agent. Thus, under the action of caproyl chloride on pyrazoline (I) or on 3-methyl-5-phenylpyrazoline, symmetrical dicaproylhydrazine was isolated.

Benzoylpyrazoline (II) is resistant to the action of benzoyl chloride (under various conditions), but 1-benzyl-3,5,5-trimethylpyrazoline (V) is cleaved rather easily, forming N,N′-dibenzoylbenzylhydrazine (VI).

$$\text{(V)} \xrightarrow[(H_2O)]{C_6H_5COCl} C_6H_5CONHNCOC_6H_5\,(CH_2{-}C_6H_5) \quad \text{(VI)}$$

Acid anhydrides acylate pyrazolines without causing ring opening, although, as is known ($^8$), azines can be cleaved by them.

## Experimental Part

**1-Benzoyl-3,5,5-trimethylpyrazoline (II).** To a solution of 45.4 g (0.2 mole) of benzoic anhydride in 50 ml of absolute benzene, 11.2 g (0.1 mole) of 3,5,5-

trimethylpyrazoline (I) was added. The benzene solution was washed with 2 N sodium hydroxide, dried, the solvent was distilled off, and the residue was recrystallized from absolute alcohol. Yield 18.7 g (83% of theory), m.p. 92.5–93°.

Found, %: C 72.25; 72.37; H 7.57; 7.65
$C_{13}H_{16}ON_2$. Calculated, %: C 72.19; H 7.45

The absorption spectrum in methyl alcohol solution has $\lambda_{\max} = 247$ m and $\lg \varepsilon = 4.348$.

**Reaction of 3,5,5-trimethylpyrazoline (I) with benzoyl chloride.** Into a mixture of 11.2 g (0.1 mole) of pyrazoline (I) and 50 ml of 2 N sodium hydroxide, 16 g (0.12 mole) of benzoyl chloride was introduced dropwise. After 10 minutes of stirring, a white mass was formed, which gradually crystallized. The crystals were washed repeatedly with cold 2 N sodium hydroxide solution and with hot water, and then treated with 100 ml of 40% sodium hydroxide. The residue was recrystallized from absolute alcohol. Yield of 1-benzoyl-3,5,5-trimethylpyrazoline, 6.4 g (29.6% of theory), m.p. 92–92.5°. It gives no depression of the melting point with 1-benzoyl-3,5,5-trimethylpyrazoline. Upon neutralization of the alkaline extract

3.3 g (22.4% of theory) of 1,2-dibenzoylhydrazine (IV) was obtained. M.p. 234-236°. Literature data (9): m.p. 236°. No depression of the melting point of a mixture with an authentic sample of 1,2-dibenzoylhydrazine was observed. The absorption spectrum in methanol solution has $\lambda_{\max} = 232$ mμ and $\lg \varepsilon = 4.279$.

On slow addition of 11 g of pyrazoline (I) to a well-stirred mixture of 14 g (0.1 mole) of benzoyl chloride, 25 ml of benzene, and 7 g of moist crystalline soda, and after analogous work-up, only 1,2-dibenzoylhydrazine was isolated. Yield 11.8 g (97% of theory), m.p. 236°. When benzoyl chloride is added under the same conditions to pyrazoline (I) in the presence of benzene and moist soda, only 1-benzoyl-3,5,5-trimethylpyrazoline is formed, in 67.5% yield of theory. M.p. 92.5-93°. If the reaction between benzoyl chloride and 3,5,5-trimethylpyrazoline is carried out under anhydrous conditions, with subsequent distillation of the reaction mass in vacuo, benzoylpyrazoline (II) is obtained in 74% yield of theory. B.p. 145-149° (4 mm), m.p. 92-93°. The order of mixing of the starting materials in this case is immaterial. The semicarbazone of mesityl oxide was isolated by treatment with semicarbazide of the ether extracts from the wash waters obtained in the cleavage of the pyrazoline. M.p. 162°. Literature data (10): m.p. 163-164°.

**Reaction of 4-ethyl-5-propylpyrazoline with benzoyl chloride.** To 7 g (0.05 mole) of 4-ethyl-5-propylpyrazoline (11) (b.p. 110-112° (22 mm); $n_D^{20}$ 1.4682; $d_4^{20}$ 0.9130; $MR_D$ 42.71; for $C_8H_{16}N_2$ calculated $MR_D$ 42.81), in the presence of 5 g of soda, 9 g (0.07 mole) of benzoyl chloride was added. The separated oil was washed free of benzoic acid and twice distilled in vacuo. 5.9

g (48.3% of theory) of 1-benzoyl-4-ethyl-5-propylpyrazoline was obtained; b.p. 180–181° (10 mm); $n_D^{20}$ 1.5689; $d_4^{20}$ 1.0357; $MR_D$ 71.18; for $C_{15}H_{20}ON_2$ calculated $MR_D$ 71.62.

Found, %: N 12.83; 12.65
$C_{15}H_{20}ON_2$. Calculated, %: N 12.45

If pyrazoline is added to the reaction mixture, 1,2-dibenzoylhydrazine is formed. Yield 21% of theory.

