Complete ^1H and ^{13}C NMR Spectral Characterization of 1,6-Dioxapyrene and Related Compounds. An Unusual Coupling Interaction Through Hydrogen Bond in Three Precursors

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The ^1H and ^{13}C nmr studies of 1,6-dioxapyrene show the disruption of extended delocalization of the π electrons in this recently synthesized heterocyclic skeleton. A surprising coupling interaction through hydrogen bonding was detected in the precursors bearing formyl and hydroxyl groups in *peri* positions.

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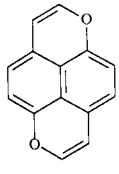
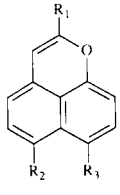
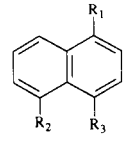
The [1]benzopyrano[6,5,4-*def*][1]benzopyran (1,6-Dioxapyrene) **1** is a new heterocyclic skeleton, the synthesis of which has been recently described [1]. This compound was prepared with the view of evaluating its biological, photobiological and photochemical properties [2], in comparison with that of pyrene. Certain particularities observed in its ^1H nmr spectrum [1] motivated our further nmr study of this compound and that of some of its precursors or analogs **2** [3,4], **3** [4], **4**, **5** [1], **6** [5,6] and **7** [6,7].



1



2 : R_1=R_2=R_3=H
3 : R_1=R_3=H; R_2=OCH_3
4 : R_1=H; R_2=OH; R_3=CHO
5 : R_1=CO_2CH_3; R_2=OH; R_3=CHO



6 : R_1=OCH_3; R_2=OH; R_3=CHO
7 : R_1=H; R_2=OH; R_3=CHO

As unexpected results were obtained, we also determined the X-ray spectrum of dioxapyrene **1** [8]. Nevertheless, no specific characteristic could be deduced from the radiocrystallographic data, except the ethylenic character of the heterocyclic double bonds. This is in fair agreement with the ^1H and ^{13}C nmr results which will be developed beneath.

For ease of comparison, an arbitrary numbering of the carbon atoms was derived from the naphthalene skeleton for compounds **1-7** (*cf.* Table 1).

Assignments of the ^1H NMR Spectra.

The signal assignments were first made on the basis of the expected effects of the substituents: for the aromatic protons, withdrawing mesomeric effect of the formyl group, donating mesomeric effect of all other substituents and for the protons in the heterocycle withdrawing inductive effect of the oxygen atom on $H_{1'}$ and mesomeric donating effect on $H_{2'}$. Secondly, the coupling interactions were ascertained, either by spin decoupling or through 2D δ ^1H δ ^1H correlations (COSY) *eg.* in the case of compound **2** which gives groups of scarcely shifted resonances. The distinction between isolated pairs of *ortho* protons and the pair of protons in the heterocycle which all gave AB patterns was made on the basis of the ^3J coupling constants. Typical values, 8-9 Hz, were found for the aromatic *ortho* protons and a smaller value, *circa* 6 Hz was measured for $^3J_{H1',H2'}$ in compounds **1, 3, 4** as well as in compound **2** where the assignments of these protons are unequivocal.

Finally, when necessary, to distinguish sets of resonances originating from protons in rings A and B, NOE difference experiments were used. The saturation of the well isolated resonance of $H_{2'}$ leads to significant enhancement of the signals of the proximate $H_{1'}$ and H_7.

The assignments of the signals of the hydroxyl and formyl protons are straightforward on the basis of their chemical shifts (a surprising coupling interaction between these two protons was found in compounds **4, 5** and **6**).

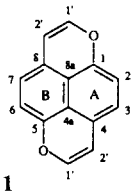
Assignments of the ^{13}C NMR Spectra.

But for the carbons of the functional groups and a few carbons, *eg.* those linked to oxygen atoms in certain cases, the values of the chemical shifts do not allow unequivocal assignments.

