Lythraceous Alkaloids. Part VIII.[1] The Mass Spectra of Lythrancine and Lythrancepine Alkaloids

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The mass spectra of the quinolizidine alkaloids isolated from *Lythrum anceps* Makino and their derivatives were taken. The fragmentation mechanism was investigated and the location of hydroxy- or acetoxy-substituent(s) at C-3, -4, and -11 was established.

We have reported [1,2] the structure and stereochemistry of seven novel alkaloids isolated from *Lythrum anceps* Makino. These alkaloids have a common skeleton containing a *cis*-quinolizidine nucleus which is different from that of *Decodon*, *Heimia*, and *Lagerstroemia* alkaloids.[3-6] Hence, the mass spectra of our *Lythrum* alkaloids are expected to be different from those [7] of the other alkaloids. An investigation of the mass fragmentation mechanism should be useful in structural studies of unknown minor alkaloids which have been shown to be present by t.l.c. of the mother liquors from the known alkaloids. These expectations prompted us to explore the mass spectra of the seven alkaloids lythrancine-I—IV and lythrancepine-I—III and of their derivatives. Mass spectral stick diagrams are given in Supplementary Publication No. SUP 10518 (14 pp.).†

First, the mass spectrum of lythrancine-III (3) was investigated in detail, as the most abundant information should be obtained from this alkaloid because of its structure. As shown in Table 1 the molecular ion peak at *m/e* 537, the base peak at *m/e* 82, and other major fragment ion peaks at *m/e* 478, 450, 437, 418, 390, 377, 295, and 253 were observed in the mass spectrum. The constitutions of these ions were determined as shown in Table 1 by high resolution mass spectrum.

The first fragmentation to give a peak with *m/e* 478 was shown to occur by a loss of an acetoxyl radical from the parent ion (3), which was supported by the presence of a metastable ion.‡ It was concluded that this fragment ion (9) was formed by a loss of an acetoxyl radical from C-11, because a peak at *m/e* 436 attributed to the ion (8) was observed in the mass spectra of lythrancine-I (Table 2) and lythrancine-II (Table 3). The ion (8) corresponded to $M^+ - 17(\dot{O}H)$ in lythrancine-I and also to $M^+ - 59(\dot{O}AC)$ in lythrancine-II.

TABLE 1

Mass spectral data of lythrancine-III

Peak at *m/e*	Formula	Calc.	Found	Structure
537(35) [a]	$C_{31}H_{39}NO_7$	537·2727	537·2707	(3)
478(55)	$C_{29}H_{36}NO_5$	478·2593	478·2619	(9)
450(7)	$C_{27}H_{32}NO_5$	450·2280	450·2289	(17)
437(10)	$C_{26}H_{31}NO_5$	437·2202	437·2222	(22)
418(40)	$C_{27}H_{32}NO_3$	418·2382	418·2393	(13)
390(5)	$C_{25}H_{28}NO_3$	390·2069	390·2086	(26)
377(6)	$C_{24}H_{27}NO_3$	377·1991	377·1985	(29)
295(7)	$C_{19}H_{19}O_3$	295·1334	295·1349	(33)
253(10)	$C_{17}H_{17}O_2$	253·1228	253·1249	(43) or (44)
82(100)	C_5H_8N	82·0656	82·0649	(32)

[a] Relative intensity (%) for base peak (100%).

TABLE 2

Lythrancine-I

m/e	453 (M^+)	436	418	408	395
Relative intensity (%)	45	19	14	22	9
Structure	(1)	(8)	(13)	(16)	(21)
m/e	390	377	295	253	82
Relative intensity (%)	18	7	6	12	100
Structure	(26)	(29)	(33)	(43) or (44)	(32)

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

‡ All fragmentations described below were supported by the observation of the corresponding metastable ions.

[1] Part VII, E. Fujita and Y. Saeki, preceding paper.

[2] E. Fujita and Y. Saeki, *J.C.S. Perkin I*, 1972, 2141.

[3] J. P. Ferris, C. B. Boyce, and R. C. Briner, *J. Amer. Chem. Soc.*, 1971, **93**, 2942.

