## EXPERIMENTAL

Indolo[2,3-b]quinoxalines I-III and 5-octadecylindolo[2,3-b]quinoxaline were obtained by the methods described in [1,2]. The electronic spectra of solutions in ethanol were recorded with a Specord UV-vis spectrophotometer. Quantum-chemical calculations of the ground and excited states of the neutral tautomeric forms of I-III, indole, and quinoxaline were made by the MO LCAO method within the PPP approximation with allowance for the configuration interaction by means of our program, which realizes the Dewar algorithm [4] with optimization of the internuclear distances with respect to the minimum of the atomization energy. In the calculations it was assumed that the molecules are planar, whereas the geometries adopted in [8, 9] were used for the quinoxaline and indole fragments, respectively. Calculations by the Huckel MO method were made by means of the following parameters: $h_N^{\bullet} = 0.4$, $h_N^{\bullet\bullet} = 2.0$, $k_{C-C} = k_{C-N} = 0.7$, and $k_{C=C} = k_{C=N} = 1.0$. 1.0.

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# SYNTHESIS AND RING-CHAIN TAUTOMERISM OF SALTS OF ALKYLIDENE(ARYLIDENE) DERIVATIVES OF AMIDRAZONES


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UDC 547.298.62'792.07:541.621.2:543.422



A number of salts of alkylidene(arylidene) derivatives of amidrazones was obtained by the reaction of S-methylthioamidium iodides with hydrazones of monocarbonyl compounds. According to the $^1H$ and $^{13}C$ NMR data, these compounds in solutions are capable of ring-chain tautomerism of the 1-alkylideneamidrazone—1,2,4-triazoline type. The position of the equilibrium is determined chiefly by steric interactions of the substituents attached to the C—$N_2$ bond.


We have previously found [1] that acetone hydrazone and methylhydrazone react smoothly with S-methylthioamidium iodide to give the corresponding salts of 2-propylidene derivatives of acetamidrazone. In the present paper we report additional results of an investigation of the reaction of hydrazones with thioamidium iodides, which are of interest in connection with the problem of the structures of the final products, which are capable of ring-chain tautomeric transformations of the 1-alkylideneamidrazone—1,2,4-triazoline type [1,2]. The information on the factors that determine the position of the equilibria in systems of this type can be used to ascertain the principles of ring-chain transformations in series of related compounds, viz., thioacylhydrazones [3], semicarbazones [4, 5], and thiosemicarbazones [6].


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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1264-1267, September, 1982. Original article submitted November 23, 1981.




0009-3122/82/1809-0978$07.50

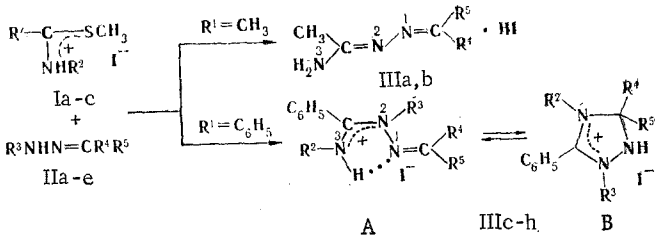
TABLE 1. Salts III

| Compound | mp, °C | Found, % | | | | Empirical formula | Calc., % | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | C | H | Ia | N | | C | H | I | N |
| III a | 166—168 b | 34,8 | 4,3 | 45,7 | 15,2 | $C_8H_{12}IN_3$ | 34,7 | 4,4 | 45,8 | 15,2 |
| III b | 117—119 c | 25,0 | 5,2 | 52,8 | 17,4 | $C_5H_{12}IN_3$ | 24,9 | 5,0 | 52,6 | 17,4 |
| III c | 224—226 d | 48,0 | 4,1 | 36,2 | 12,0 | $C_{14}H_{14}IN_3$ | 47,9 | 4,0 | 36,1 | 12,0 |
| III d | 205—207 c | 39,9 | 4,7 | 42,0 | 13,7 | $C_{10}H_{14}IN_3$ | 39,6 | 4,7 | 41,9 | 13,9 |
| III e | 146—148 b | 45,2 | 5,7 | 36,6 | 12,1 | $C_{13}H_{20}IN_3$ | 45,2 | 5,8 | 36,8 | 12,2 |
| III f | 208—210 e | 49,2 | 4,3 | 34,6 | 11,4 | $C_{15}H_{16}IN_3$ | 49,3 | 4,42 | 34,7 | 11,5 |
| III g | 178—180 e | 41,6 | 5,2 | 40,2 | 13,4 | $C_{11}H_{16}IN_3$ | 41,7 | 5,1 | 40,0 | 13,3 |
| III h | 199—201 c | 41,8 | 5,1 | 39,9 | 13,5 | $C_{11}H_{16}IN_3$ | 41,7 | 5,1 | 40,01 | 13,2 |

[a]By the Volhard method. [b]From ethyl acetate. [c]From acetonitrile. [d]From methanol. [e]From a mixture of acetonitrile with ethyl acetate.

