CHEMICAL SHIFTS IN ^{1}H AND ^{13}C NMR SPECTRA OF SOME ARYLUREAS AND THEIR DERIVATIVES

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ХИМИЧЕСКИЕ СДВИГИ В ЯМР ^{1}H И ^{13}C СПЕКТРАХ АРИЛМОЧЕВИН И НЕКОТОРЫХ ИХ ПРОИЗВОДНЫХ

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Аннотация. Для более полного представления о влиянии природы различных заместителей на изменение химических сдвигов в спектрах ЯМР биологически активных соединений и полупродуктов их синтеза были записаны и интерпретированы спектры ЯМР ^{1}H и ^{13}C ряда арилмочевин и их производных **1–5** в растворах ДМСО и ДМСО-d_6. Дана попытка объяснить влияние природы гетероатома на сигналы углеродных атомов ароматических фрагментов молекул. Зафиксирована зависимость химических сдвигов протонов аминогруппы от структурных изменений.

Introduction. In the past two decades, the simple urea related systems have received exhaustive attention with respect to their pharmacological activity. A large number of urea derivatives and its related compounds (e.g., thiourea and guanidine) have been synthesized and found application as agrochemicals, dyes for cellulose fibers, antioxidants in gasoline, resin precursors, and synthetic intermediates especially with particular focus on carbamates and isocyanates obtainment. Moreover, several of urea derivatives have displayed a wide spectrum of biological activity. The pharmacological potency of the mentioned compounds has received significant attention for their applications as HIV-1 protease inhibitors (Human immunodeficiency virus), antidiabetic, antineoplastic, antihypertensive, antipsychotic, antidiuretic, and antibacterial agents [1–4]. ^{1}H and ^{13}C NMR spectra serve as a primary tool used by chemists to perform the structure elucidation of their products on a routine basis. However, complete and systematic analysis of chemical shifts in substituted ureas remains unaccomplished. The research targets of the current work are a) to show data obtained from experimental NMR spectra and b) to perform a number qualitative observations accompanied by a brief discussion of the latter.

Experimental. All compounds were synthesized and purificated manually according to the standard strategy [5,6]. For NMR experiments, the probes of all compounds were dissolved, transferred to a standard NMR capillary, and measured at room temperature. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded in DMSO-d_6 on Tesla BS-567A spectrophotometer (100MHz). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on Tesla BS-567A (25,14 MHz). All chemical shifts were measured in parts

per million downfield from Me_4Si (TMS) as an internal standard. ^{13}C NMR were recorded with no proton decoupling.

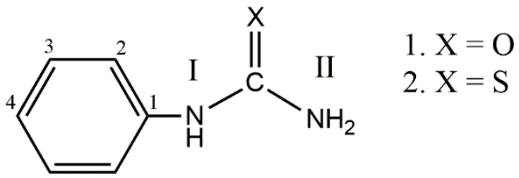

Fig. 1. Compounds 1,2

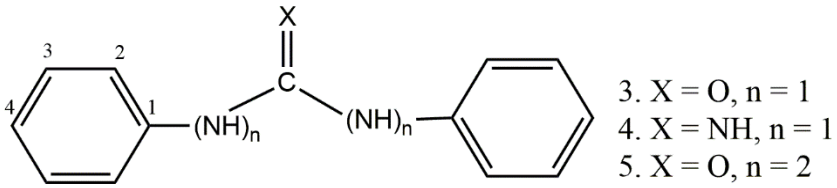

Fig. 2. Compounds 3–5

Results and discussion. Table 1 provides ^1H and ^{13}C Chemical shifts for compounds **1–5**.

Table 1

^{13}C and ^1H chemical shifts for arylureas and their derivatives

№	^{13}C NMR chemical shift, (Δ, ppm, relative to TMS), DMSO					^1H NMR chemical shifts (Δ, ppm, relative to TMS), DMSO-d_6				
	C(1)	C(2)	C(3)	C(4)	C=X	H_{ortho}, d	H_{meta}, t	H_{para}, t	NH (I)	NH_2 (II)
1	140,97	118,03	128,72	121,32	156,35	7,66	7,11	7,11	8,77	6,45
2	139,10	123,26	128,86	124,68	181,15	7,34	7,40	7,55	9,92	7,62
3	139,85	118,41	128,87	121,92	152,69	7,72	7,52	7,19	8,89	8,89
4	143,82	120,57	128,73	120,24	148,14	7,44	7,40	7,08	7,87	8,44
5	138,63	112,28	128,27	149,33	149,33	7,39	6,98	6,21	7,75	8,51

Analysis of the spectroscopic data for the examined compounds allowed us to make some qualitative observations. Firstly, C(1), C(2), C(4) have proved to be the most sensitive to structural alterations in between aromatic carbon atoms of compounds **1–5**. The differences between the largest and the smallest chemical shifts values in a data set are: ΔC(1) = 5,19 ppm; ΔC(2) = 10,98 ppm; ΔC(4) = 6,05 ppm. At the same time, for meta carbon atom C(3) this value has made only ΔC(3) = 0,6 ppm, which is relatively characteristic of monosubstituted benzenes [7]. The carbon atoms C(2) and C(4) in phenylthiourea **2** are strongly downfielded – when compared to those in other compounds. The signals of the same carbon atoms in the diphenylhydrazide **5** manifest weak diamagnetic shift. Notable shielding of C(2) and C(4) of diphenylhydrazide **5** in comparison with compounds **1–4** is obviously determined by fact that nitrogen π-electron pair delocalization towards phenyl ring and C=X groups takes place in **1–4**. Therefore, mesomeric effect of nitrogen on aromatic ring becomes reduced. This circumstance is reflected by a relative – in comparison with substituted anilines [8] – deshielding of

positions C(2) and C(4). At the same time, analogous nitrogen atom did not tie up with C=X group, and thus, its lone pair participates in mesomeric effect much more actively – due to non-competitive conditions. Chemical shifts of atoms C(1)-C(4) are relatively close to chemical shifts of the similar atoms in aniline [8].

Besides, it is worth mentioning that the ipso-atom C(1) of guanidine **4** is highly descreened for compounds **1–3,5** where chemical shifts of the C(1) fluctuate within a close band.

It is well known that transition from oxygen-containing compounds to their thio-analogues leads to a downfield shift. The same effect can be observed for phenylthiourea **2** (in comparison with phenylurea **1**).

As it can be seen from the spectroscopic data, the nature of heteroatom has enormous influence on carbon's atom within C=X group chemical shift. Shifts alternate according to the following order: C=S > C=O > C=N. The range of alteration is equal to 33,01 ppm.

In the ^{1}H NMR spectra, chemical shifts of protons in ortho-, meta- and para- phenyl ring positions display slight differences – as distinct from ^{13}C NMR spectra. Yet, it must be noted that amino proton connected to aromatic structure is vulnerable to structural variations in the "bridge-type" component of compounds **1–5**. The most distinct shift of proton attached to a nitrogen is caused by C=S group (exactly the same impact is observed for CF_3CO- group in the N-phenyl-N'-trifluoroacetylurea [9]). Chemical shift of amino proton for compounds **4–5** is decreased by nearly 1 ppm – compared to arylureas.

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