Lythraceous Alkaloids. Part IX.[1] The Structure and Absolute Configuration of Lythrancine-V, -VI, and -VII

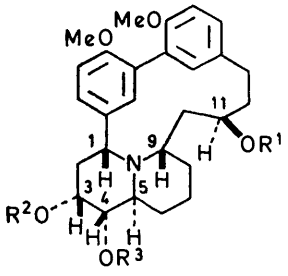
By E. Fujita * and Y. Saeki, Institute for Chemical Research, Kyoto University, Uji, Kyoto-Fu, Japan

Three minor alkaloids, lythrancine-V, -VI, and -VII have been isolated from *Lythrum anceps* Makino. Lythrancine-V is the C-3 epimer of lythrancine-IV. Lythrancine-VI and -VII are the deacetyl derivatives of lythrancine-V. Mass spectral data and a chemical conversion of lythrancine-III into lythrancine-V give their structure and absolute configuration. Lythrancine-V, -VI, and -VII are represented as (II), (VIII), and (IX), respectively.

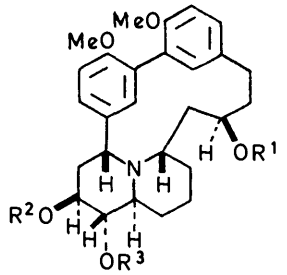
RECENTLY, we published the elucidation of the structure [2] and absolute configuration [3] of seven new alkaloids, lythrancine-I—IV and lythracepine-I—III, isolated from *Lythrum anceps* Makino. The mother liquors from the foregoing alkaloids showed the presence of some other minor alkaloids on t.l.c. Repeated chromatography of the mother liquor of lythrancepine-III resulted in the isolation of a crystalline alkaloid, named lythrancine-V. Preparative t.l.c. of the mother liquor of lythrancine-III led to the isolation of two other minor alkaloids, named lythrancine-VI and -VII.

Lythrancine-V, m.p. 133—134°, was shown to have the molecular formula $C_{33}H_{41}NO_8$, on the basis of elemental analysis and mass spectrum. Its i.r. spectrum had a carbonyl absorption band, but no hydroxy band. The mass spectrum gave a base peak at *m/e* 82 and a peak [1] which is observed in the mass spectra of all quinolizidine-type alkaloids isolated from *L. anceps*. The characteristic fragment ion peaks at *m/e* 520, 492, 479, 460, 419, 418, 400, 337, and 295 were also observed. This pattern is closely similar to that of lythrancine-IV(IV),[3] suggesting the presence of acetyl groups at C-3, -4, and -11.[1] The n.m.r. spectrum of lythrancine-V also supported this; a double doublet (*J* 4 and 10 Hz) at δ 4·23 assignable to 1-H, three acetoxy-groups singlets at 1·95, 2·05, and 2·13, and three signals, assignable to protons on an acetoxylated carbon atom, at 4·62br (s, $W_{\frac{1}{2}}$ 5·5 Hz, 4-H), 4·85 (q, *J* 3 Hz, 3-H), and 5·28br (m, 11-H) were observed. Furthermore, two singlets at δ 3·87 and 3·90 assignable to methoxy-groups were detected. The values *J* 3 and $W_{\frac{1}{2}}$ 5·5 Hz for 3- and 4-H suggested that they were in the equatorial orientation. This led to an assignment of structure (II) to lythrancine-V. The following chemical conversion unequivocally confirmed it to be correct.

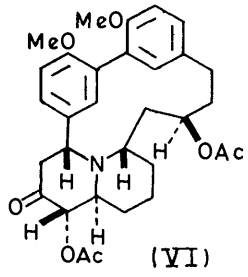
Lythrancine-III(III) [3] on treatment with activated neutral alumina in benzene gave an isomer. This substance on acetylation with acetic anhydride–pyridine yielded lythrancine-IV(IV), whereas on alkaline hydrolysis with 1% methanolic potassium hydroxide, it gave lythrancine-I(I). In the n.m.r. spectrum of this isomer, two acetoxy-signals appeared at δ 1·97 and 2·07, indicating the presence of two acetates. A narrow triplet with *J* 3 Hz at δ 4·73 was assigned to an equatorial proton on C-4, because of the close similarity to the 4-H signal [3] of lythrancine-IV(IV). Another broad multiplet at δ 5·30 was assigned to H-11. The mass spectrum of this compound showed the molecular ion peak at *m/e* 537 which corresponded to $C_{31}H_{39}NO_7$, the same molecular formula as for lythrancine-III(III), and a fragment ion peak at *m/e* 478 (*M* − 59), characteristic of 11-acetoxy-alkaloids of the quinolizidine-type isolated from *L. anceps*.[1] In addition, fragment ion peaks † at *m/e* 460, 419, 418, 337, and 295 supported the presence of a hydroxy-group at C-3 and an acetoxy-group at C-4.[1] Thus, structure (V) was assigned to this isomer.



