Tetrahedron, 1967, Vol. 23, pp. 603 to 632. Pergamon Press Ltd. Printed in Northern Ireland

PYRROLES AND RELATED COMPOUNDS—X[1]

MASS SPECTROMETRY IN STRUCTURAL AND STEREOCHEMICAL PROBLEMS—XC[2]

MASS SPECTRA OF LINEAR DI-, TRI- AND TETRAPYRROLIC COMPOUNDS

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(*Received* 3 *December* 1965; *in revised form* 23 *March* 1966)

Abstract—Mass spectra of 55 di-, tri- and tetra-pyrroles (Table 1) are recorded (Table 2); these include prodigiosin and five bile pigments. The factors affecting the various types of cleavages observed are discussed. Fragmentations of the side-chains usually follow similar patterns to those observed with mono-pyrroles, although, with pyrromethanes, cleavage of alkyl or carboxylic ester groups neighbouring the methylene bridge may be favoured by the formation of pyrromethene-like species or tricyclic pyrromethenes respectively. Cleavages between the nuclei are profoundly affected by the nature of the linkage involved e.g. pyrromethanes and pyrroketones undergo fairly ready internuclear fragmentation, whereas the pyrromethenes (as might be expected) are much more stable, and cleavage of pyrrole-pyrrole bonds (as in prodigiosin) appears to be a very unfavourable process.

IN CONTINUATION of our studies of the mass spectrometric behaviour of pyrrole[3] and porphyrin[1] derivatives we have now investigated the fragmentation of a number of pyrromethanes, pyrromethenes and pyrroketones, and of their tri- and tetra-pyrrolic analogues. Many of these compounds were prepared in the course of our work (at Liverpool) directed towards stepwise methods for porphyrin synthesis,[4,5] and the mass spectrometry was carried out at both Liverpool and Stanford. The data obtained have already proved very useful in the interpretation of the fragmentation of bile pigments, and of prodigiosin, and examples are given in this paper.

The mass spectra were determined with three different spectrometers. (C.E.C., Atlas, and A.E.I.) and the earlier (dipyrrolic samples were run on "hot-inlet" systems. Satisfactory spectra of the less volatile tri- and tetra-pyrroles however could only be obtained by the use of "direct inlet" systems. One such device has already been described,[6] and another has recently been designed by our colleague Dr. D. F. Shaw (Liverpool) for use with the MS9 spectrometer. Some of the dipyrrolic compounds were also run by direct inlet, and comparison of their spectra with those of the same compounds run by the hot-inlet, showed (as might be expected) that the molecular ions are stronger in the direct inlet spectra, and that fragment ions were less intense; however, the general pattern of fragmentation was unchanged. Later dipyrrolic

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compounds were therefore run on the direct inlet as this was more convenient.

In this paper we shall first discuss the fragmentation of the simpler dipyrrolic compounds, and then utilise the results in interpreting the behaviour of the higher mol. wt. compounds. Structurally and mass spectrometrically the dipyrroles may be conveniently divided into three groups—(a) pyrromethanes (b) pyrromethenes and (c) pyrroketones.

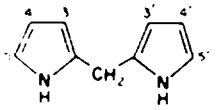
Pyrromethanes

The pyrromethanes studied (Table 1) include sixteen 2,2′-pyrromethanes; one 2,3′- and one 3,3′-pyrromethane. Their fragmentation patterns are very dependent on the nature of the substituents, but in general they all show a fairly intense molecular ion, which allows determination of the mol. wt.; exceptions are the pyrromethane carboxylic acids (VIII and IX) which undergo very ready decarboxylation, as do simple pyrrole carboxylic acids.[3] The types of fragmentations which pyrromethanes undergo may be conveniently classified into three main groups, fragmentation of side-chains, inter-nuclear cleavage to give mono-pyrrolic fragments, and formation of

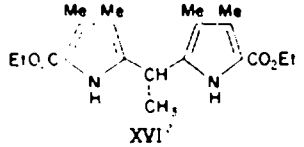
TABLE 1. STRUCTURES OF DI-, TRI- AND TETRA-PYRROLES INVESTIGATED

(Abbreviations: P^{H} = $CH_2CH_2CO_2H$, P^{Me} = $CH_2CH_2CO_2Me$, V = $CH{=}CH_2$)

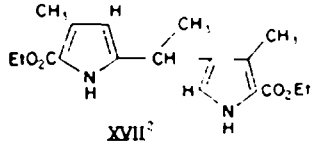
(a) *Pyrromethanes*



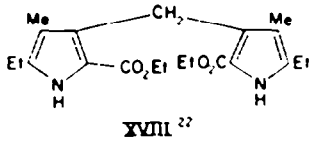
No.	5	4	3	3′	4′	5′	Ref.
I	EtO_2C	Me	Et	Me	Et	Me	8, 16
II	$PhCH_2O_2C$	Me	Et	Me	Et	Me	16
III	$PhCH_2O_2C$	Me	Me	Me	Et	Me	17
IV	EtO_2C	Me	Et	Et	Me	CO_2Et	8
V	MeO_2C	Me	P^{Me}	P^{Me}	Me	CO_2Me	18
VI	H	Me	P^{Me}	P^{Me}	Me	CO_2Me	18
VII	$PhCH_2O_2C$	Me	P^{Me}	P^{Me}	Me	CO_2CH_2Ph	19
VIII	HO_2C	Me	P^{Me}	P^{Me}	Me	CO_2CH_2Ph	18
IX	(HO_2C)	Me	P^{Me}	P^{Me}	Me	(CO_2H)	4
X	Me_2NOC	Me	P^{Me}	P^{Me}	Me	CO_2CH_2Ph	20
XI	EtO_2C	Me	CO_2Et	Me	Et	Me	16
XII	MeO_2C	Me	CO_2Me	Me	Et	Me	--
XIII	MeO_2C	Me	CO_2Me	Me	Me	Me	—
XIV	EtO_2C	Me	COMe	Me	CO_2Et	Me	4
XV	EtO_2C	Me	CO_2Et	CO_2Et	Me	CO_2Et	8



XVI[7]



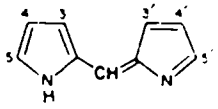
XVII[2]



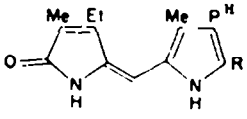
XVIII[22]

Table 1. (*Contd.*)

