How to Cite: Nurkenov, O.A., Fazylov, S.D., Seilkhanov, T.M., Nurmaganbetov, Zh., Gazaliev, A.M., & Karipova, G.Zh. (2021) Synthesis and structure of thiourea derivatives of functionally substituted pyridines. *Bulletin of the University of Karaganda – Chemistry, 101(1), 4-11.* https://doi.org/10.31489/2021Ch1/4-11

ORGANIC CHEMISTRY

UDC 547.7/.8:547.057 https://doi.org/10.31489/2021Ch1/4-11

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Synthesis and structure of thiourea derivatives of functionally substituted pyridines

The article presents data on the synthesis and study of the structure of thiourea derivatives of functionally substituted pyridines. New thiourea derivatives containing a pharmacologically active pyridine moiety in their structure were obtained. As the starting synton, 2-amino-5-bromopyridine, 2-amino-3-hydroxypyridine and 2-aminomethylpyridine were selected. It was shown that the interaction of 2-amino-5-bromopyridine, 2-amino-3-hydroxypyridine and 2-aminomethylpyridine with ethyl and phenylisothiocyanates in ethanol leads to the formation of the corresponding pyridine-containing thioureas. The synthesis of the initial isothiocyanates was carriedout in situ from the corresponding acidic chlorides (benzoyl chloride and p-brombenzoyl chloride) by heating them with potassium thiocyanate in acetone. The structure of the synthesized compounds was studied by ^{1}H and ^{13}C NMR spectroscopy, as well as by the data of two-dimensional spectra of COSY (^{1}H-^{1}H) and HMQC (^{1}H-^{13}C). The values of chemical shifts, multiplicity, and integrated intensity of ^{1}H and ^{13}C signals in one-dimensional NMR spectra were determined. Using spectra in the formats COSY (^{1}H-^{1}H) and HMQC (^{1}H-^{13}C), homo- and heteronuclear interactions were established, confirming the structure of the studied compounds.

Keywords: ethylisothiocyanates, phenylisothiocyanates, 2-amino-5-bromopyridine, 2-amino-3-hydroxypyridine, 2-aminomethylpyridine, thioureas, 2-aminopyridine, ^{1}H and ^{13}C NMR spectra.

Introduction

It is known that the pyridine cycle is part of many vital organic compounds, which determines it's one of the leading roles among heterocycles. Compounds including the pyridine ring are widely used in nature [1–5]. Pyridine derivatives have found various practical applications, for example, as pesticides, herbicides (dithiopyr, imazachine, nicosulfuron, ivinpicolinic acid) and drugs (isoniazid, phthivazide, nialamide, promedol, and many others) [2, 3]. A significant part of the biologically active derivatives of pyridine is aminopyridines [5]. An example is suprastin, which has an antihistamine effect and is used for treatment of allergic dermatoses. Another example is the triamine derivative of phenazopyridine, which is used as an analgesic at painful urination.

Currently, 2-aminopyridines are widely used as key building blocks in the search and synthesis of anti-HIV/antiviral [6–9], anti-tuberculosis [10–13], analgesic [14, 15] and anti-cancer drugs [16–18].

Experimental

^{1}H and ^{13}C NMR spectra (DMSO-d_6) were recorded on a JNM-ECA Jeol 400 spectrometer (399.78 and 100.53 MHz respectively) relative to the signals of residual protons or carbon atoms of a deuterated solvent. The melting point of the substances was determined on an SMP10 digital instrument. The reaction progress

and the purity of the obtained compounds were monitored by thin layer chromatography on Silufol UV-254 plates in an isopropyl alcohol-ammonia-water system, 7:2:1. The plates showed iodine vapor.

