Chemistry of Heterocyclic Compounds, Vol. 46, No. 12, March, 2011 (Russian Original Vol. 46, No. 12, December, 2010)

N-(2-AMINOBENZOYL)-N-METHYLHYDRAZONES OF ALDEHYDES AND ALDOSES AND THEIR CYCLIZATION TO BENZO-1,3,4-TRIAZEPINE DERIVATIVES

A. Yu. Ershov[1]*, B. V. Chernitsa[1], V. A. Doroshenko[1], S. I. Yakimovich[2], V. V. Alekseyev[3], I. V. Lagoda[4], V. V. Pakal'nis[2], I. V. Zerova[2], and V. V. Shamanin[1]

The products of the condensation of aliphatic aldehydes with N-(2-aminobenzoyl)-N-methylhydrazine exist in DMSO-d_6 solution as tautomeric mixtures of linear aldohydrazone and cyclic benzo-1,3,4-triazepine forms. The linear tautomer predominates for 2-aminobenzoyl-N-methylhydrazones of aromatic aldehydes. A tautomeric equilibrium is observed in DMSO-d_6 for the products of the condensation of the hydrazide of 2-aminobenzoic acid with a series of aldoses. This equilibrium exists between α,β-isomeric pyranose forms and the open aldosohydrazone form. Isomeric conversion to the seven-membered benzo-1,3,4-triazepine form is observed for the products of the condensation of aldoses with N-(2-aminobenzoyl)-N-methylhydrazine.

Keywords: 2-aminobenzoylhydrazones, benzo-1,3,4-triazepines, ring-chain tautomerism.

The products of the condensation of carbonyl compounds with N-(2-aminobenzoyl)-N-methylhydrazine tend to undergo intramolecular cyclization due to nucleophilic addition of the NH_2 group to the C=N bond to give the seven-membered benzo-1,3,4-triazepine ring [1-4]. In some cases, this reaction is reversible, leading to the existence of the linear N-(2-aminobenzoyl)-N-methylhydrazone and cyclic benzotriazepine forms in solution as an equilibrium mixture.

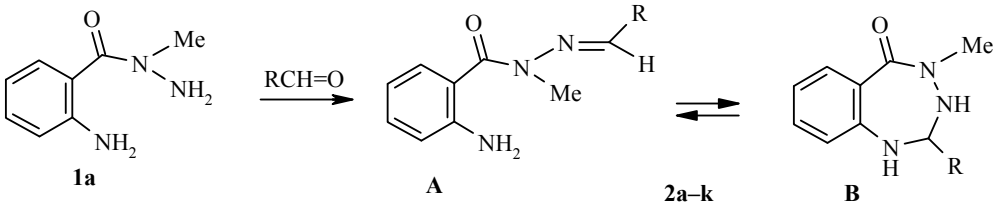
* To whom correspondence should be addressed, e-mail: ershov305@mail.ru.

[1]Institute of Macromolecular Compounds, Russian Academy of Sciences, Saint-Petersburg 199004, Russia.
[2]Saint-Petersburg State University, Saint-Petersburg 198504, Russia; e-mail: viktoriapakalnis@mail.ru.
[3]S. M. Kirov Military Medical Academy, Saint-Petersburg 194044, Russia; e-mail: alekseyevv.v@mail.ru.
[4]Scientific Research Test Center (Medical and Biological Defence), Federal Research Test Institute of Military Medicine of the Defence Ministry of Russian Federation, Saint-Petersburg 195043, Russia; e-mail: lagodai@peterstar.ru.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1838-1848, December, 2010. Original article submitted February 12, 2010.

 0009-3122/11/4612-1486©2011 Springer Science+Business Media, Inc.

In the present work, we continued our study of the structure of the products of the condensation of N-(2-aminobenzoyl)-N-methylhydrazine with a series of aliphatic and aromatic aldehydes as well as aldoses (Table 1) and their tendency to undergo reversible intramolecular cyclization leading to the seven-membered 1,3,4-triazepine ring.



2 a R = Me, **b** R = Et, **c** R = Pr, **d** R = Bu, **e** R = CH_2Ph, **f** R = *i*-Pr, **g** R = *i*-Bu;
h–k R = XC_6H_4, **h** X = 4-NO_2, **i** X = 3-NO_2, **j** X = H, **k** X = 4-MeO

The initial compounds studied were the N-(2-aminobenzoyl)-N-methylhydrazones of aliphatic aldehydes **2a-g**. These hydrazones were obtained in 50-90% yield after maintaining equimolar amounts of N-(2-aminobenzoyl)-N-methylhydrazine **1a** and the corresponding aliphatic aldehyde in methanol at room temperature (see Experimental).

