

^1H and ^{13}C NMR study of the structure of the reaction product of 4-acetylfuro[3,2-*b*]pyrrole with dimethyl butynedioate

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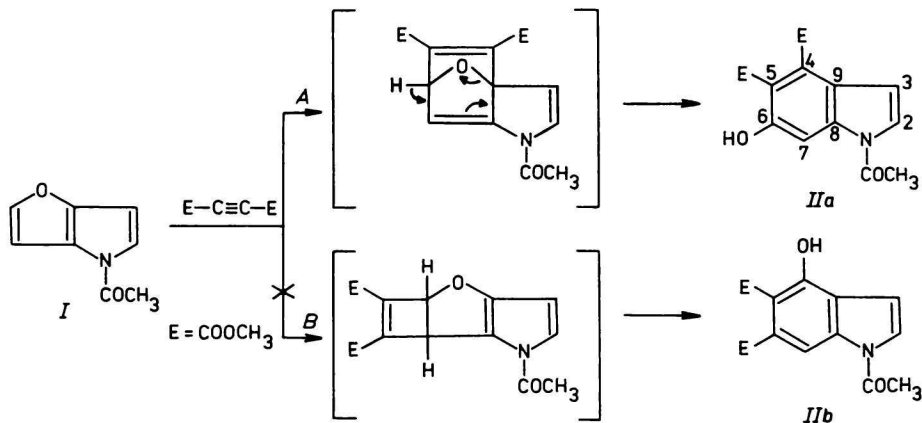
By ^1H and ^{13}C NMR spectroscopy it was confirmed that the final product of the reaction of 4-acetylfuro[3,2-*b*]pyrrole with dimethyl butynedioate is dimethyl 1-acetyl-6-hydroxy-4,5-indolecarboxylate. To determine the structure of the reaction product FT NMR techniques were used: 2D heteronuclear chemical shift correlation, selective INEPT and 1D-INADEQUATE experiments.

С помощью ^1H и ^{13}C ЯМР спектроскопии было подтверждено, что конечным продуктом реакции 4-ацетилфуоро[3,2-*b*]пиррола с диметил-бутиндиоатом является диметил-1-ацетил-6-гидрокси-4,5-индол-дикарбоксилат. Для установления строения продукта реакции были использованы ЯМР методы с преобразованием Фурье: двухразмерная гетероядерная корреляция химических сдвигов, избирательный INEPT и одномерный 1D-INADEQUATE методы.

The reactions of 2-aryl-4*H*-furo[3,2-*b*]pyrrole and its 4-substituted analogues with dimethyl butynedioate were studied [1]. The course of the reaction was proved by ^1H NMR spectroscopy determination of the structure of the final products. It was confirmed that the reaction takes place on the pyrrole ring and the structure of the final products is dependent on the character of the substituents attached at nitrogen atom. 4-Acetyl-2-arylfuro[3,2-*b*]pyrrole, the compound bearing the electronattracting substituent, with dimethyl butynedioate gives the substituted benzo[*b*]furan.

In this work the structure of the final product of the reaction of 4-acetylfuro[3,2-*b*]pyrrole (*I*) with dimethyl butynedioate was studied by means of ^1H and ^{13}C NMR spectroscopy. It was found that in this case the reaction takes place on the furan ring and the final product is substituted indole. Since it was possible to presume that this reaction proceeds either as a (4 + 2) cycloaddition or as a (2 + 2) cycloaddition [2], the exact determination of the structure of the final product was unavoidable. By analysis of ^1H and ^{13}C NMR spectra the structure of dimethyl 1-acetyl-6-hydroxy-4,5-indolecarboxylate (*IIa*) was con-

firmed, which enabled us to conclude that the studied reaction proceeds *via* (4 + 2) cycloaddition (Scheme 1, pathway A).



^1H and ^{13}C NMR data of the studied compound *IIa* are listed in Tables 1 and 2. The signals of the first order ^1H NMR spectrum were unambiguously assigned. Signals of the protons H-2 and H-3 are observed at $\delta = 7.80$ and 6.88 ppm, respectively. Signal H-2 was split into a doublet with the coupling constant $J(2, 3) = 3.8$ Hz, H-3 is a doublet of doublet due to an interaction with H-2 and H-7 of the six-membered ring. Signal H-7 at $\delta = 8.26$ ppm is split into doublet, the coupling constant $^5J(3, 7)$ value being 0.9 Hz. The H-7 signal is shifted downfield due to the anisotropic effect of the carbonyl group attached at the nitrogen atom of the pyrrole ring. To determine the position of OH group signal, the deuteration with D_2O was used. It was found that its chemical shift is not influenced with the concentration of the solution, which is due to an existence of the intramolecular hydrogen bond with the *o*-methoxycarbonyl group. The determination of the isomer was not possible using the substituent chemical shift additivity principles for substituents on a benzene ring, as for the above introduced reason the considerable deviations were obtained [3].

