REVISED ASSIGNMENT OF OLEFINIC PROTON SIGNALS IN THE ^{1}H-NMR SPECTRA OF DIENOID-TYPE ERYTHRINAN ALKALOIDS[1]

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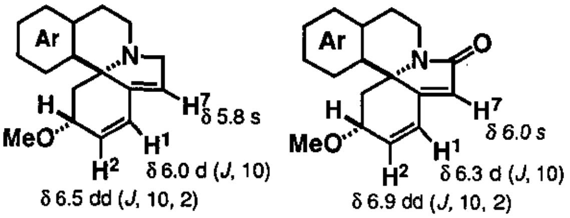
Abstract ——— Previous assignment of the olefinic proton signals (H-1 and H-2) in the ^{1}H-nmr spectra of dienoid-type erythrinan alkaloids was interchanged on the basis of the synthesis of the stereoisomers, nOe experiments, and theoretical calculations.

Dienoid-type erythrinan alkaloids are known more than 40 species in the plants of Genus *Erythrina* (Leguminosae) and *Cocculus* (Menispermaceae).[2] All of them bear 3α-methoxy (or hydroxy) group and exhibit three olefinic proton signals in the ^{1}H-nmr spectra at around δ 5.8, 6.0, and 6.5 (in $CDCl_3$) with the multiplicities of broad singlet (s), doublet (d, J=10 Hz), and doublet-doublet (dd, J=10 and 2 Hz), respectively. The corresponding signals in the 8-oxo alkaloids appear at δ 6.0, 6.3, and 6.9 with similar multiplicities. These proton signals have been assigned as those of H-7, H-1, and H-2, respectively, assuming that the vicinal coupling between H-2 and H-3β is *ca.* 2 Hz.[3,4] However, recent synthesis of the various 3β-isomers and 3,8-dioxo derivatives[5-8] throw a doubt on the previous assignment, suggesting that the previous assignment for H-1 and H-2 has to be interchanged.



Previous assignment

Olefinic Proton Signals of 3,8-Diones 3,8-Dioxo derivatives show the signals of H-7, H-1, and H-2 at *ca.* δ 6.4, 7.7, and 6.4 as s, d (J=10 Hz), and d (J=10 Hz), respectively. This assignment was supported by AM1 calculations[9] of the electron densities of the corresponding positions and proved by observation of nOe's for **40**: irradiations of the singlet at δ 6.26 and the doublet at δ 6.39 gave 4.7% and 10% enhancements of the intensity on the doublet signal at δ 7.56, respectively, while irradiation of the doublet at δ 7.56 produced 17% and 4% enhancements of the two protons at δ 6.26 (s) and 6.39 (d). The dimethoxy derivative (**37**) gave similar results.

Olefinic Proton Signals of 3β-Substituted Alkaloids All synthetic 8-oxo-3β-methoxy (or 3β-hydroxy) alkaloids showed olefinic protons at similar positions with the corresponding 3α-isomers (*ca.* δ 5.9, 6.3, and 6.8), but with different multiplicities of s, dd (J=10, 5 Hz), and d (J=10 Hz). Supposing the previous assignment is correct and the chemical shifts are comparable with those of 3α-isomers, the coupling constant of 5 Hz for H-1 is too large to assign as an allylic coupling with H-3α, instead it is rather the value of a vicinal coupling, suggesting that this proton should be attributed to H-2. Thus olefinic protons should be assigned as shown in Figure 1. Removal of 8-oxo group from these compounds produced up-field shifts on the above protons by 0.1-0.2, 0.1-0.2, and 0.2 ppm as expected. Thus they are assigned as H-7, H-2, and H-1, respectively.

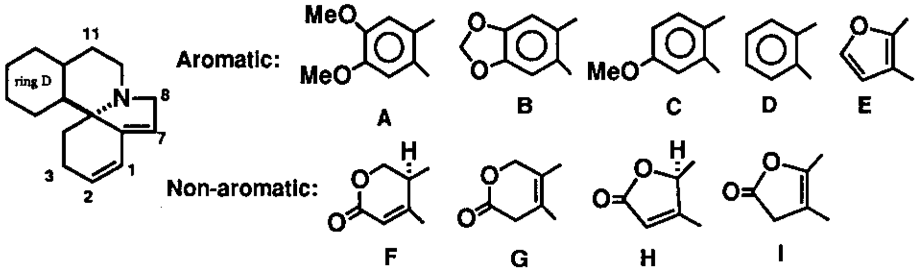
Olefinic Proton Signals of 3α-Isomers Since the chemical shifts of olefinic protons should not be much affected by the stereochemistry of the 3-OR substituents, the above evidence suggests that the olefinic proton signals at δ 5.8, 6.0, and 6.5 (for the natural alkaloids) should be assigned to H-7, H-2, and H-1, respectively. The corresponding signals for 8-oxo derivatives are at δ 6.0, 6.3, and 6.9. Comparing the latter values with those of 3,8-diones, the shift values are -0.4, -0.1, and -0.8 ppm, respectively, being compatible to the common shift rule. If the previous assignment was taken, those values were -0.4, +0.5, and -1.5 ppm, respectively, violating the common shift rule at H-2. Therefore, the small coupling (2-2.5 Hz) for H-1 is attributed to an allylic coupling between H-1 and H-3β, and the vicinal coupling constant between H-2 and H-3β is 0 Hz, suggesting the dihedral angle between H-3β and H-1 (and H-2) is *ca.* 90°. In contrast, $J_{2,3\alpha}$=4-5 Hz and $J_{1,3\alpha}$(allylic)=0 Hz for 3β-isomers.