TABLE 1. Physicochemical Characteristics of Compounds **2a-k** and **4a-h**

Compound	Form in crystalline state	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
			C	H	N		
2a	**B**	$C_{10}H_{13}N_3O$	62.78 / 62.81	6.91 / 6.85	22.04 / 21.97	153-155 (157-159 [2])	55
2b	**B**	$C_{11}H_{15}N_3O$	64.30 / 64.37	7.44 / 7.37	20.51 / 20.47	140-142	50
2c	**B**	$C_{12}H_{17}N_3O$	65.77 / 65.73	5.76 / 5.81	19.09 / 19.16	154-156	60
2d	**B**	$C_{13}H_{19}N_3O$	66.87 / 66.92	8.26 / 8.21	17.96 / 18.01	142-144	50
2e	**B**	$C_{16}H_{17}N_3O$	71.95 / 71.89	6.36 / 6.41	15.63 / 15.72	130-132	65
2f	**B**	$C_{12}H_{17}N_3O$	65.67 / 65.73	5.88 / 5.81	19.07 / 19.16	102-104	60
2g	**B**	$C_{13}H_{19}N_3O$	66.98 / 66.92	8.17 / 8.21	18.08 / 18.01	132-134	60
2h	**A**	$C_{15}H_{14}N_4O_3$	60.34 / 60.40	4.79 / 4.73	18.70 / 18.78	200-202 (204-206 [7])	90
2i	**A**	$C_{15}H_{14}N_4O_3$	60.46 / 60.40	4.65 / 4.73	18.84 / 18.78	152-154	70
2j	**A**	$C_{15}H_{15}N_3O$	71.07 / 71.13	6.04 / 5.97	16.63 / 16.59	127-130 (131-133 [2])	60
2k	**A**	$C_{16}H_{17}N_3O_2$	67.75 / 67.83	5.97 / 6.05	14.88 / 14.83	134-136 (134-140 [7])	70
4a	**A**	$C_{12}H_{17}N_3O_5$	57.71 / 57.67	5.76 / 5.81	13.39 / 13.45	159-160	55
4b	**C**	$C_{12}H_{17}N_3O_5$	57.71 / 57.67	5.76 / 5.81	13.39 / 13.45	189-190	50
4c	**C**	$C_{13}H_{19}N_3O_6$	49.80 / 49.84	6.06 / 6.11	13.37 / 13.41	160-164	45
4d	**C**	$C_{13}H_{19}N_3O_6$	49.89 / 49.84	6.19 / 6.11	13.47 / 13.41	190-193	50
4e	**B**	$C_{13}H_{19}N_3O_5$	52.47 / 52.52	6.39 / 6.44	14.08 / 14.13	112-114	45
4f	**B**	$C_{13}H_{19}N_3O_5$	52.59 / 52.52	6.50 / 6.44	14.06 / 14.13	168-171	50
4g	**B**	$C_{14}H_{21}N_3O_6$	51.29 / 51.37	6.40 / 6.47	12.93 / 12.84	130-132	40
4h	**B**	$C_{14}H_{21}N_3O_6$	51.41 / 51.37	6.55 / 6.47	12.79 / 12.84	116-118	45

The change in the ^{1}H NMR spectra over time indicates that compounds **2a-g** exist in the crystalline state in the cyclic triazepine form **B**. A single set of signals corresponding to this form is observed in the ^{1}H NMR spectrum of **2a-g** taken immediately after dissolution in DMSO-d_6. This conclusion follows from observation of the doublet for the NH protons at 5.70-5.90 ppm and signal with the corresponding multiplicity at 4.00-4.50 ppm for H-2. The signal for the sp^3-hybridized carbon atom at 70-75 ppm for C(2) corresponds to triazepine form **B** in the ^{13}C NMR spectrum (Tables 2 and 3) [2, 3].

Signals corresponding to the linear 2-aminobenzoylhydrazone form **A** appear in the ^{1}H NMR spectra 24 h after dissolution of the compounds in DMSO-d_6. A typical diagnostic of this form, whose content for these compounds does not exceed 12%, is the downfield signal for the azomethine group protons at 7.10-7.40 ppm in the ^{1}H NMR spectrum and signals for the C=N group carbon at 147 ppm and C=O group carbon at 171 ppm in the ^{13}C NMR spectrum (Table 2). The spectra of compounds **2a-g** do not undergo further change, indicating the establishment of a ring-chain equilibrium in solution.