1-(5-Bromopyridin-2-yl)-3-ethylthiourea (5). When stirring, 0.3 g (0.003 mol) of ethylisothiocyanate is added drop by drop to a solution of 0.5 g (0.003 mol) of 2-amino-5-brompyridine in 10 ml of ethanol. When stirring, 0.3 g (0.003 mol) of ethylisothiocyanate is added drop by drop to a solution of 0.5 g (0.003 mol) of 2-amino-5-brompyridine in 10 ml of ethanol. The reaction mixture was heated at 50–60 ºC for 6 hours. The completion of the reaction was monitored by TLC. Next, the reaction mixture was cooled, the precipitate formed was filtered off and recrystallized from ethanol. Obtained 0.38 g (49 %) of substance 5 with m.p. 120–121 ºC. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.15 t (2H, H-12,12,12, 3J 7.4), 3.57 q (2H, H-11,11, 3J 7.2), 7.10 d (1H, H-3, 3J 8.8), 7.91 dd (1H, H-4, 3J 11.6, 4J 2.8), 8.28 d (1H, H-6, 4J 2.8), 10.59 br.s (1H, H-7), 11.11 br. s (1H, H-11). ^{13}C NMR spectrum, δ_C, ppm: 14.47 (C-12), 39.46 (C-11), 105.61 (C-5), 112.29 (C-3), 116.04 (C-6), 146.63 (C-4), 159.16 (C-2), 179.60 (C-8). Cross peaks of the COSY (^{1}H-^{1}H) NMR spectra, ppm: H12-H11 (1.15, 3.57 and 3.54, 1.15), H3-H4 (7.11, 7.92 and 7.92, 7.11). Cross peaks of the HMQC (^{1}H-^{13}C) NMR spectra, ppm: H12-C12 (1.12, 14.36), H11-C11 (3.58, 9.67), H3-C3 (7.11, 112.30), H4-C4 (7.91, 146.50), H6-C6 (8.27, 116.05).

1-(5-Bromopyridin-2-yl)-3-phenylthiourea (6) was obtained analogously to compound 5 from 0.5 g (0.003 mol) of 2-amino-5-bromopyridine and 0.4 g (0.003 mol) of phenyl-isothiocyanate. Obtained 0.43 g (41 %) of substance 6 with m.p. 229–230 ºC. ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.16–7.24 m (2H, H-3,15), 7.35 t (2H, H-14,16, 3J 7.6), 7.64 d (2H, H-13,17, 3J 8.4), 8.00 dd (1H, H-4, 3J 9.2, 4J 2.8), 8.41 d (1H, H-6, 4J 2.4), 8.41 br. s (2H, H-7,11). ^{13}C NMR spectrum, δ_C, ppm: 112.82 (C-5), 115.43 (C-3), 124.84 (C-13,17), 126.16 (C-15), 129.03 (C-14,16), 139.21 (C-12), 142.25 (C-4), 146.73 (C-6), 152.75 (C-2), 178.62 (C-8). Cross peaks of the COSY (^{1}H-^{1}H) NMR spectra, ppm: H15-H14,16 (7.18, 7.31 and 7.31, 7.18), H14,16-H13,17 (7.31, 7.63 and 7.63, 7.31), H3-H4 (7.21, 7.98 and 7.98, 7.21). Cross peaks of the HMQC (^{1}H-^{13}C) NMR spectra, ppm: H3-C3 (7.17, 115.23), H15-C15 (7.25, 126.16), H14,16-C14,16 (7.34, 129.18), H13,17-C13,17 (7.67, 124.86), H4-C4 (8.02, 142.14) and H6-C6 (8.46, 146.76).

