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CONDENSATION PRODUCTS OF 1-ARYL-3-ETHOXYCARBONYL-2-METHYL-1,4,5,6-TETRAHYDRO-4(1H)PYRIDONES WITH HYDRAZINE, PHENYLHYDRAZINE, AND HYDROXYLAMINE

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We have studied condensation of 1-(4-bromophenyl- and 2,5-dimethylphenyl)-3-ethoxycarbonyl-2-methyl-1,4,5,6-tetrahydro-4(1H)pyridones with hydrazine, phenylhydrazine, and hydroxylamine, as a result of which we obtained nucleophilic substitution and intramolecular cyclization products: 5-(4-bromophenyl- and 2,5-dimethylphenyl)-4-methyl-2,5,6,7-tetrahydro-3H-pyrazole[4,3-c]pyridin-3-ones, 5-(4-bromophenyl- and 2,5-dimethylphenyl)-4-methyl-6,7-dihydroisoxazole[4,3-c]pyridin-3(5H)-ones. We used computer modeling of the molecules of the studied compounds to obtain additional information on the structural features of the reaction products.

Keywords: 1-aryl-3-ethoxycarbonyl-2-methyl-1,4,5,6-tetrahydro-4(1H)pyridones, hydrazides of pyridine-3-carboxylic acids, keto–enol tautomerism, condensation, exchange processes, ^{1}H and ^{13}C NMR spectroscopy, cyclization.

Pyridone derivatives include compounds known to have pharmaceutical [1, 2] and agrochemical [1-3] activity.

In this paper, we have studied the reactions of 1-aryl-3-ethoxycarbonyltetrahydro-2-methyl-4(1H)-pyridones with some nucleophiles. When tetrahydropyridones **1a,b** are refluxed with hydrazine hydrate in methanol, the hydrazides of 1-(4-bromophenyl)-4-hydroxy-2-methyl-1,6-dihydropyridine-3-carboxylic acid (**2a**) and 1-(2,5-dimethylphenyl)-4-hydroxy-2-methyl-1,6-dihydropyridine-3-carboxylic acid (**2b**) are formed, which separate out from the reaction mixture even during the reaction.

According to the ^{1}H NMR spectra, the enol form is observed not only in the synthesized hydrazides **2a,b** but also in their condensation products with aromatic aldehydes: 2-(4-methoxyphenyl)methylidene hydrazide of (1-(4-bromophenyl)-4-hydroxy-2-methyl-1,6-dihydro-3-pyridinecarboxylic acid (**3a**), 2-(3,4-dimethoxyphenyl)-methylidene hydrazide of 1-(4-bromophenyl)-4-hydroxy-2-methyl-1,6-dihydropyridine-3-carboxylic acid (**4a**), 2-(4-dimethylaminophenyl)methylidene hydrazide of 1-(2,5-dimethylphenyl)-4-hydroxy-2-methyl-1,6-dihydropyridine-3-carboxylic acid (**5b**), apparently due to the strong intramolecular hydrogen bond between the oxygen atom of the 4-OH group of the heterocycle and the hydrazine moiety. When compound **1a** is heated with phenylhydrazine in methanol, the carbonyl group in the 4 position of the heterocycle undergoes nucleophilic