The position of the equilibrium depends on the length and branching of the alkyl substituent. The fraction of linear form **A** increases in going to compounds **2f**,**g**, which contain bulky isopropyl and isobutyl groups, respectively. A clear correlation of the position of the tautomeric equilibrium with the steric constants of the alkyl substituents could not be established due to the low content of form **A**. Cyclic triazepine form **B** is markedly stabilized in going from polar, strongly basic, aprotic solvents such as DMSO-d_6 and DMF-d_7 to weakly-polar $CDCl_3$ and is the only species observed in $CDCl_3$ for all the compounds studied, **2a-g**.

TABLE 2. ^{1}H NMR Spectra of Compounds **2a-g**

Com-pound	Chemical shifts (DMSO-d_6), δ, ppm (J, Hz)
2a	Form **A** (1%): 1.39 (3H, d, J = 6.0, CH_3); 3.25 (3H, s, CH_3N); 5.15 (2H, br. s, NH_2); 7. 39 (1H, q, J = 6.0, HC=N) Form **B** (99%): 1.24 (3H, d, J = 6.2, CH_3); 3.08 (3H, s, CH_3N); 4.45 (1H, dq, J_1 = 6.8, J_2 = 6.2, H-2); 5.87 (1H, d, J = 6.8, NH); 6.23 (1H, br. s, NH); 6.65-7.63 (4H, m, Ar)
2b	Form **A** (2%): 0.94 (3H, t, J = 7.4, CH_3); 3.27 (3H, s, CH_3N); 5.17 (2H, br. s, NH_2); 7. 28 (1H, t, J = 4.8, HC=N) Form **B** (98%): 0.98 (3H, t, J = 7.2, CH_3); 1.55 (2H, m, CH_2); 3.07 (3H, s, CH_3N); 4.09 (1H, dt, J_1 = 6.6, J_2 = 6.0, H-2); 5.87 (1H, d, J = 6.6, NH); 6.27 (1H, br. s, NH); 6.65-7.64 (4H, m, Ar)
2c	Form **A** (2%): 0.91 (3H, t, J = 7.0, CH_3); 3.23 (3H, s, CH_3N); 5.17 (2H, br. s, NH_2); 7. 37 (1H, t, J = 6.2, HC=N) Form **B** (98%): 0.93 (3H, t, J = 6.8, CH_3); 1.53 (4H, m, $2CH_2$); 3.06 (3H, s, CH_3N); 4.27 (1H, dt, J_1 = 6.6, J_2 = 6.0, H-2); 5.87 (1H, d, J = 6.6, NH); 6.26 (1H, br. s, NH); 6.67-7.63 (4H, m, Ar)
2d	Form **A** (2%): 0.90 (3H, t, J = 7.2, CH_3); 3.23 (3H, s, CH_3N); 5.19 (2H, br. s, NH_2); 7. 36 (1H, t, J = 6.0, HC=N) Form **B** (98%): 0.91 (3H, t, J = 7.2, CH_3); 1.34 (2H, m, CH_2); 1.48 (4H, m, CH_2); 3.06 (3H, s, CH_3N); 4.16 (1H, dt, J_1 = 6.6, J_2 = 5.5, H-2); 5.87 (1H, d, J = 6.6, NH); 6.26 (1H, br. s, NH); 6.65-7.64 (4H, m, Ar)
2e	Form **A** (3%): 3.29 (3H, s, CH_3N); 3.48 (2H, d, J = 5.2, CH_2); 5.24 (2H, br. s, NH_2); 7. 40 (1H, t, J = 5.2, HC=N) Form **B** (97%): 2.79, 2.91 (2H, ABX system, J_{AB} = 12.5, CH_2); 2.93 (3H, s, CH_3N); 4.46 (1H, dd, ABX system, J_{AX} = 6.0, J_{BX} = 4.5, H-2); 5.98 (1H, br. s, NH); 6.31 (1H, br. s, NH); 6.60-7.65 (9H, m, Ar)
2f	Form **A** (7%): 0.96 (6H, d, J = 7.0, $2CH_3$); 2.67 (1H, m, CH); 3.21 (3H, s, CH_3N); 5.19 (2H, br. s, NH_2); 7.10 (1H, d, J = 7.6, HC=N) Form **B** (93%): 0.93 (3H, d, J = 6.8, CH_3); 1.01 (3H, d, J = 6.8, CH_3); 1.83 (1H, m, CH); 3.04 (3H, s, CH_3N); 3.93 (1H, dd, J_1 = 7.6, J_2 = 5.2, H-2); 5.70 (1H, d, J = 7.6, NH); 6.32 (1H, br. s, NH); 6.62-7.68 (4H, m, Ar).
2g	Form **A** (12%): 0.87 (6H, d, J = 6.6, $2CH_3$); 2.03 (1H, m, CH); 3.29 (3H, s, CH_3N); 5.18 (1H, br. s, NH_2); 7. 23 (1H, t, J = 5.6, HC=N) Form **B** (88%): 0.93 (6H, d, J = 6.6, $2CH_3$); 1.41 (2H, m, CH_2); 1.88 (1H, m, CH); 3.07 (3H, s, CH_3N); 4.24 (1H, dt, J_1 = 6.6, J_2 = 6.2, H-2); 5.88 (1H, d, J = 6.6, NH); 6.20 (1H, br. s, NH); 6.65-7.65 (4H, m, Ar)