(b) *Pyrromethenes*

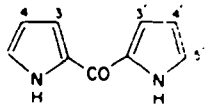


No.	5	4	3	3′	4′	5′	Ref.
XIX	Me	Me	H	H	Me	Me	10
XX	Me	Et	Me	Me	Et	Me	10
XXI	Me	P[H]	Me	Me	P[H]	Me	10
XXII	$PhCH_2O_2C$	Me	Et	Me	Et	Me	13
XIII	EtO_2C	Me	Et	Et	Me	CO_2Et	25
XXIV	Me	CO_2Et	Me	Me	CO_2Et	Me	10
XXV	Br	Me	Et	Me	Et	Me	10
XXVI	Br	Me	Et	Me	Et	CH_2Br	10, 17
XXVII	Br	Me	Et	Me	Et	CH_2OMe	10, 17
XXVIII	Br	Me	Me	Me	Me	CH_2Br	10, 17
XXIX	Br	Me	P	Me	Et	Me	21
XXX	Br	Me	CO_2Et	Me	Et	Me	17
XXXI	MeO	Me	Et	Me	p[H]	Me	10

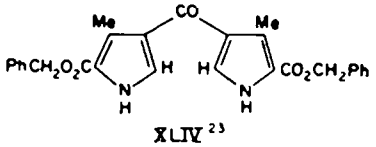


XXXII[5, 2] R = Me
XXXIII[5, 2] R = H

(c) *Pyrroketones*



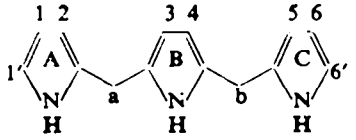
No.	5	4	3	3′	4′	5′	Ref.
XXIV	H	H	H	H	H	H	8
XXXV	Me	Me	H	H	Me	Me	8
XXXVI	Me	Et	Me	Me	Et	Me	8, 13
XXXVII	H	Me	Et	Me	Et	Me	13
XXXVIII	PhC_2O_2O	Me	Et	Me	Et	Me	13
XXXIX	$PhCH_2O_2C$	Me	Et	Me	P[Me]	Me	23
XL	$PhCH_2O_2C$	Me	P[Me]	Me	P[Me]	Me	23
XLI	$PhCH_2O_2C$	Me	P[Me]	Me	P[Me]	CH_2Cl	23
XLII	Me	CO_2Et	Me	Me	Et	Me	13
XLIII	Me	CO_2Et	Me	Me	CO_2Et	Me	8, 13



XLIV[23]

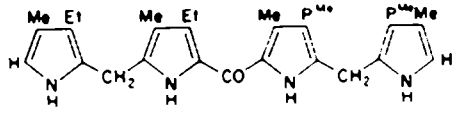
Table 1. (*contd.*)

(d) *Tripyrranes*

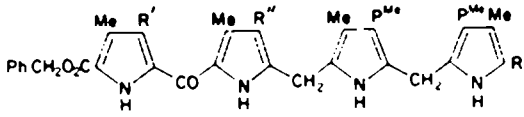


No.	1′	1	2	a	3	4	b	5	6	6′	Ref.
XLV	$PhCH_2O_2C$	Me	Et	CH_2	Me	Et	CH_2	Et	Me	CO_2Et	4
XLVI	$PhCH_2O_2C$	Me	Et	CH_2	Me	Et	CH_2	Et	Me	CO_2CH_2Ph	4
XLVII	$PhCH_2O_2C$	Me	P^{Me}	CH_2	P^{Me}	Me	CO	Me	Et	Me	24

(e) *Tetrapyrranes (Bilanes)*[8,10,84]

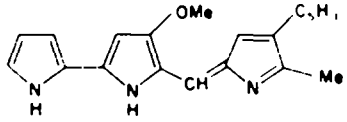


XLVIII

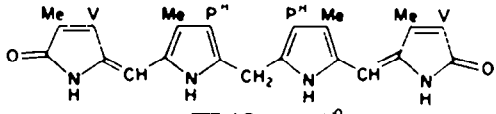


XLIX R = CHO, R′ = R″ = Et
L R = CO_2CH_2Ph, R′ = R″ = Et
LI R = CO_2CH_2Ph, R′ = Me, R″ = Et
LII R = CO_2CH_2Ph, R′ = Et, R″ = Me

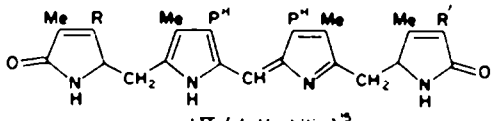
(f) *Natural products*



LIII (Prodigiosin)[26]



LIV (Bilirubin)[9]



LV (d-Urobilin)[15],
(a) R = V, R′ = Et, or
(b) R = Et, R′ = V

tricyclic fragmentation products (when the methylene bridge is flanked by neighbouring carbonyl substituents). Cleavage between the two nuclei is often the predominant process but fragmentation of the side-chains may predominate, especially if several carbonyl substituents are present (e.g. XI, XII, and XIII).

Simple cleavages from the intact skeleton are closely analogous in many cases to those observed with the monopyrroles studied earlier,[3] and the various types of fragmentations involved will be referred to in the subsequent discussion by the same numbers as those used in the pyrrole paper.[3] The side-chain fragmentations of the

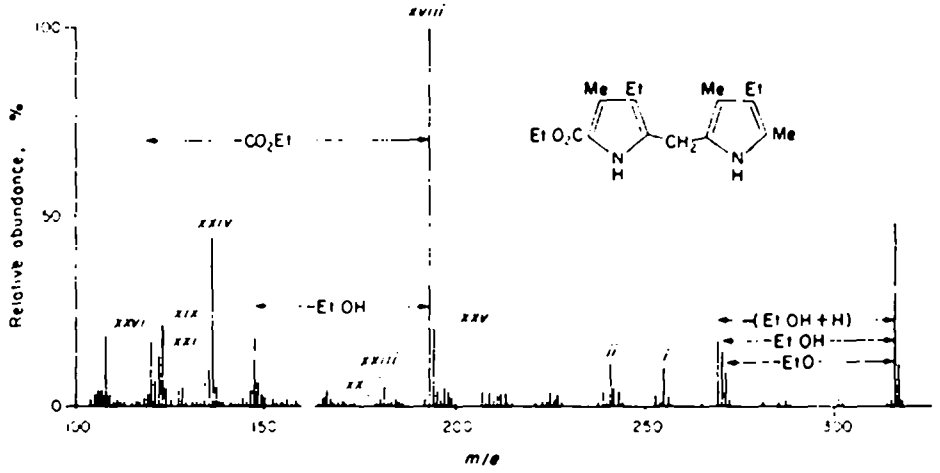


FIG. 1. Mass spectrum of pyrromethane (I) (Hot inlet).

pyrromethane ester (I: Fig. 1) are relatively weak (compared with the inter-nuclear fragmentations), but all the fragments observed correspond to those found in the

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TABLE 2. PRINCIPAL PEAKS IN THE MASS SPECTRA OF DI-, TRI-, AND TETRA-PYRROLES

Peaks are listed in descending order of *m/e* ratio with intensities expressed as a percentage of the most intense (base) peak, in parentheses. Peaks below 10%, unless specifically mentioned in the text, have generally been omitted. Peaks below *m/e* 100 have also been omitted unless they are especially prominent. In many of the spectra meta-stable peaks (m*) were also observed and these are recorded separately together with assignments of the transitions giving rise to them (when these may be made with some degree of confidence). The type of inlet system used for each spectrum is identified by the terms "hot" or "direct". The spectra of all the pyrromethenes (XIX–XXXI, LIII and LV) were determined with the salts (hydrochloride or hydrobromide), but the peaks due to halide or hydrohalide ion, even though of high intensity, have been omitted from the Table.