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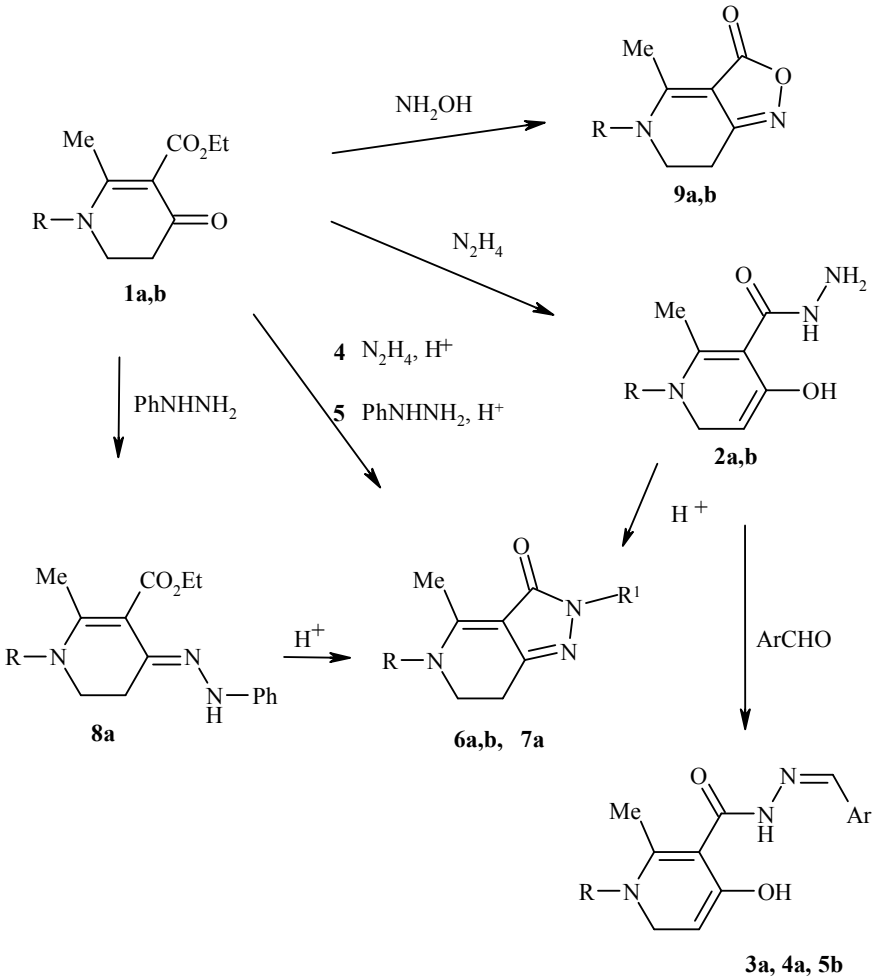
attack first of all. In fact, in the ^{1}H NMR spectrum of compound **8a**, we observe signals from the ester group OEt as a quartet at 4.24 ppm and a triplet at 1.28 ppm, and new signals also appear from the monosubstituted phenyl. The reaction of 1-(4-bromophenyl)-3-ethoxycarbonyl-2-methyl-1,4,5,6-tetrahydro-4(1H)pyridone (**1a**) with hydrazine hydrate or phenylhydrazine in glacial acetic acid at the boiling point of the mixture leads to formation of condensed bicyclic compounds: 5-(4-bromophenyl)-4-methyl-2,5,6,7-tetrahydro-3H-pyrazolo-[4,3-*c*]pyridin-3-one (**6a**) and 5-(4-bromophenyl)-4-methyl-2-phenyl-2,5,6,7-tetrahydro-3H-pyrazolo[4,3-*c*]-pyridin-3-one (**7a**). By the same method, from compound **1b** we also obtained 5-(2,5-dimethylphenyl)-4-methyl-2,5,6,7-tetrahydro-3H-pyrazolo[4,3-*c*]pyridin-3-one (**6b**). Upon condensation of tetrahydropyridones **1a,b** with hydroxylamine hydrochloride in a boiling mixture of 2-propanol and pyridine, the corresponding 5-aryl-4-methyl-6,7-dihydroisoxazolo[4,3-*c*]pyridin-3(5H)-ones **9a,b** are formed.



a R = 4-BrC$_6$H$_4$; **b** R = 2,5-Me$_2$C$_6$H$_3$; **3a** Ar = 4-MeOC$_6$H$_4$; **4a** Ar = 3,4-(MeO)$_2$C$_6$H$_3$; **5b** Ar = 4-Me$_2$NC$_6$H$_4$; **6a,b** R^1 = H; **7a** R^1 = Ph

The structures of the synthesized compounds were confirmed by ^{1}H and ^{13}C NMR spectroscopy, with assignment of the signals based on the general substituent additivity rules [4]. The appearance of new characteristic signals in the NMR spectra of compounds **6a,b, 7a, 9b** confirms the formation of new cyclic structures. The NMR spectra of the compounds **2a,b, 3a, 4a,** and **5b** proved to be unexpectedly complex: the ^{1}H NMR spectra were complicated by the presence of a large number of signals and some broadening of those signals; the ^{13}C NMR spectra were complicated by the absence of the required number of signals. Apparently