This revised assignment (listed in Table I) was proved by nOe experiments for **16** and **31**, although decoupling experiments did not give a definite conclusion. For **16**, irradiation of the proton at δ 6.69 produced 4.4% and 9.5% enhancements on the signals at δ 5.86 and 6.31, while irradiation of either proton at δ 5.86 or 6.31 resulted in an nOe enhancement only on the poton at δ 6.69 by 3.7% or 11%. For **31**, nOe enhancements between H-7 at

Table I. Revised Assignment of Olefinic Protons for Dienoid-type Erythrinan Alkaloids (in $CDCl_3$)

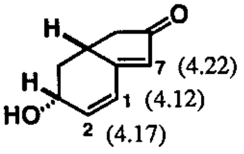
Name@		D-ring	3-OR	Others		H-1	H-2	H-7	ref.
3α-OR Series									
* 1	Erysotrine	A	α-OMe			6.56(dd, 10, 2)	5.98(d, 10)	5.70(br s)	15)
* 2	Erythraline	B	" "			6.62(dd, 10, 2)	5.90(br d, 10)	5.73(br s)	11)
* 3	Coccuvinine	C	" "			6.56(dd, 10, 2)	5.99(d, 10)	5.72(s)	6)
* 4		D	" "			6.55(dd, 10, 2)	5.97(d, 10)	5.71(s)	6)
* 5	α–Erythroidine	F	" "			6.38(dd, 10, 2.5)	5.88(d, 10)	5.75(br s)	14)
* 6	β-Erythroidine	G	" "			6.44(dd, 11, 2)	5.90(d, 11)	5.71(s)	14)
* 7	Erythravine	A	α-OH			6.57(dd, 10, 2)	6.05(d, 10)	5.77(br s)	17)
* 8	Erythristemine	A	α–OMe	11β-OMe		6.56(dd, 10, 2)	5.98(br d, 10)	5.68(br s)	
						6.32(dd, 10, 2)	5.88(d, 10)	5.38(br s)#	3)
* 9	Erythrartine	A	α-OMe	11β-OH		6.66(dd, 10, 2.5)	6.09(br d, 10)	5.80(br s)	4)
*10	Erythrascine	A	" "	11β-OAc		6.46(dd, 10, 2.5)	5.92(br d, 10)	5.68(br s)	16)
*11	Erythrinine	B	" "	11β-OH		6.60(dd, 10, 2.5)	6.00(br d, 10)	5.75(br s)	11)
*12	Erysotramidine	A	α-OMe		8=O	6.90(dd, 10, 3)	6.32(br d, 10)	6.02(s)	4)
*13	8-Oxoerythraline	B	" "		8=O	6.83(dd, 10, 2)	6.27(br d, 10)	6.00(s)	5)
*14	Coccolinine	C	" "		8=O	6.89(dd, 10, 2)	6.30(br d, 10)	6.03(s)	6)
*15		D	" "		8=O	6.88(dd, 10, 2)	6.30(d, 10)	6.02(s)	6)
*16		E	" "		8=O	6.69(dd, 10, 2)	6.31(d, 10)	5.86(s)	8)
*17	8-Oxo-α-erythroidine	F	" "		8=O	6.74(dd, 10, 2)	6.25(d, 10)	6.02(s)	14)
*18	8-Oxo-β-erythroidine	G	" "		8=O	6.77(dd, 12, 2.5)	6.25(d, 12)	5.96(s)	14)
*19		H	" "		8=O	6.73(dd, 10, 2)	6.30(d, 10)	6.02(s)	8)
*20		I	" "		8=O	6.68(dd, 10, 2)	6.25(d, 10)	5.92(s)	8)
*21		A	α-OH		8=O	6.91(dd, 10, 3)	6.30(br d, 10)	6.00(s)	5)
*22	8-Oxoerythrinine	B	α-OMe	11β-OH	8=O	6.85(dd, 11, 2)	6.34(br d, 11)	6.03(s)	13)
*23	Erytharbine	A	α-OMe	Δ^{10}	8=O	6.96(dd, 10, 2.5)	6.35(br d, 10)	6.08(s)	4)
*24	Crystamidine	B	α-OMe	Δ^{10}	8=O	6.93(dd, 10, 2.5)	6.32(br d, 10)	6.07(s)	12)
*25		A	α-OH	Δ^{10}	8=O	6.98(dd, 10, 2)	6.32(d, 10)	6.09(s)	7)
*26		B	α–OH	Δ^{10}	8=O	6.91(dd, 10, 2)	6.29(d, 10)	6.07(s)	7)
3β-OR Series									
27		A	β-OMe			6.70(d, 10)	6.15(dd, 10, 5)	5.80(s)	5)
28		B	" "			6.67(d, 10)	6.11(dd, 10, 5)	5.85(br s)	5)
29		A	" "		8=O	6.92(br d, 10)	6.35(dd, 10, 5)	5.94(s)	5)
30		B	" "		8=O	6.89(d, 10)	6.30(dd, 10, 5)	5.96(s)	5)
31		E	" "		8=O	6.70(d, 10)	6.33(dd, 10, 5)	5.80(s)	8)
32		H	" "		8=O	6.77(d, 10)	6.33(dd, 10, 2)	5.98(s)	8)
33		I	" "		8=O	6.64(d, 10)	6.23(dd, 10, 4)	5.85(s)	8)
34		D	β-OH		8=O	6.93(d, 10)	6.28(dd, 10, 5)	6.02(s)	6)
35		E	" "		8=O	6.70(d, 10)	6.29(dd, 10, 4)	5.81(s)	8)
36		A	β-OMe	Δ^{10}	8=O	6.95(d, 10)	6.30(dd, 10, 5)	6.00(s)	7)
3,8-Dioxo Derivatives:		(3=O, 8=O)							
37		A				7.75(d, 10)	6.41(d, 10)	6.36(s)	5)
38		B				7.72(d, 10)	6.35(d, 10)	6.36(s)	5)
39		C				7.75(d, 10)	6.38(d, 10)	6.38(s)	6)
40		E				7.56(d, 10)	6.39(d, 10)	6.26(s)	8)
41		H				7.63(d, 10)	6.34(d, 10)	6.41(s)	8)
42		I				7.55(d, 10)	6.33(d, 10)	6.32(s)	8)
43		A		Δ^{10}		7.85(dd, 10, 1)	6.37(d, 10)	6.46(s)	7)

