ISOMERIZATION OF 2-ARYL-5,6-TETRAMETHYLENE-3,3,4-TRICYANO-2,3,4,5-TETRAHYDROPYRIDINE-4-CARBOX-AMIDES UNDER THE INFLUENCE OF ACIDS

Ya. S. Kayukov, P. M. Lukin, O. E. Nasakin, V. N. Khrustalev, V. N. Nesterov, M. Yu. Antipin, and A. N. Lyshchikov

When 2-aryl-5,6-tetramethylene-3,3,4-tricyano-2,3,4,5-tetrahydropyridine-4-carboxamides are subjected to the action of acids, they are isomerized, forming either 2-aryl-5,6-tetramethylene-3,3,4-tricyano-1,2,3,4-tetrahydropyridine-4-carboxamides or 3-aryl-1,8-tetramethylene-6-oxo-2,7-diazobicyclo[3.2.1]octane-4,4,5-tricarbonitriles.

We had shown previously [1] that 2-aryl-5,6-tetramethylene-3,3,4-tricyano-2,3,4,5-tetrahydropyridine-4-carboxamides (Ia-c), obtained by the interaction of 1-(2-oxocyclohexyl)ethane-1,1,2,2-tetracarbonitrile with 1,3,5-triaryl-2,4-diaza-1,4-pentadienes, are converted in the presence of bases to 4-aryl-3-amino-6,7-tetramethylene-1-oxo-3a,4,5,7a-tetrahydro-1H-pyrrolo[3,4-c]pyridine-3a,7a-dicarbonitriles (IVa-c). Continuing these studies, we have investigated the conversion of compounds Ia-c under the influence of acids.

In acetic, formic, butyric, or trifluoroacetic acid, compounds Ia-c are isomerized to 2-aryl-5,6-tetramethylene-3,3,4-tricyano-1,2,3,4-tetrahydropyridine-4-carboxamides (IIa-c). When compounds Ia-c are exposed to the action of 20% aqueous sulfuric acid, they are converted to 3-aryl-1,8-tetramethylene-6-oxo-2,7-diazobicyclo[3.2.1]octane-4,4,5-tricarbonitriles (IIIa-c). It was found that compounds IIIa-c are also formed by the action of aqueous solutions of organic acids.



I-IVa) Ar = Ph; I-IVb) Ar = 2-furyi; I-IVc) Ar = p-MeOC₆H₄

The crystal structure of the IIIb molecule was established by x-ray diffraction (Fig. 1). The structures of IIIa, c were determined by comparing their IR spectra with that of IIIb, and their compositions were established from the results of elemental analyses (Tables 1, 4).

Chubash State University, Cheboksary 428015. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 528-532, April, 1997. Original article submitted October 24, 1996.

Com-	Empirical	Found, % Calculated, %			mp (decomp.),	Yield, %
pound	formula	с	н	N	°C	(and method)
Па	C19H17N5O	<u>68.64</u> 68.74	<u>5.11</u> 5,24	<u>21.10</u> 21,19	155156	69
IIb	C17H15N5O2	<u>63.38</u> 63,54	<u>4.62</u> 4,71	<u>21.66</u> 21,79	>150	73
Пс	C20H19N5O	<u>66.32</u> 66,47	<u>5.17</u> 5,30	<u>19.25</u> 19,38	>155	76
IIIa	C19H17N5O	<u>68.59</u> 68,74	<u>5.10</u> 5,24	<u>21.14</u> 21,19	>175	65 (A)
шь	C17H15N5O2	<u>63.37</u> 63,54	<u>4.58</u> 4,71	<u>21.67</u> 21,79	>110	82 (A)
Шc	C20H19N5O	<u>66.40</u> 66.47	<u>5,16</u> 5,30	<u>19.27</u> 19.38	>160	71 (A)

TABLE 1. Characteristics of Compounds IIa-c and IIIa-c



Fig. 1. Molecular structure of compound IIIb.

The structures of compounds IIa-c can be judged from the fact that they can be converted almost quantitatively to the known compounds IVa-c [1] under the influence of bases. On the other hand, compounds IIa-c, the same as compounds Ia-c, are converted to the bicyclo compounds IIIa-c in a 20% acetic acid solution. The IR spectra and elemental compositions of IIa-c are also consistent with the proposed structure (Tables 1, 4).

