

The Structures of Lythrum Alkaloids, Lythrancine-I, -II, -III, -IV, Lythrancepine-I, -II, and -III

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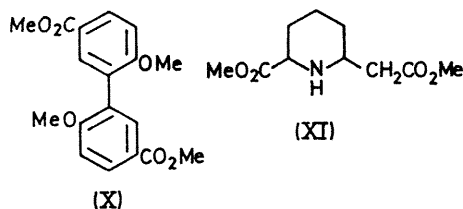
Summary The structures of seven new alkaloids, lythrancine-I, -II, -III, -IV, and lythrancepine-I, -II, and -III, have been shown to be (I)—(VII), respectively.

BESIDES the known alkaloids, lythranine, lythranidine, and lythramine,¹ seven new alkaloids, lythrancine-I, -II, -III, -IV, and lythrancepine-I, -II, and -III, have been isolated from methanolic extracts of *Lythrum anceps* Makino (Lythraceae).

TABLE

	M.p.	$[\alpha]_D^{20}$
Lythrancine—I (I)	powder	+65°
—II (II)	274—275°	+125°
—III (III)	134—136°	+38°
—IV (IV)	237—238°	+27°
Lythrancepine—I (V)	149—151°	+59°
—II (VI)	187—189°	+44°
—III (VII)	174—178°	+7°

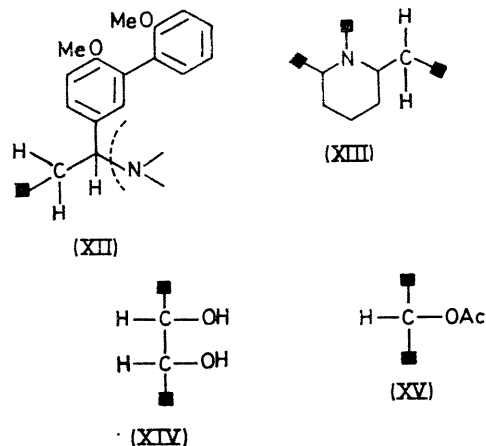
Acetylation of lythrancine-II (II) gave lythrancine-II *O*-acetate and lythrancine-II *OO*-diacetate which were identical with lythrancine-III (III) and lythrancine-IV (IV), respectively. Alkaline hydrolysis of these three alkaloids afforded lythrancine-I (I). Both lythrancepine-II (VI) and lythrancepine-III (VII), on alkaline hydrolysis, gave lythrancepine-I (V). Lythrancine-III (III) was converted into lythrancepine-I (V) by treatment with toluene-*p*-sulphonyl chloride in pyridine followed by LiAlH_4 reduction of the resulting lythrancine-III *O*-tosylate (VIII), m.p. 192—194°. Thus, these seven alkaloids have a common skeleton and a tertiary nitrogen.



Lythrancine-II showed a hydroxy band at 3480 cm^{-1} and a carbonyl band at 1720 cm^{-1} in its i.r. spectrum. Its n.m.r. spectrum demonstrated this carbonyl group to be present as a secondary acetate, showing a singlet at δ 2.01 (3H, CH_3CO_2) and a multiplet at δ 5.35 (1H, AcOCH). Furthermore, two methoxy-groups (δ 3.87, 6H, s) and a proton (δ 4.08, 1H, dd, J 4 and 10.5 Hz) on the carbon which carried a phenyl group and a nitrogen atom were recognized. The n.m.r. spectrum of lythrancine-II *OO*-diacetate, *i.e.* lythrancine-IV (IV) showed singlets at δ 1.94 (6H, $2\text{CH}_3\text{CO}_2$) and at δ 2.06 (3H, CH_3CO_2), a triplet at δ 4.91 (1H, J 2.5 Hz, AcOCH), an octet at δ 5.15 (1H, J 3, 6, and 11.5 Hz, AcOCH), and a multiplet at δ 5.35 (1H, AcOCH). Lythrancine-II, therefore, has two secondary hydroxy-groups.

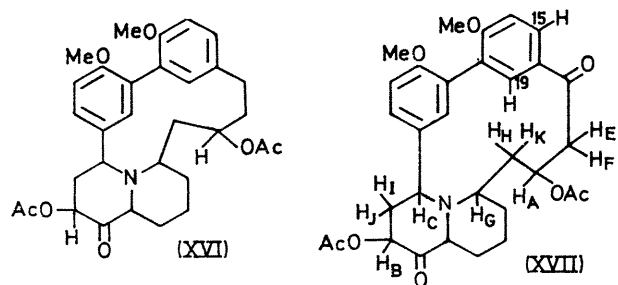
† The structure of this compound was supported by the i.r., n.m.r., and mass spectra.