The undecoupled spectra are more informative since many carbons gave typical coupling patterns. The correspondence between the carbons and their bounded protons were obtained through 2D reverse δ ^{13}C-δ ^1H correlation

Table 1

^1H and ^{13}C NMR Chemical Shift Data



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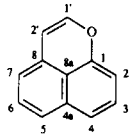

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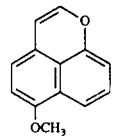

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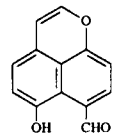

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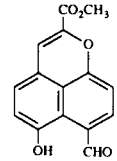

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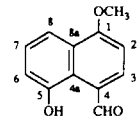

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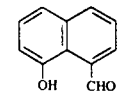


7

Position or group	1 δ ^1H	1 δ ^{13}C	2 δ ^1H	2 δ ^{13}C	3 δ ^1H	3 δ ^{13}C	4 δ ^1H	4 δ ^{13}C	5 δ ^1H	5 δ ^{13}C	6 δ ^1H	6 δ ^{13}C	7 δ ^1H	7 δ ^{13}C
1		151.28		152.73		152.68*		161.40		160.85		163.30	8.14	139.05
2	6.08	108.33	6.72	107.25	6.76	108.35	6.69	107.63	6.89	108.65	6.85	102.76	7.56	124.27
3	6.16	117.48	7.24	127.47	7.28	127.19	7.74	146.63	7.82	146.85	7.93	146.65	8.03	142.87
4		122.35	7.22	119.61	7.55	114.19		124.54		125.07		125.53		132.29
4a		127.20		135.07		127.11		126.18		123.70		122.50		121.10
5		151.28	7.34	123.79		152.59*		154.16		156.74		155.68		155.13
6	6.08	108.33	7.19	127.72	6.60	105.07	7.06	118.36	7.08	118.33	7.18	116.71	7.19	115.92
7	6.16	117.48	6.67	115.29	6.63	114.83	6.97	121.04	7.15	124.52	7.48	128.60	7.54	129.02
8		122.35		128.85		121.40		120.77		119.45	7.84	113.67	7.42	120.49
8a		127.20		124.34		124.87		123.42		126.24		128.22		136.20
1'	6.14	143.67	6.71	144.28	6.62	142.12	6.77	140.73		139.66				
2'	5.40	107.35	5.91	107.54	5.93	107.38	6.18	109.75	7.16	116.87				
OH							12.10		12.48		12.16		11.68	
CHO							9.38	194.32	9.43	194.73	9.60	195.68	9.85	197.84
OCH_3					3.94	55.47					4.10	56.35		
CO_2CH_3										161.04				
CO_2CH_3									3.92	52.71				

* assignments could be inverted

for compounds **2, 4, 5** (Figure 1) and **7**. Based on the resulting unequivocal assignments of the protonated carbons, the following criteria were derived for the assignments of the carbons in the five heterocyclic compounds **1-5**. The ^1J coupling of $C_{1'}$ has an expected high value (*circa* 200 Hz) according to the effect of the bounded oxygen [9,10]. For the other carbons, the ^1J coupling constants do not provide significant diagnosis. Thus, only the long range coupling interactions will be further described. $C_{2'}$ exhibits two long range coupling interactions of unequal magnitude with $H_{1'}$ and H_7. Similarly C_7 is always slightly coupled to $H_{2'}$. The aromatic carbons show the expected ^3J coupling (*circa* 7-8 Hz) according to the substitution patterns. The carbons C_3 and C_6 which, due to their positions, are never significantly coupled to aromatic protons, are respectively coupled to the formyl and to the hydroxyl protons in the relevant derivatives.

For the assignments of the quaternary carbons, the following arguments were used: - C_8 exhibits coupling of similar magnitude with H_6 and $H_{1'}$, thus giving rise to a triplet. - C_{8a}, which is farther away from the protons than the other carbons, gives the signal of lower intensity, due to the lack of efficient relaxation. The magnitude of the ^2J coupling to the formyl proton (*circa* 20 Hz) allows an easy assignment of C_4 in compounds **4, 5, 6, 7** [11]. - In the hydroxylated derivatives, exchange of the hydroxyl proton by a deuterium results in a slight high field shift for the proximate cabons C_5 and C_{4a}. - In compound **5**, the quaternary carbons in the heterocycle $C_{1'}$ was identified by its coupling (^2J) to $H_{2'}$.

The long range coupling interactions were ascertained by selective spin decoupling experiments. All the chemical shift data are collected in Table 1. Pertinent coupling constants are given in the Experimental section.