I: 316(49), 271(9), 270(15), 269(17), 255(10), 241(11), 194(21), 193(100), 181(5), 179(1), 166(4), 147(18), 136(45), 135(9), 123(21), 122(12), 120(18), 108(18). Hot.

II: 378(32), 271(10), 270(27), 269(18), 256(16), 255(63), 244(10), 241(10), 136(48), 123(27), 122(19), 121(15), 120(11), 109(11), 108(100), 107(59), 91(84), 79(85), 77(52). Hot.

III: 364(18), 256(18), 255(11), 241(12), 137(19), 136(46), 124(12), 123(27), 122(25), 110(15), 109(12), 108(83), 107(46), 91(100), 79(60), 77(40). Hot.

IV: 374(88), 329(10), 299(11), 281(5), 253(3), 194(32), 193(100), 181(15), 180(24), 166(7), 148(10), 147(17), 134(18), 120(13). Hot.

V: 463(27), 462(100), 432(30), 431(55), 404(23), 403(95), 376(20), 375(87), 371(35), 343(55), 315(14), 283(12), 239(10), 238(49), 237(16), 209(11), 178(10), 166(10), 146(12), 134(16), 133(20), 132(18), 126(12), 109(10). Direct. m*: 401(462 → 431), 351·5(462 → 403), 341·5(403 → 471), 314(375 → 343).

VI: 405(24), 404(84), 372(11), 346(10), 345(42), 331(10), 318(21), 317(100), 299(10), 286(12), 285(67), 257(17), 238(28), 237(15), 210(13), 197(12), 180(28), 166(11), 146(13), 120(27), 119(19), 118(12), 112(13), 108(18), 107(14), 106(18), 105(15). Hot.

VII: 614(22), 524(30), 523(100), 506(18), 479(19), 448(18), 419(12), 415(23), 371(13), 314(27), 223(14), 210(12). Direct. m*: 446(614 → 523), 439(523 → 479), 329(523 → 415).

VIII: 481(10), 480(40), 394(12), 393(50), 390(22), 389(100), 372(22), 371(14), 346(30), 345(55), 314(14), 313(35), 312(15), 286(14), 285(75), 271(14), 259(13), 257(11), 241(13), 225(21), 211(16), 210(16), 200(20), 199(12), 198(30), 197(11), 184(20), 180(75). Direct. m*: 354(389 → 371), 315·5(480 → 389), 306(389 → 345), 288(480→372), 248(480→345), 208(383 → 285).

IX: 346(36), 260(18), 259(100), 199(20), 197(22), 185(22), 180(47), 170(15), 138(15), 120(35), 108(25), 106(22). Direct.

X: 552(18), 551(100), 520(17), 480(11), 479(32), 478(11), 474(13), 465(10), 464(14), 463(11), 461(16), 460(55), 392(10), 387(19), 374(12), 373(50), 371(18), 357(13), 355(13), 343(10), 329(21), 297(13), 283(17), 251(27), 91(400). Direct. m*: 425(460 → 442), 416(551 → 479), 398(460 → 429), 384(551 → 460), 287(479 → 371).

XI: 360(22), 345(8), 331(13), 315(27), 314(45), 313(20), 300(26), 299(78), 287(12), 286(55), 285(100), 269(17), 268(22), 267(31), 254(13), 253(55), 241(16), 240(22), 239(45), 238(22), 225(12), 213(29), 212(13), 211(14), 210(12), 197(17), 196(10), 184(14), 183(14), 182(13), 168(10), 164(13), 162(12), 156(11), 143(13), 139(11), 138(19), 137(13), 136(23), 134(13), 127(21), 124(12), 123(34), 122(43), 121(11), 120(14), 108(40), 107(10). Hot. m*: 274(360 → 314), 214(299 → 253), 201(285 → 239).

XII: 333(20), 332(100), 303(10), 301(18), 300(43), 299(20), 286(18), 285(90), 273(10), 272(55), 271(64), 269(15), 268(17), 267(25), 254(12), 253(63), 241(15), 240(17), 239(48), 225(15), 213(30), 212(13), 211(16), 198(10), 197(20), 196(11), 195(10),

Table 2. (*Contd.*)

184(18), 183(16), 182(13), 170(10), 156(10), 144(10), 136(16), 134(12), 127(19), 123(34), 122(33), 121(15), 120(17), 109(28). Hot.

XIII: 318(50), 287(10), 286(25), 285(12), 272(10), 271(50), 258(23), 255(12), 254(17) 253(17), 240(12), 239(68), 227(14), 226(17), 225(14), 211(14), 199(38), 198(18), 197(17), 180(16), 179(19), 149(18), 143(30), 127(27), 122(40), 121(13), 120(19), 113(11), 110(12), 109(78), 108(76), 107(18), 106(13), 106(10). Hot.

XIV: 375(20), 374(82), 329(24), 328(18), 327(12), 313(21), 302(10), 301(28), 300(51), 299(35), 285(23), 283(15), 257(18), 256(12), 255(53), 241(10), 239(12), 213(18), 211(18), 209(18), 194(19), 184(12), 183(12), 180(24), 167(33), 166(46), 162(14), 148(36), 138(23), 134(22), 122(26), 65(21), 43(100). Hot.

XV: 462(19), 417(15), 416(29), 389(4), 387(11), 371(35), 370(100), 344(26), 343(90), 341(16), 325(25) 324(27), 298(22), 298(57), 296(11), 269(15), 251(16), 225(8), 224(8), 223(10). Direct. m*: 375(462 → 416), 329(416 → 370), 302(389 → 343), 301(387 → 341), 284(370 → 324), 257(343 → 297).

XVI: 361(17), 360(75), 346(10), 345(48), 315(14), 300(20), 299(100), 194(26), 193(17), 148(15). Direct. m*: 330·5(360 → 345), 274(360 → 314), 273(360 → 313), 259(345 → 299), 246(299 → 271), 230(315 → 269), 214(299 → 254).

XVII: 333(11), 332(60), 318(13), 317(70), 287(13), 272(17), 271(100), 225(50), 213(12), 179(15), 135(14). Direct. m*: 232(317 → 271), 187(271 → 225).

XVIII: 374(18), 328(27), 301(34), 256(31), 255(100), 241(17), 240(19), 239(11), 227(12), 226(10), 225(12), 180(20). Hot.

XIX: 201(18), 200(100), 199(50), 186(11), 185(77), 184(15), 170(10), 108(17), 95(35), 94(49). Hot.