N-((5-Bromopyridin-2-yl)carbamothioyl)benzamide (7). While striring on a magnetic stirrer, 0.11 g (0.0012 mol) of potassium thiocyanate was added to a solution of 0.17 g (0.0012 mol) of benzoyl chloride in 10 ml of acetone. It was stirred at reflux for 2 hours, and then filtered through a paper filter to a solution of 0.2 g (0.0012 mol) of 2-amino-5-bromopyridine in 10 ml of acetone. Then it was stirred at 30–40 ºC for 3 hours. The solvent was distilled off. The residue was crystallized upon cooling with isopropanol. The product was recrystallized from isopropyl alcohol. Obtained 0.22 r (55 %) white powder with m.p. 159–160 ºC. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.31–1.52 m (1H. H9ax), 1.53–1.61 m (3H, H8ax,10ax,9eq), 1.70–1.88 m (1H, H8eq), 2.18–2.40 m (1H, H10eq), 2.76–2.84 m (2H, H4ax,7ax), 2.96–2.98 m (1H, H7eq), 3.58–3.65 m (2H, H4eq, H-11), 4.58 br. s (1H, H1), 5.12–5.21 m (1H, H5), 7.18–7.22 m (3H, H14,15,16), 7.25–7.37 m (4H, H13,17,22,23), 8.40–8.50 (2H, H19,21). ^{13}C NMR spectrum, δ_C, ppm: 19.43 (C9), 25.93 (C8), 26.96 (C10), 42.12 (C11), 42.14 (C4), 49.01 (C7), 70.49 (C5), 126.29 (C14,15,16), 127.58 (C15,21), 128.61 (C13,17,19,23), 134.60 (C13,17,22,23), 141.20 (C18), 141.22 (C12), 148.61 (C19,21). Cross peaks of the COSY (^{1}H-^{1}H) NMR spectra, ppm: H4ax-H5 (2.76, 5.16 and 5.16, 2.75), H13,17-H14,16 (7.34, 7.16 and 7.16, 7.34), H21,23-H22 (8.39, 7.34 и 7.34, 8.39). Cross peaks of the HMQC (^{1}H-^{13}C) NMR spectra, ppm: H4ax-C4 (2.75, 42.19), H4eq-C4 (3.64, 42.19), H5-C5 (5.20, 70.38), H8ax-C8 (1.53, 25.86), H8eq-C8 (1.73, 25.86), H9ax-C9 (1.37, 19.54), H9eq-C9 (1.61, 19.54), H10eq-C10 (2.25, 26.85), H11-C11 (3.58, 42.12), H22-C22 (7.34, 134.83).

4-Bromo-N-((5-bromopyridin-2-yl)carbamothioyl)benzamide (8) was obtained analogously to compound 7. Obtained 0.2 g (40 %) white powder with m.p. 205–207 ºC. ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.73–7.85 m (4H, H-15,16,18,19), 8.10–8.54 m (3H, H-3,4,6), 11.97 br. s (2H, H-7,11). ^{13}C NMR spectrum, δC, ppm: 115.93 (C-5), 117.54 (C-3), 127.74 (C-17), 131.24 (C-15,19), 132.09 (C-16,18), 138.59 (C-14), 141.23 (C-4), 149.45 (C-6), 150.70 (C-2), 167.80 (C-12), 178.43 (C-8). Cross peaks of the COSY (^{1}H-^{1}H) NMR spectra, ppm: H16,18-H15,19 (7.72, 7.83 and 7.83, 7.72). Cross peaks of the HMQC (1H-13C) NMR spectra, ppm: H16,18-C16,18 (27.72, 132.17).

1-(3-Hydroxypyridin-2-yl)-3-phenylthiourea (9). 1.23 g (0.009 mol) of phenylisothiocyanate is added dropwise with stirring to a solution of 1g (0.009 mol) of 2-amino-3-hydroxypyridine in 10 ml of ethanol. The reaction mixture was heated at 50–60 ºC for 6 hours. The completion of the reaction was monitored by TLC. Then the reaction mixture was cooled, the precipitate formed was filtered off and recrystallized from isopropanol. Obtained 0.9 g (41 %) of substance 9 with m.p. 258–259 ºC. ^{1}H NMR spectrum, δ, ppm (J, Hz): 7.03–7.09 m (2H. H-5,15), 7.36 t (2H, H-14,16, 3J 7.6), 7.73 d (2H, H-13,17, 3J 8.7), 7.79 d (1H, H-4, 3J 8.2),

