^{1}H AND ^{13}C CHEMICAL SHIFT DATA OF SOME OMMOCHROME MODELS: SUBSTITUTED BENZO[3,2-a]-5H-PHENOXAZIN-5-ONE

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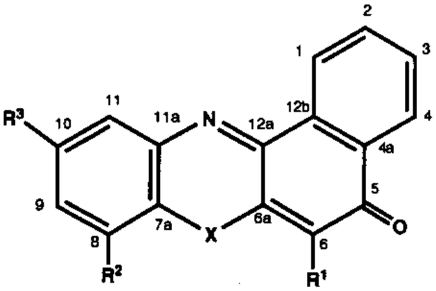
Abstract - ^{1}H and ^{13}C chemical shift data are reported for some substituted benzo[3,2-a]-5H-phenoxazin-5-ones, that are convenient models of natural ommochromes. Assignments are based on one- and two-dimensional techniques.

Ommochromes are a class of natural photosensitive phenoxazinones [1, 2] which occur mainly as bright red and purple colouring substances in the photoreceptors of invertebrates. The best known ommochromes xanthommatin and dihydroxanthommatin, present as granules in skin and eyes of cephalopods, are highly insoluble in water and in neutral solvents. These chemical and physical features contributed to the late discovery of ommochromes and of their biological role as well as to the slow progress in the knowledge of their chemistry, which is still largely unknown. In pursuance of our effort to explore the chemical behaviour and the physical properties of these little known substances, we have synthesized, as model compounds, the substituted benzo[2,3-a]-5H-phenoxazin-5-ones (1- 4). To the best of our knowledge, no ^{13}C spectroscopic data has been reported hitherto on compounds containing this tetracyclic skeleton, except for two main signals.[3] Furthermore the only reports on the ^{13}C data of the correlated 3H-phenoxazin-3-ones were obtained by comparison of the chemical shifts with those of model substances. [4, 5]

Here we present the complete proton and carbon resonance assignments of 1 - 4 and 5 - 7, these latter were obtained by a photochemical irradiation of 4. The phenothioazinone (8) was also investigated to collect data available to characterize other unknown ommochromes containing sulfur.[6]



	1	2	3	4	5	6	7	8
X	O	O	O	O	O	O	O	S
R^1	H	H	H	H	OMe	OAc	COOMe	H
R^2	H	H	Me	H	H	H	H	H
R^3	H	Me	Me	Cl	Cl	Cl	Cl	H

As the only reports [3, 7, 8] on ^{1}H nmr of benzo[a]-5H-phenoxazin-5-one derivatives concern the main signals, whose assignments are even in disagreement between ref. 3 and 7 , a preliminary study of the proton resonances of 2 - 8 was deemed necessary to take full advantage of nmr heterocorrelated experiments, in order to obtain a complete assignment of all carbon resonances.

^{1}H nmr signals (Table 1) of 1 - 8 were easily assigned on the basis of their multiplicities, decoupling experiments and, in the case of 2 and 3, by NOE experiments upon irradiation of methyl resonances. The final assignment of H-1 and H-4 signals was inferred from INAPT experiments, that provide long-range heteronuclear connectivity information in a highly sensitive way by application of a set of low-intensity radiofrequency pulses to a preselected proton multiplet [9] (see below).

Table 1. ^{1}H Nmr data of 1 - 8 in $CDCl_3$. Apparent coupling constant (Hz) in parentheses.