TABLE 3. ^{13}C NMR Spectra of Compounds **2a-c**,**e**,**f**,**j**

Compound	Form	Chemical shifts (DMSO-d_6), δ, ppm			
		CH_3N	C(2) or C=N	C=O	R
2a	**B**	38.55	70.14	171.74	21.46 (CH_3)
2b	**B**	38.51	75.82	171.79	9.93 (CH_3); 27.62 (CH_2)
2c	**B**	38.55	74.09	171.79	13.97 (CH_3); 18.29, 36.81 ($2CH_2$)
2e	**B**	38.35	75.91	172.01	40.73 (CH_2); 126.23-139.39 (Ar)
2f	**B**	38.34	78.62	171.65	16.84, 18.94 ($2CH_3$); 31.80 (CH)
2g	**A**	28.32	147.00	170.07	22.25 ($2CH_3$); 26.10 (CH); 41.07 (CH_2)
	B	38.53	72.57	171.70	22.14 (CH); 23.20, 23.98 ($2CH_3$); 43.57 (CH_2)
2j	**A**	28.63	147.28	170.54	128.70-135.08 (Ar)

Thus, the products of the condensation of aliphatic aldehydes with N-(2-aminobenzoyl)-N-methylhydrazine have benzo-1,3,4-triazepine structure in the crystalline state. Partial conversion to the linear form occurs only in solutions in strongly polar solvents. Thus, the term "N-(2-aminobenzoyl)-N-methylhydrazone" should be considered as tentative for such compounds.

We should have expected that N-(2-aminobenzoyl)-N-methylhydrazones of aromatic aldehydes would exist largely in linear form **A** due to stabilization related to inclusion of the aromatic ring into the π-*p*-π-conjugation system of the acylhydrazone fragment [5-7]. This hypothesis is fully supported by an NMR study of the structure of compounds **2h-k**.

The ^{1}H NMR spectrum of the N-(2-aminobenzoyl)-N-methylhydrazone of benzaldehyde **2j** in DMSO-d_6 taken both immediately upon preparation and several days after dissolution in a solvent show a single set of signals corresponding to the linear form **A**: the signal for the azomethine proton appears at 8.15 ppm, while the broad singlet of the NH_2 group protons appears at 5.35 ppm (Table 4). The existence of linear form **A** for compound **2j** was also supported by the ^{13}C NMR spectrum (Table 3).

Four structures are possible for the acylhydrazones of carbonyl compounds differing in the arrangement of the substituents relative to the C=N bond (geometrical (*Z,E*)-isomerism) and the amide fragment C–N bond (conformational (*Z′,E′*)-isomerism) [5, 6]. The derivatives of aromatic aldehydes exist predominantly or entirely in the (*E)*-configuration relative to the C=N bond. Thus, the signals of linear form **A** in the ^{1}H and ^{13}C NMR spectra of the N-(2-aminobenzoyl)-N-methylhydrazone of benzaldehyde **2j** should be assigned to one of the (*E′)*- or (*Z′)*-conformers of this structural isomer.

