Tetrahedron Letters No. 42, pp 3897 - 3900, 1971. Pergamon Press. Printed in Great Britain.

NIGAKILACTONES: STEREOSTRUCTURE AND NUCLEAR OVERHAUSER EFFECTS

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(Received in Japan 2 September 1971; received in UK for publication 15 September 1971)

A number of bitter principles have been isolated from Picrasma ailanthoides Planchon (=P. quassioides Bennett), and their structures have been described in recent years (1,2). We report here intramolecular nuclear Overhauser effects (NOE) (3) observed for nigakilactones C (1a, 1c) and E (1b, 1c); the results have confirmed the stereostructures for nigakilactones A, B, C, E, F, and J, and nigakihemiacetal A and C.

The structure Ia was previously given for nigakilactone E (1b, 1c) on the basis of its transformation into quassin (III) (4) together with the presence of a partial structure (Aa) deduced from the observed spin-coupling features of the three adjacent protons, H_a, H_b, and H_c (J_{ab} = 11.3 and J_{bc} = 9.3 Hz), which are apparently in axial-axial relationships. The conformation of Ia is represented by I'a whose C ring is in a chair form to account for the J-values. However, an alternative structure (IIa) with its C ring in a boat form (II'a) is compatible with the above coupling data.

The presence of NOE's between 11-H and 10-Me, between 11-H and 8-Me, between 13-OH and 8-Me, and between 12-H and 9-H, as shown in the Table, provides confirmatory evidence that 11-H, 13-OH, 8-Me, and 10-Me are in cis relationships to one another, and that 12-H and 9-H are oriented toward the same side from the molecular plane of nigakilactone E. Since the β-configuration of the 8- and 10-Me's and the α-configuration of 9-H have already been demonstrated (1b, 1c), both 11-H and 13-OH must be in the β(axial)-configuration and 12-H in the α(axial) one. These results lead to the conformation (I'a), thus confirming the structure (Ia) for nigakilactone E. An alternative structure (IIa) with the conformation

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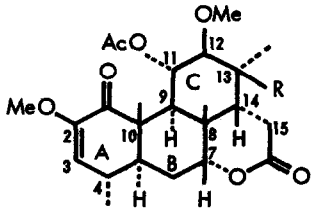
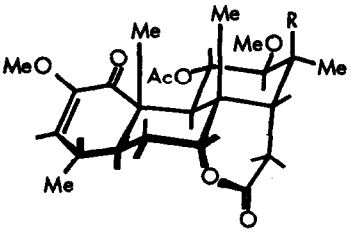


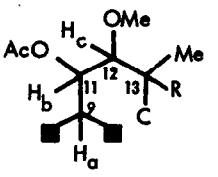
(Ia: R = OH; nigakilactone E)

(Ib: R = H ; nigakilactone C)



(I'a: R = OH)

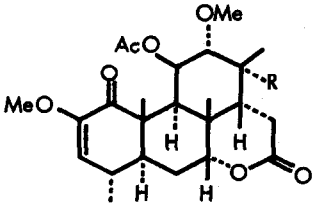
(I'b: R = H)



(Aa: R = OH)

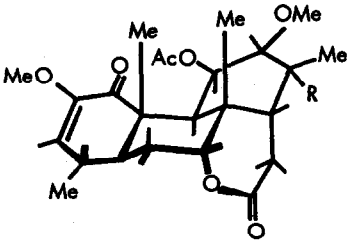
(Ab: R = H_d)

[■ indicates carbon with no proton]



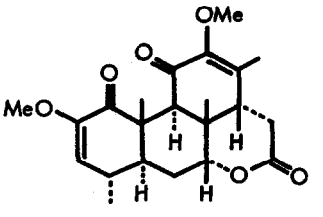
(IIa: R = OH)

(IIb: R = H)

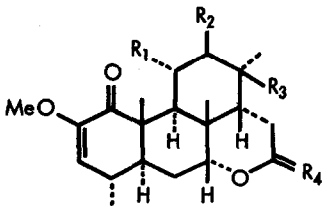


(II'a: R = OH)

(II'b: R = H)



(III: quassin)



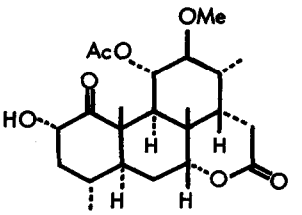
(IVa: R_1 = OH, R_2 = OH, R_3 = H, R_4 = O; nigakilactone A)

(IVb: R_1 = OH, R_2 = OMe, R_3 = H, R_4 = O; nigakilactone B)