With this in mind, we examined the reaction of S-methylthioacet- (Ia) and S-methylthiobenzamidium (Ib,c) iodides with a series of hydrazones (IIa-e) of monocarbonyl compounds. We found that in all cases the reaction of methanol solutions of the reagents proceed quantitatively at room temperature with the liberation of a molecule of methanethiol and the formation of products with the required compositions (Table 1).

An analysis of the spectral characteristics (Table 2) and a comparison with the literature data [1, 7] show that acetamidrazone derivatives (IIIa,b) exist in the linear form and have an E configuration relative to the $C{=}N_{(2)}$ bond. The absence of an intramolecular hydrogen bond follows from the pronounced temperature dependence of the chemical shifts of the protons attached to the $N_{(3)}$ atom in the PMR spectra and the presence of an intense bond of NH stretching vibrations at 3460 $cm^{-1}$ in the IR spectrum.



I a $R^1{=}CH_3$, $R^2{=}H$; b $R^1{=}C_6H_5$, $R^2{=}H$; c $R^1{=}C_6H_5$, $R^2{=}CH_3$; II a $R^3{=}R^4{=}H$, $R^5{=}C_6H_5$; b $R^3{=}H$, $R^4{=}R^5{=}CH_3$; c $R^3{=}H$, $R^4{=}CH_3$, $R^5{=}t\text{-}C_4H_9$; d $R^3{=}H$, $R^4{=}CH_3$, $R^5{=}C_6H_5$; e $R^3{=}R^4{=}R^5{=}CH_3$; III a $R^2{=}R^3{=}R^4{=}H$, $R^5{=}C_6H_5$; b $R^2{=}R^3{=}H$, $R^4{=}R^5{=}CH_3$; c $R^2{=}R^3{=}R^4{=}H$, $R^5{=}C_6H_5$; d $R^2{=}R^3{=}H$, $R^4{=}R^5{=}CH_3$; e $R^2{=}R^3{=}H$, $R^4{=}CH_3$, $R^5{=}t\text{-}C_4H_9$; f $R^2{=}R^3{=}H$, $R^4{=}CH_3$, $R^5{=}C_6H_5$; g $R^2{=}R^4{=}R^5{=}CH_3$, $R^3{=}H$; h $R^2{=}H$, $R^3{=}R^4{=}R^5{=}CH_3$

Compounds IIIa,b do not display a capacity for ring-chain tautomerism, evidently as a consequence of the unfavorable spatial orientation of the $C{=}N_{(1)}$ bond and the $NH_2$ group.

The $N_{(1)}$ and $N_{(2)}$ atoms should have comparable basicities, and the "acidic" proton ($R^3$ = H, IIIa,b) may be localized on either of them; rapid migration between them is also possible. Two bands of stretching vibrations of C=N bonds at 1615 and 1640 $cm^{-1}$, which are shifted approximately identically to the high-frequency region on passing to hydriodide IIIa (1660 and 1680 $cm^{-1}$), are observed in the IR spectrum of 1-(2-propylidene)acetamidrazone [7]. In the PMR spectrum of this salt the "acidic" proton is not localized even when the sample is cooled to −30°C. Thus the problem regarding the center of protonation in salts IIIa,b remains open to discussion. The facile hydrolysis of salts IIIa,b to acetamidrazonium iodide can be regarded only as indirect evidence in favor of $N_1$ protonation.

According to the PMR spectroscopic data (freshly prepared solutions), benzamidrazone derivatives IIIc-g in the crystalline state also exist in linear form A. As a consequence of an increase in the steric interactions relative to the $C{=}N_{(2)}$ bond, a configuration with a syn orientation of the $N_{(1)}$ and $N_{(3)}$ atoms (the Z isomer), which is stabilized by an intramolecular hydrogen bond, is fixed in these compounds. The formation of the latter configura-

tion is proved by the presence of a diffuse band of NH stretching vibrations at 3250 $cm^{-1}$ in the IR spectra and determines localization of the "acidic" proton on the $N_{(2)}$ atom.

