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Complicated Conformational Exchange of New Pyridoxine Derivative. Dynamic ^{13}C NMR Characterization

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Abstract New pyridoxine derivative with multiple chemical exchanges was studied by ^{13}C (at 298 K, 188 K) and 2D NMR (^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC) spectroscopy in acetone-d_6 solution. Complete ^{13}C NMR data (table with chemical shifts at different temperatures) is presented. Intramolecular mobility of the molecule was analyzed based on the results of ^{13}C NMR experiments in combination with the data obtained from previous study of this compound by dynamic ^{1}H NMR spectroscopy.

Keywords Pyridoxine · ^{13}C NMR spectroscopy · Conformation · Stereochemistry

1 Introduction

Nuclear magnetic resonance (NMR) methods with variation of temperature including the full line shape analysis are very effective for obtaining detailed information about the main characteristics of stereochemically and structurally flexible molecules [1–3]. Nowadays, NMR techniques are also proved to be a powerful tool for conformational analysis of biologically important samples [4–6].

Investigations of systems with multi-rate chemical exchange are primarily relevant because they allow deepening and broadening of our understanding of the mechanism of molecular transformations. Many difficulties might occur related to the assessment of the rate constants and interpretation of activation and kinetic characteristics of the observed processes in study of systems with two or more exchange rate constants (multi-exchange) in combination with more difficult task of components identification [7]. In our previous works, we have studied some pyridoxine derivatives by ^{1}H dynamic NMR spectroscopy [1, 2, 8]. However, ^{13}C NMR spectroscopy also can provide valuable information about this system. In the presented letter, the results of ^{13}C NMR study of new pyridoxine derivative representing a potential biologically active substance and nonlinear optical material – 9-(2,4-dinitrophenoxy)-3,3,8-trimethyl-6-(2-nitrophenyl)-1,5-dihydro-[1, 3] dioxepino[5,6-c]pyridine [9, 10] is discussed. Molecular structure of the compound with possible intramolecular conformational processes (R, R' – rotations, T-T – twist-twist transitions of the cycle) is shown in the top of the Fig. 1.

2 Material and Methods

Registration of 1D (^{13}C) and 2D (^{1}H-^{13}C) NMR spectra of studied compound in $(CD_3)_2CO$ was carried out using NMR spectrometer (Bruker, Avance II-500) (125.76 MHz (^{13}C)) at 298 and 188 K. Temperature control was achieved using a Bruker variable temperature unit (BVT 3000) in combination with a Bruker cooling unit (BCU-05). The sample was cooled by a flow of low-temperature nitrogen gas from a Dewar with liquid nitrogen. The experiments were performed without sample spinning. All two-dimensional experiments were performed with 2 k × 512 data points; the number of transients (2–16 scans) and the sweep widths were optimized individually. All samples were prepared in standard 5-mm NMR tubes. Concentrations of the substances were 0.5 wt%. The solution volume was 0.6 ml. The deuterium signals of the solvent were used for the stabilization of magnetic field.

