Tetrahedron Letters No. 42, pp 3725 - 3728, 1974. Pergamon Press. Printed in Great Britain.

REVISED STRUCTURE OF ANKORINE

Csaba Szántay, Éva Szentirmay, Lajos Szabó
Institut for Organic Chemistry of the Technical University
Budapest

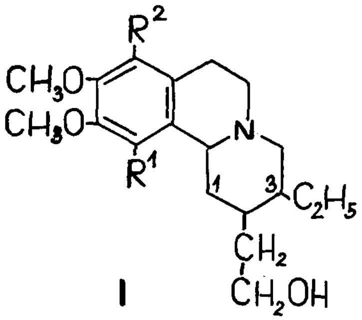
(Received in UK 30 August 1974; accepted for publication 12 September 1974)

On the basis of spectral evidence the structure (Ia) has been assigned to the Alangium lamarckii alkaloid ankorine, without any indication of its stereochemistry[1]. To elucidate the stereostructure we undertook the synthesis of the four possible racemic forms of structure (Ia).

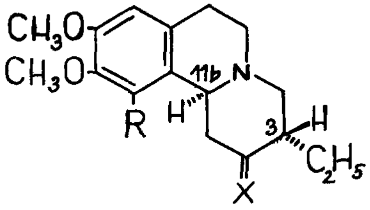
3-Benzyloxy-4,5-dimethoxyphenylethylamine has been converted by Bischler--Napieralsky ring closure to a mixture of the 8-benzyloxy- and 6-benzyloxy-isoquinoline derivatives[2]. The components of the mixture were separated through their salicylic acid salts.

The 8-benzyloxy-derivative (Salicylate, m.p. 122-123^{o}) reacted with 3--ethyl-butenone[3] to give the benzo(a)quinolizidine (IIa) (63%, mp. 97^{o}) . Hydrogenolysis of the benzyloxy group with H_2/Pd yielded (IIb)(90%, mp. 155^{o} from ethyl acetate). The stereostructure of the ketone was presumed to be (II) because of the thermodynamic control of the reaction[4], but it was further proved as follows. (IIb) was treated with 1-phenyl-5-chlorotetrazole[5], and the resulting 11-tetrazolyloxy derivative (IIc) (mp. 158-160^{o}) was reduced to give the already known[3,6] (IId).

Reaction of (IIb) with methoxycarbonylmethylenetriphenylphosphorane yielded (IIe)(28%, mp. 125-127^{o} methanol). The Wittig-reagent is known[6] not to change the configuration at C_3. The same product (IIe) was also obtained in 70% yield using the phosphonic ester method[7]. Catalytic reduction of the double bond gave two saturated esters having the normal (IIIa),(M^+ m/e 363.2040, R_f 0.45) and epiallo (IIIb),(M^+ m/e 363.2048 R_f 0.35) configurations in a ratio of about 1:1, separated by TLC. To prove the stereostructure



I



II

a R^1 = OH; R^2 = H

b R^1 = H R^2 = OH

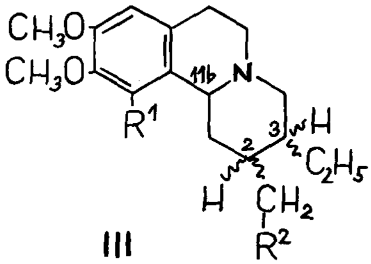
a R = $OCH_2-C_6H_5$; X = O

b R = OH ; X = O

c R = 1-phenyltetrasolyloxy; X = O

d R = H ; X = O

c R = OH ; X = $CH-COOCH_3$



III

a 11bHα,2Hα,3Hβ(normal); R^1 = OH; R^2 = $CH_2-COOCH_3$

b 11bHα,2Hβ,3Hβ(epiallo); R^1 = OH; R^2 = $CH_2-COOCH_3$

c 11bHα,2Hα,3Hα(allo); R^1 = OH; R^2 = $CH_2-COOCH_3$

d 11bHβ,2Hα,3Hβ(pseudo); R^1 = OH; R^2 = $CH_2-COOCH_3$

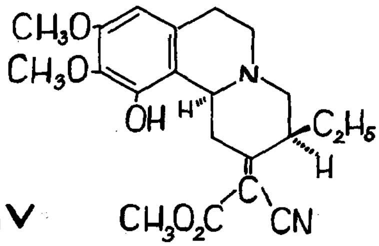
e 11bHα,2Hα,3Hβ(normal); R^1 = H ; R^2 = $CH_2-COOCH_3$

f normal ; R^1 = OH ; R^2 = CH_2-CH_2-OH

g epiallo ; R^1 = OH ; R^2 = CH_2-CH_2-OH

h allo ; R^1 = OH ; R^2 = CH_2-CH_2-OH

i pseudo ; R^1 = OH ; R^2 = CH_2-CH_2-OH



IV

(IIIa) was converted by the above mentioned method[5] to the known[6,7] compound (IIIe).

