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^{13}C NMR ANALYSIS OF SOME OXOAPORPHINE ALKALOIDS

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Key Word Index—^{13}C NMR spectra; oxoaporphine alkaloids; oxo-*O*-methylpukateine; *O*-methylmoscatoline; oxoglaucine; papaveraldine; (6,7-dimethoxyisoquinolinyl)-(4′-methoxyphenyl)-methanone; (6,7-methylenedioxyisoquinolinyl)-(4-methoxyphenyl)-methanone.

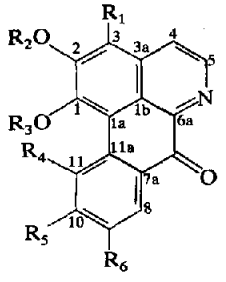
INTRODUCTION

Recently we described the isolation and structure elucidation of oxo-*O*-methylpukateine (**1a**)* and of the known alkaloid *O*-methylmoscatoline (**1b**) from *Dugetia eximia* [1]. In order to confirm the proposed structure for **1a**, its synthesis was carried out [2–4]. Following the sequence reported by Cohen *et al.* [4] and starting from 6′-nitropapaveraldine, oxoglaucine (**1c**) was also prepared. The absence of ^{13}C NMR spectral data of oxoaporphines prompted us to undertake the analysis of **1a**, **1b** and **1c** as an aid in the structure elucidation of new compounds and also as a continuation of our project on ^{13}C NMR spectroscopy of isoquinoline alkaloids [5, 6].

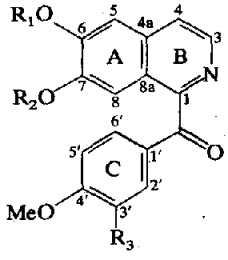
RESULTS AND DISCUSSION

In order to facilitate the shift assignment of the oxoaporphine alkaloids **1a–1c**, the analysis of papaveraldine (**2a**), (6,7-dimethoxyisoquinolinyl)-(4′-methoxyphenyl)-methanone (**2b**), (6,7-methylenedioxyisoquinolinyl)-(4′-methoxyphenyl)-methanone (**2c**), was first carried out.

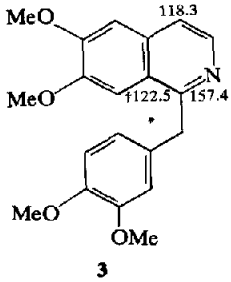
The dimethoxyisoquinoline system of **2a** shows carbon shifts and multiplicities, in the fully coupled spectrum, comparable to those observed in papaverine (**3**) [5], except for the C-1, C-4 and C-8a signals. Carbon-1 and C-4 are shielded and deshielded respectively in **2a**, due to the effect of the CO group, and C-8a appears as a clean triplet [^3J(C-8a, H-4); ^3J(C-8a, H-5)], since further long range splittings produced by the methylene group were eliminated. A comparison of the carbon signals of ring C of **2a** with the corresponding ones of veratraldehyde (**4**) [7] shows good agreement allowing a preliminary shift assignment.



1a $R_1 = R_5 = R_6 = H$; $R_2 = R_3 = —CH_2—$; $R_4 = OMe$
1b $R_1 = OMe$; $R_2 = R_3 = Me$; $R_4 = R_5 = R_6 = H$
1c $R_1 = R_4 = H$; $R_2 = R_3 = Me$; $R_5 = R_6 = OMe$



2a $R_1 = R_2 = Me$; $R_3 = OMe$
2b $R_1 = R_2 = Me$; $R_3 = H$
2c $R_1 = R_2 = —CH_2—$; $R_3 = H$



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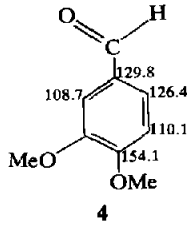

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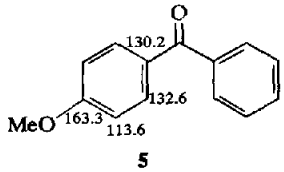

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*After submission of our manuscript [1] we became aware of a publication by Hsu, C.C., Dobberstein, R. H., Cordell, G. A. and Farnsworth, N. R. (1977) *Lloydia* **40**, 152, in which the isolation of **1a** was reported.