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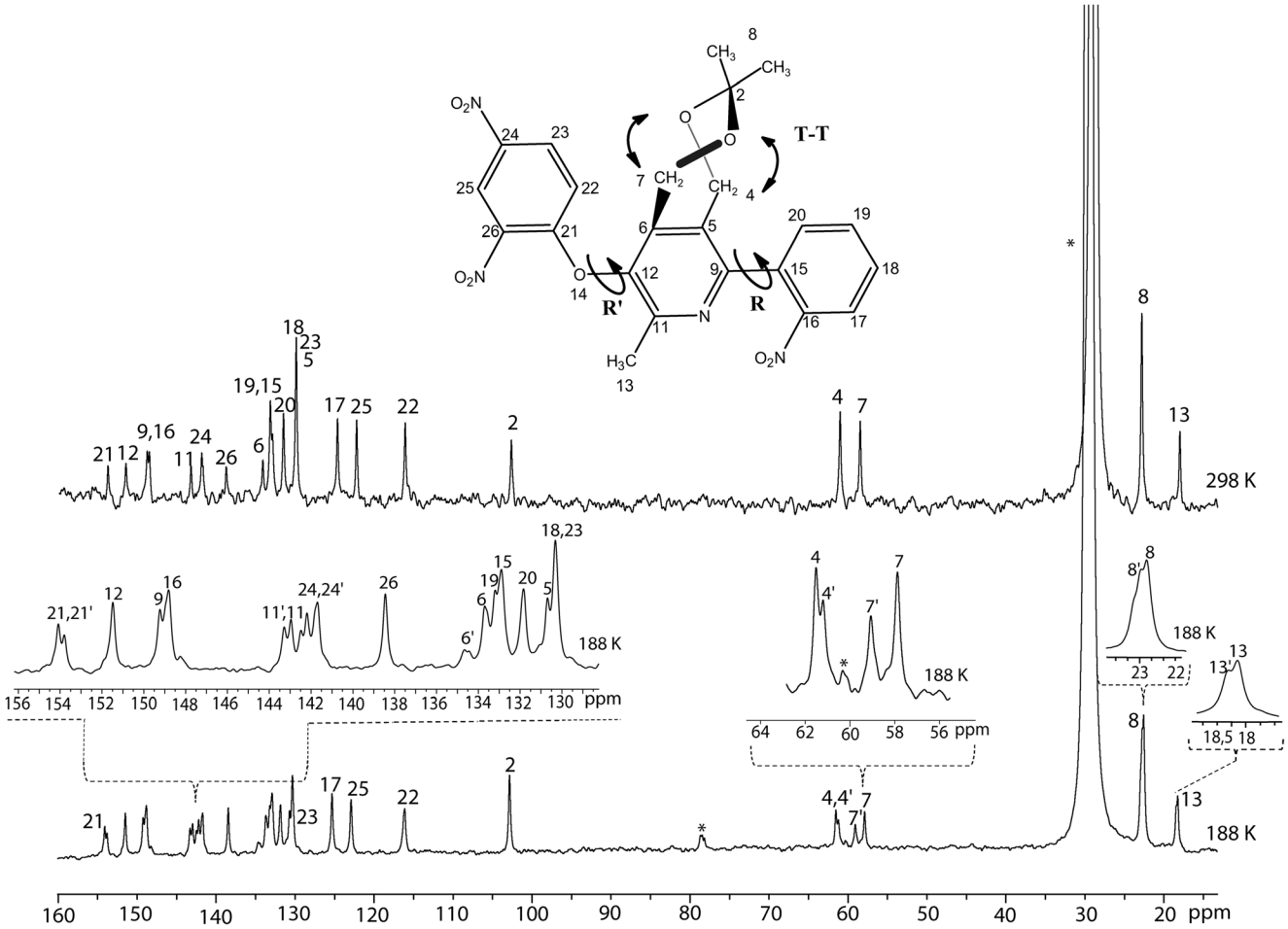

Fig. 1 ^{13}C NMR spectra of the compound in $(CD_3)_2CO$ at 298 and 188 K (solvent and impurities signals are marked by *asterisks*)

3 Results and Discussion

Studied compound contains a seven-membered acetal ring, 2,4-dinitrophenyloxy ortho-substituent through an oxygen atom at the 12-position of pyridine and 2-nitrophenyl ortho-substituent at the 9-position of pyridine (Fig. 1).

^{13}C NMR spectra of studied compound in acetone-d_6 solution at 298 and 188 K are shown in the Fig. 1. The signals in the ^{13}C NMR spectrum were assigned using literature data and the 2D ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC NMR experiments. All obtained data is presented in Table 1.