XX: 257(9), 256(44), 242(17), 241(100), 226(10), 213(10), 212(50), 211(12), 197(18), 128(16), 113(14), 105(12). Hot. m*: 187(241 → 212).

XXI: 344(7), 329(6), 285(6), 269(8), 181(14), 180(9), 168(5), 167(29), 166(5), 152(6), 124(9), 123(14), 122(60), 121(11), 120(12), 109(17), 108(100). Direct.

XXII: 377(27), 376(99), 362(12), 361(46), 347(23), 285(17), 267(19), 253(29), 241(14), 240(24), 239(18), 226(29), 225(15), 212(21), 211(12), 197(11), 138(17), 124(12), 91(100). Hot.

XXIII: 372(6), 343(15), 297(11), 270(7), 209(6), 193(9), 135(6), 110(80), 108(100). Direct m*: 316·5(372 → 343), 257(343 → 297).

XXIV: 345(20), 344(85), 329(30), 301(10), 300(30), 299(29), 274(18), 273(100), 271(5), 270(5), 257(11), 256(31), 255(30), 226(12). Direct. m*: 315(344 → 329), 274(329 → 300), 260(344 → 299), 242(300 → 271), 241(299 → 270), 288(344 − 283), 215(300 → 255).

XXV: 323(10), 322(60), 321(10), 320(60), 307(40), 305(40), 293(19). 292(17), 291(22), 290(17), 278(16), 276(17), 241(11), 227(17), 226(100), 225(14), 213(11), 212(60), 211(21), 197(20), 160(13), 159(13). Direct. m*: 293(322 → 307), 291(320 → 305), 278(307 → 292), 276) (305 → 290), 266·5(322 → 293), 264·5(320 → 291), 182(212 → 197), 166(307 and 305 → 225).

XXVI: 321(50), 320(24), 319(50), 318(23), 307(45), 305(48), 293(16), 292(14), 291(17), 290(14), 278(21), 277(13), 276(22), 275(10), 241(12), 239(10), 227(15), 226(100), 225(22), 213(12), 212(78), 211(30), 210(11), 209(11), 198(14), 197(27), 196(12), 195(11). Direct. m*: 167(307 and 305 → 226), 154(293 and 291 → 212).

XXVII: 353(19), 352(99), 351(23), 350(100), 337(23), 335(25), 323(24), 322(54), 321(74), 320(53), 319(56), 307(32), 306(15), 305(72), 304(11), 303(42), 293(15), 292(25), 291(30), 290(30), 289(23), 278(12), 277(11), 276(17), 275(11), 257(12), 256(64), 242(46), 241(10), 240(9), 239(26), 227(11), 226(59), 225(30), 224(13), 213(10), 212(42), 211(32), 210(29), 209(23), 198(12), 197(23), 196(23), 195(22), 183(12), 182(12), 181(11), 176(15), 175(15), 168(13), 167(10), 120(13), 105(20), 91(18). Hot.

Table 2.—(*contd.*)

XXVIII: 293(21), 292(10), 291(23), 290(9), 279(12), 277(13), 199(18), 198(100), 197(15), 183(10). Direct. m*: 170(198 → 183), 141·5(279 → 198), 140·5(277 → 198).

XXIX: 367(14), 366(70), 365(17), 364(70), 351(11), 349(12), 321(10), 319(10), 307(17), 306(22), 305(27), 304(22), 303(12), 293(26), 292(16), 291(30), 290(14), 285(10), 271(15), 270(69), 226(15), 225(27), 212(19), 211(100), 210(19), 209(10), 208(10), 198(19), 123(18). Direct. m*: 335·5(366 → 351), 333·8(364 → 349), 234(366 → 293), 232(363 → 291), *ca.* 219(351, 349 → 270), *ca.* 154(293, 291 → 212).

XXX: 366(18), 364(18), 305(12), 303(10), 293(19), 291(21), 256(11), 225(12), 223(13), 213(22), 212(100). Hot.

XXXI: 317(21), 316(100), 302(15), 301(80), 287(22), 286(18), 272(10), 258(10), 257(65), 241(25), 227(25), 213(20), 137(10), 128(18), 121(18), 86(45), 84(70). Direct.

XXXII: 317(20), 316(100), 301(7), 285(7), 257(8), 243(71), 230(17), 228(12), 213(17), 199(11), 121(14), 120(13). Direct. m*: 287(316 → 301), 187(316 → 243).

XXXIII: 289(17), 288(100), 273(22), 259(11), 229(47), 213(10), 199(14). Direct. m*: 259(288 → 273), 233(288 → 259), 205(288 → 243), 182(288 → 229).

XXXIV: 161(21), 160(100), 94(58), 67(70), 66(26). Hot.

XXXV: 216(50), 123(30), 95(100), 94(40). Direct. m*: 72·5(122 → 94).

XXXVI: 273(18), 272(85), 258(12), 257(65), 243(14), 228(22), 150(58), 149(61), 148(11), 134(26), 124(17), 123(100), 122(31), 121(68), 120(11), 108(78), 107(23), 106(19). Direct. m*: 243(272 → 257), 202(257 → 228), 98·3(149 → 121), 94·8(123 → 108).

XXXVII: 258(49), 243(26), 229(15), 214(10), 150(37), 136(15), 135(87), 134(24), 124(24), 123(22), 122(12), 121(12), 115(12), 114(15), 109(18), 108(67), 107(100), 106(33), 94(39). Hot.

XXXVIII: 393(28), 392(85), 377(21), 363(5), 283(10), 270(20), 269(95), 256(10), 255(15), 241(14), 240(15), 226(10), 178(11), 162(9), 160(11), 150(14), 134(10), 123(18), 122(11), 121(6), 108(15), 91(100). Direct. m*: 363(392 → 377), 336(392 → 363), 216(269 → 241).

XXXIX: 451(20), 450(60), 435(14), 327(15), 270(20), 269(100), 241(15), 240(16), 226(13), 208(16), 181(20), 180(17), 178(22), 162(18), 160(20), 148(11), 135(9), 134(25), 108(32), 91(210). Direct. m:* 421(450 → 435), 394(450 → 421), 216(269 → 241).

XL: 509(30), 508(90), 477(14), 435(16), 421(9), 399(8), 385(11), 313(21), 300(15), 299(100), 209(10), 208(55), 207(12), 182(14), 181(15), 160(12), 148(16), 134(40), 121(15), 108(37), 91(210). Direct. m*: 479(508 → 493).

XLI: 507(14), 493(13), 479(13), 345(24), 314(14), 313(18), 312(32), 301(50), 300(14), 299(50), 286(18), 285(40), 228(40), 210(15), 208(15), 194(35), 181(25), 180(20), 178(20), 167(20), 134(14), 120(24), 108(100), 107(50), 92(75), 91(800). Direct. m*: 262·5(?).