[4] J. P. Ferris, R. C. Briner, and C. B. Boyce, *J. Amer. Chem. Soc.*, 1971, **93**, 2953.

[5] J. P. Ferris, R. C. Briner, and C. B. Boyce, *J. Amer. Chem. Soc.*, 1971, **93**, 2958.

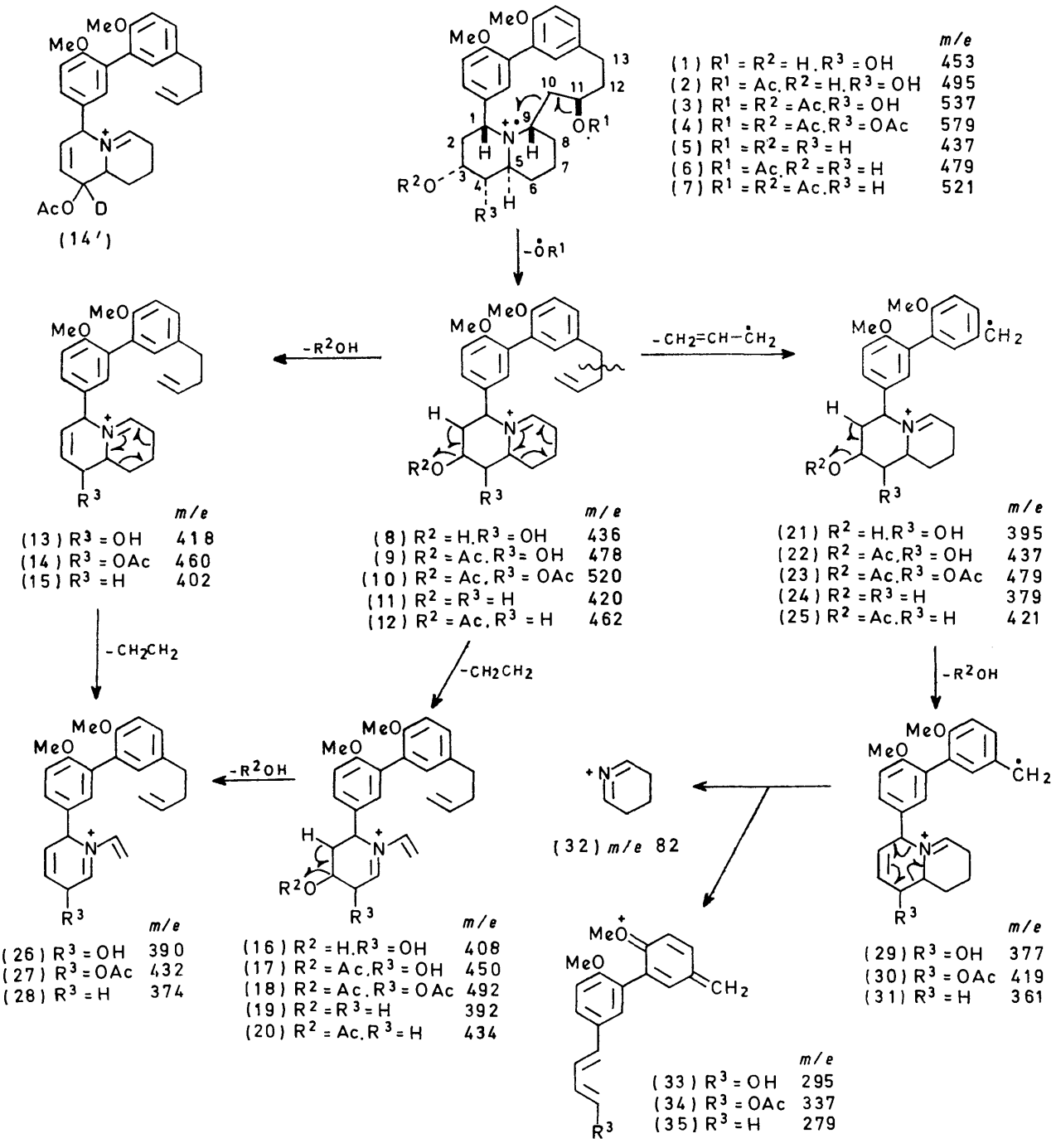
[6] J. P. Ferris, C. B. Boyce, R. C. Briner, U. Weiss, I. H. Qureshi, and N. E. Sharpless, *J. Amer. Chem. Soc.*, 1971, **93**, 2963.