A ring-chain tautomeric equilibrium (A ⇄ B) is established in solutions in $d_6$-DMSO and $D_7$-DMF after 24 h, as evidenced by the appearance of the corresponding signals in the $^1H$ and $^{13}C$ NMR spectra. Thus a high-field singlet of methyl groups in the 3 position at 1.82 ppm appears in the PMR spectrum of an equilibrium solution of 1-(2-propylidene)benzamidrazonium iodide (IIId). The presence of a signal of the $C_{(3)}$ atom of the cyclic tautomer at 80 ppm is characteristic for the $^{13}C$ NMR spectrum [2].

We have previously described 1-(2-propylidene)benzamidrazone hydrochloride [2], 15% of which in $d_6$-DMSO solution exists in the form of 3,3-dimethyl-5-phenyl-2,3-dihydro-1,2,4-triazolium chloride. Replacement of the anion by iodide (IIId), trifluoroacetate, or picrate ions is accompanied by a decrease in the percentage of the cyclic form to 7%.

Variation of the steric and electronic properties of the substituents in the alkylidene fragment (IIIe,f) has virtually no effect on the position of the tautomeric equilibrium. The quantitative determination of cyclic form B was accomplished by integration of the signals of the methyl (2.27 and 1.97 ppm) and tert-butyl (1.22 and 1.14 ppm) groups for IIIe and the methyl group (2.68 and 2.11 ppm) for the acetophenone derivative (IIIf).

The equilibrium is also insensitive to the introduction of a methyl group relative to the $N_{(3)}$ atom (IIIg), this evidently indicates an insignificant increase in the steric interactions relative to the partially double $C{=}N_{(3)}$ bond in the linear form. The methyl groups in the 3 position of cyclic form B give a singlet at 1.74 ppm in the $^1H$ NMR spectrum and a signal at 22.5 ppm in the $^{13}C$ NMR spectrum. In addition, signals corresponding to 3,3,4-trimethyl-5-phenyl-2,3-dihydro-1,2,4-triazolium iodide are observed in the $^{13}C$ NMR spectrum at 29.4 ($4\text{-}CH_3$), 79.8 [$C_{(3)}$], and 164.3 ppm [$C_{(5)}$].

On the other hand, IIIh, which contains a methyl group attached to the $N_{(2)}$ atom, has the 1,3,3-trimethyl-5-phenyl-2,3-dihydro-1,2,4-triazolium iodide structure in the crystalline state and immediately after dissolving. In the equilibrium state the percentage of noncyclic form A, to which the signals at 2.25 and 2.23 ppm (syn- and anti-methyl groups in the alkylidene fragment), 3.30 [$CH_3N_{(2)}$], and 8.79 and 9.40 ppm ($NH_2$) correspond in the PMR spectrum, is 18%.

Consequently, the tautomeric equilibrium of 1-alkylideneamidrazone-1,2,4-triazoline is extremely sensitive to steric interactions relative to the $C{=}N_{(2)}$ bond. The presence of a substituent attached to the $N_{(2)}$ atom favors the cyclic form, while the linear form predominates in its absence.

Thus the reaction of hydrazones with thioamidium iodides can be regarded as a convenient and universal method for the synthesis of alkylidene derivatives of amidrazones, in the study of which one should take into account their tendency to exist and, consequently, to react in the ring 1,2,4-triazoline form.

## EXPERIMENTAL

The IR spectra of 1% solutions of the compounds in DMSO and $CHCl_3$ were obtained with a UR-20 spectrometer at 700-3600 $cm^{-1}$. The PMR spectra of ∿10% solutions in $d_7$-DMF at −40 to +80°C were recorded with a Tesla BS-497 spectrometer (100 MHz) with hexamethyldisiloxane as the internal standard. The $^{13}C$ NMR spectra of ∿20% solutions in $d_6$-DMSO were recorded with a Varian CFT-20 spectrometer (20 MHz) under conditions of noise decoupling of the protons and monoresonance with tetramethylsilane as the internal standard. The marked preponderance of one of the tautomeric forms for IIIc-h required a large number of scannings to detect the signals of both forms in the $^{13}C$ NMR spectra. This was carried out only for IIId,h; only the signals of the predominant tautomer are presented in Table 2.

The benzaldehyde, acetone, and acetophenone hydrazones were synthesized by the method in [10], pinacolone hydrazone was synthesized by the method in [11], and acetone methylhydrazone was synthesized by the method in [12].

Hydriodide Salts of 1-Alkylidene(arylidene)amidrazones (IIIa-h, Table 1). A solution of 0.1 mole of the corresponding hydrazone in 50 ml of methanol was added with stirring and cooling with ice water to 0.1 mole of thioamidium iodide Ia-c [8,9] in 50 ml of absolute methanol, and the mixture was stirred with cooling for 2 h and allowed to stand for 24 h. The solvent was removed *in vacuo*, and the residue was recrystallized.

