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INVESTIGATION OF (E)-(4-HYDROXY-2-METHYLPHENYL) ACETOPHENONE OXIME AND (E)-4-HYDROXY-2-METHYLACETOPHENONE THIOSEMICARBAZONE IN SOLUTIONS BY NMR SPECTROSCOPY

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The presented work is devoted to the study of dynamic processes of (E)-(4-hydroxy-2-methylphenyl) ethanone oxime and (E)-4-hydroxy-2-methylacetophenone thiosemicarbazone in solutions by NMR spectroscopy.

Keywords: *oxime, thiosemicarbazone, hydrogen bonds, nuclear magnetic resonance.*

Introduction

NMR spectroscopy plays an important role at studying of various interactions in solutions, including hydrogen bond formations. The obtained results from these investigations have a particular importance for the chemistry, biochemistry, biophysics, etc. Besides, NMR very importance at studying of the structure of drugs and their influence mechanisms [1–12].

Oxime compounds are well known as antidotes for nerve agents, analytical reagents, etc. [13–17]. Also, thiosemicarbazones and their various derivatives have a medical and biological importance. The above indicated type compounds are widely used as antitumor, antifungal, antibacterial, antiviral, antimalarial reagents [18–21].

Therefore the presented work is devoted to the investigation of dynamic processes of (E)-(4-hydroxy-2-methylphenyl) ethanone oxime and (E)-4-hydroxy-2-methylacetophenone thiosemicarbazone molecules in solutions by NMR. Obtained results showed the existence of anisotropic reorientation for the (E)-(4-hydroxy-2-methylphenyl) acetophenone oxime and four rotational conformers for the (E)-4-hydroxy-2-methylacetophenone thiosemicarbazone in solutions.

Experimental part

The research of the samples were carried out by using Bruker AVANCE 300 NMR spectrometer with BVT 3200 temperature regulator (working frequencies of 300 MHz for

¹H and 75 MHz for ¹³C and Software TopSpin 2.1). Acetone-d₆, DMSO-d₆, CCl₄ and D₂O as solvents were used at NMR investigations.

Spin-lattice relaxation times are measured by the inversion-recovery method:

– at 180° pulse inverts the magnetization to the z-axis,

– during the following delay time, relaxation along the longitudinal plane takes place,

– magnetization come back to the original equilibrium z-magnetization,

– a read 90° pulse creates transverse magnetization,

– acquisition is performed as usual.

The activation energies of intramolecular mobility have been calculated by the formula

$$E = 19.13 [T^{(1)} T^{(2)} / (T^{(2)} - T^{(1)})] \lg (T_1^{(2)} / T_1^{(1)}),$$

where $T^{(1)}$ and $T^{(2)}$ are temperatures and $T_1^{(1)}$ and

$T_1^{(2)}$ are relaxation times (E)-(4-hydroxy-2-methylphenyl) acetophenone oxime (I) was

obtained at ethanol boiling temperature (reaction time 3 hours, 0.02 mol 4-hydroxy-2-methylacetophenone, 0.29 mol NH₂OH·HCl and 40 ml of ethanol) [22]. Yield – 47%, T_{melt} –

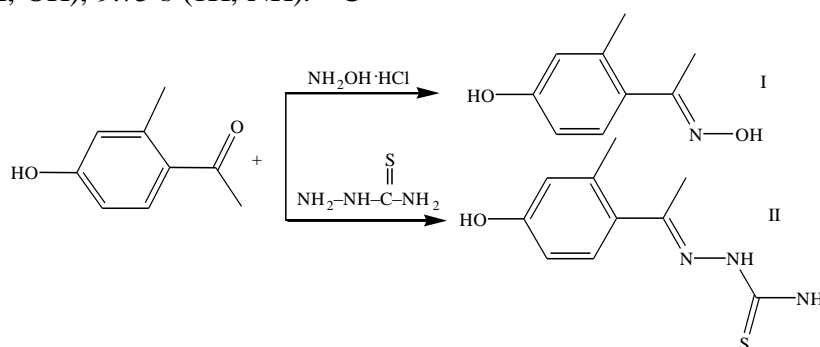
196–197°C. ¹H NMR (DMSO-d₆, δ, m.h.): 1.9 s (3H, CH₃), 2.35 s (3H, CH₃), 6.6–7.3 (3H, arom.), 9.72 s (1H, OH), 11.3 s (1H, N–OH).

¹³C NMR (DMSO-d₆; δ, m.h.): 18.1 (CH₃), 22.94 (CH₃), 113.6 (CH, arom.), 115.3 (CH, arom.), 123.3 (C, arom.), 129.3 (CH, arom.), 139.3 (C, arom.), 153.2 (C=N, azomethine), 159.6 (C–O).