[7] H. Appel and H. Achenbach, *Tetrahedron Letters*, 1966, 5789.

The fragment ion (9), *m/e* 478, was the most important intermediate, from which three directions of cleavage started. The loss of acetic acid from C-3 and C-2 of ion (9) gave a peak at *m/e* 418, which corresponded to (13). The fact that a peak of the fragment ion, to which structure (14′) was assignable, was observed at *m/e* 461, but no peak at *m/e* 460 in the mass spectrum of 4-deuteriolythrancine-IV (Table 5) was evidence for the cleavage of (9) to (13).

The second route was the loss of ethylene by a retro-Diels–Alder reaction, which gave the fragment ion (17) at *m/e* 450. The third route occurred by cleavage at the benzylic position, and the fragment ion (22) appeared at *m/e* 437 due to loss of an allyl radical.

A subsequent retro-Diels–Alder cleavage of (13) with loss of ethylene gave ion (26) at *m/e* 390, which was alternatively formed by the loss of acetic acid from ion (17). From ion (22), ion (29), *m/e* 377, was produced by



SCHEME 1

the elimination of acetic acid. The possibility that this ion (29) was produced by loss of an allyl radical from (13) was obviated by the lack of the corresponding metastable ion. Further retro-Diels–Alder reactions of ion

TABLE 3

Lythrancine-II

m/e	495 (M^+)	436	418	408	395
Relative intensity (%)	60	100	36	19	16
Structure	(2)	(8)	(13)	(16)	(21)
m/e	390	295	253	82	
Relative intensity (%)	3	5	16	80	
Structure	(26)	(33)	(43) or (44)	(32)	

TABLE 4

Lythrancine-IV

m/e	579 (M^+)	520	492	479	460	432
Relative intensity (%)	25	51	4	13	64	5
Structure	(4)	(10)	(18)	(23)	(14)	(27)
m/e	419	418	337	295	253	82
Relative intensity (%)	6	7	5	6	14	100
Structure	(30)	(42)	(34)	(36)	(43) or (44)	(32)

TABLE 5

4-Deuteriolythrancine-IV

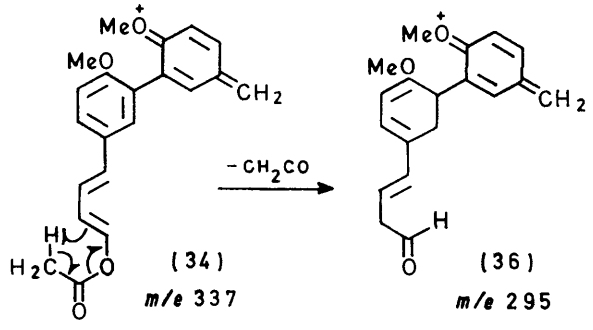
m/e	580 (M^+)	521	493	480	461	433
Relative intensity (%)	21	40	8	16	41	8
m/e	420	419	338	296	253	82
Relative intensity (%)	6	8	6	6	13	100

(29) gave rise to the base peak ion (32) at *m/e* 82 and the remaining fragment ion (33) at *m/e* 295.

In the mass spectrum of lythrancine-I (Table 2), the molecular ion (1), *m/e* 453, the base peak ion (32), *m/e* 82, and the fragment ion (8), *m/e* 436 ($M^+ - 17$), were observed. The intermediate ion (8) was transformed into (13), *m/e* 418, (16), *m/e* 408, and (21), *m/e* 395, by the loss of water, ethylene, or allyl radical, respectively. Further cleavages of (13) and (16) with loss of ethylene and water, respectively, resulted in the formation of ion (26), *m/e* 390, while ion (29), *m/e* 377, was formed by the loss of water from ion (21). Ion (29) was cleaved into the base peak ion (32), *m/e* 82, and another ion (33), *m/e* 295, as in the case of lythrancine-III.