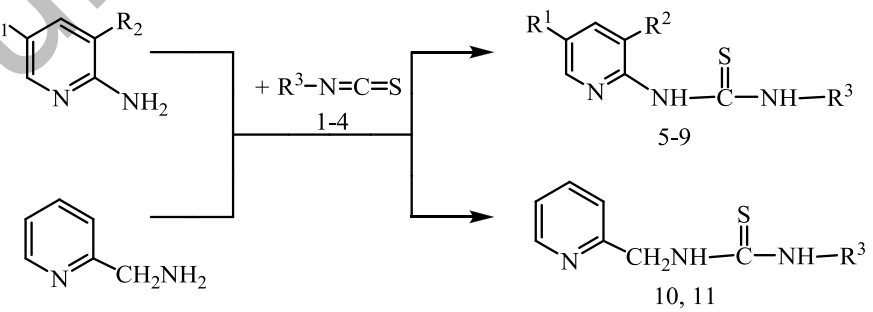
8.19 d (1H, H-6, 3J 5.0), 9.91 br. s (1H, H-10), 10.88 br. s (2H, H-7,11). ^{13}C NMR spectrum, δ_C, ppm: 115.64 (C-5), 116.97 (C-4), 118.15 (C-13,17), 122.81 (C-15), 128.89 (C-14,16), 138.02 (C-12), 139.57 (C-6), 144.26 (C-3), 157.04 (C-2), 159.94 (C-8). Cross peaks of the COSY (^{1}H-^{1}H) NMR spectra, ppm: H15-H14,16 (7.03, 7.35 и 7.35, 7.03), H5-H6 (7.03, 8.17 and 8.17, 5.03), H5-H4 (7.05, 7.78 и 7.78, 7.05), H14,16-H13,17 (7.35, 7.72 and 7.72, 7.35). Cross peaks of the HMQC (^{1}H-^{13}C) NMR spectra, ppm: H13,15-C13,15 (7.38, 117.59), H14,16-C14,16 (7.34, 129.51), H4-C4 (7.72, 118.80), H6-C6 (8.19, 139.58).

1-Ethyl-3-(pyridin-2-ylmethyl)thiourea (10). When stirring, 0.78 g (0.009 mol) of ethylisothiocyanate was added dropwise to a solution of 1 g (0.009 mol) of 2-aminomethylpyridine in 10 ml of ethanol. The reaction mixture was heated at 50–60 ºC for 2 hours. The completion of the reaction was monitored by TLC. Then the reaction mixture was cooled, the precipitate formed was filtered off and recrystallized from isopropanol. Obtained 1.44 g (66 %) of substance with m.p. 66–67 ºC. ^{1}H NMR spectrum, δ, ppm (J, Hz): 1.05 t (3H, H-13,13,13, 3J 7.6), 3.37 br. s (2H, H-12,12), 4.70 s (H, H-7,7), 7.20–7.26 m (2H, H-3,5), 7.68–7.73 m (2H, H-2,4), 7.83 br. s (1H, H-8), 8.43 br. s (1H, H-11). ^{13}C NMR spectrum, δ_C, ppm: 14.93 (C-13), 38.96 (C-12), 49.24 (C-7), 121.81 (C-5), 122.62 (C-3), 137.16 (C-4), 149.24 (C-2), 158.76 (C-6) and 182.91 (C-9). Cross peaks of the COSY (^{1}H-^{1}H) NMR spectra, ppm: H13-H12 (1.05, 3.2 and 3.34, 1.04), H3,5-H2,4 (7.22, 7.72 and 7.69, 7.25). Cross peaks of the HMQC (1H-13C) NMR spectra, ppm: H13-C13 (1.01, 13.37), H12-C12 (3.34, 38.97), H7-C7 (4.68, 49.06), H3,5-C3,5 (7.21, 121.84), H4-C4 (7.70, 137.25) and H2-C2 (8.45, 149.25).