(I) $R^1 = R^2 = R^3 = H$
(III) $R^1 = R^2 = Ac, R^3 = H$
(IV) $R^1 = R^2 = R^3 = Ac$
(V) $R^1 = R^3 = Ac, R^2 = H$



(II) $R^1 = R^2 = R^3 = Ac$
(VII) $R^1 = R^3 = Ac, R^2 = H$
(VIII) $R^1 = H, R^2 = R^3 = Ac$
(IX) $R^1 = R^2 = Ac, R^3 = H$



(VI)

Jones oxidation of compound (V) gave a dehydro-derivative (VI), which was reduced by sodium borohydride in methanol to give the desired 3-β-ol (VII) as sole product. The mass spectrum was very similar to that of (V). The stereoselective formation of this axial alcohol was anticipated by consideration of the stereomodel of the ketone (VI). Acetylation of compound (VII) yielded lythrancine-V as was expected. Thus, the structure and absolute configuration of lythrancine-V was established as (II).

Lythrancine-VI was obtained as an oil, but its homogeneity was shown by t.l.c., n.m.r., and mass spectra. Its i.r. spectrum had hydroxy and carbonyl absorptions.

† This compound alone gave a fragment ion at *m/e* 83 but not at 82. The reason is not clear.

[1] Part VIII, E. Fujita and Y. Saeki, preceding paper.
[2] E. Fujita and Y. Saeki, *J.C.S. Perkin I*, 1972, 2141.
[3] E. Fujita and Y. Saeki, *J.C.S. Perkin I*, 1973, 297.

The alkaloid on acetylation with acetic anhydride–pyridine afforded lythrancine-V (II). The mass spectrum of lythrancine-VI showed the molecular ion peak at *m/e* 537 which corresponded to $C_{31}H_{39}NO_7$, and a fragment ion peak at *m/e* 520 showed the presence of a hydroxy-group at C-11. The fragment ion peaks at *m/e* 479, 460, 419, 418, 337, and 295 suggested acetoxy-groups at C-3 and C-4.[1] Hence, structure (VIII) was assigned to lythrancine-VI.

Lythrancine-VII was shown to have the same molecular weight as lythrancine-VI from the molecular ion peak at *m/e* 537 in its mass spectrum. The i.r. spectrum showed hydroxy and carbonyl bands. The n.m.r. spectrum suggested the presence of two secondary acetates. The alkaloid on acetylation with acetic anhydride–pyridine also gave lythrancine-V(II). A fragment ion peak at *m/e* 478 (*M* − 59) showed that one of the two acetoxy-groups must be at C-11. Furthermore, the fragment ion peaks at *m/e* 437, 418, 377, and 295 suggested the second acetoxy-group was at C-3 and a hydroxy-group was present at C-4. Thus, the structure of lythrancine-VII is (IX).

Mass spectral data of lythrancine-V–VII and related compounds

m/e	579	537	520	492	479	478	460	450	437	432	419	418	390	374	337	295	253	82
	Relative intensity (%)																	
Lythrancine-V (II)	14 (M^+)		33	4	8		33			6	4	6			5	7	5	100
Isomer (V)		35 (M^+)				42	21	7	14	3	7	11			3	3	10	100 *
Compound (VII)		17 (M^+)				40	14	4	10	2	12	17			2	5	14	100
Lythrancine-VI (VIII)		22 (M^+)	8	14	8	13	12			8	16	23			7	6	5	100
Lythrancine-VII (IX)		8 (M^+)				21		2	6			28	3	4		6	7	100

* In this case only a base peak at *m/e* 83 was observed.