TABLE 1. ^{1}H NMR Spectra (DMSO-d_6) for Compounds **2-9**

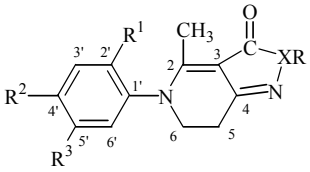
Com-pound	Chemical shifts, δ, ppm (*J*, Hz)
2a	2.34 (3H, br. s, 2-CH_3); 2.82 (2H, m*, CH_2CO); 3.25 (2H, m*, CH_2N); 5.30 (2H, br. s, NH_2); 5.87 (1H, br. s*, CH=); 6.53 (2H, d, *J* = 8.9, H-2', H-6' arom.); 7.19 (2H, d, *J* = 8.9, H-3', H-5' arom.); 10.84 (1H, br. s, NH)
2b	2.0 (3H, s, 2'-CH_3); 2.20 (3H, s, 5'-CH_3); 2.36 (3H, br. s, 2-CH_3); 2.91 (2H, m*, CH_2CO); 3.32 (2H, m*, CH_2N); 4.76 (1H, br. s*, CH=); 5.33 (2H, br. s, NH_2); 6.32 (1H, d, *J* = 7.4, H-3' arom.); 6.37 (1H, s, H-6' arom.); 6.82 (1H, d, *J* = 7.4, H-4' arom.); 10.87 (1H, br. s, NH)
3a	2.62 (3H, br. s, 2-CH_3); 2.92 (2H, m*, CH_2CO); 3.33 (2H, m*, CH_2N); 3.82 (3H, s, OCH_3); 5.90 (1H, br. s*, CH=); 6.56 (2H, d, *J* = 8.8, H-2', H-6' arom.); 7.02 (2H, d, *J* = 8.8, H-2", H-6" arom.); 7.19 (2H, d, *J* = 8.8, H-3', H-5' arom.); 7.60 (2H, d, *J* = 8.8, 3"-, 5"-H); 8.39 (1H, s, CH=); 11.21 (1H, br. s, NH); 14.20 (1H, br. s, OH)
4a	2.64 (3H, br. s, 2-CH_3); 2.89 (2H, m*, CH_2CO); 3.40 (2H, m*, CH_2N); 3.82 (6H, s, OCH_3); 5.89 (1H, br. s*, CH=); 6.56 (2H, d, *J* = 8.8, H-2', H-6' arom.); 7.05 (1H, d, *J* = 8.4, H-5" arom.); 7.20 (2H, d, H-3', H-5' arom.); 7.35 (1H, d. d, H-6" arom.); 7.41 (1H, s, H-2" arom.); 8.38 (1H, s, CH=); 11.21, 12.20 (1H, br. s, NH); 14.20 (1H, br. s, OH)
5b	2.01 (3H, s, 2'-CH_3); 2.20 (3H, s, 5'-CH_3); 2.65 (3H, br. s, 2-CH_3); 2.96 (2H, m*, CH_2CO); 3.00 (6H, s, $N(CH_3)_2$); 3.37 (2H, m*, CH_2N); 4.80 (1H, m*, CH=); 6.32 (1H, d, *J* = 7.4, H-3' arom.); 6.41 (1H, s, H-6' arom.); 6.76 (2H, d, *J* = 8.9, H-3", H-5" arom.); 6.84 (1H, d, *J* = 7.4, H-4' arom.); 7.63 (2H, d, *J* = 8.9, H-2", H-6" arom.); 8.28 (1H, s, CH=); 11.17, 12.01 (1H, br. s, NH); 14.03, 14.26 (1H, br. s, OH)
6a	2.18 (3H, s, 2-CH_3); 2.78 (2H, t, *J* = 6.7, CH_2C=N); 3.90 (2H, t, *J* = 6.7, CH_2N); 7.42 (2H, d, *J* = 8.6, H-2', H-6' arom.); 7.70 (2H, d, *J* = 8.6, H-3', H-5' arom.); 10.50 (1H, s, NH)
6b	2.06 (3H, s, 2'-CH_3); 2.18 (3H, s, 5'-CH_3); 2.30 (3H, s, 2-CH_3); 2.81 (2H, m , CH_2C=N); 3.78 (2H, m , CH_2N); 7.10-7.32 (3H, m , H-3', H-4', H-6' arom.); 10.50 (1H, s, NH)
7a	2.36 (3H, s, 2-CH_3); 2.99 (2H, t, *J* = 7.2, CH_2C=N); 3.91 (2H, t, *J* = 7.2, CH_2N); 7.08 (2H, d, *J* = 8.8, H-2', H-6' arom.); 7.12 (1H, t, *J* = 7.4, H-4" arom.); 7.38 (2H, t, *J* = 7.4, H-3", H-5" arom.); 7.59 (2H, d, *J* = 8.8, H-3', H-5' arom.); 8.02 (2H, d, *J* = 7.4, H-2", H-6" arom.)
8a	1.28 (3H, t, $CH_2\underline{CH_3}$); 1.76 (3H, s, 2-CH_3); 2.93 (2H, t, CH_2C=N); 3.93 (2H, t, CH_2N); 4.24 (2H, q, $\underline{CH_2}CH_3$); 6.60-8.20 (9H, m , H arom.); 8.86 (1H, s, NH)
9a	2.15 (3H, s, CH_3); 2.94 (2H, t, CH_2C=N); 3.98 (2H, t, CH_2N); 7.43 and 7.74 (4H, 2d, *J* = 8.8, H arom.)
9b	2.18 (3H, s, 2'-CH_3); 2.21 (3H, s, 5'-CH_3); 2.37 (3H, s, 2-CH_3); 3.83 (2H, t, *J* = 6.6, CH_2C=N); 3.77-3.91 (2H, m , CH_2N); 6.96 (1H, s, H-6' arom.); 7.15-7.27 (2H, m , H-3', H-4' arom.)

