Determination of regio- and stereochemistry of spiropyrrolizine oxindoles using NMR spectroscopy methods

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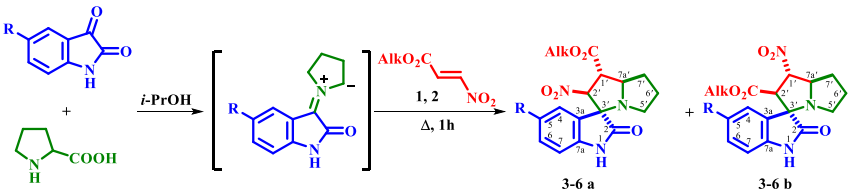
A study of the nitroacrylates **1, 2** interaction with isatinproline ylides upon boiling for 1 hour in isopropyl alcohol showed that the reaction leads to the formation of regioisomeric spirooxindoles **3-6**, similar to the reactions of 3,3,3-trihalogen-1-nitropropenes [1] or β-nitrostyrenes [2]. Spiropyrrolizine oxindoles **3-6** were isolated from the reaction as a mixture of two regioisomers in the ratio a : b = 2 : 1 (by ^{1}H NMR spectra). Individual major isomers of spiropyrrolizine oxindoles **3-6a** was isolate by recrystallization.



Alk = Me (**1**, **3**, **5**), Et (**2**, **4**, **6**); R = H (**3**, **4**), Br (**5**, **6**)

The rigidly fixed structure of the isolated spiropyrrolizine oxindoles **3-6a** makes them very attractive objects for studying the structure using 2D NMR spectroscopy experiments.

In the ^{1}H NMR spectra of individual compounds **3-6a** the proton ($H^{2'}$) at the carbon atom associated with the nitro group appears as a doublet at 5.59-5.61 ppm (^3J 11.1-11.3 Hz), in turn, the proton ($H^{1'}$) at the carbon atom associated with the alkoxycarbonyl group resonated as a doublet of doublets at 3.96-4.21 ppm (^3J 9.2-9.3, ^3J 11.1-11.3 Hz), which allows them to be characterized as regioisomers **a** (Fig. 1).

This assignment of signals in the ^{1}H NMR spectra is confirmed by the results of studying these substances using the ^{1}H-^{1}H COSY NMR method. Thus, in the ^{1}H-^{1}H COSY spectrum of compound **6a**, cross peaks are observed between the signals of the pyrrolizine ring protons $H^2/H^{1'}$, $H^{1'}/H^{7'a}$, $H^{7'a}/H^{7'}$, $H^{7'}/H^{6'}$, $H^{6'}/H^{5'}$, which confirms the presence of spin-spin interaction between them (Fig. 2).