@ Natural alkaloids are given with names. Others are synthetic compounds. Only selected compounds are listed.
* The assignment in the references must be revised as those shown in this Table.
\# The values in benzene-d_6.



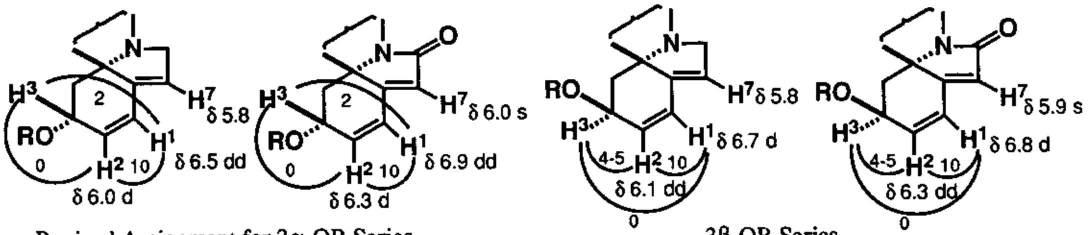
δ 5.80 and H-1 at δ 6.70 (4.4%) and between H-1 and H-2 at δ 6.33 (11-13%) were observed. Theoretical calculations also supported the above assignment: the electron densities calculated by AM1[9] for a model compound of 3-OR structure revealed that the order is C-7>C-2>C-1.

The above assignment is applicable not only to aromatic alkaloids but also to non-aromatic ones such as erythroidines, in which H-1 and H-2 appeared at slightly higher field than those of aromatic alkaloids.



Atom electron density

For homoerythrinan alkaloids of dienoid-type, Johns and co-workers[10] assgined the olefinic protons of H-1, H-2, and H-7 at *ca.* δ 6.2, 5.8, and 5.5 (in benzene-d_6), based on detailed decoupling experiments of the 3α- and 3β-isomers. This is in agreement with our revised assignment for erythrinan alkaloids.



Revised Assignment for 3α-OR Series

3β-OR Series

Figure 1

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