* Signals for exchange multiplets of the keto–enol form.

keto–enol tautomerism is typical of compounds **2a,b, 3a, 4a,** and **5b** [5-8]. Detailed study of the ^{1}H NMR spectra of compounds **2a,b**, **3a, 4a**, and **5b** showed that in solution the compounds exist simultaneously in both the ketone and enol forms. The process of keto–enol tautomerism explains the broadening of the multiplets and the intensity distribution among them. We know that depending on the proton exchange rate between the keto–enol forms, in the ^{1}H NMR spectra [4] we observe either individual multiplets or broadened exchange signals. Computer modeling of the molecules, based on the concepts of molecular mechanics (MM2 method) and semiempirical molecular orbital methods (MOPAC program), is quite useful in studying keto–enol forms [9]. By minimization of the total energy of the model molecules, we established that the enol form is typically lower in energy (**2a** enol form, -6.79 kcal/mol) than the keto form (-3.43 kcal/mol).

In the ^{1}H NMR spectra of compounds **2a,b, 3a, 4a,** and **5b**, we observe individual multiplet signals for the protons of the NCH_2 moiety (~3.3 ppm) and the CH_2CO moiety (~2.9 ppm) and broad singlets for the CH=COH moiety (~5.9 ppm and 4.8 ppm). The integrated intensity of the multiplet signal from the protons of

TABLE 2. ^{13}C NMR Spectra (DMSO-d_6) for Compounds **6a, 6b, 71, 9b**



6a R^2 = Br, X = N, R, R^1, R^3 = H
6b R = H, X = N, R^1, R^3 = CH_3
R^2 = Br, X = N, R^1, R^3 = H,
7a R =
9b X = O, R^1, R^3 = CH_3

Carbon atoms	Chemical chifts, δ, ppm			
	6a	**6b**	**7a**	**9b**
$C_{(2)}$	160.92	161.37	163.89	164.98
$C_{(3)}$	100.40	99.45	102.40	91.45
$C_{(4)}$	144.82	144.83	145.28	156.30
$C_{(5)}$	23.30	23.35	23.88	22.38
$C_{(6)}$	52.96	52.02	53.38	51.87
C=O	166.76	166.77	162.56	172.05
2-CH_3	14.97	14.52	15.40	15.40
$C_{(1')}$	141.92	141.02	141.40	140.43
$C_{(2')}$	128.79	131.13	128.66	131.02
$C_{(3')}$	132.50	131.34	133.33	131.77
$C_{(4')}$	120.90	129.46	122.58	130.50
$C_{(5')}$	132.50	136.90	133.33	138.22
$C_{(6')}$	128.79	127.62	128.66	127.13
2'-CH_3		16.66		17.05
5'-CH_3		20.32		20.81
$C_{(1'')}$			139.17	
$C_{(2'')}$			118.89	
$C_{(3'')}$			127.95	
$C_{(4'')}$			123.93	

the NCH_2 group is equal to the sum of the intensities of the signals from the CH_2CO and CH=COH moieties. The multiplet from the NCH_2 moiety is broadened and quartet-shaped, probably due to overlap of a doublet (for the enol form) and a triplet (for the ketone form). The multiplet from the CH_2CO moiety (the ketone form) is broadened and triplet-shaped.

In the spectra of compounds **2a,b, 3a, 4a,** and **5b**, we observed significant broadening and a signal from the protons of the 2-CH_3 group, although this group is not involved in the direct process of keto–enol exchange. Detailed study of the data obtained by computer modeling (Table 3) indicated the presence of charge transfer (the appearance of a partial double bond N–$C_{(2)}$) between the benzene ring and the heterocycle in the studied structures. In this case, an extended double bond system is formed. Since the CH=CH group has a greater *-I* effect [10] than the phenyl moiety, the shielding of the 2-CH_3 group will change. A change in the electron density in the heterocycle is also indicated by the appearance of conjugation between $C_{(2)}$=$C_{(3)}$ and $C_{(4)}$=$C_{(5)}$ upon formation of the enol form, and also formation and breaking of the intramolecular hydrogen bond [4, 6, 11-13] between the 4-OH and 3-C–C=O groups. The change in the electron density in the heterocycle affects the chemical shift of the signals from the protons of the 2-CH_3 group and thus is responsible for broadening of such signals.