It can be assumed that in the formation of either group of compounds, II or III, the substrate I is protonated to form a cation K, and that subsequent path of conversion of this cation may depend on its concentration in the particular medium that is being used. In an aqueous sulfuric acid solution, a strongly acidic medium, the concentration of the cation K is sufficient for intramolecular cyclization and the formation of compound III. In glacial acetic acid, the acidity constant of the cation K is apparently commensurate with the constant of autoprotolysis of acetic acid; and as a consequence, a proton is readily abstracted, with the formation of the more thermodynamically stable base II. The formation of compound III upon prolonged holding in an organic medium can also be explained by the reversibility of this reaction.

EXPERIMENTAL

IR spectra were taken in a UR-20 instrument on samples in white mineral oil. The purity of the synthesized compounds and the degree of completion of the reaction were established by TLC on Silufol UV-254 plates.

Atom	x	у	Z	Ueq
O(32)	689(2)	5941(1)	4102(1)	33(1)
O(61)	-3040(2)	10509(1)	2508(1)	19(1)
N(2)	-239(3)	6952(1)	2774(1)	15(1)
N(7)	-1307(2)	8882(1)	2105(1)	15(1)
N(41)	-3781 (2)	5602(1)	3841(1)	33(1)
N(42)	-2916(2)	9681(1)	4304(1)	29(1)
N(51)	-6903(4)	8715(2)	2777(1)	25(1)
C(1)	-1231(3)	7433(1)	2139(1)	14(1)
C(11)	-436(3)	6852(2)	1532(1)	18(1)
C(12)	-1660(3) ·	7028(2)	867(1)	22(1)
C(13)	-3502(3)	6524(2)	932(1)	22(1)
C(14)	-4351 (3)	7254(2)	1491(1)	16(1)
C(3)	-506(4)	7735(1)	3365(1)	15(1)
C(31)	561 (3)	7259(1)	3997(1)	18(1)
C(33)	1736(3)	5783(2)	4711(1)	38(1)
C(34)	2230(3)	6927 (2)	4982(1)	29(1)
C(35)	1475(3)	7897(2)	4518(1)	25(1)
C(4)	-2558(4)	7816(1)	3420(1)	15(1)
C(41)	-3260(3)	6566(1)	3657(1)	18(1)
C(42)	-2823(3)	8853(1)	3922(1)	18(1)
C(5)	-3585(4)	8172(1)	2695(1)	11(1)
C(51)	-5438(6)	8452(2)	2741(1)	15(1)
C(6)	-2624(3)	9378(1)	2422(1)	14(1)
C(8)	-3182(3)	7117(1)	2176(1)	13(1)

TABLE 2. Coordinates of Nonhydrogen Atoms ($\times 10^4$) and Coefficients of Equivalent Isotropic Displacement ($\dot{A}^2 \times 10^3$) of Compound IIIb

X-Ray Diffraction Study of Compound IIIb. Crystals of compound IIIb ($C_{17}H_{15}N_5O_2$, M 321.34) are monoclinic, space group P2₁/c; at -100°C, a = 7.574(3), b = 10.252(3), c = 19.745(7) Å, $\beta = 96.55(2)^\circ$, V = 1523(1) Å³, Z = 4, d = 1.238 g/cm³. The elementary cell constants and the intensities of 2036 reflections were measured in a Siemens P3/PC automatic four-circle diffractometer ($T = -100^\circ$ C, λ MoK α , graphite monochromator, $\theta/2\theta$ scanning, $\theta_{max} = 27^\circ$). The structure was deciphered by the direct method and refined by full-matrix LSM in the anisotropic approximation for the nonhydrogen atoms. The hydrogen atoms, localized objectively in a difference Fourier synthesis, were refined in the isotropic approximation. The final divergence factors were $R_f = 0.029$ based on 1779 independent reflections with I > $2\sigma(I)$ and wR₂ = 0.103 based on all 1815 independent reflections. The calculations were performed on an IBM PC/AT-486 computer, using the programs SHELXTL PLUS and SHELXL-93. The coordinates of the atoms, bond lengths, bond angles, and the thermal parameters were entered into the files of the Cambridge Crystallographic Data Center.

