NMR SPECTROSCOPY IN STRUCTURE DETERMINATION OF A NUMBER OF POLYSUBSTITUTED PYRIDINES AND THIAZOLOPYRIMIDINES

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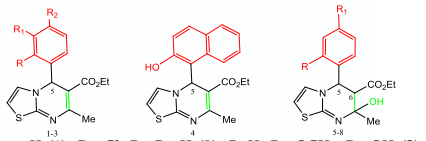
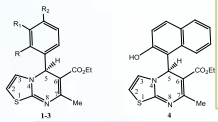
Abstract: Using the one-dimensional and two-dimensional NMR methods (1H, 13C, HMBC, COSY, HSQC) the structure of compounds of a variety of hydroxythiazolopyrimidincarboxylates, its dehydrated forms and chromenopyridinecarbonitriles was established and isomerization transformations were studied. These compounds were obtained in stages or by three-component condensation of heterocyclic amines (1,3-thiazole-2-amine, 2-aminopyridine), substituted aromatic aldehydes and active methylene compounds (ethyl acetoacetate, malononitrile).



R= R_1= R_2 = H (1); R= Cl, R_1=R_2=H (2); R=H, R_1=OCH_3, R_2=OH (3); R=NO_2, R_1=H (5); R=CH_3, R_1=H (6); R=H, R_1=Cl (7); R=H, R_1=Br (8)

The structure of previously synthesized compounds of the thiazolopyrimidine series, characterized by the presence or absence of a hydroxyl group in the pyrimidine fragment and the number, nature and position of substituent groups in the aryl substituent [1], was established by spectral methods (1H NMR, 13C NMR, HSQC $^1H/^{13}C$, HMBC $^1H/^{13}C$).

Two-dimensional (HSQC $^1H/^{13}C$, HMBC $^1H/^{13}C$) NMR spectroscopy



^1H NMR spectrum (δ, ppm)
H^5 (s, 5.20-6.45),
CH_3 (s, 2.17-2.92),
$CH_2\underline{CH_3}$ (t, 1.11-1.20),
$\underline{CH_2}CH_3$ (m, 3.80-4.17),
H_{arom}+H^2 +H^3 (m, 6.59-7.37)

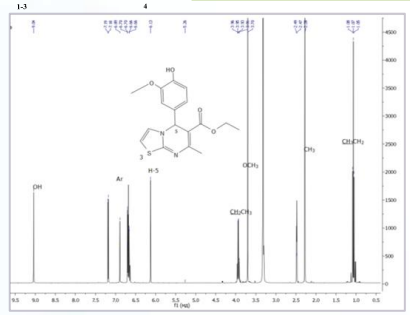
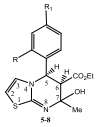


Fig. 1. ^1H NMR spectrum (δ, ppm) ethyl 5-(4-hydroxy-3-methoxyphenyl)-7-methyl-5H-thiazolo[3,2-a]pyrimidine-6-carboxylate (3) (Varian 400, acetone –d_6)



^1H NMR spectrum (δ, ppm)
H-5 (d, 6.27 ; d, 6.41),
H-6 (d, 4.35 ; d, 4.49),
OH (s, 2.15 ; s, 2.83),
CH_2CH_3 (m, 3.95-4.06; m, 4.08-4.18),
$CH_2\underline{CH_3}$ (t, 1.03 ; t, 1.13),
CH_3 (s, 2.27),
H_{arom}+H^2 +H^3 (m, 6.57-8.05)

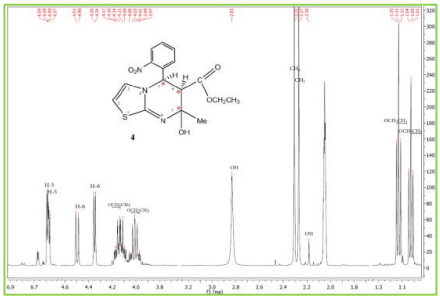


Fig. 2. 1H NMR spectrum (δ, ppm) ethyl 5- (2-nitrophenyl) -7-hydroxy-7-methyl-5H-6H-thiazolo [3,2-a] pyrimidine-6-carboxylate (5) (Varian 400, acetone –d6)

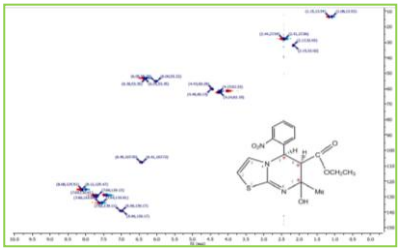


Fig. 3. Spectrum of HSQC $^1H/^{13}C$ethyl 5- (2-nitrophenyl) -7-hydroxy-7-methyl-5H-6H-thiazolo [3,2-a] pyrimidine-6-carboxylate (5)

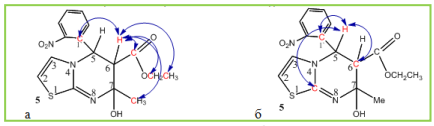
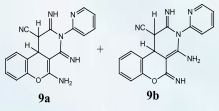


Fig. 4. Correlations in the HMBC $^1H/^{13}C$ spectrum of the H-6 proton (a) and the H-5 proton (b) ethyl 5- (2-nitrophenyl) -7-hydroxy-7-methyl-5H-6H-thiazolo [3,2 -a] pyrimidine-6-carboxylate (5)

