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^{13}C-NMR SPECTRA OF AZAFLUORENONES

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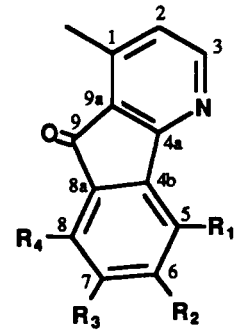
ABSTRACT.—The ^{13}C-nmr chemical shifts of onychine (1-methyl-4-azafluoren-9-one) [**1**] were assigned with the aid of heteronuclear 2D-nmr spectra and these results were used to interpret the ^{13}C nmr spectra of several other synthetic azafluorenones.

Although onychine [**1**], the first azafluorenone alkaloid, was described over a decade ago (1), the number of natural products in this class has grown considerably only in the past couple of years with the discovery of a wide variety of mono-, di, and tri-substituted derivatives of this skeleton (2–7). The first ^{13}C-nmr data published for this series corresponded to onychine itself (8), and the signal assignments were then based on the erroneous structure initially proposed for the alkaloid (1). We have now reproduced a literature synthesis of onychine (9) and recorded heteronuclear 2D-nmr spectra to assign all the signals. In particular, a long-range ^{1}H-^{13}C chemical shift correlation spectrum (COLOC) suggested ^{13}C signal attributions that differ from some which have been recently published (10).

The ^{13}C-nmr spectrum of onychine [**1**] showed the presence of seven carbon atoms bonded to hydrogen, of which the one resonating at 17.0 ppm could be immediately assigned to the methyl group, while the heteronuclear COSY spectrum left no doubt that C-2 and C-3 were represented by the signals at 125.5 and 152.4 ppm, respectively. At this point, neither the C-5/H-5 and C-8/H-8 peaks on one hand nor the C-6/H-6 and C-7/H-7 peaks on the other could be assigned unambiguously. Of the quaternary carbon signals, assignment of the one at 192.8 ppm to C-9 was trivial and the one at 147.1 ppm could be attributed to C-1 because of its relatively strong intensity due to the nOe of the methyl protons. A long-range ^{1}H-^{13}C chemical shift correlation spectrum (COLOC) confirmed the latter assumption and allowed the identification of several long range ^{1}H-^{13}C couplings. Thus, a correlation was observed between the carbonyl carbon and the proton resonating at 7.58 ppm, which was therefore located at C-8; this proton was similarly correlated with a quaternary carbon resonating at 142.7 ppm, assigned in consequence to C-4b. Stepwise analysis of the other long-range correlations in combination with the COSY results finished off the assignments shown in Table 1. A correlation observed between C-4b and the proton resonating at 7.50 ppm led us to locate the latter to C-6. Both the H-5 (7.7 ppm) and H-7 (7.34 ppm) are coupled with the carbon at 134.5 ppm which corresponds to the C-8a. The COSY spectrum shows the correlation between the carbon atoms at 120.4 and 130.5 ppm and the protons situated at positions 5 and 7, respectively, which completes the assignment of the whole spectrum.



	R_1	R_2	R_3	R_4
1	H	H	H	H
2	OMe	H	H	H
3	H	OMe	H	H
4	H	H	OMe	H
5	H	H	H	OMe
6	H	OMe	OMe	H

TABLE 1. ^{1}H- and ^{13}C-nmr Chemical Shifts of Onychine [1] in $CDCl_3$ (360/90.5 MHz).

Proton	δ	Carbon	δ	δ(10)
CH_3	2.54	CH_3	17.0	17,2
—	—	C-1	147.1	147,1
H-2	6.87	C-2	125.5	125,6
H-3	8.31	C-3	152.4	152,7
—	—	C-4a	164.8	165,1
—	—	C-4b	142.7	134,9
H-5	7.70	C-5	120.4	123,5
H-6	7.50	C-6	134.6	130,6
H-7	7.34	C-7	130.5	134,7
H-8	7.58	C-8	123.3	120,6
—	—	C-8a	134.5	143,0
—	—	C-9	192.8	192,7
—	—	C-9a	130.4	125,8

Syntheses of the four benzene-ring monomethoxylated onychines **2–5** (11) and of the 6,7-dimethoxy derivative **6**, modeled on the above-mentioned onychine synthesis (9), have led to an extension of these results. With the ^{13}C-nmr spectrum of onychine as a reference, the assignment of the spectra of its oxygenated derivatives was quite straightforward (Table 2). The deviations of the observed ^{13}C-nmr chemical shifts of these synthetic onychine derivatives from calculated values (13) based on our onychine assignments are clearly smaller than those found using the alternative interpretation of the onychine spectrum (10). We feel that this circumstance supports our signal assignments.