The presence of a NHN=CHAr moiety in compounds **3a, 4a,** and **5b** is why *Z/E*-isomerism is possible, In the ^{1}H NMR spectra of compounds **4a** and **5b**, there are rather intense signals from protons of the NH group at 11.21 ppm and 11.17 ppm respectively, and there are low-intensity broadened signals at 12.0 ppm. Based on

TABLE 3. Models of Synthesized Compounds (Total Energy Optimized to a Global Minimum)

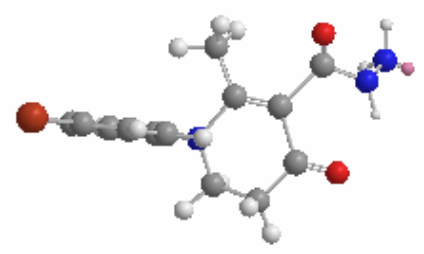
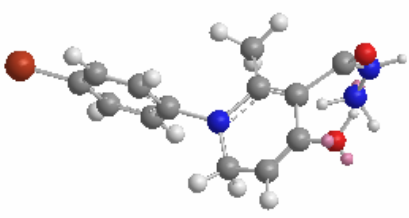
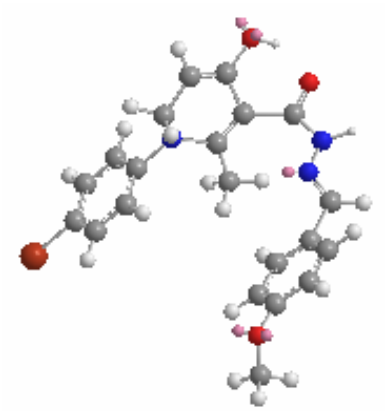
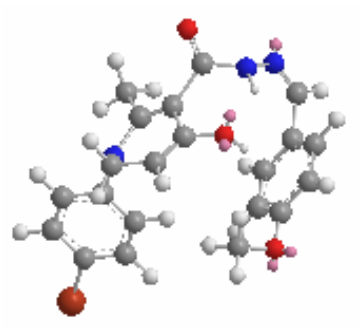
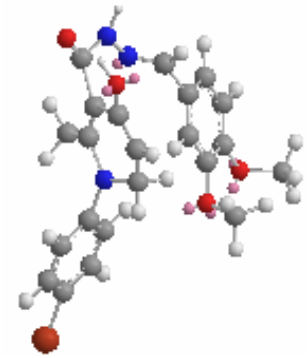
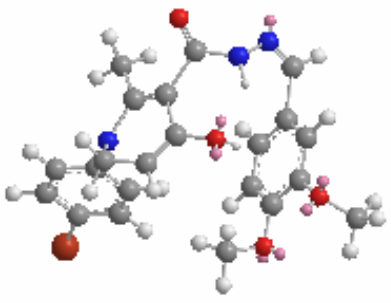
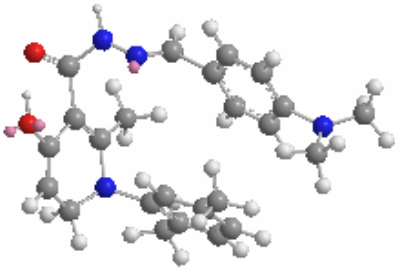
2a (keto form)	**2a** (enol form)
	
-3.43 kcal/mol	-6.79 kcal/mol
3a (*E*)	**3a** (*Z*)
	
-4.06 kcal/mol	-16.51 kcal/mol
4a (*E*)	**4a** (*Z*)
	
-5.75 kcal/mol	-16.41 kcal/mol

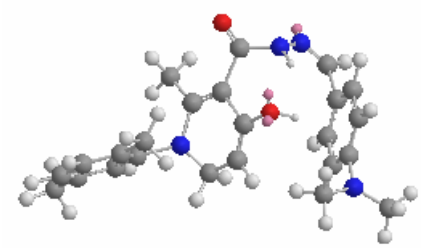
TABLE 3 (continued)

5b (*E*)