The complete assignment of the carbons in the ^{13}C NMR spectra and the structure determination was achieved by the application of the pulsed FT NMR techniques. ^1H noise decoupled ^{13}C NMR spectrum shows 14 resonance signals (Table 2). The carbons C-2, C-3, and C-7 were unambiguously assigned using the 2D ^1H — ^{13}C chemical shift correlated spectrum [4]. The signal at $\delta = 152.43$ ppm belongs to the carbon atom bearing the OH group, which was on the basis of the next introduced methods assigned to the carbon C-6 of the

Table 1

¹H NMR data of the compound *Ila*

Proton	δ/ppm		$J(\text{H}, \text{H})/\text{Hz}$
	<i>a</i>	<i>b</i>	
H-2	7.80 d	7.38 d	$J(2, 3) = 3.8$
H-3	6.88 dd	6.48 dd	
H-7	8.26 d	8.12 d	$J(3, 7) = 0.9$
OH	10.34 bs	10.62 bs	
<u>COOCH</u> ₃	3.78 s	3.96 s	
	3.88 s	3.94 s	
N— <u>COCH</u> ₃	2.62 s	2.60 s	

a) Measured in hexadeuterodimethyl sulfoxide; *b*) in deuteriochloroform.

Table 2

¹³C NMR data of the compound *Ila*

Carbon	δ/ppm^a	$J(\text{C}, \text{H})/\text{Hz}^b$	$J(\text{C}, \text{C})/\text{Hz}^c$
C-2	128.09	$^1J(\text{C-2}, \text{H-2}) = 190.1$	$J(\text{C-2}, \text{C-3}) = 71.5$
C-3	107.99	$^2J(\text{C-2}, \text{H-3}) = 9.7$	$J(\text{C-3}, \text{C-9}) = 55.9$
C-4	120.02	$^1J(\text{C-3}, \text{H-3}) = 180.0$	
C-5	119.91	$^2J(\text{C-3}, \text{H-2}) = 7.0$	
C-6	152.43	$^2J(\text{C-6}, \text{H-7}) = 2.0$	$J(\text{C-6}, \text{C-5}) = 69.5$
C-7	107.02	$^1J(\text{C-7}, \text{H-7}) = 169.0$	$J(\text{C-7}, \text{C-6}) = 67.7$
C-8	136.34	$^3J(\text{C-4}, \text{H-3}) = 0$	$J(\text{C-7}, \text{C-8}) = 62.4$
C-9	121.99	$^3J(\text{C-5}, \text{H-7}) = 2.5$	$J(\text{C-8}, \text{C-9}) = 54.3$
<u>COOCH</u> ₃	167.42	$^3J(\text{C-8}, \text{H-2}) = 6.0$	$J(\text{C-9}, \text{C-4}) = 53.5$
	165.79		
N— <u>COCH</u> ₃	169.86	$^3J(\text{C-8}, \text{H-3}) = 3.5$	$J(\text{C-4}, \text{COO}) = 74.4$
<u>COOCH</u> ₃	52.45	$^2J(\text{C-8}, \text{H-7}) = 9.0$	$J(\text{C-5}, \text{COO}) = 75.1$
	52.17	$^3J(\text{C-9}, \text{H-2}) = 9.0$	
N— <u>COCH</u> ₃	23.79	$^3J(\text{C-9}, \text{H-7}) = 3.0$	

a) Measured in hexadeuterodimethyl sulfoxide; *b*) the values from the proton coupled spectrum; *c*) the values from the 1D-INADEQUATE spectrum.

compound *Ila*. The values of coupling constants $J(\text{C}, \text{H})$ were determined from the proton coupled spectra. The quaternary carbon atoms were identified using the selective INEPT experiment [5]. In the selective INEPT spectrum only those resonances of carbon atoms are shown, which have a transfer from the competent proton being irradiated by "soft" pulses. The selective INEPT spectra of *Ila* are in Fig. 1. By the irradiation of H-2 the polarization is transferred to the carbon atoms C-8, C-9, and C-3 and transfer from H-3 shows at C-8, C-9, and