As may be seen in Table 2, the C-methyl group and pyridine ring resonances show little variation. The C-1 signal was consistently stronger than those of most other quaternary carbon nuclei, as in the case of onychine, and a similar effect could be observed in some cases for C-9a. The methoxyl groups exhibited "normal" chemical shifts of 55.8–56.5 ppm indicating that they lie in the plane of the benzene ring (12). The fact that in the C-5- and C-8-methoxylated compounds **2** and **5** the methoxyl resonances are not strongly affected by the neighboring pyridine ring or carbonyl function suggests that the conformationally mobile group is turned away from the magnetically anisotropic moiety most of the time.

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LITERATURE CITED

1. M.E.L. De Almeida, R. Braz F°, M.V. von Bülow, O.R. Gottlieb, and J.G.S. Maia, *Phytochemistry*, **15**, 1186 (1976).

TABLE 2. ^{13}C-nmr Chemical Shifts of Onychine Derivatives in $CDCl_3$.

Carbon	Compound				
	2	**3**	**4**	**5**	**6**
1-Me	17.4	17.1	17.3	17.0	17.0
C-1	147.3	147.0	147.3	147.2	146.5
C-2	124.7	125.7[a]	124.8	126.0	125.2
C-3	152.9	152.2	152.7	152.1	151.9
C-4a	165.7	164.3[b]	165.6	163.9	165.0
C-4b	125.4	145.9	135.5[a]	144.9	137.9
C-5	155.4	105.9	122.1	113.2[a]	103.5
C-6	118.5	165.7[b]	120.4	137.1	154.9
C-7	132.4	116.4	162.3	114.6[a]	151.2
C-8	116.1	126.1[a]	108.8	157.9	106.3
C-8a	136.8	127.1	136.9[a]	122.7	126.3
C-9	193.3	191.9	193.0	191.2	192.4
C-9a	128.7	127.9	126.0	131.2	128.0
OMe	56.3	55.9	55.8	55.9	56.3
OMe	—	—	—	—	56.5

[a,b]Values in the same column with the same superscript are interchangeable.

2. M.O.F. Goulart, A.E.G. Sant'Ana, A.B. De Oliveira, G.G. De Oliveira, and J.G.S. Maia, *Phytochemistry*, **25**, 1691 (1986).
3. D. Tadić, B.K. Cassels, M. Lebœuf, and A. Cavé, *Phytochemistry*, **26**, 537 (1987).
4. D. Tadić, B.K. Cassels, A. Cavé, M.O.F. Goulart, and A.B. De Oliveira, *Phytochemistry*, **26**, 1551 (1987).
5. G.J. Arango, D. Cortes, B.K. Cassels, A. Cavé, and C. Mérienne, *Phytochemistry*, **26**, 2093 (1987).
6. J. Zhang, A.R.O. El Shabrawy, M.A. El-Shanawany, P.L. Schiff Jr., and D.J. Slatkin, *J. Nat. Prod.*, **50**, 800 (1987).
7. O. Laprévote, F. Roblot, R. Hocquemiller, and A. Cavé, *J. Nat. Prod.*, **51**, 555 (1988).
8. P.G. Waterman and I. Muhammad, *Phytochemistry*, **24**, 523 (1985).
9. J. Koyama, T. Sugita, Y. Suzuta, and H. Irie, *Heterocycles*, **12**, 1017 (1979).
10. C.D. Hufford, L. Shihchih, A.M. Clark, and B.O. Oguntimein, *J. Nat. Prod.*, **50**, 961 (1987).
11. D. Tadić, B.K. Cassels, and A. Cavé, *Heterocycles*, **27**, 407 (1988).
12. A. Makriyannis and S. Fesik, *J. Am. Chem. Soc.*, **104**, 6462 (1982), and references cited therein.
13. E. Pretsch, T. Clerc, J. Seibl, and SW. Simon, "Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Methoden," 2nd ed., Springer-Verlag, Berlin, 1981.

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