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LANTHANIDE INDUCED SHIFTS AS AN AID IN THE STRUCTURAL DETERMINATION OF EUSIDERINS

Raimundo Braz F^{o} and Jamil C Mourão
Instituto de Ciências Exatas, Universidade Federal Rural do Rio de Janeiro

Otto R Gottlieb
Instituto de Química, Universidade de São Paulo

and

José G S Maia
Instituto Nacional de Pesquisas da Amazônia, CNPq, Manaus, Brasil

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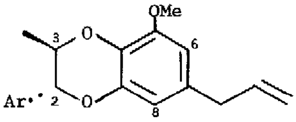
Merlini and Zanarotti[1] recognized that the choice between the structural alternatives 1a and 2a assigned to eusiderin[2,3] is difficult, even on the basis of NMR spectra Although favouring 1a upon consideration of biosynthetic mechanism, in the same way as proposed previously,[4] and a biogenetically patterned, but not unambiguous, synthesis, they, nevertheless, were forced to defer a final decision to X-ray analysis [1]

Eusiderin, a neolignan of the Lauraceae genera Eusideroxylon,[2] Aniba[5] and Licaria,[6] is accompanied in a Licaria species by eusiderin-B to which again, considering MS and ^{1}HMR data, the alternative structures 1b and 2b can be assigned

Isolated aromatic ethers associate only weakly with the NMR shift reagent Pr(fod)$_3$. The same occurs with ortho diethers in which the oxy-functions are part of an additional ring (e g in methylenedioxybenzene and benzodioxane), unless an OR group substitutes at least one of the vicinal positions Ortho di- and triethers associate strongly with the reagent

These facts, verified by examination of simple model compounds, leave no doubt about the significance of LIS data concerning eusiderin-B (1b, Table 1). Coordination with Pr affects

H-3 more strongly than H-2, leading to the conclusion that the methoxyl must be located at C-5 and not at C-8 Structure 1b for eusiderin-B is corroborated examining LIS data for licarin-B[7] (3b, Table 1), whose structure was confirmed by synthesis [8] The relative Δ values for H-2, H-3 and Me-3 (Table 2) show clearly that the methoxyl is closer to H-2 in 3b and to H-3 and Me-3 in 1b. The relative Δ values for protons *ortho*- and *para*-related with the methoxyl are typical of 1,2-dimethoxybenzenes (Table 3) While absolute Δ values are not directly useful in such correlations, they indicate that the complexation ratio in 1b (Δ_{OMe} 16 2 ppm) is higher than in 3b (Δ_{OMe} 10 9 ppm) by a factor of 1.5



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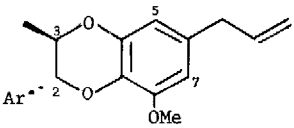

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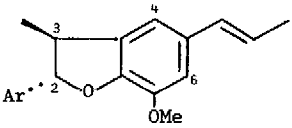

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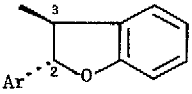
a Ar = tri-O-methylgallyl, b.. Ar = piperonyl

The configurational assignments are relative Absolute configurations are known only for 3a (2R,3R)[9] and 3b (2S,3S) [7]



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Turning now to the case of eusiderin, the complexation ratio at the oxy-methoxy site (Δ_{OMe} 4 6 ppm) is also higher than in licarin-C[9] (3a, Table 1) (Δ_{OMe} 3 0 ppm), and again by a factor of 1.5 Since this phenomenon is here as clearly linked to differential steric hindrance at the coordination site as it was in the case of 1b vs. 3b, only 1a can represent correctly the structure of eusiderin. This conclusion is consistent with the relative Δ values 52 and 44 for H-6 and H-8 which indicate that the proton *para*-related with the methoxyl is under the influence of the neighbouring coordination site at the aryl group Indeed, if eusiderin had structure 2a, its LIS data should be comparable to the data of 3a (Table 1). The experimental values are, however, in better agreement with calculated values for 1a 4 1 (Δ_{H-2}), 6 6 (Δ_{H-3}) and 2 4 (Δ_{Me-3}).

For calculation it was assumed that LIS data are additive.[10] Thus, each of the Δ values for H-2, H-3 and Me-3 of 3a are due partly to Pr-trimethoxy and partly to Pr-oxy-methoxy association Since their relative populations are known (through Δ_{OMe-7} and $\Delta_{OMe-4'}$ values) and the influence of the Pr-oxy-methoxy coordination may be inferred from data on 3b (where it causes the only strong effect), the influence of the Pr-trimethoxy coordination can be

TABLE 1. Δ VALUES (ppm) RECORDED FOR PROTON SIGNALS OF EUSIDERINS AND LICARINS[x]

Cmpd.	Aryl System						Bicyclic System					
	OMe-4'	OMe-3',5'	H-2'	H-6'	H-5'	O_2CH_2-3',4'	H-2	H-3	Me-3	OMe	H-o[y]	H-p[y]
1a	24.4	11.8	8.8		-	-	5.6	6.0	4.6	4.6	2.4	2.0
3a	24.4	8.2	7.1		-	-	4.8	2.8	0.9	3.0	1.8	0.8
1b	-	-	4.2	3.6	1.4	0.8	9.2	19.2	16.6	16.2	8.8	3.6
3b	-	-	2.0	4.3	0.0	-0.7, -0.2	12.0	6.2	1.6	10.9	6.6	2.5

[x] Shift studies were carried out by stepwise addition of known amounts of $Pr(fod)_3$ to *ca.* 0.15 M solutions of substrate in $CDCl_3$ The LIS data were obtained by graphic extrapolation of observed shifts to 1 1 shift reagent - substrate ratio.

[y] In relation to OMe

TABLE 2. Δ VALUES (% of Δ_{OMe}) CALCULATED FOR PROTON SIGNALS OF COMPOUNDS WITH SINGLE COORDINATION SITE

Cmpd	OMe at position	H-2	H-3	Me-3	H-o[y]	H-p[y]
1b	5	57	118	41	54	22
3b	7	110	57	15	61	23
4a	4'	6	5	2		

[y] In relation to OMe

TABLE 3 Δ VALUES (% of Δ_{OMe}) CALCULATED FOR 1,2-DIMETHOXYBENZENES

Substituents	OMe at position	H-3	H-6	H-4	H-5
-	1,2	55		23	
4-allyl	1,2	55	54	-	24
4-propenyl	1,2	55	55	-	23
6-allyl-3,4-O_2CH_2	2	-	-	-	22
3-methoxy	2	-	40[x]		23

[x] In this case, two equivalent complexes are possible[10] and, indeed, 40 is within experimental error of the average between 55 and 23.

calculated Expressed in relative Δ values for a hypothetical compound **4a** in Table 2, they can be used to calculate the required Δ values for a H-n of structure **1a** by the equation

$$\Delta^{\mathbf{1a}}_{H-n} = \Delta^{\mathbf{1a}}_{OMe-4'} \frac{rel\ \Delta^{\mathbf{4a}}_{H-n}}{100} + \Delta^{\mathbf{1a}}_{OMe-5} \frac{rel\ \Delta^{\mathbf{1b}}_{H-n}}{100}$$

LIS data were recently applied in the revision of the structure[11] of another neolignan, porosin,[12] and it is to be foreseen that the method will prove useful in the solution of other problems concerning aromatic ethers, e g the structural elucidation of the flavanolignans,[13] the only other known natural products with a benzodioxane nucleus besides the eusiderins [1]

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