2-Aryl-5,6-tetramethylene-3,3,4-tricyano-1,2,3,4-tetrahydropyridine-4-carboxamides (IIa-c). A 5-mmole quantity of the corresponding compound Ia-c was added to 5 ml of glacial acetic acid. Upon stirring, first the reactant dissolved; then, in 2-3 min, a precipitate was formed. At the end of the reaction, the precipitate was filtered off, washed with chilled isopropyl alcohol, recrystallized from isopropyl alcohol, and vacuum-dried.

Compounds IIa-c were also prepared in the same manner, with formic, butyric, or trifluoroacetic acid in place of the acetic acid.

3-Aryl-1,8-tetramethylene-6-oxo-2,7-diazobicyclo[3.2.1]octane-4,4,5-tricarbonitriles (IIIa-c). A. To 15 ml of 20% sulfuric acid, 5 mmoles of the appropriate amide Ia-c was added. Upon stirring, the reactant gradually dissolved, and a new precipitate was formed simultaneously. At the end of the reaction, the precipitate was filtered off and washed with water. The compounds IIIa-c were purified by reprecipitation from acetonitrile by the addition of water. The substances were vacuum-dried over P_2O_5 .

B. Compounds IIIa-c were also prepared by an analogous procedure using a 50% aqueous solution of formic or trifluoroacetic acid. When a 50% aqueous solution of acetic acid was used, it was necessary to heat the reaction mass to the boiling point in order to drive the reaction to completion.

Bond	Length, Å	Angle	ω, deg	Angle	ω, deg
O ₍₃₂₎ —C ₍₃₁₎	1,369(2)	C(31)-O(32)-C(33)	105,86(12)	C(3)-N(2)-C(1)	113,3(2)
O ₍₃₂₎ —C ₍₃₃₎	1,373(2)	C(6)—N(7)—C(1)	112,69(14)	N(2)-C(1)-N(7)	112,76(12)
O(61)-C(6)	1,218(2)	N(2)-C(1)-C(8)	107,0(2)	N(7)-C(1)-C(8)	100,51(14)
N ₍₂₎ -C ₍₃₎	1,450(2)	N(2)—C(1)—C(11)	109,3(2)	N(7)-C(1)-C(11)	111,85(13)
N(2)-C(1)	1,471(2)	C(8)-C(1)-C(11)	115,3(2)	$C_{(1)} - C_{(11)} - C_{(12)}$	112,0(2)
N ₍₇₎ —C ₍₆₎	1,337(2)	C(13)-C(12)-C(11)	111,3(2)	$C_{(12)}-C_{(13)}-C_{(14)}$	111,2(2)
N(7)-C(1)	1,487(2)	C(13)—C(14)—C(8)	110,0(2)	N(2)-C(3)-C(31)	112,4(2)
N ₍₄₁₎ —C ₍₄₁₎	1,139(2)	N(2)-C(3)-C(4)	108,3(2)	C(31)-C(3)-C(4)	113,98(14)
N(42)-C(42)	1,142(2)	C(35)-C(31)-O(32)	110,08(13)	C(35)-C(31)-C(3)	131,68(14)
N(51)-C(51)	1,152(3)	O(32)-C(31)-C(3)	118,24(12)	C(34)-C(33)-O(32)	110,9(2)
C(1)-C(8)	1,522(3)	C(33)-C(34)-C(35)	106,5(2)	C(31)-C(35)-C(34)	106,6(2)
C ₍₁₎ —C ₍₁₁₎	1,524(2)	C(42)-C(4)-C(41)	109,06(14)	C(42)-C(4)-C(3)	107,1(2)
C(11)-C(12)	1,528(2)	C(41)-C(4)-C(3)	111,6(2)	C(42)-C(4)-C(5)	110,36(14)
C ₍₁₂₎ —C ₍₁₃₎	1,507(3)	C(41)-C(4)-C(5)	109,0(2)	C(3)C(4)C(5)	109,7(2)
C ₍₁₃₎ —C ₍₁₄₎	1,535(2)	N(41)-C(41)-C(4)	179,3(2)	N(42)C(42)C(4)	175,4(2)
C(14)-C(8)	1,535(2)	C(51)-C(5)-C(8)	116,6(2)	C(51)-C(5)-C(6)	110,99(14)
C ₍₃₎ —C ₍₃₁₎	1,489(2)	C(8)-C(5)-C(6)	100,9(2)	C(51)-C(5)-C(4)	111,6(2)
C ₍₃₎ -C ₍₄₎	1,572(3)	C(8)-C(5)-C(4)	108,9(2)	C(6)-C(5)-C(4)	107,0(2)
C(31)-C(35)	1,343(2)	N(51)-C(51)-C(5)	177,9(2)	O(61)-C(6)-N(7)	130,21(14)
C ₍₃₃₎ —C ₍₃₄₎	1,324(3)	O(61)-C(6)-C(5)	124,5(2)	N(7)-C(6)-C(5)	105,24(14)
C ₍₃₄₎ —C ₍₃₅₎	1,428(2)	C(1)-C(8)-C(14)	113,84(14)	C(1)-C(8)-C(5)	98,6(2)
C ₍₄₎ —C ₍₄₂₎	1,484(2)	C(14)C(8)C(5)	112,5(2)		
C ₍₄₎ —C ₍₄₁₎	1,484(2)				
C ₍₄₎ —C ₍₅₎	1,591(2)			1	
C ₍₅₎ —C ₍₅₁₎	1,445(4)				
C ₍₅₎ —C ₍₈₎	1,545(2)				
C ₍₅₎ —C ₍₆₎	1,562(2)				