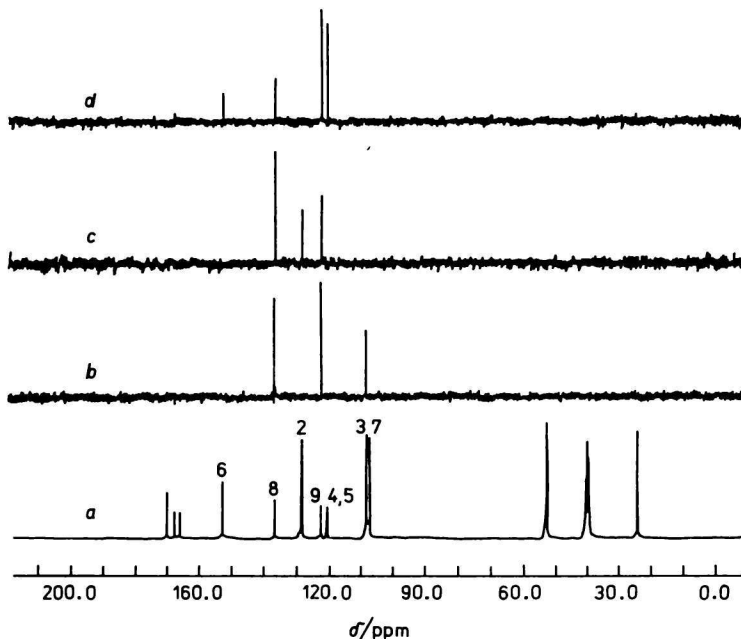


Fig. 1. ^1H noise decoupled ^{13}C NMR spectrum of the compound *IIa* (a). The selective INEPT spectra: transfer from the proton H-2 (b), from the proton H-3 (c), from the proton H-7 (d).

C-2. The transfer from the proton H-7 confirms the assignment of C-6, C-8, C-9, and C-5. The transfer from H-3 to C-4 was not observed, because in the undecoupled ^{13}C NMR spectrum the long-range coupling was not observed ($^3J(\text{C-4}, \text{H-3}) \approx 0$).

For the determination of the connectivities of the carbon atoms and the complete assignment of the carbons of six-membered ring 1D-INADEQUATE method [6] was used, which enables to obtain simultaneously the values of the coupling constants $J(\text{C}, \text{C})$ (Table 2). The signals C-4 and C-5 are overlapped, therefore it was not possible to ascertain the coupling constant $J(\text{C-4}, \text{C-5})$ from 1D-INADEQUATE spectrum. The values of the coupling constants $J(\text{C-7}, \text{C-6}) = 67.7 \text{ Hz}$ and $J(\text{C-6}, \text{C-5}) = 69.5 \text{ Hz}$ unambiguously confirmed the connectivities of the carbon atoms C-7—C-6—C-5 in the six-membered ring and the position of the hydroxy group as well.

Experimental

^1H NMR spectra were recorded with FT NMR Bruker AM-300 apparatus operating at 300 MHz at room temperature, in deuteriochloroform and hexadeuterodimethyl

sulfoxide. ¹³C NMR spectra were measured at 75.43 MHz in the same solvents ($c = 0.5 \text{ mol dm}^{-3}$) at room temperature and 40 °C, respectively. Tetramethylsilane in deuteriochloroform was used as an internal reference substance, in hexadeuterodimethyl sulfoxide the reference signal of the solvent at $\delta = 39.5 \text{ ppm}$ relative to tetramethylsilane was used. The spectral width 17 kHz using 32 K during accumulation, relaxation delay 1.5 s. The uncoupled ¹³C NMR spectra were measured with the spectral width 5 kHz (without COCH₃ and COOCH₃ region).

The H-X correlated 2D spectrum was measured at the spectral width in dimension F2 4424.78 Hz and in dimension F1 523.01 Hz. The magnitude of the matrix data in F1 dimension was 128 words, whereas in dimension F2 1 K. Before the Fourier transformation FID was multiplied with the sine-bell function (F2) and in dimension F1 with the Gaussian function. 1D-INADEQUATE experiment was realized with the spectral width 5 kHz at 40 °C using 10 mg of the relaxation agent [Cr(acac)₃] (acac = acetylacetonate). The relaxation delay 8 s, the experiment was optimized for $J(\text{C}, \text{C}) = 60 \text{ Hz}$. The total number of the accumulations was 64 000. The selective INEPT experiment was measured under the same conditions as the basic decoupled spectrum and was optimized for $J(\text{long-range}) = 7 \text{ Hz}$.

4-Acetylfuro[3,2-*b*]pyrrole (*I*) was prepared according to [7]. The procedure for the preparation of dimethyl 1-acetyl-6-hydroxy-4,5-indoledicarboxylate is described in [2].

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