On the other hand, reaction of the ketone (IIb) with methyl cyanoacetate, which causes epimerisation at C_3[6,8], yielded (IV) (83%, mp. 142-143° from petrol ether). Reduction of the latter compound ($NaBH_4$, 66%), followed by hydrolysis and decarboxylation, furnished the nitrile (M^+ m/e 330.1938), which was transformed to the allo-ester (IIIc) (M^+ m/e 363.2040 R_f 0.55) by methanol/HCl.

To prepare the fourth racemate, the pseudo - stereoisomer, the normal--ester (IIIa) was oxidized by Hg^{II}-acetate and the resulting immonium salt was reduced by Zn and hydrochloric acid. The mixture of normal and pseudo (IIId,) (M^+ m/e 363.2050, R_f 0.30) compounds obtained was separated by TLC.

All the four stereoisomeric esters were reduced to the alcohols (IIIf-i) (MS data see Table) by $LiAlH_4$ but none of the racemates corresponded with natural ankorine.

Assignment of the stereostructure of our synthetic compounds was based 1./ on the applied synthetic route; 2./ on the TLC behaviour[9] and 3./ on the mass spectra. According to our earlier observations[10], the ratio of intensity of fragment ions m/e 262/221 varies greatly according to wether the compound belongs to the normal, pseudo or allo, epiallo series. This rule was applied succesfully both to (IIIa-d) esters and to (IIIf-i) alcohols.

Taking into account our synthetic results and the data published earlier the structure of ankorine must be (Ib) and according to our mass spectral considerations its stereostructure is presumably normal. It is likely that the structures of alangicine and alangimarckine[1] should also be revised accordingly. The synthesis of the new ankorine structure is in progress.

These experiments prove that even nowadays, in the era of highly sophisticated spectroscopic methods synthesis can be a useful tool in structure elucidation as was also shown by us recently in connection with alloyohimbine synthesis[11].

We are indebted to Dr. S.P. Popli (Lucknow, India) for furnishing us with natural ankorine.

Table

m/e	I %					M-X
	ANKORIN	pszeudo	epiallo	normal	allo	
335	71,8	58	34,2	75	40	M
334	100,0	51	25,6	58	30	M-1
320	37,3	6	3,5	4,8	3,1	M-15
318	53,8	3	2,7	1,6	-	M-17
306	9,8	10	4,0	11,0	5,0	M-29
304	6,8	8	3,7	6,9	3,5	M-31
290	14,5	15	10,3	14	13,0	M-45
288	7,4	-	2,3	3,8	-	M-47
278	15,6	13	4,8	16,0	-	M-57
262	66,6	71	37,1	76	48	M-73
248	8,8	-	6,4	10	-	M-87
221	65,9	100	100	100	100	M-114
207	47,6	64	47,3	69	71	M-128
192	31,4	-	8,7	11	-	M-143
M	335,2086	-	335,2088	335,2088	335,2098	

REFERENCES

1./ A.R. Battersby, R.S. Kapil, D.S. Bhakuni, S.P. Popli, J.R. Merchant and S.S. Salgar, Tetr. Letters, 1966, 4965;
S.C. Pakrashi and Esahak Ali, ibid. 1967, 2143.

2./ A. Brossi et al., Helv. Chim. Acta, 49, 403 (1966).

3./ Beke D. and Cs. Szántay, Chem. Ber., 95, 2132 (1962).

4./ Szántay Cs. and Rohály J., Magyar Kém. Folyóirat 70, 478 (1964).

5./ W.J. Musliner and J.W. Gates, J. Amer. Chem. Soc., 88, 4272 (1966).

6./ H.T. Openshaw and N. Whittaker, J. Chem. Soc., 1963, (1461).

7./ Cs. Szántay, L. Tőke and P. Kolonits, J. Org. Chem. 31, 1447 (1966).

8./ A. Brossi and O. Schnider, Helv. Chim. Acta, 45, 1899 (1962);
Cs. Szántay and M. Bárczai-Beke, Chem. Ber. 102, 3963 (1969).

9./ J.D. Philipson and E.J. Shellard : J. of Chromatography, 31, 427 (1967).

10./ M. Bárczai-Beke, G. Dörnyei, J. Tamás and Cs. Szántay, Chem. Ber. 105, 3244 (1972).

11./ L. Tőke, K. Honty, L. Szabó, G. Blaskó and Cs. Szántay, J. Org. Chem. 38, 2496 (1973).