† Complex multiplet.

The analysis of the fine structure of these methines from the ^{1}H-coupled ^{13}C spectrum indicates, however, that the signals at 111.7 and 109.7 ppm should be assigned to C-2′ and C-5′ respectively, although the shifts of related carbons of **4** show the opposite trend. The assignment of rings A and B carbon shifts of **2b** is based on comparisons with the isoquinoline system of **2a**, and for ring C, the methoxybenzophenone **5** was used as model [8]. Finally, the replacement of the 6,7-dimethoxyisoquinoline in **2a** by a methylenedioxyisoquinoline in **2c** produces the expected changes on the benzenoid carbons [9], while the remaining carbon shifts are essentially unaffected. The non-aromatic carbons of **2a**, **2b** and **2c** were readily assigned by standard chemical shift theory. The shifts of compounds **2a–2c** are listed in Table 1.

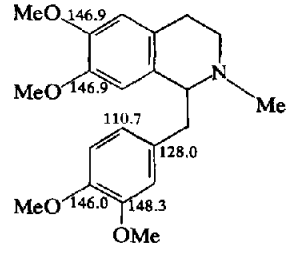
The first oxoaporphine alkaloid analysed was oxoglaucine (**1c**) and its sp^2 carbon signals were split into two groups on the basis of their signal multiplicities from a SFORD spectrum. Of the proton-bearing carbon shifts, the signals at 105.7, 122.9 and 144.3 ppm were assigned to C-3, C-4 and C-5, respectively, by analysis of their fine structure in the fully coupled spectrum, leaving those at *ca* 109 ppm to C-8 and C-11 or vice versa. Unambiguous assignment, however, was made by selective decoupling at 8 ppm which is the resonance frequency of H-8 [10]. The non-protonated carbon signals at 119.1, 121.1, 134.8 and 144.9 ppm were assigned, again on the basis of their fine structure from a fully coupled spectrum, to C-1a, C-1b, C-3a and C-6a, respectively, while for the assignments of the remaining signals at 126.3 and 128.7 ppm and those of the non-protonated, oxygenated aromatic carbons, a comparison between the $\Delta\delta$ values observed in the transformation of laudanosine (**6**) into glaucine (**7**) [9] with the ones observed going from papaveraldine (**2a**) into oxoglaucine (**1c**) was used. The OMe groups on C-2, C-9 and C-10 show signals at 55.8 ppm and the one on C-1, as expected, resonates at lower field, 60.2 ppm. The signal at 180.7 ppm was assigned to the CO group.

Table 1. ^{13}C NMR data of compounds **2a–2c**

Carbon	2a	2b	2c
1	153.5	153.5	154.7
3	139.7	139.9	140.2
4	120.9	121.1	121.7
4a	133.6	133.8	133.3
5	104.6	104.7	102.6
6	152.9	153.0	151.0
7	150.7	150.9	149.1
8	103.8	104.0	102.1
8a	122.5	122.6	123.7
1′	129.6	129.7	129.7
2′	111.7	133.1	133.0
3′	148.7	113.6	113.6
4′	153.5	163.0	163.8
5′	109.7	113.6	113.6
6′	126.6	133.1	133.0
—OMe	55.9	56.0	55.0
	55.9	56.0	
	55.9	55.6	
	55.9		
C=O	186.4	187.0	*
$-OCH_2O-$			101.7

The spectra were obtained at 25.2 MHz in Fourier transform mode in $CDCl_3$ solutions. The data for each carbon are shown in ppm downfield from TMS.

*Due to the lower sample concentration the CO signal was not detected.