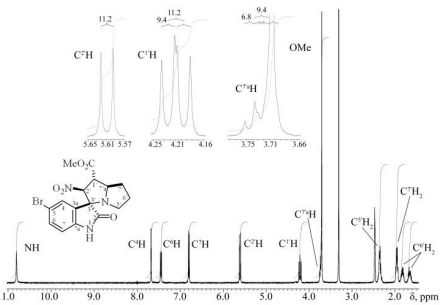


*Figure 1. ^{1}H NMR spectrum of compounds **6a** (DMSO-d_6)*

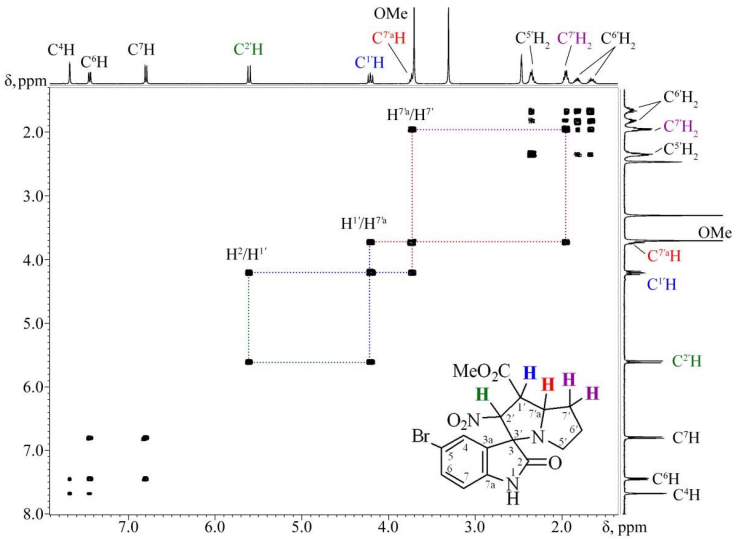


*Figure 2. ^{1}H-^{1}H COSY spectrum of compound **6a** (DMSO-d_6)*

The fine structure of the obtained individual spiropyrrolizine oxindoles **3-6a** was studied using a ^{1}H-^{1}H NOESY NMR experiment. Results of ^{1}H-^{1}H NOESY experiments for individual diastereomers, obtained with a variable value of mix. time (τ 0.5, 1, 1.5, 2 sec), demonstrate NOE correlations of protons $H^{1'}/H^{4}$ and $H^{7'a}/H^{2'}$ (Fig. 3).

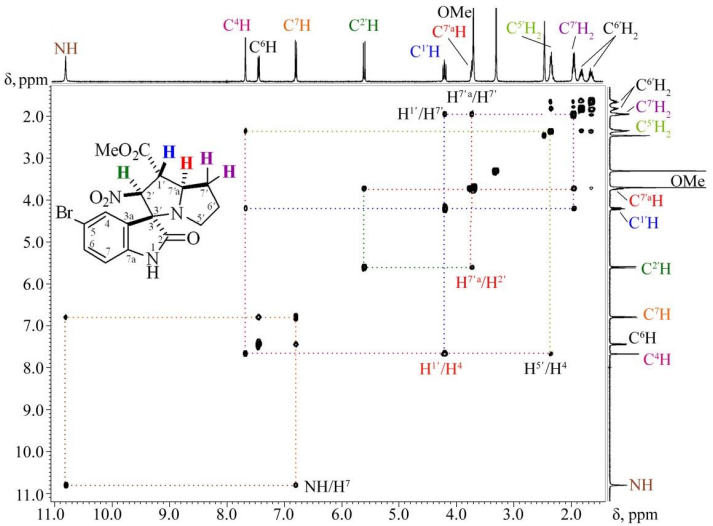


*Figure 3. ^{1}H-^{1}H NOESY spectrum of compound **6a** (DMSO-d_6)*

The presence of these correlations indicates that for diastereomer **a** such an arrangement of spirocycles is realized in which the proton of the pyrrolizine ring ($H^{1'}$) at the carbon atom associated with the alkoxycarbonyl group and the proton of the indole ring (H^4) are as close as possible in space (Fig. 4).

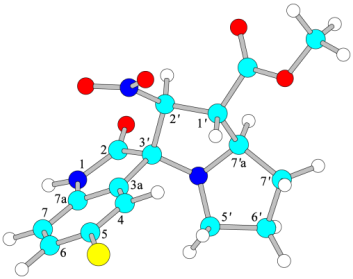


*Figure 4. Spatial model of compound **6a** (HyperChem, MM+)*

Thus, the study of individual isomers of spiropyrrolizine oxindoles 3-6a using ^1H-^1H COSY and NOESY NMR spectroscopy experiments made it possible to establish their regeo- and stereochemistry.

The studies were carried out in the Center of collective use at the Faculty of Chemistry of the Herzen State Pedagogical University of Russia on the Jeol ECX-400A spectrometer (Royal Probe) at 399.78 (^1H) and 100.53 (^{13}C) MHz with standard experimental settings. The residual signals of a non-deuterated solvent (for ^1H nuclei) or the signals of a deuterated solvent (for ^{13}C nuclei) were used as a standard.

Acknowlegments

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References

1. A. Y. Barkov, N. S. Zimnitskiy, V. Y. Korotaev, I. B. Kutyashev, V. S. Moshkin, V. Y. Sosnovskikh. – *Tetrahedron*, 72(43), 6825-6836 (2016).
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