TABLE 2. $^{1}H$ and $^{13}C$ NMR spectra of III

| Compound (form; concn., %) | $\delta_H$, ppm (J, Hz) | | | | | | $\delta_C$, ppm (J, Hz) | | |
|---|---|---|---|---|---|---|---|---|---|
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | NH | $C=N_{(1)}$ | $C=N_{(2)}$ | Other signals |
| III a (A; 100) | 2,56 | 9,61 | [a] | 8,73 | 7,4—8,2 m | 9,85 | 152,0 ($^1J_{CH}$=163,5) | 161,5 ($^2J_{CH}$=6,0) | 16,8 ($^1J_{CH}$=132,0), 128,5, 128,8, 131,7, 132,2 |
| III b (A; 100) | 2,49 | 9,11 | [a] | 2,16 | 2,07 | 9,55 | 169,8 ($^2J_{CH}$=6,6) | 161,5 ($^2J_{CH}$=5,7) | 17,0 ($^1J_{CH}$=130,5), 20,0 ($^1J_{CH}$=129,0, $^3J_{CH}$=3,2), 25,6 ($^1J_{CH}$=129,0, $^3J_{CH}$=3,2) |
| III c (A; 100) | 7,3—8,4 m | 10,02 | [a] | 8,98 | 7,3—8,4 m | 10,15 | 154,1 ($^1J_{CH}$=166,0, $^3J_{CH}$=4,5) | 160,4 ($^3J_{CH}$=3,0) | 126,2, 128,8, 129,2, 131,9, 132,5, 134,1 |
| III d (A; 93) | 7,5—8,1 m | 9,60 | [a] | 2,30 | 2,17 | 10,75 | 169,2 ($^2J_{CH}$=6,3) | 160,2 ($^3J_{HC}$=4,0) | 19,8, 25,2 |
| III e (A; 95) | 7,4—8,0 m | 9,25 | [a] | 2,27 | 1,22 | 9,35 | 163,1 | 160,9 | 14,5 ($^1J_{CH}$=127,5), 27,3, 50,3 |
| III f (A; 95) | 7,3—8,2 m | 10,12 | 12,50[b] | 2,68 | 7,3—8,2 m | 10,40 | 162,1 | 161,5 | 16,2, 126,7, 128,0, 128,5, 128,9, 129,1, 131,0, 133,7, 136,1 |
| III g (A; 90) | 7,5—7,9 m | 3,03[c] | 11,95 | 2,18 | 2,16 | 9,85 | 166,6 | 160,7 | 19,4, 25,6, 31,6, 125,3, 129,0, 132,5 |
| III h (B, 82) | 7,6—8,0 | 10,85 | 3,47 | 1,66 | | 7,27 | 78,1[d] | 159,6 | 26,5, 39,9, 121,3, 129,9, 134,2 |

[a]The signal is not localized at room temperature. [b]The spectrum at −40°C is presented. [c]Doublet, J = 5.0 Hz. [d]The $C_{(3)}$ atom of the cyclic form.

Let us note that benzylidene derivatives IIIa,c upon recrystallization from methanol precipitated in the form of rather stable complexes with a molecule of alcohol (1:1), which decomposed only upon heating to 100°C *in vacuo* (5 mm) for 30 min.

1-Isopropylidenebenzamidrazone Picrate. The free base [7] was treated with an equivalent amount of a saturated alcohol solution of picric acid to give a product with mp 137-138°C (from $C_2H_5OH$). PMR spectrum: the A form: 2.14 (3H), 2.23 (3H), 7.4-8.0 (m, 5H), and 9.70 ppm (broad s, 2H); the B form: 1.76 ppm (3-$CH_3$). Found: C 47.7, H 4.3, N 20.9%. $C_{10}H_{13}N_3 \cdot C_6H_3N_3O_7$. Calculated: C 47.5, H 4.0, N 20.8%.

1-Isopropylidenebenzamidrazone Trifluoroacetate. This compound was obtained by treatment of the free base with excess trifluoroacetic acid and subsequent drying *in vacuo*. The product was an oil. PMR spectrum: the A form: 2.11 (3H), 2.19 (3H), 7.4-8.0 (5H), 9.37 (1H), and 10.0 ppm (1H); the B form: 1.73 ppm (3-$CH_3$). Found: C 50.0, H 4.7, N 14.5%. $C_{10}H_{13}N_3 \cdot CF_3COOH$. Calculated: C 49.8, H 4.9, N 14.5%.

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