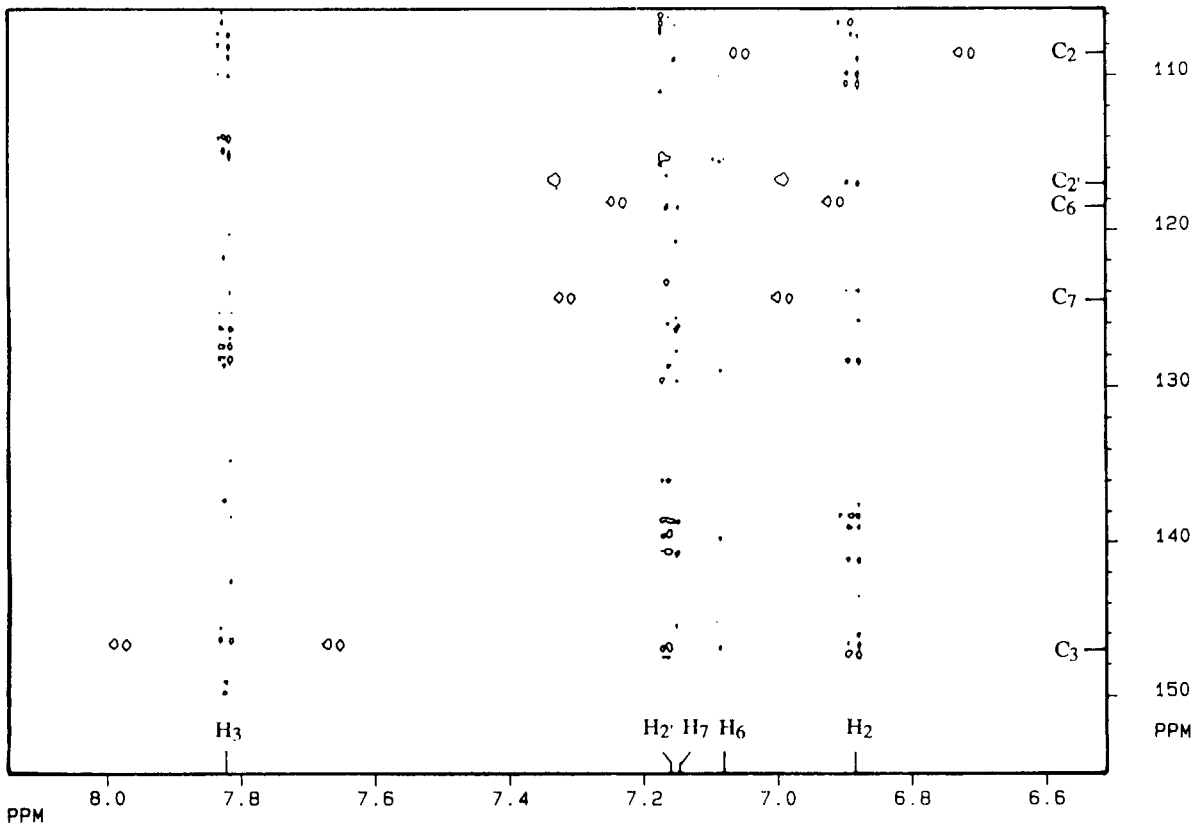


Figure 1. Reverse ^{13}C-^1H correlated spectra of compound **5**.

Discussion.

As regards the ^1H spectra, the most striking feature is the low values of the chemical shifts of all the protons in dioxapyrene **1**.

To get insight in the factors which determine these shifts, we first examined the effect of the oxygen atom in a simple donor substituent -OCH_3 and that of the oxygen atom in the heterocycle by comparing compounds **6** and **4** to compound **7**. In the former case conjugation occurs only with ring A and extends moderately to the formyl group. The shifts of the protons attached to ring B are not significantly modified, except in the particular case of H_8 which experiences the *peri* effect of the oxygen atom [12,13]. In the second case, the mesomeric effect appears in both rings, due to the existence of two pathways for the development of conjugation, the direct one towards ring A and the indirect one through the double bond $C_{1'}C_{2'}$ towards ring B. It is noteworthy that, despite these two possibilities for electron delocalisation, and the significant effect observed at H_7, the high field shifts observed for H_2 and for the formyl proton exceed those observed upon introduction of the methoxy group. It seems that a more conjugated system is attained when the oxygen atom is included in the heterocycle.