EXPERIMENTAL

M.p.s were taken on a micro hot-stage apparatus and were uncorrected. I.r. spectra were measured for chloroform solutions on a Hitachi EPI-S_2 spectrometer and optical rotations on a JASCO DIP-180 automatic polarimeter for chloroform solutions at room temperature. N.m.r. spectra were taken on a Varian T-60 spectrometer in deuteriochloroform with tetramethylsilane as internal standard. Mass spectra were determined on a Hitachi RMU-6D mass spectrometer. Mass spectral stick diagrams are given in Supplementary Publications No. SUP 20519 (6 pp.).†

Silicic acid for chromatography refers to Kieselgel 0·05—0·2 mm (Merck) unless otherwise noted. Preparative t.l.c. was done on 20 cm plates with a 2 mm layer of Kieselgel F 254 (Merck) and was developed with methylene dichloride–ethyl acetate (1 : 1). Recovery of the compounds were effected by elution with methylene dichloride–methanol (1—3%).

Homogeneity of oils was determined by t.l.c., n.m.r., and mass spectra, and the identity of compounds was established by m.p. and the i.r. spectra.

Isolation of Lythrancine-V (II).—The mother liquor ‡ (440 mg) of lythrancepine-III in methylene dichloride was chromatographed twice on silicic acid. Elution with methylene dichloride gave crystals. Recrystallisation from methanol gave *lythrancine*-V (II) (154 mg, 0·00033%), m.p. 133—134°, $[\alpha]_D$ + 91° (*c* 0·55), $\nu_{max.}$ 1732 cm^{-1}, $\lambda_{max.}$ (EtOH) 290 nm (ε 8200), δ 1·95 (3H, s, OAc), 2·05 (3H, s, OAc), 2·13 (3H, s, OAc), 3·87 (3H, s, OMe), 3·90 (3H, s, OMe), 4·23 (1H, dd, *J* 4 and 10 Hz, 1-H), 4·62br (1H, s, $W_{\frac{1}{2}}$ 5·5 Hz, 4-H), 4·85 (1H, q, *J* 3 Hz, 3-H), and 5·28 (1H, m, 11-H) (Found: C, 67·35; H, 7·15; N, 2·2%; M^+, 579·2840. $C_{33}H_{41}NO_8$ requires C, 68·35; H, 7·15; N, 2·4%; *M*, 579·2832).

Isolation of Lythrancine-VI (VIII) *and* -VII (IX).—The mother liquor ‡ (dried residue; 115 mg) obtained after crystallisation of lythrancine-III (III) was subjected to preparative t.l.c. (ca. 40 mg per plate; three developments). This gave two bands which were visualized with u.v. light. The lower band gave *lythrancine*-VI (VIII) (Found: M^+, 537·2706. $C_{31}H_{39}NO_7$ requires *M*, 537·2727) (45 mg, 9 × 10^{-5}%), oil, $[\alpha]_D$ + 25·5° (*c* 1·8), $\nu_{max.}$ 3480 and 1735 cm^{-1}, δ 1·96 (3H, s, OAc), 2·06 (3H, s, OAc), 3·90 (3H, s, OMe), 3·94 (3H, s, OMe), 4·20 (1H, dd, *J* 6 and 8 Hz, 1-H), and 4·80—5·40 (2H, m, 3- and 4-H). The upper band afforded oily lythrancine-VII (IX) (Found: M^+, 537·2753. $C_{31}H_{39}NO_7$ requires *M*, 537·2727) (37 mg, 8 × 10^{-5}%), $[\alpha]_D$ + 101·5° (*c* 0·37), $\nu_{max.}$ 3450 and 1725 cm^{-1}, δ 2·01 (3H, s, OAc), 2·10 (3H, s, OAc), 3·90 (6H, s, 2 × OMe), 4·25 (1H, dd, *J* 4 and 10 Hz, 1-H), 4·90 (1H, m, $W_{\frac{1}{2}}$ 6Hz, 3-H), and 5·30 (1H, m, 11-H).