XLII: 317(25), 316(100), 302(15), 301(75), 271(12), 270(15), 255(45), 193(35), 177(20), 175(25), 151(10), 150(95), 149(35), 148(30), 138(10), 134(25), 128(25), 124(15), 123(45), 122(20), 121(30), 120(9), 108(35). Direct. m*: 285(316 → 301), 216(301 → 255), 141(193 → 165).

XLIII: 361(15), 360(65), 345(35), 315(15), 300(10), 299(70), 194(40), 193(100), 168(10), 167(40), 166(15), 165(40), 148(70), 138(25), 123(17), 122(25). Direct. m*: 330·5(360 → 345), 259(345 → 299), 245·5(299 → 271), 141(192 → 165).

Table 2.—(*contd.*)

XLIV: 457(38), 456(100), 365(9), 347(10), 274(16), 241(12), 239(12), 230(11), 215(12), 213(12), 108(10), 91(34). Direct. m*: 427(456 → 441), 278(441 → 350), 265(456 → 348), 251(441 → 333), 239(274 → 256).

XLV: 557(4), 511(3), 449(5), 376(4), 363(4), 301(9), 285(15), 269(18), 255(100), 241(19), 239(12), 225(12), 202(14), 201(15). Hot.

XLVI: 620(10), 619(22), 511(21), 510(15), 376(7), 363(7), 269(13), 257(21), 256(38), 255(100) 212(13), 211(11), 198(11), 167(11). Hot.

XLVII: 630(30), 629(100), 614(6), 542(6), 538(11), 506(11), 480(11), 479(25), 419(12), 415(40), 389(11), 371(19), 329(9), 315(13), 314(22), 313(13), 210(12), 150(40), 149(13), 134(9), 123(50), 122(18), 121(10), 108(100), 91(80). Direct. m*: 600(629 → 614), 461(629 → 538), 407(629 → 506), 353·5(?), 341(506 → 415), 320(538 → 415), 287·5(479 → 371).

XLVIII: 603(37), 602(90), 481(10), 420(10), 372(14), 347(10), 346(50), 345(25), 285(15), 259(65), 257(20), 256(30), 255(50), 254(20), 246(12), 230(40), 229(18), 212(10), 201(10), 199(15), 197(14), 182(10), 180(60), 167(10), 166(10), 165(17), 139(14), 122(100), 121(80), 120(40), 109(40), 108(50), 94(60), 86(55), 84(85). Direct. m*: 404(602 → 493), 384(602 → 481), 318·5(?), 215·5(?), 194(346 → 259).

XLIX†: 764(5), 557(10), 447(14), 446(14), 357(87), 314(50), 313(75), 301(88), 299(60), 287(50), 286(40), 285(50), 283(49), 270(61), 269(92), 256(45), 255(100), 243(45), 241(75), 227(57), 225(45), 211(45), 210(59), 194(55), 181(80), 180(80), 167(40), 162(40), 136(55), 123(40), 122(100), 121(40), 120(70), 108(330), 94(210), 91(420). Direct.

L†: 870(1), 762(14), 735(17), 691(9), 627(10), 602(35), 601(90), 570(14), 559(10), 517(16), 510(17), 439(35), 492(45), 480(65), 479(60), 448(18), 418(19), 405(35), 401((34), 393(40), 390(45), 389(100), 371(35), 357(32), 345(45), 314(65), 313(55), 301(30), 299(50), 297(80), 287(50), 285(80), 283(51), 271(50), 279(70), 269(75), 257(32), 256(50), 255(90), 241(50), 225(40), 211(50), 180(45), 162(85), 121(10), 108(14), 91(100). Direct. m*: 696(?), 354(?).

LI: 856(3), 765(1), 721(2), 492(14), 480(18), 479(21), 405(11), 401(15), 393(17), 390(10), 389(35), 377(13), 376(30), 371(16), 345(25), 314(35), 313(30), 301(10), 299(19), 297(13), 287(22), 285(40), 283(18), 273(19), 271(20), 270(19), 269(23), 256(15), 255(20), 241(26), 225(22), 212(30), 211(35), 210(20), 209(19), 198(20), 197(40), 196(20), 195(15), 194(22), 184(20), 183(15), 180(70), 179(40), 148(50), 122(80), 121(100), 120(50), 108(100), 107(70), 106(40), 91(1000). Direct. m*: 678(765 → 721), 316(480 → 389), 300(?), 287·5(?).

LII†: 856(32), 765(13), 721(14), 587(25), 492(20), 480(73), 479(53), 405(25), 401(30), 393(50), 390(25), 389(100), 371(36), 357(35), 345(37), 314(37), 285(45), 271(30), 270(45), 269(45), 255(30), 241(40), 225(40), 211(50), 199(40), 198(50), 197(90), 196(49), 185(40), 184(48), 183(50), 182(34), 181(35), 180(80), 162(80), 136(50) 134(50), 122(40), 120(60), 108(400), 91(1000). Direct.

LIII: 324(36), 323(100), 322(10), 308(11), 267(17), 266(60). Direct. m*: 219(323 → 266).

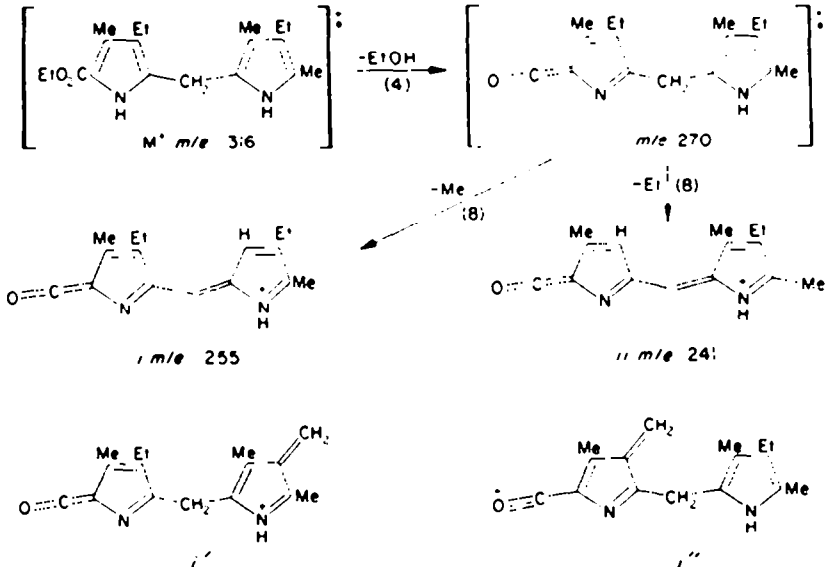
LIV: 585(15), 584(50), 301(14), 300(41), 299(100), 288(13), 287(19), 286(95), 241(14), 239(14), 226(45), 224(18), 223(12), 210(20), 163(14), 145(12), 110(55). Direct.