(*E*)-(4-hydroxy-2-methylacetophenone thiosemicarbazone (II) was obtained (reaction time 5 hours, 1 mmol 4-hydroxy-2-methylacetophenone, 1 mmol thiosemicarbazone) at ethanol boiling temperature [22]. Yield – 76%, T_{melt} – 185–187°C, ^1H NMR (DMSO- d_6 , δ , m.h.), 2.03 s (3H, CH₃), 2.13 s (3H, CH₃), 6.7–6.98 (3H, arom.), 7.92 d (2H, NH₂), 8.4 s (1H, OH), 9.75 s (1H, NH). ^{13}C

NMR (DMSO- d_6 , δ , m.h.): 19.02 (CH₃), 24.83 (CH₃), 112.93 (C, arom.), 114.29 (C, arom.), 117.67 (CH, arom.), 124.49 (C, arom.), 128.44 (CH, arom.), 151.89 (C=N, azomethine), 158.69 (C–O, arom), 178.07 (C=S).

The synthesis scheme of compounds are given below.

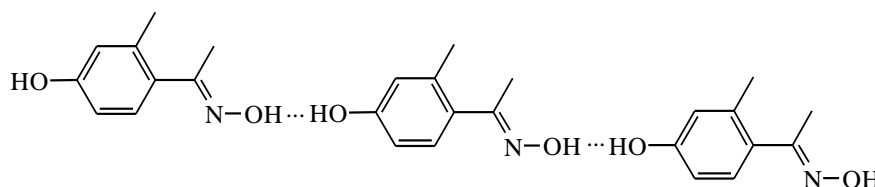


Discussions

Firstly, (*E*)-(4-hydroxy-2-methylphenyl) acetophenone oxime (I) was investigated. Obtained results confirmed the formation of one isomer between the reaction 4-hydroxy-2-methylacetophenone and hydroxylamine hydrochloride. Subsequently spin-lattice relaxation (T_1) type was calculated for the ^1H and ^{13}C nucleus in 5% acetone- d_6 solution for different groups at 22°C and 50°C and the results given in Table.

As can be seen from the table, the values of intramolecular activation energy in two different methyl groups (for ^1H and ^{13}C nucleus) are different (5.29 and 6.96; 5.69 and 6.12 kJ/mol).

This shows the existence of anisotropic reorientation for the investigated molecule in solution.



In continuation of the researches (*E*)-(4-hydroxy-2-methylacetophenone thiosemicarbazone (II) was investigated in solutions. The studies were carried out at +22°C ÷ +95°C intervals and depending on time. At NMR in-

T_1 relaxation time (for ^1H and ^{13}C nucleus, in sec) of the (*E*)-1-(4-hydroxy-2-methylphenyl) acetophenone oxime (I) CH₃- and CH-groups and activation energy of intramolecular mobility

Frag-ment	CH ₃ - and CH-positions	Nucleus	T_1 , 22°C	T_1 , 50°C	E_a , kJ/mol
CH ₃	Ar–CH ₃	^1H	2.33	2.81	5.29
CH ₃	=C–CH ₃	^1H	3.23	3.95	5.69
CH ₃	Ar–CH ₃ ,	^{13}C	6.01	7.69	6.96
CH ₃	=C–CH ₃ ,	^{13}C	9.98	12.39	6.12
CH	CH	^{13}C	3.74	–	–
CH	CH	^{13}C	4.37	–	–
CH	CH	^{13}C	5.06		

