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Positional Assignments of a Substituent Group of 3-Substituted Juglones by the Off-Resonance ^{13}C NMR Spectra1)

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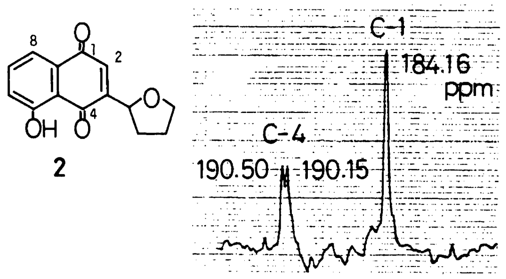
Synopsis. Taking into account the fact that the long-range ^{13}C–^{1}H coupling constant $^{3}J_{\mathrm{CH}}$ is greater than $^{2}J_{\mathrm{CH}}$, positional assignments of a substituent group of 3-substituted juglones were easily accomplished by off-resonance ^{13}C NMR spectra using a 60-MHz instrument for ^{1}H. This method was applicable to a structural determination of naphthazarin derivatives.

Such compounds having a juglone skeleton as juglomycin and hydroxyjuglone occur in nature.2) Some reports have appeared concerning structural determinations for the 2- and 3-substituted juglones by NMR. For example, Sammes et al.3) and d'Angelo et al.4) determined the positions of a substituent group of juglone derivatives based on the proton-coupled ^{13}C NMR spectra. C–H two-dimensional NMR was used to characterize 2-and 3-hydroxyjuglones by Maurette et al.5) Yoshida et al.6) assigned the positions of a substituent group of mono-substituted quinoline-5,8-diones bearing a structure similar to mono-substituted juglones, based on detailed research concerning their ^{1}H NMR spectral data.

In the course of our synthetic study of naphthoquinone derivatives, we have found the title method. The present paper describes a structural determination of 3-substituted juglones based on the off-resonance ^{13}C NMR spectra.

Results and Discussion

We have already reported that the treatment of juglone (**1**) with 2,3-dihydrofuran in the presence of $BF_3 \cdot OEt_2$ gave the juglone derivatives (**2**) and (**3**) in yields of 39% and 27%, respectively (Scheme 1), and that the structure of **2** was determined based on the two-dimensional NMR spectra (C–H COSY spectra).7) We have found that the structure could also be determined by an off-resonance ^{13}C NMR spectrum using a simpler instrument, a 60-MHz spectrometer for ^{1}H. In the off-resonance ^{13}C NMR spectrum of **2**, C-4 and C-1 signals were observed as a doublet (δ=190.15 and 190.50) and a singlet (δ=184.16), respectively (Chart 1). This result can be accounted for by the



2

Chart 1.

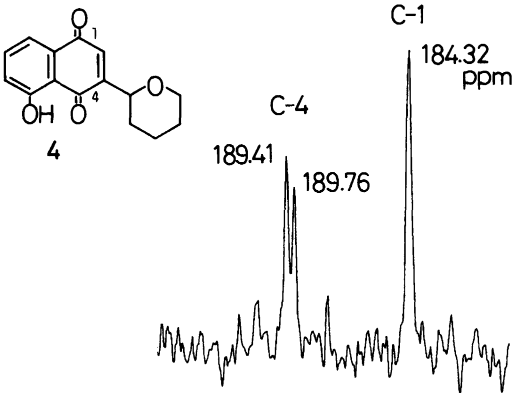


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Chart 2.

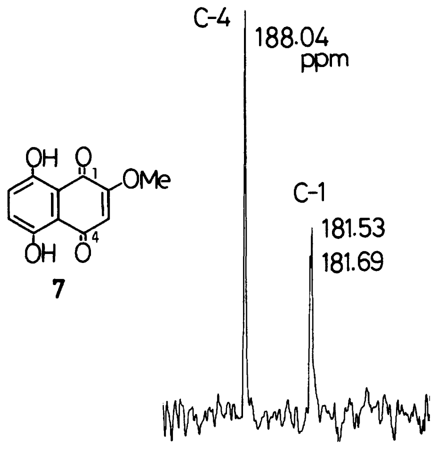

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Chart 3.