Conversion of Lythrancine-III (III) *into the Isomer* (V).—A solution of lythrancine-III (III) (1·1 g) in benzene (10 ml) was adsorbed onto a column of activated neutral alumina (Woelm grade I; 30 g) and elution with methylene dichloride–methanol (0·5%) afforded the isomer (V) (950 mg), $C_{31}H_{39}NO_7$ (M^+, 537), as an oil which was shown to be homogeneous on t.l.c., $\nu_{max.}$ 3540 and 1730 cm^{-1}, δ 1·97 (3H, s, OAc), 2·07 (3H, s, OAc), 3·87 (3H, s, OMe), 3·88 (3H, s, OMe), 4·73 (1H, t, *J* 3 Hz, 4-H), and 5·30 (1H, m, 11-H).

Acetylation of Compound (V).—Compound (V) (50 mg) in acetic anhydride–pyridine (1 : 1; 2 ml) was heated at 80° for 5 h. After evaporation of the solvent *in vacuo*, the residue (48 mg) in methylene dichloride was chromatographed on silicic acid and elution with methylene dichloride gave prisms, m.p. 236—237° (from methanol), identical with lythrancine-IV(IV).

Hydrolysis of Compound (V).—Compound (V) (50 mg) was dissolved in 1% methanolic potassium hydroxide (3 ml) and left at room temperature for 2 h. The mixture was poured into water and extracted with methylene dichloride.

† For details of Supplementary Publications see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, Issue No. 20.

‡ These mother liquors were obtained from an experiment carried out in 1964.

Evaporation of the solvent yielded an oil (36 mg), identical with lythrancine-I(I).

Jones Oxidation of the Isomer (V).—Compound (V) (670 mg) in ice-cooled acetone (20 ml) was oxidised by dropwise addition of Jones reagent (1 ml). Methanol (1 ml) was added to decompose the excess of reagent and the solution was evaporated to dryness *in vacuo*. The residue was dissolved in water, made alkaline with aqueous ammonia and extracted with methylene dichloride. The organic layer was washed with water, dried (Na_2SO_4) and evaporated to give an oil. Purification by column chromatography on neutral silicic acid gave the dehydro-derivative (VI) (262mg), an oil which was shown to be homogeneous on t.l.c., $\nu_{max.}$ 1730 cm^{-1}, δ 1·98 (3H, s, OAc), 2·10 (3H, s, OAc), 3·90 (3H, s, OMe), 3·93 (3H, s, OMe), 4·40 (1H, dd, *J* 4 and 11 Hz, 1-H), 4·66 (1H, dd, *J* 1 and 3 Hz, 4-H), and 5·45 (1H, m, 11-H).

Sodium Borohydride Reduction of Compound (VI).—To a solution of compound (VI) (98 mg) in methanol (5 ml), sodium borohydride (150 mg) was added and the mixture was stirred at room temperature for 3 h. The mixture was diluted with water and extracted with methylene dichloride. After evaporation of the solvent, the residue was dissolved in methylene dichloride and chromatographed on silicic acid. Elution with methylene dichloride afforded the alcohol (VII) (78 mg), $\nu_{max.}$ 3470 and 1725 cm^{-1}, δ 1·97 (3H, s, OAc), 2·05 (3H, s, OAc), 3·88 (3H, s, OMe), 3·91 (3H, s, OMe), 4·33 (1H, dd, *J* 4 and 10 Hz, 1-H), 4·57br (1H, s, $W_{\frac{1}{2}}$ 5 Hz, 4-H), and 5·33 (1H, m, 11-H).

Acetylation of Compound (VII).—Compound (VII) (45 mg) was treated with acetic anhydride–pyridine (1 : 2; 3 ml) at 80° for 5 h. After evaporation of the solvent *in vacuo*, the residue in methylene dichloride was passed through a short column of silicic acid. Elution with the same solvent gave prisms (37 mg), m.p. 133—134° (from methanol), identical with lythrancine-V(II).

Acetylation of Lythrancine-VI(VIII).—Lythrancine-VI (VIII) (30 mg) was acetylated with acetic anhydride–pyridine (1 : 5; 6 ml) at 80° for 5 h. The solvent was evaporated to dryness *in vacuo*. The residue in methylene dichloride was passed through a short column of silicic acid to give prisms (24 mg), m.p. 132—134°, identical with lythrancine-V(II).

Acetylation of Lythrancine-VII(IX).—Lythrancine-VII (IX) (10 mg) was acetylated in the same manner as described for lythrancine-VI to give prisms (8 mg), m.p. 133—134°, identical with lythrancine-V(II).

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