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Short Communication

The Complete Assignment of the ^{1}H and ^{13}C Chemical Shifts of 1,2-Diacetoxy-9,10-anthraquinone

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Anthraquinones comprise the largest group of naturally occurring quinones and they have been used both as pigments and medicines since ancient times.[1] In modern times the use of synthetic dyes has reduced the importance of natural pigments, but medical interest in them is increasing. This is reflected in the huge number of articles considering synthesis of anthraquinone-derived anthracyclinones with anti-tumour activity.[2–6] Anthraquinone monomers and dimers have also shown activity against human immunodeficiency virus type 1 (HIV-1).[7] The importance of a complete analysis of the nuclear magnetic resonance spectra of those compounds is thus obvious.

In 1977 Höfle published the first major NMR work on anthraquinone aglycones.[8] He started out with unsubstituted 9,10-anthraquinone, which is fully symmetrical and therefore easy to assign. He then considered 1-acetoxy- and 2-acetoxy-9,10-anthraquinone and compared the chemical shifts of the substituted anthraquinones with the unsubstituted anthraquinone. When examining his assignments of shifts of 1- and 2-acetoxy-9,10-anthraquinones it is clear that all the chemical shifts to carbons of the A-ring and C-9 and C-10 are assigned, leaving the assignment of the shifts to the carbons of the C-ring tentative. This is due to the overlap/small differences in chemical shifts for the H-5/H-8 and H-6/H-7 protons. This is the case for all 9,10-anthraquinones with an asymmetrically substituted A-ring and no substituents in the C-ring. This leads to complete assignment for only the symmetrically substituted anthraquinones, leaving a large number of tentative assignments for the asymmetric cases.

The other major work was that of Berger and Castonguay and dealt with hydroxy- and methoxy-substituted 9,10-anthraquinones.[9,10] Unlike Höfle they appear to have had no problems in assigning the ^{13}C shifts of the C-ring. Having in mind that their original work was done on a 90 MHz spectrometer using ^{1}H-noise and noise off-resonance decoupling techniques as assignment tools, there is little doubt that the signals belonging to the C-ring are only tentatively assigned.

Our conclusion is that no full assignments of the ^{1}H and ^{13}C shifts of anthraquinones asymmetrically substituted in the A-ring and unsubstituted in the C-ring have been presented. The current presentation of the complete ^{1}H and ^{13}C chemical shift assignment of 1,2-diacetoxy-9,10-anthraquinone (Fig. 1) is thus, to the best of our knowledge, the first full NMR analysis carried out on a compound of this type.

This analysis is possible because unlike most anthraquinones of this kind, H-5 is separated from H-8, and H-6 somewhat separated from H-7 at 400 MHz.

This makes possible selective decoupling of H-5 and H-8 and also irradiation of H-5 and H-8 to create NOE effects. To decide which is H-5 and H-8, examination of the molecule shows that C-9 couples only to H-8, whereas C-10 couples to H-4 as well as to H-5 via three-bond couplings. Selective decoupling of H-8 will thus make C-9 a singlet, whereas decoupling of H-5 will give both C-9 and C-10 as doublets. The results are presented in Fig. 2.

In addition to assigning H-5 and H-8, this experiment also assigns C-9 and C-10 and this assignment is the reverse of Höfle's, a possibility mentioned in his work. NOE measurements on irradiating H-5 and H-8 give H-6 and H-7, respectively.

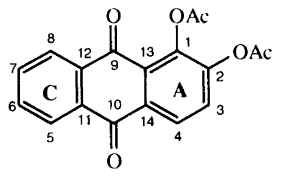

Fig. 1. 1,2-Diacetoxy-9,10-anthraquinone showing numbering system for anthraquinones.

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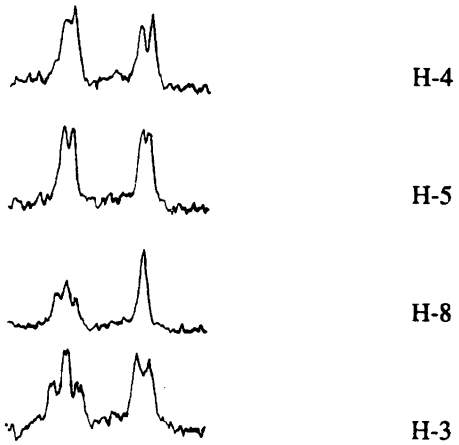

Fig. 2. ^{13}C NMR spectra showing signals of C-9 and C-10 while selectively decoupling H-3, H-8, H-5 and H-4. The proton decoupled is indicated at the right side of each spectrum.

With a fully assigned proton spectrum the protonated carbons were determined using proton–carbon correlated two-dimensional NMR and the spin–echo Fourier transform (SEFT) experiment. The assignment of the shifts of C-6 and C-7 is again the reverse of Höfle's, a possibility left open in his work. C-1 and C-2 are easily determined from an undecoupled ^{13}C-spectrum since C-1 couples with H-3 by a three-bond coupling, whereas C-2 couples with H-4 in a three-bond coupling and H-3 in a two-bond coupling.