TABLE 3. Bond Lengths and Bond Angles in Molecule of Compound IIIb

TABLE 4. IR Spectra of Compounds IIa-c and IIIa-c

	ν, cm ⁻¹				
Com- pound	ν _{NH2} . ν _{N-H}	νc = N	ν _{C=0} , ν _{C=C} , δ _{NH2}		
Па	3460, 3400, 3345, 3270	2260	1695 1650		
Пъ	3470, 3410, 3360	2265	1690, 1640		
Пс	3480, 3370, 3323	2250, 2260	1685, 1650		
Ша	3350, 3230	2260	1708		
Шb	3360, 3295	2265	1710		
IIIc	3320, 3250	2260	1711		

C. A 5-mmole quantity of the appropriate amide Ia-c was dissolved in acetic acid, and the mixture was held for 24 h, after which the precipitate was filtered off, washed with water, and vacuum-dried.

D. By a procedure analogous to Method A, compounds IIIa-c were obtained from compounds IIa-c.

3-Amino-6-methyl-7-propyl-1-oxo-4-phenyl-3a,4,5,7a-tetrahydro-1H-pyrrolo[3,4-c]pyridine-3a,7a-dicarbonitrile (IVa). To a suspension of 0.33 g (1 mmole) of compound IIa in 2 ml of isopropyl alcohol, 0.1 ml of a 5% solution of triethylamine in isopropyl alcohol was added, and the mixture was heated to boiling. The solid material first dissolved; then a new precipitate was formed in the boiling solution. The reaction mixture was cooled, and the precipitate was filtered off, washed with chilled isopropyl alcohol, and vacuum-dried to constant weight. Obtained 0.32 g (97%) of a colorless crystalline compound, mp 208-210°C (decomp.). IR spectrum: 1566, 1650 (ν C=N, ν C=C, δ NH₂); 1730 (ν C=O); 2265 (ν C = N); 3325 cm⁻¹, (ν N-H).

The IR spectrum of the synthesized substance was identical to that of a sample of IVa prepared by the method of [1], and a mixed sample did not exhibit any melting point depression.

Analogously, compounds IIIb, c were obtained from IIb, c.

REFERENCES

1. Ya. S. Kayukov, O. E. Nasakin, Ya. G. Urman, V. N. Khrustalev, V. N. Nesterov, M. Yu. Antipin, A. N. Lyshchikov, and P. M. Lukin, Khim. Geterotsikl. Soedin., No. 10, 1395 (1996).