The mass spectrum (Table 3) of lythrancine-II revealed the molecular ion (2), *m/e* 495. The other fragment ion peaks were similar to those of lythrancine-I.

The molecular ion (4) at *m/e* 579 and a key fragment ion (10) at *m/e* 520 formed by the loss of an acetoxyl radical from (4) were observed in the mass spectrum of lythrancine-IV (Table 4). The ions (14), (18), and (23) were subsequently formed from (10) by eliminations of acetic acid, ethylene, or allyl radical, and occurred at *m/e* 460, 492, and 479 respectively. Cleavages of (14) and (18) gave the same ion (27) at *m/e* 432. Further fragmentation of (23) produced (32) and (34) *via* (30), *m/e* 419. Ion (34), *m/e* 337, was an enol-acetate, from which another fragment ion (36), *m/e* 295, was formed by elimination of ketene by the mechanism shown in Scheme 2.



SCHEME 2

As expected, the investigation of the mass spectra of lythrancepine-I (Table 6) and lythrancepine-II (Table 7) clarified that the fragmentation pattern was the same for both alkaloids; except for a molecular ion (5), *m/e* 437, for lythrancepine-I and (6), *m/e* 479, for lythrancepine-II, the major fragmentations were identical. The common key intermediate ion (11), *m/e* 420, produced (15), (19), and (24) at *m/e* 402, 392, and 379, by loss of water, ethylene, or allyl radical, respectively. Ions (15) and (19) gave the common fragment ion (28) at *m/e* 374 by loss of ethylene and water, respectively. Ion (24) gave ion (31) at *m/e* 361, which was cleaved into (32) and (35), *m/e* 279.

In the mass spectrum of lythrancepine-III (Table 8), the molecular ion (7), *m/e* 521, and a key fragment ion

TABLE 6

Lythrancepine-I

m/e	437 (M^+)	420	402	392	379
Relative intensity (%)	70	16	16	32	7
Structure	(5)	(11)	(15)	(19)	(24)
m/e	374	361	279	253	82
Relative intensity (%)	28	12	12	16	100
Structure	(28)	(31)	(35)	(43) or (44)	(32)

TABLE 7

Lythrancepine-II

m/e	479 (M^+)	420	402	392	379
Relative intensity (%)	16	40	30	5	12
Structure	(6)	(11)	(15)	(19)	(24)
m/e	374	361	279	253	82
Relative intensity (%)	4	5	5	10	100
Structure	(28)	(31)	(35)	(43) or (44)	(32)

(12), *m/e* 462, were observed. As in foregoing pattern, fragmentations of ion (12) to (15), *m/e* 402, (20), 434, and (25), 421, of (15) and (20) to (28), 374, and of (25), to (31), 361, were observed. Further fragment ions (32) and (35), *m/e* 279, were also observed.