protons	1	2	3	4	5	6	7	8
H-1	8.67m	8.67m	8.63m	8.70m	8.69m	8.71m	8.72m	8.82m
H-2	7.73	7.72	7.72	7.79	7.79	7.80	7.82	7.74
H-3	7.73	7.72	7.72	7.79	7.79	7.80	7.82	7.74
H-4	8.26m	8.30m	8.27m	8.29m	8.32m	8.34m	8.33m	8.27m
H-6	6.39s	6.38s	6.38s	6.44s	-	-	-	6.80s
H-8	7.27dd	7.17d	-	7.26d	7.33d	7.32d	7.35d	7.44m
	(7.8; 1.5)	(8.3)		(8.5)	(8.5)	(8.5)	(8.8)	
H-9	7.45td	7.26dd	7.08bs	7.44dd	7.42dd	7.43dd	7.50dd	7.38
	(7.8; 1.5)	(8.3; 2.0)		(8.5; 2.4)	(8.5; 2.4)	(8.5; 2.4)	(8.8; 2.3)	
H-10	7.32td	-	-	-	-	-	-	7.38
	(7.8; 1.5)							
H-11	7.78dd	7.58d	7.38bs	7.83d	7.81d	7.82d	7.89d	7.90m
	(7.8; 1.5)	(2.0)		(2.4)	(2.4)	(2.4)	(2.3)	
10-Me	-	2.43s	2.37s	-	-	-	-	-
8-Me	-	-	2.37s	-	-	-	-	-
6-OMe	-	-	-	-	4.15s	-	-	-
6-OCOMe	-	-	-	-	-	2.38s	-	-
6-COOMe	-	-	-	-	-	-	4.04s	-

The ^{13}C nmr study (Table 2) was approached performing, in addition to on-resonance and DEPT spectra on all compounds, a complete and detailed analysis on 2 by INAPT, one-bond and long-range 2D heterocorrelated experiments.

In the case of 1, 3, 4 and 8 the assignments of ^{13}C shifts were based on one-bond heterocorrelated spectra and on comparison with chemical shifts of 2; for 5, 6 and 7, available in a small amount, the assignment was made by comparison with the data of 4.

Table 2. ^{13}C nmr chemical shifts of 1 - 8 in $CDCl_3$

C	1	2	3	4	5	6	7	8
1	124.8d	124.7d	124.6d	125.0d	124.8d	125.0d	125.0d	125.7d
2	132.0d§	132.0d§	131.8d§	132.3d§	132.2d§	132.5d§	132.8d	131.7d§
3	132.1d§	131.8d§	131.6d§	131.3d§	130.9d§	131.3d§	132.8d	131.4d§
4	126.0d	126.0d	125.8d	126.1d	126.1d	126.4d	126.6d	125.9d
4a	132.3s	132.3s	132.5s	132.4s	131.7s	130.5s	131.6s	132.8s
5	184.1s	184.0s	183.9s	183.9s	179.8s	177.2s	180.1s	180.3s
6	107.5d	107.2d	106.9d	108.0d	137.6s	128.0s	113.0s	120.4d
6a	151.4s	151.5s	151.6s	150.9s	140.6s	141.4s	147.7s§	138.8s
7a	144.3s	142.2s	140.2s	142.8s	142.7s	142.0s	142.2s	123.0s
8	116.0d	115.5d	125.0s	117.1d	117.0d	117.1d	117.5d	127.8d
9	131.6d	132.5d	134.1d	132.3d§	132.2d§	132.7d§	131.8d	130.0d
10	125.4d	135.3s	134.5s	133.6s	133.5s	133.3s	133.4s	124.8d
11	130.0d	129.9d	127.6d	129.2d	129.2d	129.4d	129.5d	133.5d
11a	133.0s	132.7s	132.3s	130.3s	130.1s	130.0s	130.5s	137.9s
12a	147.6s	147.4s	146.7s	148.7s	149.0s	148.1s	147.4s§	145.0s
12b	131.4s	131.4s	131.4s	131.1s	129.9s	129.1s	131.1s	134.4s
10-Me		20.9q	20.8q	-	-	-	-	-
8-Me		-	14.8q	-	-	-	-	-
6-OMe	-	-	-	-	61.1q	-	-	-
6-OCOMe	-	-	-	-	-	167.9 20.5q	-	-
6-COOMe	-	-	-	-	-	-	164.0 52.9q	-

§ Interchangeable values in each column.

In Table 3, the results of one-bond and long-range 2D heterocorrelated spectra on 2 are reported. These data, obtained using a delay corresponding to a $J_{C,H}$ value of 7 Hz, did not allow us to assign with certainty all carbon signals . Actually the H-6 proton showed, via long-range, three correlations with carbons at 151.5, 147.4 and 132.3 ppm. Therefore, while the signal at 132.3 ppm could be immediately assigned to C-4a on the basis of the up-field shift, the assignments of the signals at 151.5 and at 147.4 to C-12a and C-6a , respectively, could be only suggested.