Finally, the assignment of the shifts of the quaternary carbons, C-11, 12, 13 and 14 remains. The region from ca. 135–132 ppm gives three of the quaternary carbons and the protonated C-6 and C-7 (Fig. 3). Selective decoupling of H-8 removes the three-bond coupling to C-11 and the C-11 signal will change. The same will happen to C-12 on selective decoupling of H-5. Fig. 3 shows a change in the signals at 132.4 and 134.0 ppm while irradiating H-8 and H-5, respectively. The doublet at 132.2 ppm is the shift of either C-13 or C-14. The appearance of a singlet while irradiating H-3 proves it to be the shift of C-14, a result which Fig. 3 clearly shows. The complete assignment and the coupling constants of the

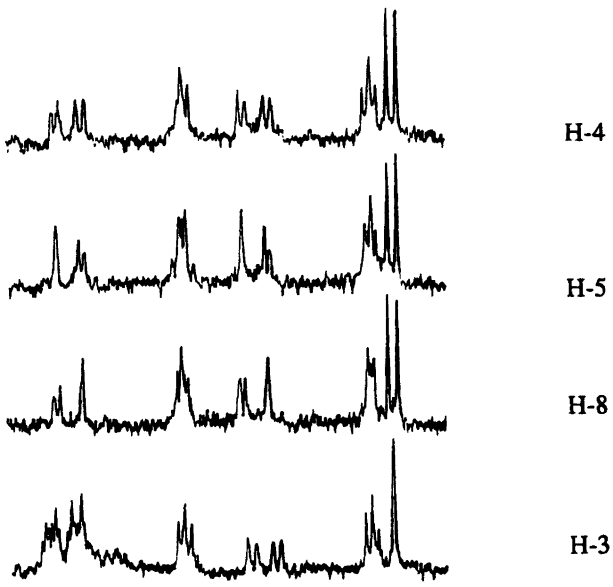

Fig. 3. ^{13}C NMR spectra showing the region from ca. 135–132 ppm while selectively decoupling H-3, H-8, H-5 and H-4. The proton decoupled is indicated at the right side of each spectrum.

^{1}H and ^{13}C spectra of 1,2-diacetoxy-9,10-anthraquinone are summarised in Table 1.

Experimental

1,2-Diacetoxy-9,10-anthraquinone. 1,2-Dihydroxy-9,10-anthraquinone (Fluka) was stirred in equal amounts of pyridine and acetic anhydride for 3 h at room temperature.[11] The solution was poured into water, filtered and the derivative was washed with several portions of water until no trace of pyridine remained.

The 400.13 and 100.62 MHz ^{1}H and ^{13}C NMR spectra were obtained at 297 K on a Bruker AM 400 WB instrument equipped with a 5 mm $^{1}H/^{13}C$ dual probe. All 90° transmitter and decoupler pulses were carefully calibrated (7–15 μs). Ca. 50 mg of the sample were dissolved in 500 μl of deuteriochloroform. The carbon signal and

Table 1. ^{1}H and ^{13}C NMR shifts (δ) and coupling constants (Hz) of 1,2-diacetoxy-9,10-anthraquinone.

Proton	δ	*o*	*m*	*p*	Carbon				
H-3	7.60	8.54	—	—	C-1	C-5	C-9	C-13	
H-4	8.27	8.54	—	—	141.91	126.90	181.33	126.29	
H-5	8.22	7.62	1.58	0.62	C-2	C-6	C-10	C-14	
H-6	7.73	7.62 7.42	1.23	—	148.33	134.03	181.56	132.17	
H-7	7.74	7.42 7.99	1.58	—	C-3	C-7	C-11	O–C=O	Methyl
H-8	8.16	7.99	1.23	0.62	128.62	134.24	132.39	168.33	20.76
Methyl	2.47				C-4	C-8	C-12	O–C=O	Methyl
Methyl	2.34				126.15	127.11	134.01	167.68	20.56
			1-Bond	C-3	C-4	C-5	C-6	C-7	C-8
			Couplings	167.47	168.61	165.56	163.27	163.27	165.56

the residual proton signal of the solvent were used as secondary references for the chemical shifts (77.00 and 7.25 ppm, respectively). The homonuclear Overhauser enhancements were measured by means of NOE difference spectroscopy by saturating the relevant proton signals on resonance for 5 s using weak irradiation. The enhanced resonances were identified by subtracting the unperturbed FID with off-resonance irradiation from the perturbed FID, followed by Fourier transformation and phasing.

Selective decoupling was performed by irradiation of a specific proton at its exact frequency at a low power level, while recording carbon. The directly bonded ^{13}C signal changes into a singlet, while the remaining ^{13}C absorptions show residual coupling. The spin–echo experiment was performed using the gated decoupler mode whereas the 2D heteronuclear one-bond correlation experiment was performed in the normal mode. Both experiments were optimised for a 165 Hz one-bond coupling. The simulation of the ^{1}H spectrum to give the *ortho*, *meta* and *para* couplings, was performed by means of the PANIC program available in the Bruker Software Library.

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