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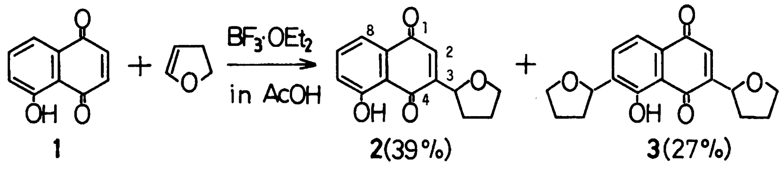
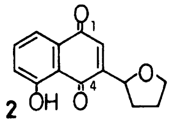
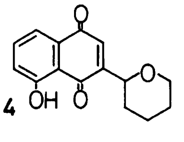
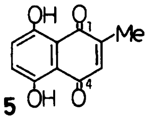
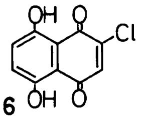
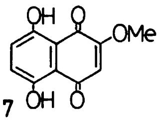
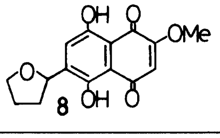


Scheme 1.

Table 1. Chemical Shifts (ppm) of Off-Resonance ^{13}C NMR Spectra

Compound	C-1	C-4
 2	184.16	190.15 190.50
 4	184.32	189.41 189.76
 5	182.32 182.55	182.04
 6	172.77 172.95	177.06
 7	181.53 181.69	188.04
 8	180.78 181.00	187.63

coupling constants: The long-range ^{13}C–^{1}H coupling constant $^3J_{\mathrm{CH}}$ is greater than $^2J_{\mathrm{CH}}$, and in the juglone derivatives $^3J_{\mathrm{C4-H2}}$ (about 7 to 9 Hz) is larger than $^3J_{\mathrm{C1-H8}}$ (about 3 to 4 Hz).[3—5] Therefore, although the C-4 signal was a doublet coupled with H-2, the C-1 signal was a singlet uncoupled with H-2 and H-8. This result indicates that the tetrahydrofuryl group is substituted at the 3-position in juglone.

Similarly, an off-resonance ^{13}C NMR spectrum of 5-hydroxy-3-(tetrahydro-2*H*-pyran-2-yl)-1,4-naphthoquinone (**4**)[6] showed C-4 and C-1 signals as a doublet (δ=189.41 and 189.76) and a singlet (δ=184.32), respectively (Chart 2). Therefore, the tetrahydro-2*H*-pyranyl group is found to be substituted at the 3-position in juglone.

We next applied the off-resonance ^{13}C NMR method to the known naphthazarin derivatives. In a spectrum of 2-methoxynaphthazarin (**7**),[8] although the C-1 signal was a doublet (δ=181.53 and 181.69) coupled with H-3, the C-4 signal was observed as a singlet (δ=188.04) (Chart 3). Similar reduced couplings were clearly observed in the off-resonance ^{13}C NMR spectra of 2-methylnaphthazarin (**5**),[8] 2-chloronaphthazarin (**6**),[9] and 2-methoxy-6-(tetrahydrofuran-2-yl)naphthazarin (**8**).[7] The results are summarized in Table 1.

In conclusion, we found that the positions of a substituent group of 3-substituted juglones can be easily determined by the off-resonance ^{13}C NMR spectra using a 60-MHz instrument for ^{1}H.

Experimental

^{13}C NMR spectra were recorded on a JEOL JNM-FX 60 spectrometer in CDCl$_3$ operating at 15.04 MHz with Me$_4$Si used as an internal standard. The off-resonance spectra were obtained by placing a decoupler offset by 23 ppm upfield from the center (δ=5.8) of the ^{1}H chemical shifts, using: decoupling power, 4 W; spectral width, 3500 Hz; pulse width, 7 μs (45° flip angle); data points, 8192.

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