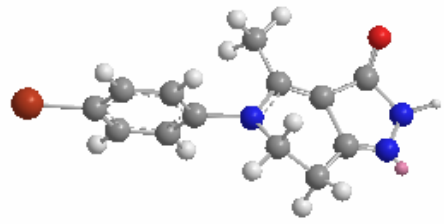
-10.51 kcal/mol

5b (*Z*)



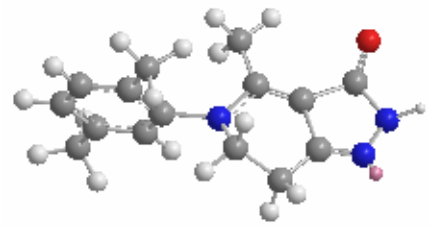
-18.71 kcal/mol

6a



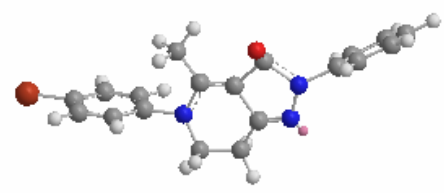
15.40 kcal/mol

6b



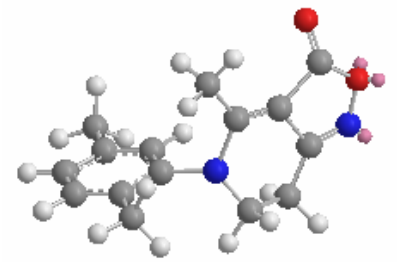
15.35 kcal/mol

7a



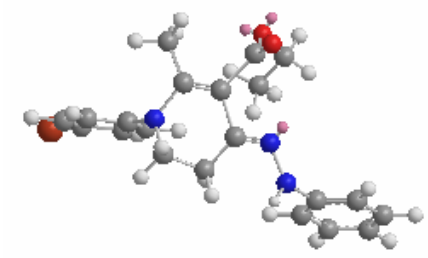
15.33 kcal/mol

9b



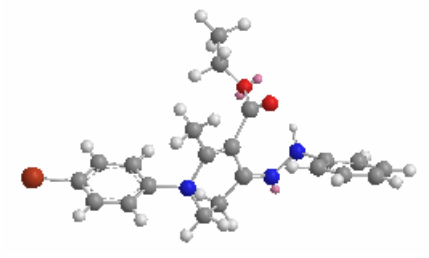
18.62 kcal/mol

8a (*Z*-isomer relative to the $C_{(5)}$ atom in the heterocycle)



1.53 kcal/mol

8a (*E*-isomer relative to the $C_{(5)}$ atom in the heterocycle)



2.61 kcal/mol

this, we can conclude that the studied compounds **4a** and **5b** exist predominantly in the form of *Z*-isomers, but with a fairly small *E*-isomer impurity. We do not observe *Z/E*-isomerism for compound **3a**. The computer modeling data for **3a, 4a**, and **5b** showed that the existence of *Z*-isomers is most favorable, since their energy is about 10 kcal/mol lower than the energy of the *E*-isomer.

According to computer modeling data, compound **8a** more likely exists in the form of the *Z*-isomer (relative to the $C_{(5)}$ atom of the heterocycle), having lower total energy than the corresponding *E* isomer. The bulky substituent at the $C_{(3)}$ atom probably hinders formation of the *E*-isomer [13].

The signals for the carbon atoms in the ^{13}C NMR spectra of compounds **6a,b, 7a, 9b** were fully assigned. In these compounds, exchange processes are stopped by formation of cyclic structures. In the ^{13}C NMR spectra of compounds **2a,b, 3a, 4a, 5b**, due to a dynamic equilibrium between the interconverting keto–enol isomers, formation of a system of double bonds between the benzene and heterocyclic moieties, and formation of intramolecular hydrogen bonds, the shielding effect for the carbon atoms becomes somewhat indeterminate. So some signals in the compounds with a change in electron density may not be detected by the instrument. The problem of assigning the lines in the ^{13}C NMR spectra of such compounds is complicated by the averaged nature of the effect of the substituents due to the keto–enol forms of the compounds formed, and also the possibility of recording individuals signals for atoms of the keto–enol forms.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were obtained on a Varian Unity Inova (300 MHz) and a Bruker AC 250-P (250 MHz), internal standard TMS. The IR spectra in KBr disks were recorded on a Perkin-Elmer Spectrum BX FT-IR system. The course of the reactions and the purity of the compounds obtained were monitored by TLC on Silufol UV-254 plates, visualization in UV light or iodine vapors.