Without going into a detailed discussion of the spectral differences between the (*E,E′)*- and (*E,Z′)*-forms, we only note the position of the chemical shifts of the C=N and C=O group carbon atoms in the ^{13}C NMR spectra: the signals of the (*E′)*-isomer of these groups are in the vicinity of 145 and 170 ppm, respectively, while these signals for the (*Z′)*-isomer lie at 150 and 160 ppm, respectively [8, 9]. Thus, the chemical shifts of the C=N and C=O group carbon atoms given in Table 3 for form **A** of compound **2j** correspond to (*E,E′)*-structural arrangement of the N-(2-aminobenzoyl)-N-methylhydrazone fragment in this molecule.

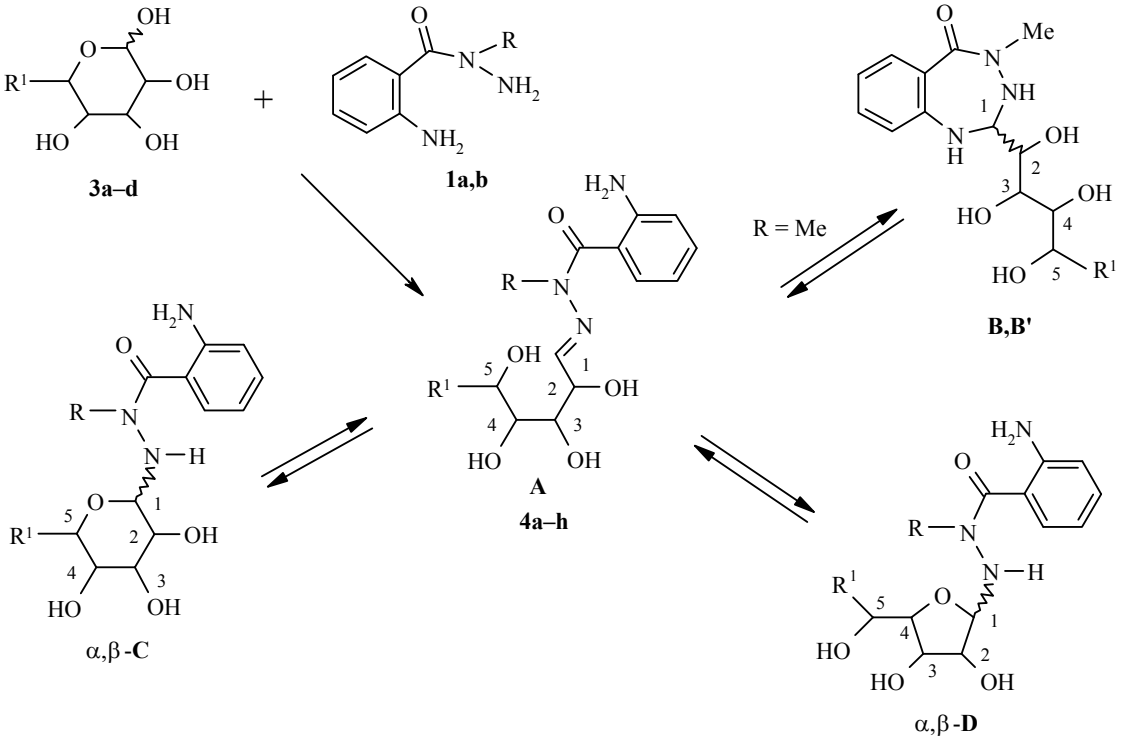
TABLE 4. ^{1}H NMR Spectra of Compounds **2h-k**

Compound	Chemical shifts (DMSO-d_6), δ, ppm.			
	CH_3N, s, 3H	HC=N, s, 1H	NH_2, br. s, 2H	Ar, m
2h	3.48	8.11	5.35	6.56-8.22 (8H)
2i	3.33	8.14	5.34	6.58-8.36 (8H)
2j	3.36	7.99	5.30	6.57-7.52 (9H)
2k	3.36	7.94	5.28	3.75 (3H, s, OCH_3); 6.57-7.45 (8H)

Formation of the cyclic 1,3,4-triazepine form **B** was also not detected for the products of the condensation of N-(2-aminobenzoyl)-N-methylhydrazine with other aromatic aldehydes **2h-k** in DMSO-d_6. These compounds exist in linear form **A**, represented by a single structural (*E,E'*)-isomer, in the crystalline state and in solution. The linear structure of compounds **2h-k** is in full accord with the results of Neuvonen et al. [7] in a ^{13}C NMR spectral study of the structure of 2-aminobenzoylhydrazones of aromatic aldehydes.