**Reaction of 3,5,5-trimethylpyrazoline with caproyl chloride.** To 7 g (0.05 mole) of caproyl chloride in the presence of 5 g of moist soda, 5.6 g (0.05 mole) of pyrazoline (I) was added. After the usual work-up, 1,2-dicaproylhydrazine was isolated. Yield 4.6 g (80.6% of theory), m.p. 159° (from alcohol). Literature data (12): m.p. 159°. No depression of the melting point of a mixture with an authentic sample of 1,2-dicaproylhydrazine (12) was observed.

**Reaction of 3-methyl-5-phenylpyrazoline with caproyl chloride.** When the reaction was carried out under analogous conditions, from 14 g (0.1 mole) of caproyl chloride and 16 g (0.1 mole) of 3-methyl-5-phenylpyrazoline, 7.1 g (62% of theory) of dicaproylhydrazine, m.p. 159°, was obtained.

**Reaction of 1-benzyl-3,5,5-trimethylpyrazoline (V) with benzoyl chloride.** A mixture of 11.2 g (0.08 mole) of benzoyl chloride, 7.4 g (0.036 mole) of pyrazoline (V), and 4.5 g of crystalline soda was heated to boiling and then, after cooling, treated in the usual manner. Yield of $N, N'$-dibenzoylbenzylhydrazine: 1.9 g (16% of theory), m.p. 148° (from alcohol). Literature data (13): m.p. 148°. No depression of the melting point of a mixture with an authentic sample of $N, N'$-dibenzoylbenzylhydrazine (13) was observed.

**Reaction of acetone azine (III) with benzoyl chloride.** To 14 g (0.1 mole) of benzoyl chloride was gradually added a solution of 11.2 g of acetone azine in 25 ml of benzene. Then 30 ml of water was added to the reaction mixture and, after the usual work-up, dibenzoylhydrazine (IV) was isolated. Yield 17.3 g (72.5% of theory), m.p. 235–236°. If the reaction ···

distilled off immediately in vacuo, then in this case benzoylpyrazoline (II) is obtained. Yield 2.7 g (12.4% of theory), b.p. 145–147° (4 mm), m.p. 92–93°. From the wash waters obtained in the cleavage of azine, acetone semicarbazone was isolated by the action of semicarbazide, m.p. 185–186°. Literature data (⁀14): m.p. 187°.

**1-Propionyl-3,5,5-trimethylpyrazoline.** To 11.2 g (0.1 mole) of pyrazoline (I), in the presence of 5 g of crystalline soda, 10.6 g (0.1 mole) of propionic acid chloride was added dropwise. The reaction mass was washed with 2 N sodium hydroxide and extracted with ether. By distillation, 7.2 g (43%) of 1-propionyl-3,5,5-trimethylpyrazoline was isolated, b.p. 125–127° (21 mm); $n_D^{20}$ 1.4779; $d_4^{20}$

0.9813; $MR_D$ 48.39; for $C_9H_{16}ON_2$ calculated $MR_D$ 48.60.

Found %: N 16.93; 16.97

$C_9H_{16}ON_2$. Calculated %: N 16.66

**1-Butyryl-3,5,5-trimethylpyrazoline.** Obtained from 11.2 g (0.1 mole) of pyrazoline (I) and 11 g (0.1 mole) of butyric acid chloride analogously to the preceding. Yield 8.3 g (45.7%), b.p. 121-123° (13 mm); $n_D^{20}$ 1.4665; $d_4^{20}$ 0.9663; $MR_D$ 52.22; for $C_{10}H_{18}ON_2$ calculated $MR_D$ 52.43.

Found %: C 66.75; 66.76; H 10.04; 10.11

$C_{10}H_{18}ON_2$. Calculated %: C 66.44; H 9.95

**1-Isovaleryl-3,5,5-trimethylpyrazoline.** Obtained likewise from 4.5 g (0.04 mole) of pyrazoline (I) and 7.2 g (0.06 mole) of isovaleric acid chloride in 25 ml of benzene. Yield 3.3 g (42.5%); b.p. 108-110° (10 mm); $n_D^{20}$ 1.4712; $d_4^{20}$ 0.9520; $MR_D$ 57.65; for $C_{11}H_{20}ON_2$ calculated $MR_D$ 57.84.

Found %: N 14.45; 14.33

$C_{11}H_{20}ON_2$. Calculated %: N 14.27

**1-(m-Nitrobenzoyl)-3,5,5-trimethylpyrazoline.** Obtained analogously from 4.5 g (0.04 mole) of pyrazoline (I) and 8 g (0.05 mole) of *m*-nitrobenzoic acid chloride in the form of a thick oil, which crystallized on standing. Yield 6.2 g (72.3%), m.p. 99.5-100° (from alcohol).

Found %: N 16.24; 16.34

$C_{13}H_{15}O_3N_3$. Calculated %: N 16.09

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