Two-dimensional (HSQC $^1H/^{13}C$, HMBC $^1H/^{13}C$) NMR spectroscopy



Amino/imino tautomeric forms of 9a and 9b

^1H NMR spectrum (δ, ppm)
NH (s, 3.88; 3.30),
H_{10}-H_{11} (dd, 4,81-5,07),
NH_2 (s, 6.64; 6.17),
H_{arom}+H^2 +H^3 (m, 7.23-8.30)

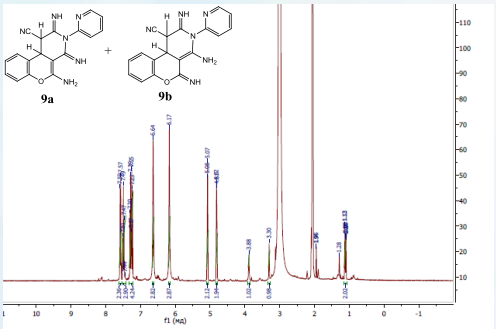
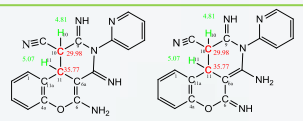


Fig.5. NMR ^1H spectrum of the tautomeric mixture of 5-amino-2,4-diimino-3-(pyridin-2-yl)-2,3,4,10b-tetrahydro-1H-chromeno[3,4-c]pyridine-1-carbonitrile (9a) and 4-amino-2,5-diimino-3-(pyridin-2-yl)-2,3,5,10b-tetrahydro-1H-chromeno[3,4-c]pyridine-1-carbonitrile (9b).



Main correlations in the NMR HSQC $^1H/^{13}C$ spectrum
H_{10}/C_{10}(4,81/29,98 ppm),
H_{11}/C_{11}(5,07/35,77 ppm).

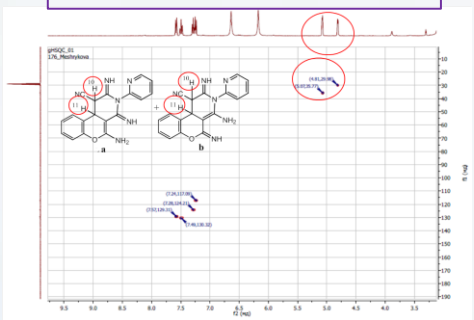
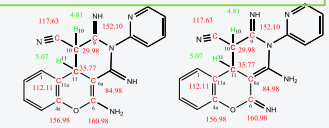


Fig. 6. NMR HSQC $^1H/^{13}C$ spectrum of the tautomeric mixture of 5-amino-2,4-diimino-3-(pyridin-2-yl)-2,3,4,10b-tetrahydro-1H-chromeno[3,4-c]pyridine-1-carbonitrile (9a) and 4-amino-2,5-diimino-3-(pyridin-2-yl)-2,3,5,10b-tetrahydro-1H-chromeno[3,4-c]pyridine-1-carbonitrile (9b).



Main correlations in the NMR HMBC $^1H/^{13}C$ spectrum
H_{10}/C_{11} (4,81/35,77 ppm), H_{10}/ CN (5,07/117,63 ppm)
H_{11}/C_{10} (5,07/29,98 ppm), H_{11}/ C_{6a} (5,07/84,98 ppm),
H_{11}/ C_{11a} (5,07/112,11 ppm), H_{11}/ C_1 (5,07/129,30 ppm),
H_{11}/ C_9 (5,07/152,10 ppm), H_{11}/ C_{4a} (5,07/156,98 ppm),
H_{11}/ C_6 (5,07/160,98 ppm), H_{11}/CN (5,07/117,63 ppm).

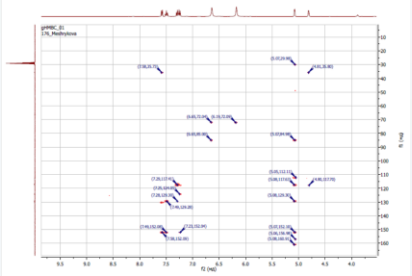


Fig. 7. NMR HMBC $^1H/^{13}C$ spectrum of the tautomeric mixture of 5-amino-2,4-diimino-3-(pyridin-2-yl)-2,3,4,10b-tetrahydro-1H-chromeno[3,4-c]pyridine-1-carbonitrile (9a) and 4-amino-2,5-diimino-3-(pyridin-2-yl)-2,3,5,10b-tetrahydro-1H-chromeno[3,4-c]pyridine-1-carbonitrile (9b).

Conclusion: the analysis of 1D and 2D NMR spectroscopy data allows to determine the structure of the obtained hydroxy-substituted thiazolopyrimidinecarboxylates, their dehydrated forms and chromeneopyridinecarbonitriles, propose a probable mechanism of the formation of thiazolopyrimidinecarboxylates and to differentiate the fine structure of the components of tautomeric mixture of chromenopyridinecarbonitriles.

1. N.O. Vasilkova, A.V. Nikulin, A.P. Krivenko. Synthesis and Structure of Thiazolopyrimidine Derivatives // Russ.J.Org.Chem. 2020. Vol.56. No. 6. P. 990-993. DOI: 10.1134/S1070428020060044

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