It would seem that some steric access of the C=N bond for intramolecular nucleophilic attack by the hydrazone NH_2 group is a necessary condition for appearance of the cyclic 1,3,4-triazepine tautomer **B** for N-(2-aminobenzoyl)-N-methylhydrazones of carbonyl compounds. Such access may be achieved in the case of the products of the condensation of N-(2-aminobenzoyl)-N-methylhydrazine with aliphatic aldehydes or aldoses, which represent a latent form of the aliphatic aldehyde function. A study of the structure of the 2-aminobenzoylhydrazones and N-(2-aminobenzoyl)-N-methylhydrazones of aldoses fully supports our hypothesis.

2-Aminobenzoylhydrazones and N-(2-aminobenzoyl)-N-methylhydrazones **4a-h** are the products of condensation of aldoses, D-ribose **3a**, L-arabinose **3b**, D-glucose **3c**, and D-mannose **3d** with N-(2-aminobenzoyl)-N-methylhydrazine **1a** and 2-aminobenzoylhydrazine **1b** are complex tautomeric mixtures capable of cyclization to give a five-membered form **C** and six-membered form **D** as well as a seven-membered 1,3,4-triazepine form **B**.



4a–d R = H, **e–h** R = Me; **1b** R = H; **3a,b** R^1 = H, **a** D-riboze, **b** L-arabinose; **c,d** R^1 = CH_2OH, **c** D-glucose, **d** D-mannose, **a,b,e,f** R^1 = H, **a**,**e** D-ribose, **b**,**f** L-arabinose; **c,d,g,h** R^1 = CH_2OH, **c**,**g** D-glucose, **d**,**h** D-mannose

We should note that each of these forms is capable of existing as two structural isomers (α,β-isomers of forms **C** and **D**, (*Z',E'*)-conformers of form **A**, and 2*R*- and 2*S*-stereoisomers of form **B**). Formation of the cyclic benzo-1,3,4-triazepine form for 2-aminobenzoylhydrazones **4a-d** through attack of the NH_2 group at the C=N bond should be considered unlikely. It is known that no tendency has been found for products of the condensation of the hydrazide of 2-aminobenzoic acid with aldehydes to undergo such a cyclization [7, 10].

TABLE 5. ^{13}C NMR Spectra of Compounds **4a–h**

Compound	Form (%)	Chemical shifts (DMSO-d_6), δ, ppm*								
		CH_3N	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	Ar	C=O
4a	**A** (60)	—	151.73	74.55	72.25	72.20	63.46	—	113.34-150.15	165.76
	β-**C** (25)	—	88.13	70.20	69.13	67.64	64.33	—		168.91
	β-**D** (15)	—	95.89	72.84	70.12	83.32	61.58	—		168.50
4b	**A** (25)	—	151.35	68.98	70.80	71.17	63.78	—	114.67-147.22	165.69
	β-**C** (65)	—	89.13	73.65	72.75	69.05	65.08	—		168.74
	β-**D** (10)	—	95.94	78.81	76.89	85.53	61.82	—		168.01
4c	α-**C** (30)	—	88.41	72.19	73.99	70.65	71.49	60.46	114.89-149.73	168.19
	β-**C** (70)	—	91.38	71.71	78.14	70.76	77.05	61.81		168.94
4d	α-**C** (40)	—	89.48	71.89	70.92	67.85	73.31	61.75	113.32-150.18	168.98
	β-**C** (60)	—	88.11	71.75	74.51	67.36	78.50	62.13		168.65
4e	**B** (55)	37.98	74.85	72.70	73.14	72.70	62.79	—	116.51-145.60	171.68
	B'(45)	38.38	75.10	73.00	73.51	71.52	63.43	—		171.58
4f	**B** (65)	38.35	75.37	65.35	70.21	71.52	63.96	—	117.65-145.39	172.33
	B'(35)	38.60	76.88	65.35	70.30	71.52	63.75	—		172.15
4g	**B** (70)	37.86	75.11	70.69	73.22	72.03	72.49	64.53	117.70-146.74	170.20
	B'(30)	38.09	76.38	70.78	73.40	71.60	72.35	63.91		170.10
4h	**B** (60)	38.48	75.10	71.52	69.53	69.76	71.64	64.20	117.54-146.02	171.89
	B'(40)	38.72	75.48	70.37	69.66	69.92	73.30	63.85		170.88

* Numbering of the atoms proceeds according to the carbohydrate fragment.