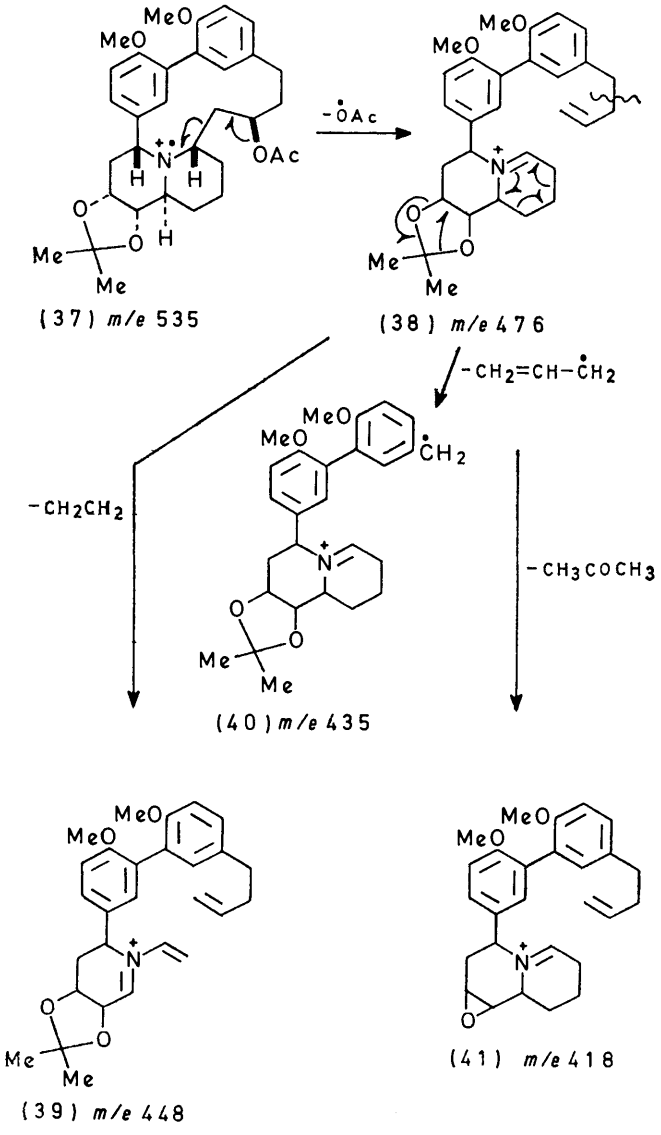
The mass spectrum of lythrancine-II acetonide (Table 9) showed the molecular ion (37), *m/e* 535, and

TABLE 8

Lythrancepine-III

m/e	521 (M^+)	462	434	421	402
Relative intensity (%)	22	70	4	10	70
Structure	(7)	(12)	(20)	(25)	(15)
m/e	374	361	279	253	82
Relative intensity (%)	5	5	11	7	100
Structure	(28)	(31)	(35)	(43) or (44)	(32)

peaks at *m/e* 476, 448, 435, and 418. These were attributed to ions (38), (39), (40), and (41), as shown in Scheme 3.



SCHEME 3

The mass spectra of the 4-epimer of lythrancine-IV [2] (Table 10) and the 3-epimer of lythrancepine-III (Table 11) were very similar to those of lythrancine-IV (Table 4) and lythrancepine-III (Table 8), respectively. The mass spectra of 4-deuteriolythrancine-IV (Table 5) and 3-deuterio-3-epilythrancepine-III (Table 12) also provide support for the cleavage mechanism shown in Scheme 1. Thus, the fragmentation pattern shown in Scheme 1 occurs for all the quinolizidine-type alkaloids of *L. anceps*.

TABLE 9

Lythrancine-II acetonide

m/e	535 (M^+)	476	448	435	418	253	82
Relative intensity (%)	14	51	7	13	17	11	100
Structure	(37)	(38)	(39)	(40)	(41)	(43) or (44)	(32)

The foregoing results can be summarised as follows. (*a*) A peak at $M^+ - 17$ is observed in the mass spectra of 11-hydroxyalkaloids, whilst a peak at $M^+ - 59$ occurs in those of 11-acetoxyalkaloids. (*b*) If peaks at *m/e* 402, 374, 361, and 279 are observed in the mass spectra, they derive from alkaloids with no substituent at C-4. (*c*) A peak at *m/e* 295 suggests the presence of a hydroxy- or

TABLE 10

4-Epilythrancine-IV

m/e	579 (M^+)	520	492	479	460	432
Relative intensity (%)	40	30	6	17	60	5
Structure		(10)	(18)	(23)	(14)	(27)
m/e	419	418	337	295	253	82
Relative intensity (%)	8	10	7	10	18	100
Structure	(30)	(42)	(34)	(36)	(43) or (44)	(32)

an acetoxy-group at C-4. Where there is an additional peak (34), *m/e* 337, an acetoxy-group is present at C-4.

