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^{1}H NMR Characterization of Two New Pyridoxine Derivatives

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Abstract Two new pyridoxine derivatives were studied by dynamic ^{1}H NMR spectroscopy. The complete ^{1}H NMR data for two pyridoxine derivatives are presented. Assignment of the signals in the spectra was achieved using 1D and 2D COSY NMR experiments.

Keywords Pyridoxine · Dynamic ^{1}H NMR spectroscopy · Conformation

1 Introduction

Synthesis of molecular systems with desirable biochemical or physical properties often requires knowledge about spatial structure of compounds and information about their conformational mobility [1–3]. Nowadays, NMR techniques are proved to be a powerful tool for conformational analysis of biologically important samples [4–6]. In this letter, we present the results of ^{1}H NMR study of two new pyridoxine derivatives representing a potential biologically active substances: 3-isopropyl-8-methyl-6-(2-nitrophenyl)-1,5-dihydro-[1, 3] dioxepino [5,6-c] pyridine-9-ol (**I**) and 3,3,8-trimethyl-6-(2-nitrophenyl)-1,5-dihydro-[1, 3] dioxepino [5,6-c] pyridine-9-ol (**II**) (Fig. 1).

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2 Material and Methods

Compounds (**I**, **II**) were synthesized by the procedure described in the patent [7]. All of the NMR experiments were performed on a Bruker Avance II-500 NMR spectrometer. ^{1}H NMR spectra were recorded using 90° pulses, a delay between pulses of 2 s, a spectrum width of 10 ppm, and a minimum of ten scans at 308 and 198 K. The sample was cooled by a flow of low-temperature nitrogen gas from a dewar with liquid nitrogen. Assignment of the ^{1}H NMR signals for the entire set of compounds were achieved from the signal multiplicities, the integral values and the characteristic chemical shifts from the through-bond correlations in the 2D correlated spectroscopy (COSY) spectra. The NMR samples were prepared by additional dissolving in dichloromethane-d_2 and acetone-d_6 solvents. ^{1}H chemical shifts are given in values of parts per million, referenced to residual solvent signals (5.32 ppm for dichloromethane-d_2, 2.05 ppm for acetone-d_6). All samples were prepared in standard 5-mm ampoules. Concentrations of the substances were 0.5 % by weight; the solution volume was 0.6 mL. Stabilization of the magnetic field was carried out using the deuterium signals of the solvents.

3 Results and Discussion

Compounds **I** and **II** have a similar structure, but different substituents at the acetal carbon atom C-2: $CH(CH_3)_2$ and $(CH_3)_2$, respectively (Fig. 1). To confirm the chemical structure of compounds **I** and **II** 1D ^{1}H, ^{13}C and 2D NMR experiments were performed. The signals in the ^{1}H NMR spectrum (Fig. 2) were assigned using literature data [8] and the 2D ^{1}H-^{1}H COSY NMR spectra at room