In all the experiments, we recorded the ^{1}H and ^{13}C NMR spectra over time and followed the change in the NMR spectra of the reaction products from immediately after dissolution until the completion of any chemical transformation. The ^{13}C NMR spectral data served as the major criterion for identification of specific forms in the solutions of compounds **4a-h**. Thus, we would have expected a signal for anomeric carbon C(1) in the pyranose form **C** at 85-90 ppm. The analogous signal for five-membered furanose form **D** would be found at 95-100 ppm. In case of seven-membered triazepine form **B**, the signal for atom C(1) should be found upfield at 70-75 ppm, which is characteristic for an sp^3-hybridized carbon atom of a seven-membered ring attached to two nitrogen atoms [2, 3, 11]. A downfield ^{13}C NMR signal at 150 ppm related to the C=N bond should be diagnostic for aldosohydrazone form **A**.

One set of signals belonging to linear form **A** is observed in the ^{13}C NMR spectrum of the product of the condensation of the hydrazide of 2-aminobenzoic acid with D-ribose **4a** taken immediately after dissolution. This finding suggests that compound **4a** has the same structure in the crystalline state. After 2 days, sets of signals arise corresponding to the cyclic pyranose form **C** and furanose form **D** in the ^{13}C NMR spectrum of the solution. The ^{13}C NMR signal for atom C(1) at 88.13 ppm is characteristic for form **C**. The presence of the five-membered furanose form **D** is indicated by the signals for C(4) and C(1) at 83.32 and 95.89 ppm, respectively. The spectrum of compound **4a** stops changing after some time, indicating the establishment of a ring-chain equilibrium, in which linear form **A** (60%) exists along with the cyclic pyranose **C** (25%) and furanose **D** forms (15%) (Table 5).

A single set of signals corresponding to cyclic pyranose form **C** is observed for the product of condensation of the hydrazide of 2-aminobenzoic acid with L-arabinose **4b** immediately after dissolution. As in the case of compound **4a**, we may assume that the spectral data reflect the structure of compound **4b** in the crystalline state. Sets of signals corresponding both to the five-membered furanose form **D** and linear aldosohydrazone form **A** gradually arise in the ^{13}C NMR spectrum in DMSO-d_6. The ^{13}C NMR signal at 151.35 ppm for the C=N carbon is characteristic for linear form **A** (Table 5).

Going from ribose derivative **4a** and arabinose derivative **4b** to products of condensation with hexoses **4c**,**d** is accompanied by disappearance of the cyclic furanose form **D** and linear aldosohydrazone form **A** from the equilibrium. In the crystalline state, compounds **4c**,**d** have pyranose structure **C**, while the ^{13}C NMR spectra indicate that these compounds in DMSO-d_6 solution are represented by geometric α,β-isomers of this form.

Thus, in contrast to the results of a study of El-Barbary et al. [12] on the structure of a series of 3,5-di-substituted 2-aminobenzoylhydrazones of aldoses, in which the linear aldosohydrazone structure was adopted, we have shown that, in the case of aldose 2-aminobenzoylhydrazones **4a-d**, these compounds may convert to alternative cyclic pyranose and furanose forms and that both ring-chain and ring-linear-ring tautomeric equilibria are possible.

Different behavior is found for compounds **4e-h**, which are the products of the condensation of aldoses with N-(2-aminobenzoyl)-N-methylhydrazine. The change in the ^{13}C NMR spectra of all these products indicates that they have the cyclic benzo-1,3,4-triazepine structure **B** in the crystalline state. The ^{13}C NMR signal for atom C(1) at 75-80 ppm characteristic for an sp^3-hybridized carbon atom in a seven-membered ring attached to two nitrogen atoms [2, 3, 11] is diagnostic for benzo-1,3,4-triazepine form **B**. Signals corresponding to a second configurational isomer of the benzo-1,3,4-triazepine form **B'** are found in the ^{1}H and ^{13}C NMR spectra of compounds **4e-h** in DMSO-d_6. It was impossible to determine the *2R*- or *2S*-configuration of these derivatives. The ^{1}H and ^{13}C NMR spectra of solutions of the products of the condensation of aldoses with N-(2-aminobenzoyl)-N-methylhydrazine stop changing after 4-7 days, indicating that transition to the possible linear form **A** and cyclic pyranose form **C** does not occur.