Bearing in mind the preceding observations, let us now compare compounds **3** and **1** to compound **2**. In fair agreement with expectation, the introduction of the methoxy group at C_5 in **3** results in a significant high field shift for H_6 only (the values $\Delta\delta \cong$ -0.6 ppm, compares well with the effect previously observed for H_2 in **6** with respect to **7**) and to the lack of significant changes for the protons of ring A taking account of the *peri* effect at H_4. As regards the protons of the double bond, a small shielding of $H_{1'}$ ($\cong$ -0.1 ppm) indicates a moderate participation of the double bond to the conjugated system involving the methoxy group and ring B.

In contrast, the introduction of the second heterocycle in **1** results in high field shifts of all the protons by far greater than expected.

The phenomenon is particularly noteworthy at positions where no significant conjugation with the newly introduced donor atom is expected, namely H_2 (-0.64 ppm), H_7 (-0.51 ppm), $H_{2'}$ (-0.57 ppm). Similarly, at positions where conjugation is likely to occur, the shifts largely exceed those observed upon introduction of the first heterocycle or that of the methoxy group.

These observations suggest that the shielding experienced by the various protons in dioxapyrene results only

in part from the mesomeric donor effect of the two oxygen atoms. Another cause might be the disruption of the ring current which, in fully aromatic systems, results in low field shifts of the protons. The same mechanism might play a role, even of minor importance, upon the introduction of the first heterocycle since non-negligible high field shifts occur, for H_3 and H_6, in compound **4** with respect to compound **6** despite the fact that these protons are not in positions where conjugation is expected with the new oxygen donor atom.

Further insight in the electronic behaviour might be gained by examination of the ^{13}C nmr spectra.

The comparison of compounds **4** and **6** clearly confirms the occurrence of two distinct pathways for the conjugation starting from the oxygen atom in the heterocycle, one through ring A which extends to the formyl carbon, and the other through the double bond towards ring B. Nevertheless, the carbons C_2 and C_6 are deshielded in compound **4** with respect to compound **6**. As a result, the reverse trend observed for their attached protons cannot be attributed to an increased electron releasing effect of the oxygen atom at these positions.

The comparison of compounds **1** and **3** to compound **2** shows that the presence of the second oxygen atom results in less shielding for the carbons of ring B in the dioxapyrene **1** than in the methoxy oxaphenalene **3**. This observation once more excludes the hypothesis of an increased electron releasing effect of the oxygen atoms as the basis of the unexpectedly large upfield shifts of the protons in compound **1**.

As regards the double bond in the heterocycles, once more the large high field shift of the protons in the dioxapyrene **1** is not reflected in noticeable correlated changes of the ^{13}C chemical shifts between compound **1** and compounds **2** and **3**.

Finally, the ^{13}C nmr results as well as the ^1H nmr data provide arguments which fully support the hypothesis of the disruption of extended delocalisation of π electrons in the new heterocyclic structure **1**. The loss of ring current anisotropic effect might be estimated to *circa* 0.5 ppm on the basis of the ^1H nmr data.

It is noteworthy that in pyrene, which bears no electron releasing group, extensive ring current effect results in shifting the proton signals to low field by *circa* 0.9 ppm with respect to the naphthalene.

Another surprising feature was the coupling interaction observed in **4**, **5** and **6** between the hydroxyl and the formyl protons with a sizeable magnitude, *circa* 1.2 Hz (Figure 2).

Due to the formation of an hydrogen bond between the phenolic proton and the carbonyl oxygen, the two protons are remote from each other and a through space interaction is certainly not possible. We postulate that the coupling occurs through the hydrogen bond. Since this interaction was not detected in **7** it seems that an extended conjugation from a donor atom at position **1** to the carbonyl group is necessary to insure, at the carbonyl oxygen atom, the electron density needed to provide the required strength of the hydrogen bond.