TABLE 11

3-Epilythrancepine-III

m/e	521 (M^+)	462	434	421	402
Relative intensity (%)	28	48	4	11	56
Structure		(12)	(20)	(25)	(15)
m/e	374	361	279	253	82
Relative intensity (%)	6	5	11	8	100
Structure	(28)	(31)	(35)	(43) or (44)	(32)

TABLE 12

3-Deuterio-3-epilythrancepine-III

m/e	522 (M^+)	463	435	422	403
Relative intensity (%)	26	54	4	12	70
m/e	375	362	280	253	82
Relative intensity (%)	6	5	12	8	100

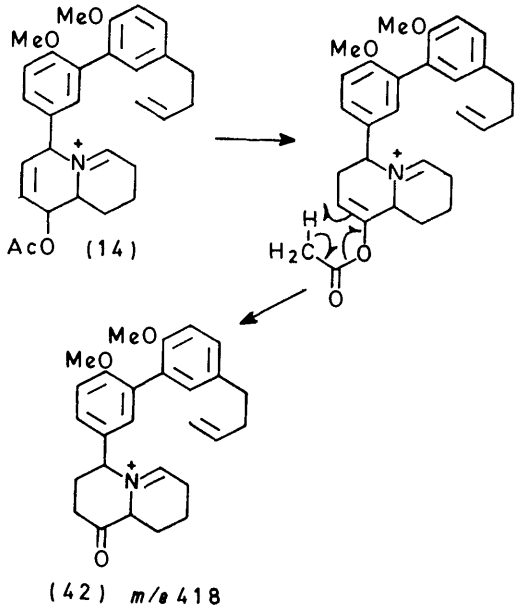
TABLE 13

11-Deuteriolythrancine-II acetonide

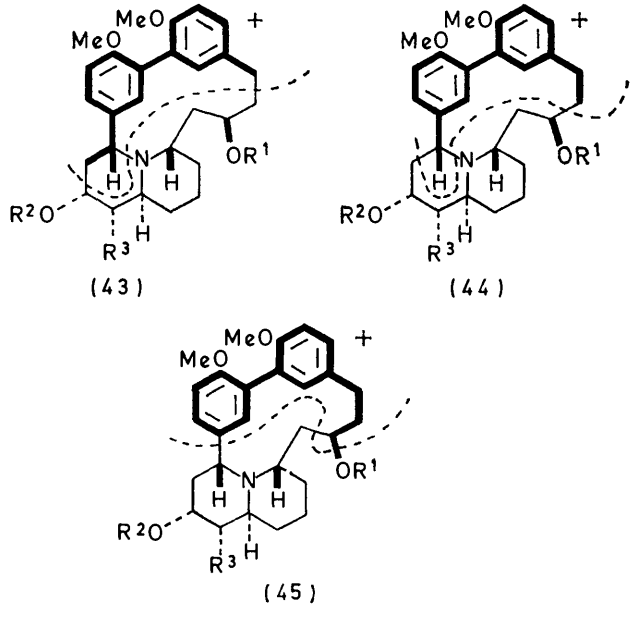
m/e	536 (M^+)	477	449	435	419	253	82
Relative intensity (%)	14	48	7	12	17	6	100

When no such peak is present, there is a hydroxy group at C-4. (*d*) Only one major ion peak (13), *m/e* 418, is observed in the case of 4-hydroxy-substitution, whilst two peaks, *m/e* 418 and 419, are observed for 4-acetoxy-

substitution. The peak, *m/e* 418, for 4-acetoxy-compounds is attributed to ion (42) which is formed from (14) by the mechanism shown in Scheme 4. A peak at *m/e*



SCHEME 4



SCHEME 5

419 is due to ion (30). (*e*) Whether a hydroxy- or an acetoxy-group is the substituent at C-3 is decided by the fragment ion ($M^+ - \dot{O}R^1 - R^2OH$). Thus, 3-hydroxy-substitution gives a fragment ion, $M^+ - \dot{O}R^1 - 18$, while the 3-acetoxy-substitution gives a fragment ion, $M^+ - \dot{O}R^1 - 60$. (*f*) A common fragment ion at *m/e* 253 was observed for all compounds. The constitution, $C_{17}H_{17}O_2$, was obtained by high resolution mass spectra, and three structures (43)—(45) were considered (Scheme 5). In the mass spectrum of 11-deuteriolythrancine-II acetonide (Table 13), however, a fragment ion at *m/e* 253 was also observed. This excludes the possibility (45). We have not decided between the possibilities (43) or (44). (*g*) A common fragment ion peak at *m/e* 82 due to (32) is observed for all compounds.