LV: 590(5), 589(14), 588(36), 467(9), 466(26), 386(13), 369(11), 368(30), 366(14), 364(10), 348(28), 328(18), 322(25), 320(20), 181(6000), 180(3600), 167(15,000), 166(9600), 139(14,000), 125(70,000), 124(21,000), 122(46,000), 110(69,000), 108(97,000), 95(100,000), 93(23,000), 82(31,000). Direct. Note: only the very intense peaks below *m/e* 300 have been recorded.

† Owing to the very large number of peaks observed in these spectra below *m/e* 300, only those ions > 30% have been recorded.

spectrum of ethyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate, i.e. loss of C_2H_4 (1), Et (2), EtO (3), EtOH, (4), EtOH + H (5), CO_2Et (6) and $H{\cdot}CO_2Et$ (7). The spectrum of the corresponding benzyl ester (II) like those of other pyrromethane and pyrrole benzyl esters is dominated by fragmentations arising from loss of benzyl alcohol, benzyl etc.[7]

Substantial fragments involving the loss of 61 and 75 mass units from the molecular ion of pyrromethane (I) are worthy of comment. The former could arise by successive losses of EtOH (4) and Me from the side-chain or nucleus or *vice-versa*, and the latter by loss of EtOH (4) and Et from the nucleus. Similar cleavages of the propionate side-chain are also observed in the spectra of the pyrromethanes (V–IX); indeed in the pyrromethane (VI) it is the principal fragmentation giving rise to the base peak at *m/e* 317. In contrast, this type of cleavage is relatively unimportant in fragmentations of simple monopyrrole carboxylic esters, alkyl substituents undergoing the more normal cleavage of the β-bond ("β"-type). If one assumes that these "α-type" cleavages (8) are accompanied by rearrangement of one hydrogen from a neighbouring substituent, then their relatively more important role in the fragmentations of certain pyrromethanes can be readily explained, e.g. in the fragmentation of I migration of one of the methylene bridge hydrogen atoms would give the very stable methene salt-like cations i and ii* (although ions i′ and i″ may also contribute to the observed peak).† The ion *m/e* 317, derived by α-cleavage of the propionate side-chain in the pyrromethane (VI) would presumably have the analogous structure iii (or iii′). A parallel for these processes is provided by the hydrogen abstraction which occurs in the oxida-

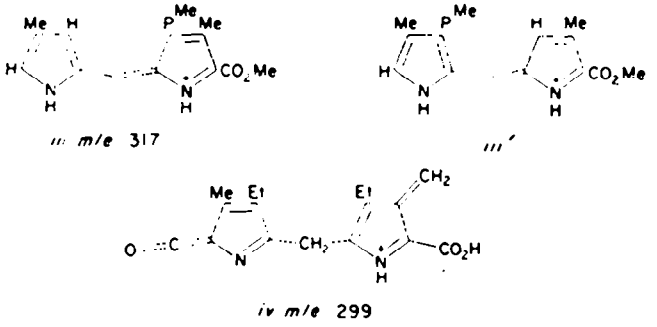


tion of pyrromethanes to pyrromethenes,[8] and which is usually assumed to be a free-radical process. The pyrromethane (IV) also shows an M-75 peak (*m/e* 299) which could arise in the same manner as the corresponding peak in the spectrum of I;

* Italicized small Roman numerals denote fragment ions.

† Ions i′ and i″ may also be formulated as the ring expanded pyridinium analogues as discussed briefly in our earlier paper on pyrrole mass spectra.[8] However this possibility seems less likely.

alternatively the loss of C_2H_5 may be due to fission of the second ester group (cleavage 2) to give an ion iv rather than fission of the nuclear ethyl group, or both processes may occur simultaneously. Evidence for the occurrence of the second type of fission is given by the peaks at *m/e* 281 and 253 which could arise from ion iv by loss of H_2O (4) and $H{\cdot}CO_2H$ (7) respectively.



iii m/e 317 *iii'*

iv m/e 299

The fragmentations of pyrromethanes with two carbonyl substituents in the same ring (XI–XV) bear considerable resemblances (in the high mass ranges) to those of 3,5-dimethylpyrrole-2,4-dicarboxylic acid and its esters.[3] The spectrum of pyrromethane (XI) is recorded in Fig. 2 and the following scheme is suggested for the various fragmentations involved. (Scheme I.)

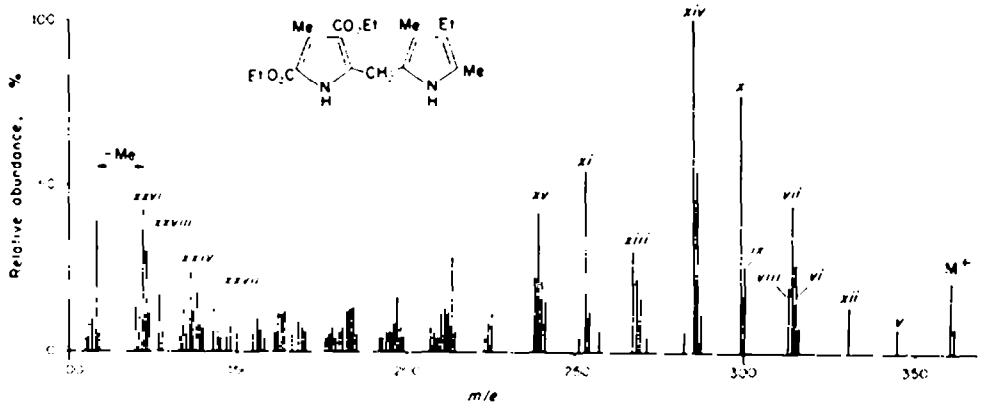
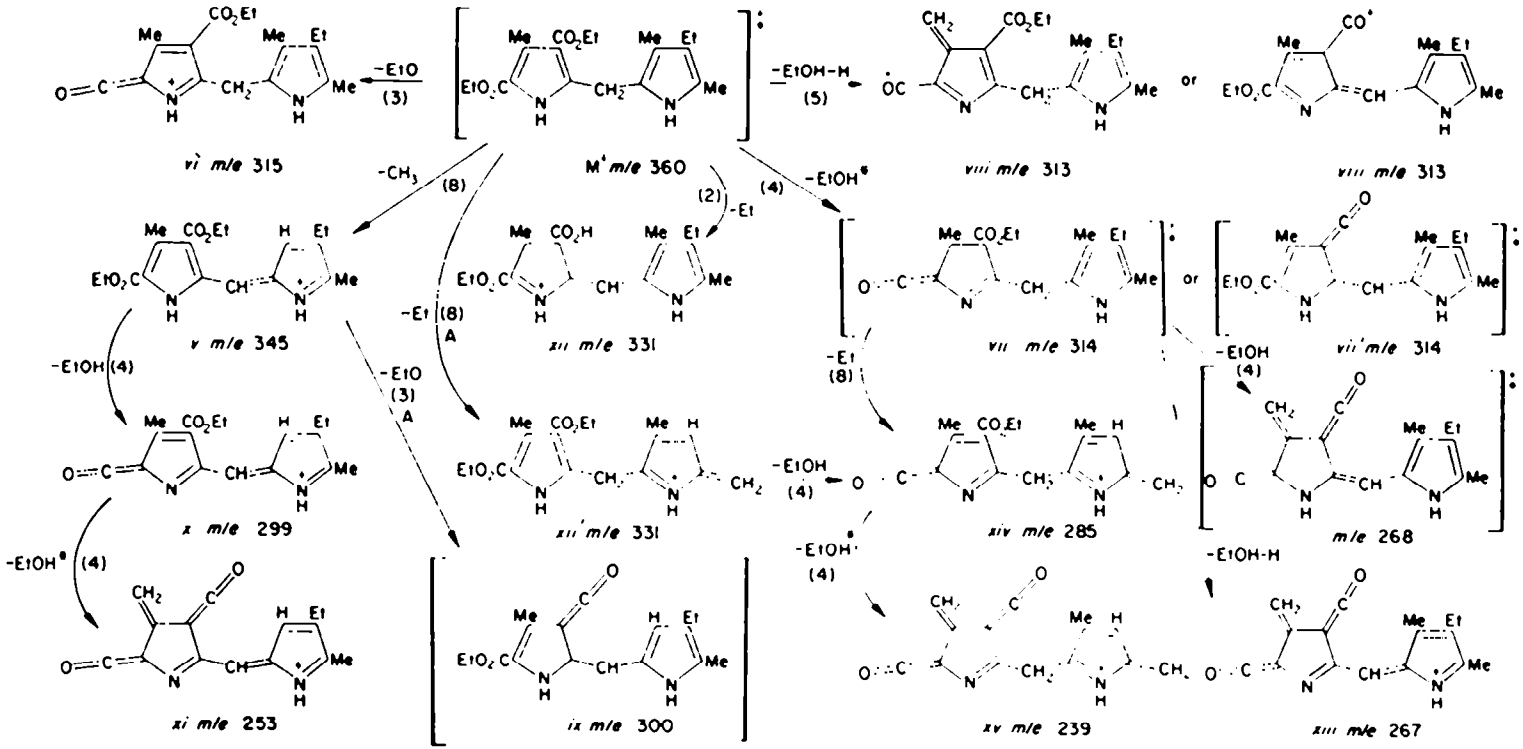