A tendency to cyclize with formation of a seven-membered benzo-1,3,4-triazepine ring is a common feature of compounds **4e-h** and the previously studied products of the condensation of aldoses with the hydrazide of 2-methylbenzoic acid. Intramolecular attack by the sulfur atom at the C=N bond of the hydrazone fragment of the initially-formed linear form leads to coexistence in solution of an additional seven-membered benzo-1,3,4-triazepine tautomer along with the cyclic pyranose tautomer [11].

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were taken on a Bruker AV-400 spectrometer at 400 MHz and AT-500 spectrometer at 125 MHz, respectively with HMDS as the internal standard. The quantitative composition of the tautomeric forms was determined by integration of the corresponding signals in the ^{1}H NMR spectra. Monitoring of the reaction course and purity of the products was carried out by thin-layer chromatography on Silufol UV-254 plates using 4:1 benzene–acetone as the eluent for compounds **2a-k** and 12:5:4 ethyl acetate–pyridine–water as the eluent for compounds **4a-h**. Hydrazides **1a**,**b** were obtained according to reported methods [2, 10].

N-(2-Aminobenzoyl)-N-methylhydrazones of Aldehydes 2a-k. A mixture of corresponding aldehyde (15 mmol) and N-(2-aminobenzoyl)-N-methylhydrazine **1a** (1.65 g, 10 mmol) in methanol (50 ml) was maintained at room temperature for 2 h. The crystalline precipitate was filtered off, washed with ether, dried, and recrystallized from 1:4 benzene–petroleum ether.

2-Aminobenzoylhydrazones and N-(2-aminobenzoyl)-N-methylhydrazones of Aldoses 4a-h. A mixture of corresponding monosaccharide **3a-d** (10 mmol) and N-(2-aminobenzoyl)-N-methylhydrazine **1a** or 2-aminobenzoylhydrazine **1b** (10 mmol) in methanol (25 ml) was heated at reflux for 2-6 h. After removal of the solvent, the crystalline precipitate was filtered off, washed with ether, dried, and recrystallized from 1:8 methanol–acetonitrile.

REFERENCES

1. O. Hromatka, M. Knollmüller, and F. Krenmüller, *Monatsh. Chem.*, **100**, 941 (1968).
2. M. Gál, E. Tihanyi, and P. Dvortsák, *Acta Chim. Hung.*, **123**, 55 (1986).
3. K. Pihlaja, M. F. Simeonov, and F. Fülöp, *J. Org. Chem.*, **62**, 5080 (1997).
4. B. V. Chernitsa, A. Yu. Ershov, D. A. Komarova, S. I. Yakimovich, V. V. Pakal'nis, I. V. Zerova, I. V. Lagoda, and V. V. Shamanin, *Khim. Geterotsikl. Soedin.*, 1725 (2010). [*Chem. Heterocycl. Chem.*, **46** 1400 (2010)].
5. Yu. P. Kitaev and B. I. Buzykin, *Hydrazones* [in Russian], Nauka, Moscow (1974), p. 381.
6. N. A. Parpiev, V. G. Yusupov, S. I. Yakimovich, and Kh. T. Sharipov, *Acylhydrazones and Their Transition Metal Complexes* [in Russian], Fan, Tashkent (1988), p. 163.
7. K. Neuvonen, F. Fülöp, H. Neuvonen, M. Simeonov, and K. Pihlaja, *J. Phys. Org. Chem.*, **10**, 55 (1997).
8. A. Yu. Ershov, I. V. Lagoda, S. I. Yakimovich, V. V. Pakal'nis, I. V. Zerova, A. V. Dobrodumov, and V. V. Shamanin, *Zh. Org. Khim.*, **45**, 678 (2009).
9. A. Yu. Ershov, I. V. Lagoda, S. I. Yakimovich, I. V. Zerova, V. V. Pakal'nis, and V. V. Shamanin, *Zh. Org. Khim.*, **45**, 1503 (2009).
10. P. S. N. Reddy and P. P. Reddy, *Indian J. Chem.*, **27B**, 135 (1988).
11. V. V. Alekseyev, A. Yu. Ershov, B. V. Chernitsa, V. A. Doroshenko, I. V. Lagoda, S. I. Yakimovich, I. V. Zerova, V. V. Pakal'nis, and V. V. Shamanin, *Zh. Org. Khim.*, **46**, 865 (2010).
12. A. El-Barbary, A. Z. A. El-Ezz, A. M. Sharaf, and C. Nielsen, *Phosphorus, Sulfur, Silicon*, **181**, 1895 (2006).