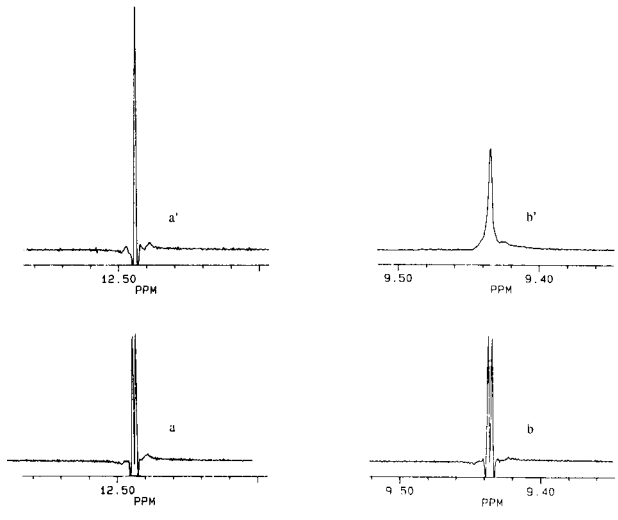


Figure 2. Partial ^1H nmr spectrum of compound **5** showing the coupling interaction between: (a) the hydroxyl proton and (b) the formyl proton; double irradiation experiments at the frequencies of (a') the formyl proton, (b') the hydroxyl proton.

The increased strength of the hydrogen bond is well reflected, of course, in the low field shift of the phenolic proton in **4**, **5**, **6** with respect to **7**. The chemical shifts of the carbonyl carbon are less significant since they most likely result from a balance between the high field shift induced by the electron releasing effect of the donor oxygen atom at position 1 and the low field shift induced by the electron-withdrawing effect of hydrogen bonding.

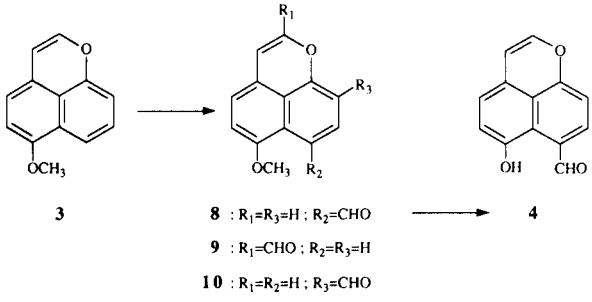
EXPERIMENTAL

Chemistry.

Melting points were measured on an Electrothermal digital melting-point apparatus and are uncorrected. The proton nuclear magnetic resonance spectra were recorded at 90 MHz using a Varian EM 390 spectrometer, with tetramethylsilane as the internal standard. The ir spectra were recorded on a Perkin-Elmer 1720 spectrometer, the uv spectra were measured with a Varian-Techtron 635. The hplc was conducted with a Gilson chromatograph.

Except oxaphenalene **4**, the synthesis of which is described below, all the compounds used in this study were previously described (**1** [1], **2** [3,4], **3** [4], **5** [1], **6** [5,6] and **7** [6,7]).

The hydroxy aldehyde **4** was synthesized according to the following pathway:



7-Formyl-6-methoxynaphtho[1,8-*bc*]pyran (**8**), 2-Formyl-6-methoxynaphtho[1,8-*bc*]pyran (**9**), and 9-Formyl-6-methoxynaphtho-[1,8-*bc*]pyran (**10**).

To an ice-cooled, well-stirred solution of titanium tetrachloride (4.2 g, 22 mmoles) under an argon atmosphere and α,α-dichloromethyl methyl ether (1.3 g, 11 mmoles) in anhydrous dichloromethane (50 ml), a solution of 6-methoxyoxaphenalene (**3**) (2 g, 10 mmoles) in dichloromethane (50 ml) was slowly added. After one hour at 20°, the reaction mixture was quenched with ice-water, and the organic phase was washed twice with water, dried over sodium sulfate and the solvent evaporated. The crude product obtained (1.8 g, 79%) was chromatographed (hplc, Microsorb Si60 Merck). Elution with *n*-hexane-ethyl acetate 2.5/1 gave successively the following compounds:

a) The aldehyde **9** (710 mg, 31%) was obtained as fine yellow needles, mp 151-152° (cyclohexane); ^1H nmr (deuteriochloroform): δ 3.96 (s, OCH_3), 6.85-7.68 (m, 6H arom), 10.18 (s, CHO); ir (deuteriochloroform): ν 1669 cm^{-1} (CHO); uv (ethanol): λ max (log ε) 230 (3.81), 270 (3.97).