FIG. 2. Mass spectrum of pyrromethane (XI) (Hot inlet) cf. Scheme I.

The flow sheet gives only one positional isomer for each ion, although in many instances two or more isomers are possible and may well contribute to a single peak in the spectrum, as is the case with the monopyrrolic analogues. The origin of ions v–xii (and their isomers) follows by analogy with the simple pyrroles, but fragmentation of the β-carboxylate may be more pronounced owing to the relative ease of abstraction of a hydrogen atom from the methylene bridge, and thus ions of type vii' and viii' may be formed more readily than their isomers.

The peak at *m/e* 331 cannot be due solely to loss of an ethyl radical from one of the ethoxycarbonyl groups (cleavage 2 giving rise to ion xii) since the corresponding dimethyl ester (XII) also exhibits an M-29 peak (which is absent in the spectrum of the methyl-analogue; XIII). It must therefore be presumed that loss of the nuclear ethyl



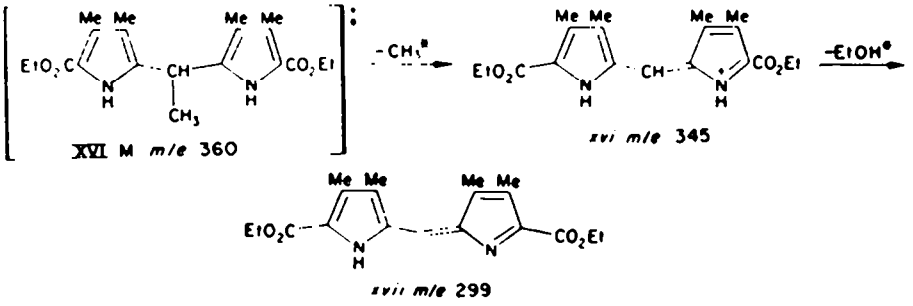
An asterisk indicates that the cleavage postulated has been confirmed by a metastable peak

Scheme I

group also occurs with concomitant transfer of one of the hydrogen atoms from one of the neighbouring methyl groups to give the ion xii', or an isomer (cleavage 8). Further evidence for this loss of nuclear ethyl is that ion xii' undergoes two further cleavages (4) to give ions xiv and xv, and the second of these cleavages is confirmed by a metastable peak. On the other hand the ion *m/e* 285 can arise either by loss of EtOH from xii', or by loss of ethyl from vii, i.e. xiv, or an isomer.

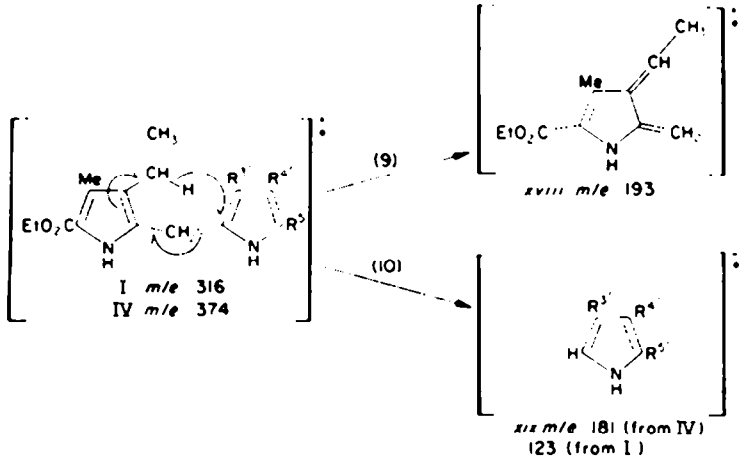
Loss of nuclear propionate groups also appears to be a marked feature of the spectra of pyrromethanes (V), (VI), (VIII), (IX) and (X).