(IVc: R_1 = OH, R_2 = OMe, R_3 = OH, R_4 = O; nigakilactone F)

(IVd: R_1 = OH, R_2 = OMe, R_3 = OH, R_4 = H, OH; nigakihemiacetal A)

(IVe: R_1 = OH, R_2 = OH, R_3 = H, R_4 = H, OH; nigakihemiacetal C)



(V: nigakilactone J)

TABLE

PMR Spectral Data on Nigakilactones E (Ia) and C (Ib) in $CDCl_3$[a]

Nuclear Overhauser effects (increases in integrated signal intensities, %)			Chemical shifts (δ, ppm downfield from TMS) and coupling constants (J, Hz)		
Observed protons	Saturated protons	NOE		(Ia)	(Ib)
	(Ia)		4-Me	1.08 d	1.10 d
3-H	2-OMe	25	13-Me	1.24 s	1.04 s
11-H	12-OMe	nil	10-Me	1.26 s	1.28 s
13-OH	12-OMe	5[b]	8-Me	1.52 s	1.28 s
7-H	8-Me	8	11-OAc	1.97 s	1.97 s
11-H	8-Me	14	13-OH	2.39 s	---
13-OH	8-Me	2[b]	15α-H	2.45 q	
11-H	10-Me	13	9-H	2.56 d	2.57 d
11-H	13-Me	nil	15β-H	2.70 q	
12-H	13-Me	12	12-H	3.36 d	3.19 q
13-OH	13-Me	5[b]	12-OMe	3.53 s	3.45 s
15β-H	13-Me	12[b]	2-OMe	3.56 s	3.56 s
11-H	13-OH	4	7-H	4.17 m	4.18 m
12-H	9-H	15	3-H	5.14 d	5.15 d
9-H	12-H	8[b]	11-H	5.52 q	5.25 q
15α-H	12-H	6[b]			
	(Ib)		$J_{3,4}$	2.5	2.5
3-H	2-OMe	23	$J_{9,11}$	11.3	11.4
11-H	12-OMe	nil	$J_{11,12}$	9.3	9.3
3-H	4-Me	11	$J_{12,13}$	---	11.0
11-H	8- and 10-Me's	16	$J_{14,15\alpha}$	11.5	
11-H	13-Me	nil	$J_{14,15\beta}$	8.3	
9-H	12-H	5[b]	$J_{15\alpha,15\beta}$	(-)18.6	

[a] The PMR spectra were taken with a Varian HA-100 spectrometer operating at 100 MHz in the frequency-swept and internal TMS-locked mode, for ca. 7% (w/v) degassed solutions in $CDCl_3$. NOE experiments were performed with sweep rates of 1 Hz per sec for integrations and 0.2 Hz per sec for signals on the spectrometer with a Hewlett-Packard HP-200ABR audiooscillator and an HP-5212A electronic counter. Accuracies are ±0.01 ppm for chemical shifts, ±0.2 Hz for coupling constants, and about ±2% for NOE values.

[b] Observed by increases in signal heights; long-range spin couplings were hardly detected in these cases.

(II'a) was therefore excluded. Other observations on NOE's (see the Table) are very consistent with the conformation (I'a).

A similar situation is seen for the structure of nigakilactone C (Ib) (1a, 1c), which could also be transformed into quassin (III); thus, besides structure Ib whose C ring adopts a chair conformation (I'b), an alternative structure (IIb) with its C ring in a boat form (II'b) is also compatible with the observed spin-coupling features (J_{ab} = 11.4, J_{bc} = 9.3, and J_{cd} = 11.0 Hz) (Ab). The results of the NOE experiments shown in the Table provide sufficient information about the conformation of nigakilactone C; the observed NOE's between 11-H and 8(β)- and 10(β)-Me's, and between 9(α)-H and 12-H indicate that 11-H and 12-H are β(axial) and α(axial), respectively, confirming the conformation (I'b). This leads to the structure (Ib) for nigakilactone C.

Nigakilactones A (IVa) (1a, 1c), B (IVb) (1a, 1c), J (V) (1f), and nigakihemiacetal C (IVe) (1e) have already been correlated with nigakilactone C. Transformations among nigakilactones E, F (IVc) (1b, 1c), and nigakihemiacetal A (IVd) (1d) have also been reported. Therefore, the present confirmation of the structures Ia and Ib for nigakilactones E and C proves that it is unnecessary to correct the structures IVa, IVb, IVc, V, IVd, and IVe, previously given for nigakilactones A, B, F, and J, and nigakihemiacetals A and C, respectively.

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