EXPERIMENTAL

Mass spectra were taken on a Hitachi model RMU-6D mass spectrometer, equipped with a direct inlet system, at 70eV and sample at 250—300°. High resolution mass spectrum was measured on JMS-OISG double focusing mass spectrometer at 75eV using perfluorokerosene as internal standard.

4-Deuteriolythrancine-IV.—To a solution of dehydrolythrancine-III [2] (430 mg) in dry THF (20 ml) lithium aluminium deuteride (200 mg) was added and the mixture was stirred at room temperature overnight. Usual work-up yielded an oil (290 mg), which was treated with acetic anhydride–pyridine (1 : 5; 6 ml) at 80° for 5 h. The mixture was evaporated to dryness *in vacuo*, and the residue (320 mg) was chromatographed on silicic acid in methylene-dichloride. Elution with methylene dichloride gave 4-deuteriolythrancine-IV (120 mg), m.p. 212—213° (from methanol).

Lythrancine-II *Acetonide*.—To a solution of lythrancine-II (200 mg) in dimethylformamide (1 ml), were added 2,2-dimethoxypropane (4 ml) and toluene-*p*-sulphonic acid (2 mg). The mixture was refluxed at 100° for 8 h with stirring and was evaporated to dryness *in vacuo*. The residue was dissolved in water, made alkaline with ammonia, and extracted with methylene dichloride. Evaporation of the solvent gave an oily lythrancine-II acetonide (215 mg), $\nu_{max.}$ ($CHCl_3$) 1725 cm^{-1}, δ ($CDCl_3$) 1·27 (3H, s, Me), 1·39 (3H, s, Me), 1·96 (3H, s, OAc), 3·85 (3H, s, OMe), 3·88 (3H, s, OMe), and 5·46 (1H, m, 11-H).

3-Deuterio-3-epilythrancepine-III.—Lythrancine-III *O*-tosylate (410 mg) in dry THF (20 ml) was reduced with lithium aluminium deuteride (200 mg) at room temperature. An oil (310 mg) obtained by the usual work-up was acetylated with acetic anhydride–pyridine (1 : 5; 6 ml) at 80° for 4 h. After evaporation of the solvent, the residue (270 mg) in methylene dichloride was chromatographed on silicic acid and elution with methylene dichloride–methanol (1%) afforded the title compound as an oil (75 mg).

11-Deuteriolythrancine-II *Acetonide*.—Lythrancine-II acetonide (1·15 g) was converted to dehydrolythrancine-I acetonide (270 mg), $\nu_{max.}$ ($CHCl_3$) 1698 cm^{-1}, δ 1·30 (3H, s, Me), 1·36 (3H, s, Me), 3·85 (3H, s, OMe), 3·80 (3H, s, OMe), and 4·25 (1H, dd, *J* 5 and 10 Hz, 1-H), by successive treatment with 5% methanolic potassium hydroxide (30 ml) and Jones reagent (1 ml) in acetone (30 ml) at room temperature. Dehydrolythrancine-I acetonide (100 mg) in THF (1 ml) was reduced with sodium borodeuteride (50 mg) at room temperature for 2 h. The mixture was diluted with water and extracted with methylene dichloride. After evaporation of the solvent, the residue (75 mg) was treated with acetic anhydride–pyridine (1 : 1; 1 ml) at 80° for 4 h. The mixture was evaporated to dryness *in vacuo*, and the residue (72 mg) in methylene dichloride was chromatographed on silicic acid. Elution with methylene dichloride gave the title compound as an oil (31 mg).

We thank Mr. A. Kato, Kyoto University, for mass spectra.

[2/748 *Received*, 30*th March*, 1972]