Treatment of lythrancine-II (II) with phosgene in toluene-pyridine readily gave a five-membered cyclic carbonate (IX), m.p. > 300°, i.r. 1798 cm^{-1} . Thus, the two secondary hydroxy-groups are present as a *cis*-glycol.



Chromic acid oxidation of lythrancine-II (II) and subsequent methylation of the oxidation products yielded dimethyl 2,2'-dimethoxydiphenyl-5,5'-dicarboxylate (X),² m.p. 172—175°, and *trans*-2-methoxycarbonyl-6-methoxycarbonylmethyl hexahydropyridine (XI),[†] $\text{C}_{10}\text{H}_{17}\text{NO}_4$. Consequently, lythrancine-II contains the partial structures, (XII), (XIII), (XIV), and (XV).

Jones oxidation of lythrancine-II (III) gave a monoketone (XVI), m.p. 133—136°, $\text{C}_{31}\text{H}_{37}\text{NO}_7$, and a diketone (XVII), m.p. 161—162°, $\text{C}_{31}\text{H}_{35}\text{NO}_8$. Sodium borohydride reduction of (XVI) afforded lythrancine-II (II) and its



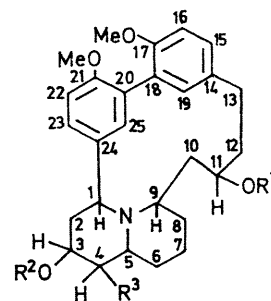
C-4 epimer. The n.m.r. spectrum of diketone (XVII) showed the presence of an ABX pattern at δ 2.61 (H_E , dd, J 10 and 14.5 Hz), 3.25 (H_F , d, J 14.5 Hz) and 5.81 (H_A , m); a double doublet of the A part (δ 2.61) collapsed into a doublet (J 14.5 Hz) on irradiation at δ 5.81 (the X part), and the value of J (H_EH_F) suggested a geminal coupling and the chemical shifts of H_E and H_F were in agreement with those of a methylene adjacent to a carbonyl grouping. By

a simultaneous irradiation at H_G (δ 3.17, br. d, J 11 Hz) and H_A (δ 2.61, m), H_K (δ 1.47, oct, J 3, 6, and 15 Hz) split into a doublet with a geminal coupling of 15 Hz. Moreover, a downfield shift of the signals of two aromatic protons (15-H and 19-H) was observed in the n.m.r. spectrum of the diketone, as compared with that of the monoketone (XVI). The second oxidation therefore occurred at a benzylic position. The benzoyl group was recognized from the i.r. spectrum (CHCl₃, 1670 cm⁻¹) and the u.v. spectrum [λ_{\max} (EtOH) 245 nm; ϵ 17,000]. In addition, double irradiation of H_C at δ 4.53 (dd, J 2.5 and 11 Hz) and H_B at δ 5.58 (dd, J 6.5 and 13 Hz) gave an AB quartet with geminal coupling of 13 Hz at δ 1.95 and 2.35.

On the basis of the above results, structure (XVII) was assigned to the diketone; hence the original base, lythrancepine-III, is (III). Thus, the structures of the seven alkaloids were clarified as shown. The chemical shift (δ 5.33) of the proton on the acetoxyated carbon of lythrancepine-II excluded another possible structure (VI'), because the 11-H signal was always observed at δ 5.34 \pm 0.01 in the

11-acetates, while 3-H in the 3-acetates resonated at somewhat higher field, δ 4.99—5.15.

	R ¹	R ²	R ³
(I)	H	H	OH
(II)	Ac	H	OH
(III)	Ac	Ac	OH
(IV)	Ac	Ac	OAc
(V)	H	H	H
(VI)	Ac	H	H
(VII)	Ac	Ac	H
(VIII)	Ac	Ac	OTs
(IX)	Ac		CO-O
(VI')	H	Ac	H



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² K. V. J. Rao and L. R. Row, *J. Org. Chem.*, 1960, 25, 981; K. P. Mathai and S. Sethna, *J. Indian Chem. Soc.*, 1963, 40, 347.