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ERYMELANTHINE, A NEW TYPE OF ERYTHRINA ALKALOID CONTAINING A 16-AZAERYTHRINANE SKELETON[1]

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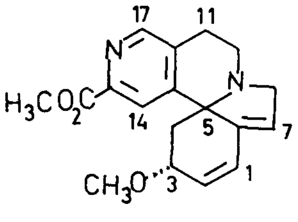
Summary: Erymelanthine, isolated from the seeds of *Erythrina melanacantha*, represents the first member of a new type of erythrina alkaloid containing a 16-azaerythrinane skeleton.

As part of our studies on the alkaloids of *Erythrina* species from Ethiopia[2] we have isolated a new alkaloid erymelanthine (1) along with erysovine (2) from the seeds of *E. melanacantha*, a tree known to occur in southern Ethiopia, Somalia, northern Kenya and Tanzania.[3]

1 has the following physical and spectral properties: mp 160-161 °C; $[\alpha]_D^{22}$ $+87^o$ (c = 0.11, MeOH); MS: *m/z* 312 (M^+, $C_{18}H_{20}N_2O_3$, 79%), 297 (36), 281 (100), 279 (28), 221 ($C_{15}H_{13}N_2$, 49), 193 (12); IR ($CHCl_3$): 2950, 1720, 1590, 1430, 1380, 1340, 1290, 1230, 1100, 930, 820/cm; UV (EtOH) $\lambda_{max}(\varepsilon)$: 270 (3000), 230 nm (8000); ^1H NMR (400 MHz, $CDCl_3$): δ 1.91 (dd, J=12+10 Hz, H-4_{ax}), 2.51 (br. dd, J=12+5 Hz, H-4_{eq}), 2.77 (m, H-10_{eq}), 3.10 (m, 2H, H-11), 3.31 (s, OCH_3), 3.55 (m, 2H, H-8), 3.75 (m, H-10_{ax}), 3.96 (s, CO_2CH_3), 4.00 (m, H-3), 5.76 (br. s, H-7), 6.10 (d, J=10 Hz, H-1), 6.61 (dd, J=10+2 Hz, H-2), 8.00 (d, J=1 Hz, H-14), 8.50 (br. d, J=1 Hz, H-17).

1 differs from all the other alkaloids isolated so far from *Erythrina* species by the presence of a second nitrogen atom.[4] Its MS exhibits the normal fragmentation pattern for an alkaloid of the 1,6-diene series[5], and the ^1H NMR signals for the protons attached to rings A, B and C correspond closely to those observed in the spectrum of erysovine (2). A dramatic difference, however, occurs in the aromatic region. Whereas in 2 and other erythrina alkaloids two singlets having chemical shifts between 6.5 and 7.0 ppm may be observed

for H-14 and H-17, the corresponding signals of 1 appear at unusually low field (δ 8.00 and 8.50, respectively). This may be explained by the presence of a pyridine unit in ring D, substituted by a carbomethoxy group at one of the α-positions. From the coupling constant of *J*=1 Hz between the aromatic signals it can be concluded that these protons occupy α- and β'-positions of the pyridine ring. The signal at δ 8.50 is broadened by benzylic coupling with the protons at C(11) as could be shown by decoupling experiments. This excludes a 15-erythrinane derivative and is in full accord with a 16-azaerythrinane structure 1 for erymelanthine.



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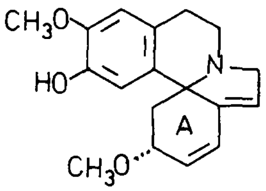

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Structure 1 is further supported by comparison of the ^{13}C NMR data of erymelanthine with those recently published for erysovine[6] (table 1). Signals for C(1) to C(11) in rings A, B and C exhibit nearly identical chemical shifts for both alkaloids. The chemical shifts of the carbons in the pyridine ring of 1

Table 1. ^{13}C NMR data of erymelanthine (1) and erysovine (2) in $CDCl_3$

Carbon No.	1			2[6]		1			2[6]
1	δ 124.9	d	*J*=156 Hz	125.6	12	134.0	s	-	125.2
2	131.7	d	154	132.0	13	140.4	s	-	131.5
3	75.4	d	137	75.9	14	122.1	d[a]	158	111.0
4	40.4	t	126	41.4	15	149.6	s	-	145.6
5	66.5	s	-	66.8	17	150.4	d[b]	171	112.5
6	145.7	s[c]	-	142.4	CO_2CH_3	165.9	s	-	-
7	123.4	d	163	122.4	$\bar{C}O_2CH_3$	52.8	q	141	-
8	56.1	t	134	56.8	$O\bar{C}H_3$	56.5	q[d]	135	55.7
10	42.3	t	132	44.0					
11	21.3	t	125	24.2					