1-Phenyl-3-(pyridin-2-ylmethyl)thiourea 11 was obtained analogously to compound 10 from 1 g (0.009 mol) of 2-aminomethylpyridine and 1.22 g (0.009 mol) of phenylisothiocyanate. Obtained 1.2 g (43 %) of substance 11 with m.p. 109–110 ºC. ^{1}H NMR spectrum, δ, ppm (J, Hz): 4.80 d (2H. H-7,7, 3J 5.4), 7.09 d (1H, H-15, 3J 7.4), 7.25 t (1H, H-3, 3J 4.8), 7.28–7.34 m (3H, H-5,14,16), 7.47 d (2H, H-13,17, 3J 8.4), 7.74 dd (1H, H-4, 3J 7.6. 4J 1.2), 8.23 br. s (1H, H-8), 8.49 d (1H, H-2, 3J 4.8), 10.94 br. s (1H, H-11). ^{13}C NMR spectrum, δ_C, ppm: 49.46 (C-7), 121.99 (C-3), 122.73 (C-13,17), 123.75 (C-5), 124.84 (C-14,16), 129.19 (C-15), 137.24 (C-4), 139.77 (C-12), 149.27 (C-2), 158.08 (C-6), 181.33 (C-9). Cross peaks of the COSY (^{1}H-^{1}H) NMR spectra, ppm: H7-H8 (4.78, 8.23 and 8.21, 4.80), H15-H14,16 (7.08, 7.30 and 7.30, 7.08), H14,16-H13,17 (7.26, 7.46 and 7.46, 7.26), H5-H4 (7.26, 7.72 and 7.72, 7.26), H7-H8 (4.78, 8.23 and 8.21, 4.80). Cross peaks of the HMQC (^{1}H-^{13}C) NMR spectra, ppm: H7-C7 (4.79, 49.45), H5-C5 (7.28, 123.87), H4-C4 (7.72, 137.16), H2-C2 (8.53, 149.15).

Results and Discussion

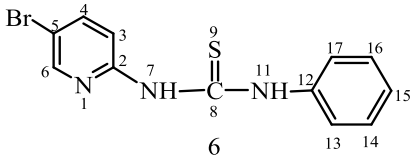
In the present work, in order to obtain new thiourea compounds, we selected 2-amino-5-bromopyridine, 2-amino-3-hydroxypyridine, and 2-aminomethylpyridine as the initial synton. By the interaction of the above 2-aminopyridines with ethyl and phenylisothiocyanates in ethanol, their thiourea derivatives 5, 6 and 9–11 were synthesized. The syntheses of new acyl derivatives of thiourea 7, 8 were also studied. The synthesis of new compounds was carried out by the interaction of isothiocyanates 1–4 with 2-amino-5-bromopyridine, 2-amino-3-hydroxypyridine and 2-aminomethylpyridine. Isothiocyanates 1–4 were obtained by the interaction of potassium thiocyanate with the corresponding chlorides (benzoyl chloride and p-bromobenzoyl chloride) under in situ interaction conditions.



5: R^1 = Br, R^2 = H, R^3 = CH_3CH_2-;
6: R^1 = Br, R^2 = H, R^3 = Ph;
7: R^1 = Br, R^2 = H, R^3 = PhC(O)-;
8: R^1 = Br, R^2 = H, R^3 = 4-BrPhC(O)-;
9: R^1 = H, R^2 = HO, R^3 = Ph;
10: R^3 = CH_3CH_2-;
11: R^3 = Ph.

The obtained compounds 5–11 after recrystallization are white crystalline substances, soluble in most organic solvents, except saturated hydrocarbons. The structure of the synthesized compound 5–11 was proved by ^{1}H and ^{13}C NMR spectroscopy, as well as by the data of the two-dimensional spectrum of HMQC (^{1}H-^{13}C).