Table 3. One-bond and long-range 2D H-C correlations of 2

proton	^{13}C shifts correlated via one-bond	^{13}C shifts correlated via long-range
CH_3	20.9	135.3; 132.5; 129.9
H-6	107.2	151.5; 147.4; 132.3
H-8	115.5	135.3; 132.7
H-9	132.5	142.2
H-11	129.9	142.2
H-1	124.7	-
H-2; H-3	132.0§; 131.8§	-
H-4	126.0	-

§Interchangeable values

This suggestion was confirmed by three INAPT experiments obtained using a delay corresponding to a $J_{C,H}$ value of 8 Hz. The first spectrum, obtained by irradiation on H-6, showed only signals at 151.5, 147.4 and 132.3 ppm confirming the results of the H-C long-range 2D nmr heterocorrelated experiment. The second obtained by irradiation at 8.67 ppm, showed only the signals at 147.4 and 132.3 ppm that were therefore assigned to C-12a and C-4a, respectively, and the third, by irradiation at 8.30 ppm, showed the signals at 131.4 ppm, assigned to C-12b, and at 184.0 ppm, assigned to C-5. These results led us also to identify, in unambiguous way, H-1 and H-4 protons at 8.67 and 8.30 ppm, respectively.

EXPERIMENTAL

General procedure for substituted Benzo[3,2-a]- 5H-phenoxazin-5-ones (1 - 4)[7] and Benzo[3,2-a]-5H-phenothiazin-5-ones (8)[10] preparation.

To a stirring solution of 2-hydroxynaphtoquinone (87 mg, 0.5 mmol) in acetic acid (50 ml) was added, dropwise, a solution of o-aminophenols (2-aminophenol, 2-amino-4-chlorophenol, 2-amino-4-methylphenol, 2-amino-4,6-dimethylphenol and 2-aminothiophenol (0.5 mmol)) in acetic acid (50 ml) and the solution was kept at room temperature for a day. The reaction mixtures were diluted with water and neutralized with saturated sodium carbonate solution and extracted with chloroform. The organic layers were dried over anhydrous sodium sulphate and evaporated in vacuo to afford the yellow compounds (1- 4 and 8), which were recrystallized from chloroform.

Photoirradiation of 10-Chloro-5H-benzo[3,2-a]phenoxazin-5-ones (4).

A solution 10^{-2} M of 4 in methanol (300 ml) in a quartz tube was exposed to a direct superphot lamp, Osram 650 W, at distance of 10 cm and at 25 °C. After 10 h of uninterrupted photoirradiation the mixturen was evaporated in vacuo and analyzed chromatographically to give small amounts of the compounds (5, 7) and of the 6-hydroxy-10-chlorobenzo[3,2-a]-5H-phenoxazin-5-

one. This latter, after acetylation with acetic anhydride and pyridine, gave 6.

Nmr samples were prepared by dissolving ca. 50 mg ml^{-1} in $CDCl_3$. All spectra were performed on WH-270 Bruker spectrometer equipped with dual probe, using tetramethylsilane as a reference compound and a controlled temperature of 300K.

^1D ^1H were recorded using a pulse width of 6.5 μs and a sweep width of 1500 Hz. NOE experiments were measured in a difference mode using a Bruker microprogram.

^1D ^{13}C experiments were run with a pulse width of a 3 μs, a sweep width of a 14000 Hz, a repetition time of 3s and 16K data points for Fourier trasformation. DEPT experiments were performed using a polarisation transfer pulse of 135° and a delay adjusted to an average C,H coupling of 160 Hz. INAPT spectra were measured with the Bruker INEPTRD microprogram using delays D_2=D_3 =31 ms, corresponding to $J_{C,H}$ =8 Hz. ^2D HC heterocorrelated experiments were run with delays calculated using a coupling constants of 160 Hz and of 7 Hz for direct and long-range correlations, respectively.

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