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.33; H, 4.42. Found: C, 74.50; H, 4.66.

b) The aldehyde **10** (230 mg, 10%) was obtained as yellow needles, mp 144-145° (hexane); ^1H nmr (deuteriochloroform): δ 3.93 (s, OCH_3), 6.16 (d, H_3, J_{3-2} = 6 Hz), 6.80 (m, H_2, H_4, H_5), 7.50 (d, H_7, J_{7-8} = 9 Hz), 7.70 (d, H_8), 10.36 (s, CHO); ir (deuteriochloroform): ν 1666 cm^{-1} (CHO); uv (ethanol): λ max (log ε) 270 (4.40), 307 (3.75), 320 (3.86), 339 (3.75).

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.33; H, 4.42. Found: C, 74.48; H, 4.40.

c) The aldehyde **8** (810 mg, 36%) was obtained as yellow needles, mp 163-164° (hexane); ^1H nmr (deuteriochloroform): δ 3.95 (s, OCH_3), 6.03 (d, H_3, J_{3-2} = 5 Hz), 6.66-6.95 (m, 4H arom), 8.00 (d, H_8, J_{8-9} = 8.5 Hz), 10.95 (s, CHO); ir (deuteriochloroform): ν 1666 cm^{-1} (CHO); uv (ethanol): λ max (log ε) 230 (4.30), 267 (4.06), 310 (3.76), 324 (3.90), 377 (3.82).

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.33; H, 4.42. Found: C, 74.51; H, 4.37.

7-Formyl-6-hydroxynaphtho[1,8-*bc*]pyran (**4**).

This compound was obtained by demethylation of 7-formyl-6-methoxynaphtho[1,8-*bc*]pyran (**8**). To a stirred solution of **8** (0.7 g, 3.1 mmoles) in anhydrous dichloromethane (75 ml) at −50° in an inert atmosphere, is added slowly, with a syringe, commercial Boron tribromide (1 *M*) in dichloromethane (3.5 ml, 3.5 mmoles). After one hour at −50° and then two hours at 20°, the reaction mixture is poured into 200 ml of ice-water and treated as usual. The crude product is recrystallized from a mixture of toluene-cyclohexane (1/1) to give **4** as fine garnet needles, mp 179-180° (0.6 g, 91%); ir (deuteriochloroform): ν 1646 cm^{-1} (CHO); uv (ethanol): λ max (log ε) 223 (4.41), 258 (4.13), 327 (3.76), 445 (3.89).

Anal. Calcd. for $C_{13}H_8O_3$: C, 73.58; H, 3.77. Found: C, 73.36; H, 3.81.

Spectroscopy.

The spectra were recorded on an AM500 Bruker spectrometer. The various compounds were dissolved in deuteriochloroform and tetramethylsilane was used as internal reference. For the ^{13}C undecoupled spectra, the resolution was 0.5 Hz. For the ^1H spectra, a resolution of 0.3 Hz was used, except for the determination of the coupling constant between the hydroxyl and aldehyde protons where the resolution was 0.1 Hz.

For the 2D experiments, the standard Bruker programs were used.

^1H ^1H Coupling Constants.

$^3J_{H1'-H2'}$: 6 Hz (**1**), 5.8 Hz (**2**), 5.8 Hz (**3**), 5.6 Hz (**4**).

$^3J_{HO-CHO}$: 1.2 Hz (**4**), 1.3 Hz (**5**), 1.2 Hz (**6**).

^1H ^{13}C Coupling Constants.

$^1J_{C1'-H1'}$: 195 Hz (**1, 2, 3**), 201 Hz (**4**).

$^1J_{C2'-H2'}$: 165 Hz (**1, 2, 3**), 167 Hz (**4**).

$^2J_{C1'-H2'}$: 7 Hz (**1**), 6.5 Hz (**2, 3, 4**), 3.8 Hz (**5**).

$^2J_{C2'-H1'}$: 8.8 Hz (**1, 2, 3, 4**).

$^3J_{C2'-H7}$: 6 Hz (**1**), 5.3 Hz (**2, 3, 4, 5**).

$^3J_{C7-H2'}$: 3.8 Hz (**1, 2, 3, 4, 5**).

$^3J_{C8-H1'}$: 7 Hz (**1, 2, 3, 4**).

$^3J_{C1-H1'}$: 4.7 Hz (**1, 4**).

$^3J_{C6-OH}$: ≅7 Hz.

$^2J_{C5-OH}$: ≅3 Hz.

$^3J_{C4a-OH}$ and $^3J_{C4a-CHO}$: ≅6 Hz.

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