The ^{1}H NMR spectrum of compound 6 is characterized by the presence of phenyl radical protons in the low-field part of the spectrum of signals. Symmetrically located methine protons H-14,16 and H-13,17 are manifested by a two-proton triplet at 7.35 (3J 7.6 Hz) and a two-proton doublet at 7.64 (3J 8.4 Hz) ppm respectively. The remaining phenyl proton H-15 was manifested together with the pyridine proton H-3 by a two-proton multiplet at 7.16–7.24 ppm. The pyridine protons H-4 and H-6 resonated with a single-proton doublet of doublets at 8.00 ppm with 3J 9.2 Hz and 4J 2.8 Hz and a doublet at 8.41 ppm with 4J 2.4 Hz respectively. In the weakest field of the spectrum at 10.94 ppm with a broadened two-proton singlet, thioamide protons H-7 and H-11 appeared.



6

In the carbon spectrum of compound 6, NMR signals of ^{13}C nuclei of the phenyl radical are observed at 124.84 (C-13.17), 126.16 (C-15), 129.03 ppm (C-14.16) and 139.21 ppm (C-12). The carbon atoms of the pyridine heterocycle give signals at 112.82 (C-5), 115.43 (C-3), 142.25 (C-4), 146.73 (C-6) and 152.75 (C-2) ppm. The most weak-field signal at 178.62 ppm refers to carbon at the sulfur atom C-8.

The structure of compound 6 was also confirmed by the methods of two-dimensional spectroscopy COSY (^{1}H-^{1}H) and HMQC (^{1}H-^{13}C), which allows one to establish spin-spin interactions of a homo- and heteronuclear nature. The observed correlations in the molecule are shown in Figures 1 and 2. In the spectra of the ^{1}H-^{1}H COSY compound, spin-spin correlations are observed through three proton bonds of the neighboring methine groups H15-H14,16 (7.18, 7.31 and 7.31, 7.18) and H14,16-H13,17 (7.31, 7.63 and 7.63, 7.31) the phenyl fragment and neighboring methine protons H3-H4 (7.21, 7.98 and 7.98, 7.21) of the pyridine nucleus. Heteronuclear interactions of protons with carbon atoms through one bond were established using 1H-13C HMQC spectroscopy for the following pairs present in the compound: H3-C3 (7.17, 115.23), H15-C15 (7.25, 126.16), H14,16-C14,16 (7.34, 129.18), H13,17-C13,17 (7.67, 124.86), H4-C4 (8.02, 142.14) and H6-C6 (8.46, 146.76).

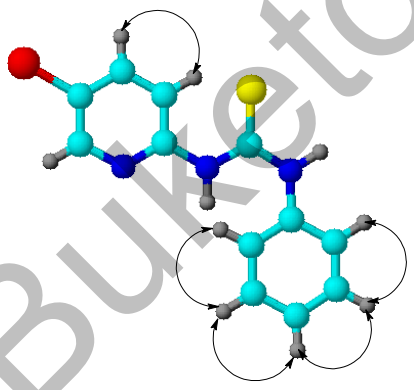


Figure 1. Correlation of COSY (^{1}H-1H) of compound 6

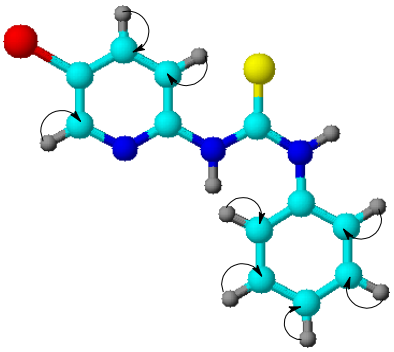
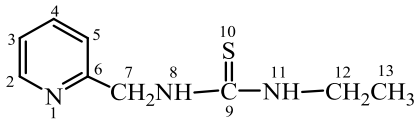


Figure 2. Correlation of HMQC (^{1}H-^{13}C) of compound 6

The presence of additional aromatic fragments in compounds 7–9 increases the number of signals in the weak zone of the spectra. Signals indicating the presence of an N-ethyl fragment in the molecule are present in compound 1.

The NMR spectra of compounds 5, 7–9 contain signals characteristic of atoms of the pyridine nucleus and thioamide moiety. The presence of additional aromatic fragments in compounds 7–9 increases the number of signals in the weak region of the spectra. In compound 1, there are signals indicating the presence of an N-ethyl fragment in the molecule.