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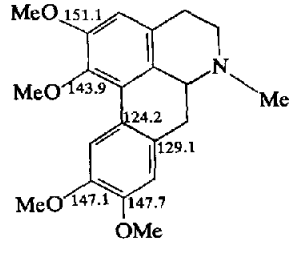

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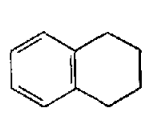
The introduction of a third OMe group on C-3 produces expected changes on the isoquinoline carbons of *O*-methylmoscatoline (**1b**) compared with those of **1c**. Carbon-3 and its corresponding *para* and *ortho* positions, C-1a, C-2 and C-3a, are deshielded and shielded, respectively, and C-4, which suffers a γ-effect by the new oxygenated function, is also shielded. The assignment of C-7a, C-11a and C-10 is based on the effects produced on some of the aromatic carbons by the replacement of a benzylic methylene by a CO group (**8**→**9**) [9, 11] using nuciferine ring D shifts, **10** [9] as a reference compound, leaving C-8, C-9 and C-11 unresolved. The shifts of the OMe groups of **1b** at *ca* 61 ppm indicate that they are sterically hindered, but specific assignments become difficult.



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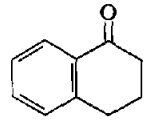

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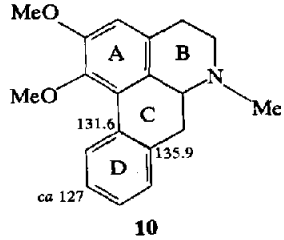

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Table 2. ^{13}C NMR data of oxoaporphines **1a–1c**

Carbon	**1a**	**1b**	**1c**	**1c***
1	147.3	148.2	148.9	155.9
1a	104.4	115.4	119.1	120.1
1b	121.6	122.5	121.1	123.4
2	151.9	147.0	156.1	162.9
3	102.1	156.2	105.7	106.5
3a	135.2	130.8	134.8	135.3
4	123.3	118.9	122.9	126.2
5	144.0	144.3	144.3	133.1
6a	144.3	145.0	144.9	141.7
7	182.0	182.3	180.7	174.8
7a	133.2	131.4	126.3	133.1
8	120.2	127.9	109.2	110.1
9	129.1	128.7	150.2	150.2
10	116.1	134.1	153.2	156.7
11	156.0	127.4	109.7	111.3
11a	123.1	134.3	128.7	130.4
—OMe	55.7	61.7	60.2†	61.6†
		61.3	55.8	57.3
		60.9	55.8	56.3
			55.8	56.3
$-OCH_2O-$	101.5			

The spectra were obtained at 25.2 MHz in the Fourier transform mode in $CDCl_3$ to which some drops of MeOH were added for better solution of the compounds. The δ values are in ppm downfield from TMS.

*In $CDCl_3$ solution with some TFA.

†Signal assigned to the OMe carried by C-1.

The signal assignments of oxo-*O*-methylpukateine (**1a**) were greatly simplified by the analysis of **1b** and **1c**. As expected, the effects of the replacement of two OMe groups by a methylenedioxy moiety in sterically hindered systems (**1c→1a**) are observed on the benzenoid carbons [6], while the remaining carbons are little affected. In agreement with these observations, C-3, C-4, C-5 and C-6a show the expected multiplicities in a fully coupled spectrum. The introduction of a OMe group on C-11 produces predictable changes on ring D carbon shifts, allowing its complete assignment.

In view of the low solubility generally observed in some oxoaporphines and of the comparative study of ^1H NMR in $CDCl_3$ and TFA solutions [10], the ^{13}C NMR analysis of oxoglaucine (**1c**) in $CDCl_3$ solution with some TFA was also undertaken. As expected, rings A and B carbons suffer changes similar to those observed on isoquinoline by protonation [12] and further, the minor changes observed on ring D carbon shifts and on the CO group could be explained assuming a keto–enol tautomerism, as was previously suggested by UV spectroscopy [13]. The shifts of **1a**, **1b** and **1c** in $CDCl_3$ solutions and those of **1c** in $CDCl_3$ solution with some TFA are listed in Table 2.

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