Table 1 ^{13}C NMR chemical shifts (δ, ppm) of the compound in acetone at 298 and 188 K

298 K	C	C	C	C	C	C	C	C	CH	C	CH
	−21	−12	−9	−16	−11	−24	−26	−6	−19	−15	−20
	153.9	151.7	148.9	148.7	143.4	141.9	138.8	134.1	133.2	132.9	131.5
	CH	CH	C	CH	CH	CH	C	CH_2	CH_2	$(CH_3)_2$	CH_3
	−18	−23	−5	−17	−25	−22	−2	−4	−7	−8	−13
	129.9	129.9	129.9	124.7	122.3	116.1	102.7	61.1	58.5	22.8	18.0
188 K	C	C	C	C	C	C	C	C	CH	C	CH
	−21	−12	−9	−16	−11	−24	−26	−6	−19	−15	−20
	154.1; 153.8[a]	151.5	149.2	148.9	142.9; 143.3[a]	141.9; 142.3[a]	138.4	133.7; 134.6[a]	133.2	132.9	131.8[b]
	CH	CH	C	CH	CH	CH	C	CH_2	CH_2	$(CH_3)_2$	CH_3
	−18	−23	−5	−17	−25	−22	−2	−4	−7	−8	−13
	130.3	130.3	130.7	125.3[b]	122.9	116.1[b]	102.8	61.5; 61.2[a]	57.9; 59.1[a]	22.5; 22.7[a]	18.2; 18.4[a]

[a] signal of minor conformer

[b] broadened

Carbons of methyl groups ($\underline{C}H_3$–13, $(\underline{C}H_3)_2$–8) as well as protons of methyl groups [8] are observed in the high-fields region with chemical shifts 18.2 and 22.5 ppm, respectively. Low-intensive minor signals at 18.4 and 22.7 ppm next to the major signals at 188 K correspond to C-13[a] and C-8[a]. Carbons of the methylene groups $\underline{C}H_2$–4,7 resonate in the area of about 60 ppm. At the low temperature, some minor signals are also observed. Significant nonequivalence of the signal $\underline{C}H_2$–7[a] compared with the $\underline{C}H_2$–4[a] can be explained by its close arrangement to the rotor around C12-O bond (R'). Signals from the carbons of the aromatic groups of the molecule, as well as signals from quaternary carbons, are located in the low-fields region of the spectrum. Some carbons (C-24, C-21) in this area, corresponding to the molecular rotor R' elements or carbon like C-11, C-8, C-13, located in close proximity to the last one, also have minor signals in the spectrum. This fact indicates conformational mobility of this fragment of the molecule. Additionally, the ratio of the integral intensities of the major and minor signals is 1.2:1.0 in average, which is, seeing $^{13}C/^{1}H$ nuclear difference, close enough to the value of the ratio 2:1, characteristic for R' rotation process in the proton spectrum [8]. The signals of $\underline{C}H$-17, $\underline{C}H$-20 groups experience only a small broadening at low temperature. This means that R rotation process around C9-C15 bond cannot be observed by ^{13}C NMR spectroscopy. This can be explained by comparing obtained results with the results of low-temperature ^{1}H NMR study [8], in which the signals of R rotor conformations had very low intensity (10:1). There is a slight increase in intensities between major and minor signals for secondary carbon 7 (1.4:1.0) and significant difference in intensities for quaternary carbon 6 (2.8:1.0). This can be explained by the additional influence of the twist-twist (T-T) interconversion process of the seven-membered cycle.

4 Conclusions

Despite the fact, that ^{13}C NMR spectroscopy is less informative then ^{1}H NMR due to low natural abundance of ^{13}C isotope, it can be very useful in the study of conformation processes of stereochemically nonrigid molecules. The new pyridoxine derivative with complicated exchange mechanism was studied by ^{13}C NMR experiments at room (298 K) and low (188 K) temperatures. Small but important changes in the spectrum at low temperature (188 K) in combination with the information about dynamics of the molecule obtained from previous dynamic ^{1}H and NOESY NMR spectroscopy study provided a complete picture of the conformational exchange transitions characteristic to the studied compound.

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