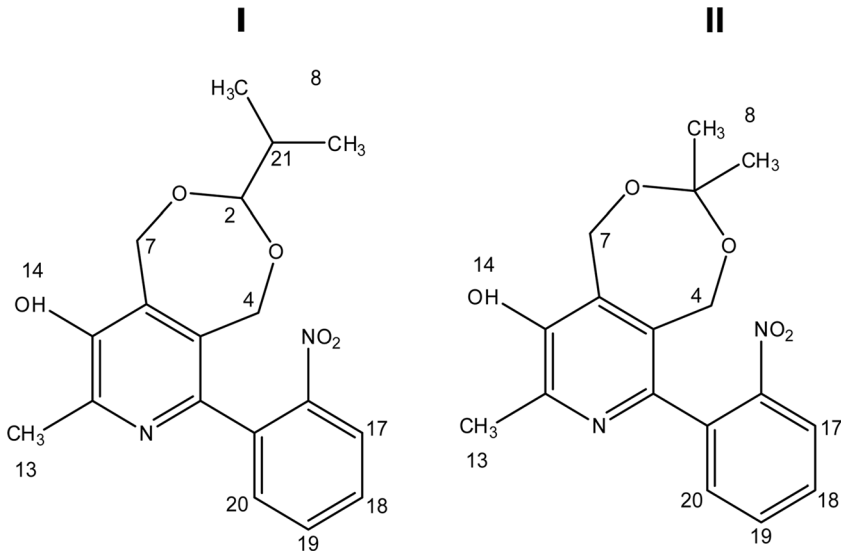

Fig. 1 Chemical structure of studied compounds **I** and **II**

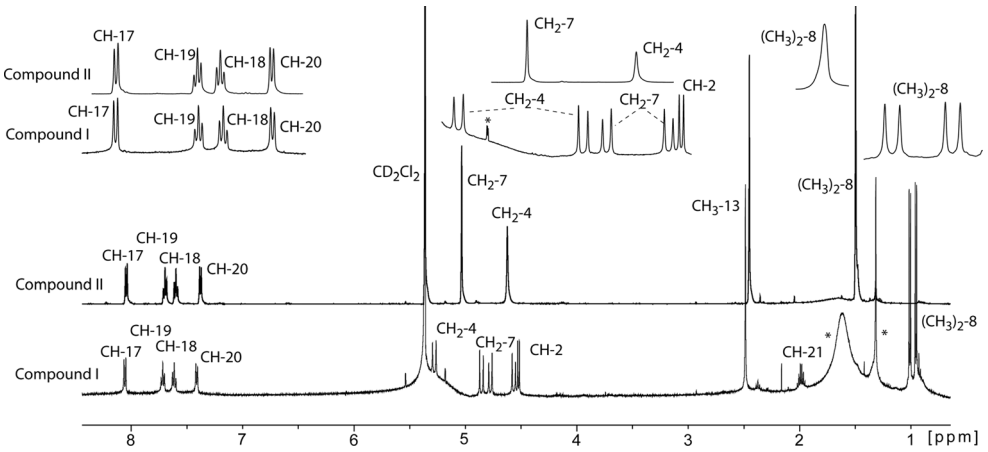

Fig. 2 The ^{1}H NMR spectra of the compounds **I** and **II** dissolved in CD_2Cl_2 at the temperature of 308 K. Impurity signals are marked by *asterisk*. Enlarged images of the observed signals are shown on *top* of the figure

temperature. The ^{1}H NMR chemical shifts and spin-spin interaction constants are presented in the Table 1.

At room temperature, almost all proton signals of studied compounds are well resolved in ^{1}H NMR spectrum. The signal O<u>H</u>-14 is not observed in the spectrum because of its participation in the intermolecular exchange. The signals corresponding to aromatic protons C<u>H</u>-17,18,19,20 resonate in a low field range, 7.3–8.1 ppm. The signals C<u>H</u>-17,20 have the shape of doublets because of spin-spin interaction with neighboring protons C<u>H</u>-18,19. C<u>H</u>-18,19 are observed as triplets in the spectra due to double-faced spin-spin interaction caused by their intermediate position in the aromatic ring. Signals C<u>H</u>-17,18 and C<u>H</u>-19,20 have similar spin-spin interaction constants. Methyl group protons C<u>H</u>$_3$-13 resonate in a high field area in the form of singlets. Each of the methyl groups (C<u>H</u>$_3$)$_2$-8 of compound **I** appears in the spectrum in the form of doublet due to spin-spin interaction with proton C<u>H</u>-21. In the spectrum of compound **II**, the same groups are observed as singlet. Line shape of CH_2-4,7 signals is different for studied compounds. They represent singlets in the spectrum of the

Table 1 ^{1}H NMR spectra parameters (δ, ppm) and spin-spin interaction constants (J, Hz, in parentheses) for compounds **I** and **II** in CD_2Cl_2 at 308 K