Hydrazide of 1-(4-Bromophenyl)-4-hydroxy-2-methyl-1,6-dihydropyridine-3-carboxylic Acid (2a). 1-(4-Bromophenyl)-3-ethoxycarbonyl-2-methyl-1,4,5,6-tetrahydro-4(1H)-pyridone (**1a**) (0.5 g, 1.5 mmol) and hydrazine hydrate (0.15 g, 3.0 mmol) in methanol (10 ml) were refluxed for 2 h. The reaction mixture was cooled down, the precipitated crystals were filtered out and washed with methanol and then ether, and then dried. Yield 0.38 g (78%); mp 200-202°C (dioxane). IR spectrum, ν, cm^{-1}: 3383.83, 3317.19, 3148.66; 1640.36. Found, %: C 48.29; H 4.22; N 12.87. $C_{13}H_{14}BrN_3O_2$. Calculated, %: C 48.17; H 4.35; N 12.96.

Hydrazide of 1-(2,5-Dimethylphenyl)-4-hydroxy-2-methyl-1,6-dihydro-3-pyridinecarboxylic Acid (2b) was obtained as for compound **2a,** from 1-(2,5-dimethylphenyl)-3-ethoxycarbonyl-2-methyl-1,4,5,6-tetrahydro-4(1H)-pyridone (**1b**) (1.0 g, 3.5 mmol), hydrazine hydrate (0.4 g, 8.0 mmol) and methanol (10 ml). Yield 0.75 g (78%); mp 195-196°C (dioxane). Found, %: C 65.76; H 6.82; N 15.18. $C_{15}H_{19}N_3O_2$. Calculated, %: C 65.91; H 7.01; N 15.37.

2-(4-Methoxyphenyl)methylidene Hydrazide of 1-(4-Bromophenyl)-4-hydroxy-2-methyl-1,6-dihydropyridine-3-carboxylic Acid (3a). A mixture of hydrazide **2a** (0.33 g, 1.0 mmol) and 4-methoxybenzaldehyde (0.27 g, 2.0 mmol) in 2-propanol (10 ml) was boiled for 2 h and cooled down; the precipitate was filtered out and washed with propanol and then ether, and then dried. Yield 0.37 g (84%); mp 219-221°C (2-propanol). IR spectrum, ν, cm^{-1}: 3320.48, 3148.92; 1632.12, 1605.66. Found, %: C 57.17; H 4.47; N 9.58. $C_{21}H_{20}BrN_3O_3$. Calculated, %: C 57.02; H 4.56; N 9.50.

2-(3,4-Dimethoxyphenyl)methylidene Hydrazide of 1-(4-Bromophenyl)-4-hydroxy-2-methyl-1,6-dihydropyridine-3-carboxylic Acid (4a) was obtained as for methylidene hydrazide **3a** from hydrazide **2a** (0.33 g, 1.0 mmol), 3,4-dimethoxybenzaldehyde (0.25 g, 1.5 mmol) in 2-propanol (10 ml). Yield 0.40 g (85%); mp 217-219°C (2-propanol). Found, %: C 55.49; H 4.40; N 9.18. $C_{22}H_{22}BrN_3O_4$. Calculated, %: C 55.94; H 4.69; N 8.90.

2-[4-(N,N-Dimethylamino)phenyl]methylidene Hydrazide of 1-(2,5-Dimethylphenyl)-4-hydroxy-2-methyl-1,6-dihydropyridine-3-carboxylic Acid (5b) was obtained similarly, from hydrazide **2b** (0.5 g, 1.8 mmol), 4-dimethylaminobenzaldehyde (0.3 g, 1.8 mmol) in 2-propanol (10 ml). Yield 0.34 g (47%); mp 245-246°C (2-propanol). Found, %: C 71.44; H 6.75; N 13.98. $C_{24}H_{28}N_4O_2$. Calculated, %: C 71.26; H 6.98; N 13.85.

5-(4-Bromophenyl)-4-methyl-2,5,6,7-tetrahydro-3H-pyrazolo[4,3-*c*]pyridin-3-one (6a). A. Compound **1a** (0.5 g, 1.5 mmol), hydrazine hydrate (0.15 g, 3.0 mmol), and glacial acetic acid (5 ml) were refluxed for 3 h. The mixture was diluted with water (15 ml) and cooled down; the precipitated crystals of compound **6a** were filtered out and washed with water and then ethanol, and then dried. Yield 0.38 g (82%); mp 277-278.5°C (dioxane). IR spectrum, ν, cm^{-1}: 3258.10, 3142.43; 1644.53. Found, %: C 51.16; H 4.07; N 13.65. $C_{13}H_{12}BrN_3O$. Calculated, %: C 51.00; H 3.95; N 13.73.