In the ^{1}H NMR spectrum of compound 10 in the high-field part of the spectrum, the N-ethyl protons H-13,13,13 and H-12,12 were manifested by a three-proton triplet at 1.05 ppm with 3J 7.6 Hz and an extended two-proton singlet at 3.37 ppm respectively. Methylene protons H-7,7 were resonated by a two-proton singlet at 4.70 ppm. The pyridine protons H-3,5 and H-2,4 were manifested by two-proton multiplets at 7.20–7.26 and 7.68–7.73 ppm respectively. In the most weak-field part of the spectrum at 7.83 and 8.43 ppm broadened single-proton singlets showed the thioamide protons H-8 and H-11 respectively.



10

In the carbon spectrum of compound 10, signals of the methyl and methylene groups of the N-ethyl radical appear at 14.93 (C-13) and 38.96 (C-12) ppm respectively. Signal at 49.24 ppm corresponds to methylene carbon atom C-7. The pyridine fragment is characterized by resonance at 121.81 (C-5), 122.62 (C-3), 137.16 (C-4) and 149.24 (C-2) ppm. The most weak-field signals at 158.76 and 182.91 ppm correspond to the quaternary carbon atom C-6 and the thiocarbonyl atom C-9 respectively.

The structure of compound 10 was also confirmed by the methods of two-dimensional spectroscopy COSY (^{1}H-^{1}H) and HMQC (^{1}H-^{13}C). The observed correlations in the molecule are shown in Figures 3 and 4. In the spectra of the ^{1}H-^{1}H COSY compound, spin-spin correlations are observed through three bonds of protons of the neighboring methyl and methylene groups H13-H12 (1.05, 3.2 and 3.34, 1.04) of the N-ethyl fragment and methine protons H3,5-H2,4 (7.22, 7.72 and 7.69, 7.25) of the pyridine nucleus. Heteronuclear interactions of protons with carbon atoms through a single bond were established using ^{1}H-^{13}C HMQC spectroscopy for the following pairs present in the compound: H13-C13 (1.01, 13.37), H12-C12 (3.34, 38.97), H7-C7 (4.68, 49.06), H3,5-C3,5 (7.21, 121.84), H4-C4 (7.70, 137.25) and H2-C2 (8.45, 149.25).

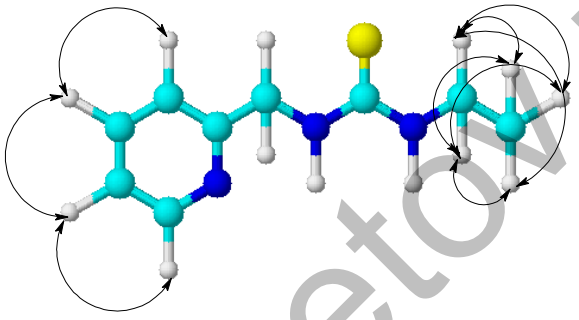


Figure 3. Correlations of COSY (^{1}H-^{1}H) of compound 10

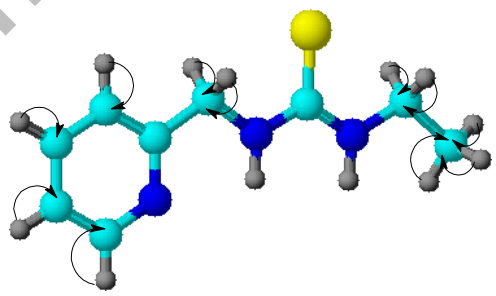


Figure 4. Correlation of HMQC (^{1}H-^{13}C) of compound 10

Conclusions

Thus, a new derivatives of thiourea were synthesized at interaction of 2-aminopyridines (2-amino-5-bromopyridine, 2-amino-3-hydroxypyridine and 2-aminomethylpyridine) with ethyl- and phenylisothiocyanate. They were characterized; their structures being confirmed by NMR spectroscopy ^{1}H and ^{13}C, as well as data the two-dimensional spectra, COSY (^{1}H-^{1}H) and HMQC (^{1}H-^{13}C).