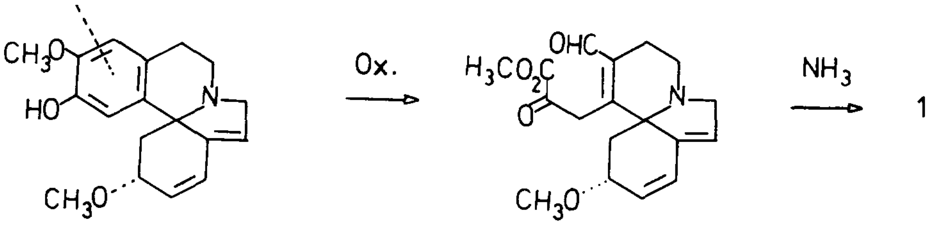
a) Sharp singlet in H-coupled ^{13}C NMR spectrum; b) Dt, $^3J_{CH}$= 3 Hz; c) d, $^3J_{CH}$= 11 Hz; d) Qd, $^3J_{CH}$= 4.5 Hz.

are in close agreement with literature data of similar systems.[7] The signals at δ 149.6 and 150.4, which correspond to the α- and α'-positions of the pyridine ring occur as a singlet and doublet, respectively, the latter being further split into triplets by $^3J_{CH}$ coupling with the protons at C(11). This lends further support for the positioning of the carbomethoxy group at C(15).

The carbomethoxy group gives rise to two signals at δ 52.8 and 165.9 in the ^{13}C NMR spectrum and is responsible for the presence of an IR band at 1720/cm.

The stereochemistry at C-3 may be deduced from the coupling constants $J_{3,4eq}$ and $J_{3,4ax}$ in the ^{1}H NMR spectrum.[8] Since 1 and 2 show the same values (5 and 12 Hz) for these coupling constants, 1 must possess the same stereochemistry. The similarity of the CD spectra of 1 and 2 particularly in the 220-260 nm region adds further support to this stereochemical assignment.

A plausible biosynthetic route to erymelanthine may involve extradiol cleavage of erysovine between C(16) and C(17) followed by formation of the pyridine ring by condensation of the intermediate 3 with ammonia. The co-occurrence of 1 and 2 in the seeds of *E. melanacantha* lends support to this hypothesis.



2 3

Barton et al.[9] have proposed two pathways for the conversion of aromatic erythrina alkaloids into α- and β-erythroidines, which involve either intradiol [C(15)-C(16)] or extradiol [C(16)-C(17)] cleavage. The isolation of erymelanthine seems to advocate the latter pathway.

The possibility that 1 is an artefact formed from intermediate 3 during work-up with ammonia[10] was excluded by isolating 1 from the seeds of *E. melanacantha* by a procedure omitting ammonia during the extraction.

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References and Notes

1) Dedicated to Professor Sir Derek Barton on the occasion of his 65th birthday.

2) E. Dagne and W. Steglich, *Phytochemistry*, in press.

3) The seeds of *E. melanacantha* were collected in April 1982 in south Ethiopia from trees growing in the province of Borana, 58 km west of Negelle town at an altitude of 980 m above sea level. The plant was identified by Ato Mesfin Tadesse of the Biology Department, Addis Ababa University. For a botanical description of this plant see: J.B. Gillet, R.M. Polhill and B. Verdcourt in E. Milne-Redhead and R.M. Polhill (Eds.), *Flora of Tropical East Africa*, Crown Agents, London 1971, p. 552.

4) Recently an erythrina alkaloid, erythramide, possessing an extra nitrogen atom in form of a carboxamino group has been isolated from *Cocculus laurifolius*: M. Juichi, Y. Fujitani, T. Shingu and H. Furukawa, *Heterocycles*, *16*, 555 (1981).

5) R.B. Boar and D.A. Widdowson, *J. Chem. Soc.* B, *1970*, 1591.

6) A.S. Chawla, S. Chunchatprasert and A.H. Jackson, *Org. Magn. Reson.* *21*, 39 (1983).

7) E. Breitmaier and G. Bauer, *^{13}C-NMR-Spektroskopie*, G. Thieme, Stuttgart 1977, p. 367.

8) S.F. Dyke and S.N. Quessy in R.H.F. Manske and R.G.A. Rodrigo (Eds.), *The Alkaloids*, Vol. 17, Academic Press, New York 1981, p. 11.

9) D.H.R. Barton, R.D. Bracho, C.J. Potter and D.A. Widdowson, *J.C.S. Perkin I*, *1974*, 2278.

10) Cf. the formation of gentianine from gentiopicroside or swertiamarine: H.-G. Floss, U. Mothes and A. Rettig, *Z. Naturforsch.* *19 b*, 1106 (1964).

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