B. Obtained by boiling hydrazide **2a** (0.49 g, 1.5 mmol) and glacial acetic acid (5 ml) for 1.5 h. Isolated as in method A. Yield 0.39 g (85%).

5-(2,5-Dimethylphenyl)-4-methyl-2,5,6,7-tetrahydro-3H-pyrazolo[4,3-*c*]pyridin-3-one (6b). A. Synthesized and isolated as for pyrazolepyridinone **6a**, from tetrahydropyridone **1b** (1.0 g, 3.5 mmol), hydrazine hydrate (0.3 g, 6.0 mmol), and glacial acetic acid (5 ml). Yield 0.62 g (70%); mp 300-301°C (dioxane). Found, %: C 70.72; H 6.52; N 16.67. $C_{15}H_{17}N_3O$. Calculated, %: C 70.56; H 6.71; N 16.46.

B. Obtained by boiling hydrazide **2b** (0.5 g, 1.8 mmol) and glacial acetic acid (5 ml) for 1.5 h. Isolated as in method A. Yield 0.65 g (73%).

5-(4-Bromophenyl)-4-methyl-2-phenyl-2,5,6,7-tetrahydro-3H-pyrazolo[4,3-*c*]pyridin-3-one (7a). A. A mixture of compound **1a** (0.5 g, 1.5 mmol), phenylhydrazine (0.32 g, 3.0 mmol) and glacial acetic acid (5 ml) was boiled for 3 h. The reaction mixture was diluted with water (15 ml) and cooled down; the precipitated crystals were filtered out and washed with methanol and then ether, and then dried. Yield 0.40 g (75%); mp 262-263.5°C (dioxane). IR spectrum, ν, cm^{-1}: 1649.42; 1592.23; 1571.49; 1498.90; 1482.46; 1330.71. Found, %: C 59.83; H 4.12; N 10.87. $C_{19}H_{16}BrN_3O$. Calculated, %: C 59.70; H 4.22; N 10.99.

B. Compound **7a** was obtained by boiling hydrazone **8a** (0.43 g, 1.0 mmol) in glacial acetic acid (9 ml). Isolated as in method A. Yield 0.42 g (80%).

Ethyl Ester of 1-(4-Bromophenyl)-2-methyl-4-(2-phenylhydrazono)-1,4,5,6-tetrahydropyridine-3-carboxylic Acid (8a). A mixture of compound **1a** (0.5 g, 1.5 mmol), phenylhydrazine (0.32 g, 3.0 mmol) in methanol (10 ml) was boiled for 2 h. The reaction mixture was cooled down; the precipitated crystals were filtered out and washed with methanol and then ether, and then dried. Yield 0.47 g (73%); mp 267-268.5°C (2-propanol). IR spectra, ν, cm^{-1}: 3275.83; 1649.96; 1591.96; 1571.21; 1482.75; 1330.82. Found, %: C 58.70; H 5.26; N 9.97. $C_{21}H_{22}BrN_3O_2$. Calculated, %: C 58.89; H 5.18; N 9.81.

5-(4-Bromophenyl)-4-methyl-6,7-dihydroisoxazolo[4,3-*c*]pyridin-3(5H)-one (9a). A mixture of tetrahydropyridone **1a** (0.5 g, 1.5 mmol), hydroxylamine hydrochloride (0.16 g, 2.25 mmol), 2-propanol (5 ml), and pyridine (1 ml) was boiled for 2 h and then diluted with water (10 ml). The precipitate was filtered out and washed with propanol and then ether, and then dried. Yield 0.36 g (78%); mp 262-264°C (2-propanol). IR spectrum, ν, cm^{-1}: 3419.26, 3363.66, 3044.95, 2980.17, 1720.85, 1601.97. Found, %: C 50.98; H 3.52; N 9.20. $C_{13}H_{11}BrN_2O_2$. Calculated, %: C 50.84; H 3.61; N 9.12.

5-(2,5-Dimethylphenyl)-4-methyl-6,7-dihydroisoxazolo[4,3-*c*]pyridin-3-(5H)-one (9b) was obtained from pyridone **1b** (0.43 g, 1.5 mmol), hydroxylamine hydrochloride (0.16 g, 2.25 mmol), 2-propanol (5 ml), and pyridine (1 ml) by the method for synthesis and isolation of compound **7a**. Yield 0.31 g (81%); mp 228-229°C (2-propanol). Found, %: C 70.41; H 6.11; N 11.09. $C_{15}H_{16}N_2O_2$. Calculated, %: C 70.29; H 6.29; N 10.93.

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