The study was performed with financial support from RK Ministry of Education and Science Committee (grant № AP08855567).

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Функционалдық-орынбасылған пиридиндердің тиомочевинді туындыларының синтезі және құрылысы

Мақалада функционалдық-орынбасылған пиридиндердің тиомочевинді туындыларының синтезі және құрылысын зерттеу бойынша деректері келтірілген. Құрамында фармакологиялық белсенді пиридин тобы бар жаңа тиомочевинді туындылар алынды. Бастапқы синтон ретінде 2-амино-5-бромпиридин, 2-амино-3-гидроксипиридин және 2-аминометилпиридин таңдалды. 2-амин-5-бромпиридиннің, 2-амин-3-гидроксипиридиннің және 2-аминометилпиридиннің этанолдағы этил және фенилизотиоцианаттармен өзара әрекеттесуі тиісті пиридин бар тиомочевин түзілуіне әкеп соқтыратыны көрсетілген. Бастапқы изотиоцианаттардың синтезі ацетон ортасында роданисті калиймен *in situ* жағдайында тиісті хлорангидридтерден (бензоилхлорид және *n*-бромбензоилхлорид) қыздыру кезінде алынды. Синтезделген қосылыстардың құрылысы ЯМР ^{1}H- және ^{13}C-спектроскопия әдістерімен, сондай-ақ екі өлшемді COSY (^{1}H-^{1}H) және HMQC (1H-13C) спектрлерінің деректерімен зерттелді. Бір өлшемді ЯМР спектрлерінде ^{1}H және ^{13}C сигналдардың интегралдық қарқындылығы, мультиплеттілігі және химиялық ығысу мәндері анықталды. COSY (^{1}H-^{1}H) және HMQC (^{1}H-^{13}C) форматтарында спектрлер көмегімен зерттелетін қосылыстардың құрылымын растайтын гомо- және гетероядролық өзара әрекеттесулері белгіленді.

Кілт сөздер: этилизотиоцианат, фенилизотиоцианат, 2-амино-5-бромпиридин, 2-амино-3-гидроксипиридин, 2-аминометилпиридин, тиомочевиндер, 2-аминопиридин, ЯМР ^{1}H-және ^{13}C-спектрлер.

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Синтез и строение тиомочевинных производных функционально-замещенных пиридинов

В статье приведены данные по синтезу и изучению строения тиомочевинных производных функционально-замещенных пиридинов. Получены новые тиомочевинные производные, содержащие в своей структуре фармакологически активную пиридиновую группировку. В качестве исходного синтона были выбраны 2-амино-5-бромпиридин, 2-амино-3-гидроксипиридин и 2-аминометилпиридин. Показано, что взаимодействие 2-амино-5-бромпиридина, 2-амино-3-гидроксипиридина и 2-аминометилпиридина с этил- и фенилизотиоцианатами в этаноле приводит к образованию соответствующих пиридинсодержащих тиомочевин. Синтез исходных изотиоцианатов был проведен *in situ* из соответствующих кислых хлоридов (бензоилхлорид и *п*-бромбензоилхлорид) путем нагревания их с тиоцианатом калия в ацетоне. Строение синтезированных соединений исследовано методами ^{1}H и ^{13}C ЯМР-спектроскопии, а также данными двумерных спектров COSY (^{1}H-^{1}H) и HMQC (^{1}H-^{13}C). С помощью спектров в форматах COSY (^{1}H-^{1}H) и HMQC (^{1}H-^{13}C) установлены гомо- и гетероядерные взаимодействия, подтверждающие структуру исследуемых соединений.

Ключевые слова: этилизотиоцианат, фенилизотиоцианат, 2-амино-5-бромпиридин, 2-амино-3-гидроксипиридин, 2-аминометилпиридин, тиомочевины, 2-аминопиридин, ^{1}H- и ^{13}C ЯМР-спектры.

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