	C<u>H</u>-20	C<u>H</u>-19	C<u>H</u>-18	C<u>H</u>-17	C<u>H</u>-21	C<u>H</u>-2	C<u>H</u>$_3$-13	(C<u>H</u>$_3$)$_2$-8	C<u>H</u>$_2$-4	C<u>H</u>$_2$-7
I	7.41 d (7.5)	7.72 t (7.5)	7.61 t (7.8)	8.06 d (7.8)	1.99 m (6.8)	4.52 d (7.4)	2.49	0.98 dd (27.5; 6.8)	5.07 q (15.3)	4.67 q (14.7)
II	7.38 d (7.5)	7.70 t (7.5)	7.60 t (7.8)	8.04 d (7.8)	–	–	2.45	1.50	4.62	5.03

d doublet, *dd* two doublets, *t* triplet, *q* AB quartet, *m* multiplet

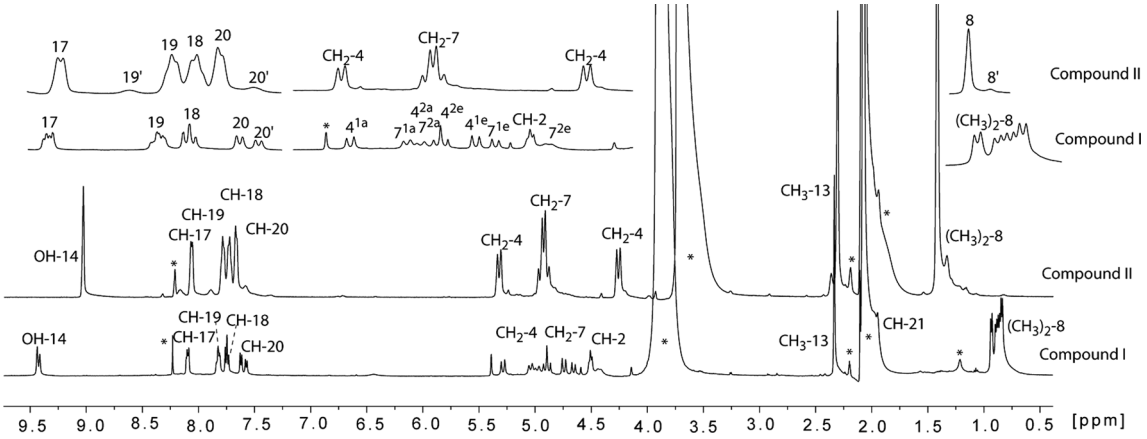

Fig. 3 The ^{1}H NMR spectra of the compounds **I** and **II** dissolved in $(CD_3)_2O$ at the temperature of 198 K. Impurities signals are marked by *asterisk*. Enlarged images of the observed signals are shown on *top* of the figure. Superscripts ^{1} and ^{2} correspond to major and minor conformations, respectively; superscripts ^{a} and ^{e} correspond to axial and equatorial relative to the seven-membered cycle protons

compound **II** and AB quartets in the spectrum of the compound **I** respectively due to non-equivalence of geminal protons caused by an influence of additional CH-2 proton in the compound **I**.

At low temperature, the number of most signals in the ^{1}H NMR spectrum of both compounds is doubled (Fig. 3). Increasing of amount of resonance lines is explained by slowing down of conformational exchange process caused by rotation of nitrophenyl fragment around C–C bond of the molecule [5, 6]. Relative population of the most stable conformations was determined by integral intensities of the resonance lines: 2:1 for compound **I** and 10:1 for compound **II**. Spatial structure of studied molecules allow us to assume that the second conformational exchange associated with interconversion of seven-membered cycle (*chair-twist* and *twist-twist*) can be observed by NMR experiments at a certain conditions. For a more detailed study of conformational transitions, additional dynamic NMR and 2D NOESY NMR experiments are needed.

4 Conclusions

Isopropyl- and dimethyl-substituted pyridoxine derivatives were characterized by ^{1}H NMR experiments at high and low temperatures. The conformational differences of two new pyridoxine derivatives were investigated by dynamic ^{1}H NMR spectroscopy. The NMR experiments with decreasing temperatures allowed deceleration of the rate of the conformational exchange caused by the rotation of the nitrophenyl fragment around C–C bond.

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