($T = 22^\circ\text{C}$ and 50°C) in the 5% acetone- d_6 solution

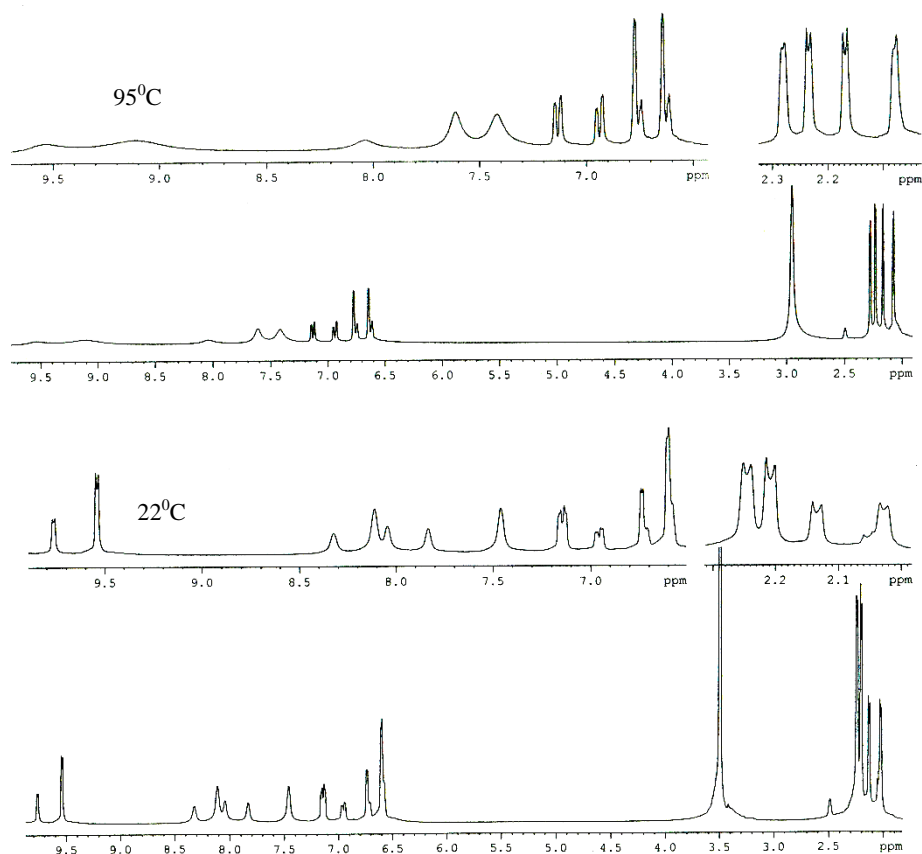
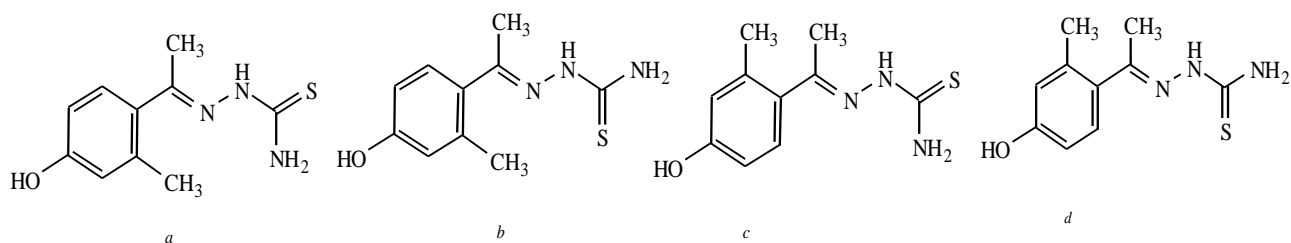
Table data for the CH-groups of aromatic ring having different relaxation time also confirm the presence of anisotropic reorientation. NMR studies showed the formation of intramolecular hydrogen bounds between the oxime molecules.

investigation of thiosemicarbazone molecule (II) in DMSO- d_6 solution are observed splitting of signals. In the ^1H NMR spectra (Figure) of 5% fresh DMSO- d_6 solution, we observed one signals for all hydrogen at the 22°C as a result

of fast exchange between the conformers. The mixture of conformers were not present in this solution. But in the ^1H spectra obtained after one week (5% DMSO-d_6 solution at $+22 \div +95^\circ\text{C}$), were observed eight singlet signals instead of two for the two different CH_3 and four singlet signals instead of one for the NH

protons resulting from rotations around the $-\text{NH}-\text{C}=\text{S}$ and $\text{C}-\text{Ar}$ bonds.

The obtained results confirmed the existence of four conformer in solution of (*E*)-(4-hydroxy-2-methylacetophenone thiosemicarbazone (II).



^1H NMR spectral sections of (I) in 5% DMSO-d_6 solution within the temperature interval of $+22 \div +95^\circ\text{C}$.

Conclusion

Our DNMR studies showed the existence of anisotropic reorientation in the acetone- d_6 solution for the (*E*)-(4-hydroxy-2-methylphenyl) acetophenone oxime (I).

The NMR investigation results confirmed the presence of $-NH=S$ and $C-Ar$ rotation in DMSO- d_6 solution and the existence of four conformers for the (*E*)-(4-hydroxy-2-methylacetophenone thiosemicarbazone (II).

NMR results have confirmed that relaxation times are very important for studying of molecular mobility in solutions, have theoretical-practical significance and may be applicable at determination of molecular configuration.

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**(E)-1-(4-HİDROKSI-2-METİLFENİL)ASETOFENONOKSİM VƏ
(E)-4-HİDROKSI-2-METİLASETOFENON TİOSEMİKARBAZON MƏHLUL
SİSTEMLƏRİNİN NMR METODU İLƏ TƏDQIQI**

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Təqdim olunan iş (E)-1-(4-hidroksi-2-metilfenil)etanon oksim və (E)-4-hidroksi-2-metilasetofenon tiosemikarbazon molekullarının məhlul sistemlərində baş verən dinamik proseslərin NMR metodu ilə tədqiqinə həsr edilmişdir.

Açar sözlər: oksim, tiosemikarbazon, hidrogen rabitələri, nüvə maqnit rezonansı.

**ИССЛЕДОВАНИЕ (E)-1-(4-ГИДРОКСИ-2-МЕТИЛФЕНИЛ)АЦЕТОФЕНОКСИМА
И (E)-4-ГИДРОКСИ-2-МЕТИЛАЦЕТОФЕНОНТИОСЕМИКАРБАЗОНА
В РАСТВОРАХ МЕТОДОМ ЯМР**

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Представленная работа посвящена синтезу производных 4-гидрокси-2-метилацетофенона (E)-1-(4-гидрокси-2-метилфенил)этанон оксима и (E)-4-гидрокси-2-метилацетофенонтиосемикарбазона и исследованию различных растворов полученных веществ методом ЯМР.

Ключевые слова: оксим, тиосемикарbazон, водородные связи, ядерный магнитный резонанс.