The spectrum of the meso-methylpyrromethane (XVI) is of some interest as cleavage of the meso-methyl substituent is a dominant feature of the spectrum, giving rise to the methene-like ions *m/e* 345 (M–Me) xvi and 299 (M—Me—HOEt) xvii; the existence of metastable peaks for the appropriate transitions indicates that the fragmentations take place in the order indicated:

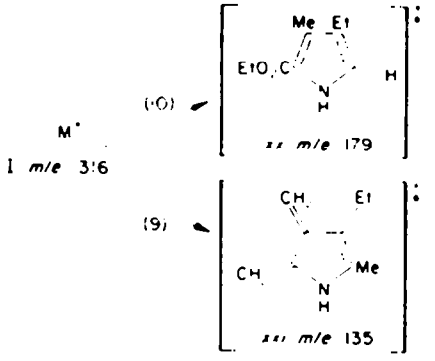


The spectrum of the only 2,3'-pyrromethane studied (XVII) is also dominated in a very similar manner to that of XVI by the meso-methyl substituent

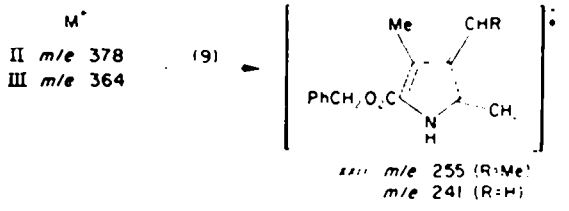
In considering the second type of cleavage observed with pyrromethanes, namely fission between the nuclei, it is convenient to discuss the spectra of pyrromethanes (I and IV) in detail first, since this fragmentation is predominant in both cases, giving rise to the same base peak (*m/e* 193) xviii. The formation of this ion must presumably involve rearrangement of one hydrogen, and this can be explained by the following mechanism:[cf.9]



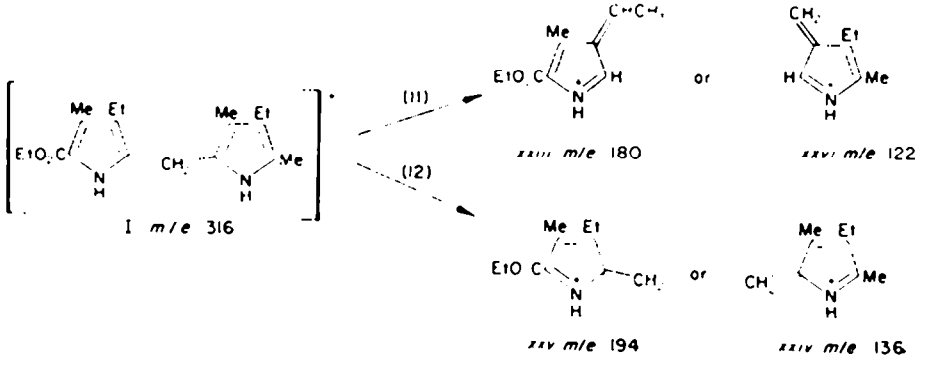
An alternative mechanism can also be written involving migration of the NH-hydrogen atom from ring A to ring B, but this was ruled out by determining the spectrum of the N-dideuterio analogues; ions *m/e* 194 and 124 were observed showing that deuterium was retained in the fragment derived from ring A. The analogous cleavage in which the methylene bridge remains attached to the B ring in the spectrum of the unsymmetrical methane (I) is strikingly less pronounced, and this could be explained on the assumption that ion xviii is more stable than ion xxi because of the carbonyl substituent in ion xviii. On the other hand consideration of the spectra of the related pyrromethanes (II and III) shows that it is the presence of the 3-Et group which is the major factor; these show the same general fragmentation behaviour as I except for the additional very strong ions derived from cleavage of the benzyl ester groups, but the



intensity of the ion xxii in the case of II (3-Et) is 65% of the base peak, while in III (3-Me) its intensity is reduced to about 12%,

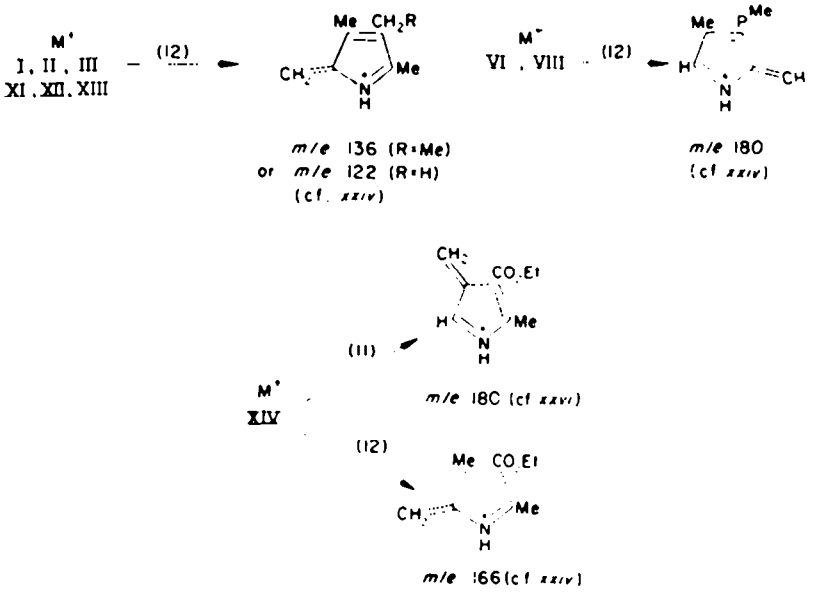


A second type of inter-nuclear cleavage can also occur but without involving rearrangement. Species xxiv is rather pronounced in the spectrum of I, ions xxv and xxvi are not abundant, and xxiii is virtually absent;



however in the spectra of the symmetrical pyrromethanes (IV, V, VII, IX and XVI) ions of the second type are relatively more abundant, i.e. *m/e* 194, 238, 314, 180 and 194 respectively, which are structurally analogous to xxv.

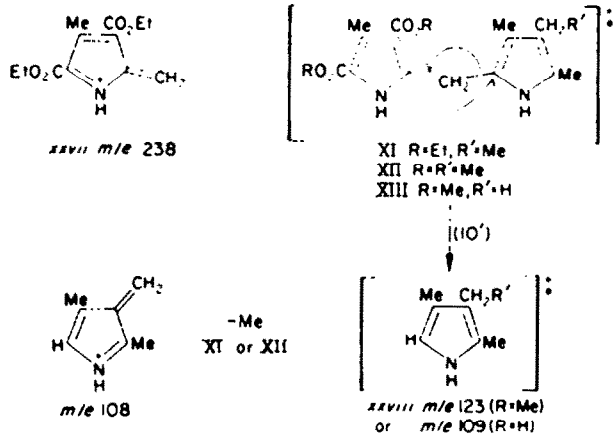
The precise nature of the factors controlling which type of internuclear cleavage is likely to occur in any particular case is not entirely clear, for cleavages 11 and 12 are also quite important in the unsymmetrical methanes, e.g. I, II, III, VI, VIII and XI–XIV give rise to ions of type xxiv, and XIV to an ion of type xxvi also:



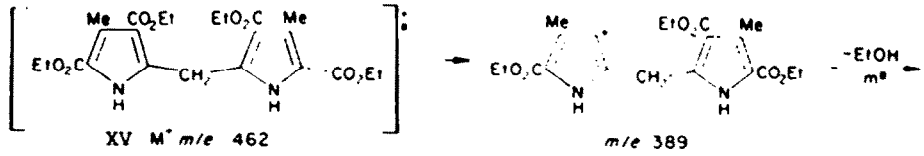
However it is important to note that the fragment retaining the positive charge in this type of cleavage is the ring bearing the fewer carbonyl substituents, i.e. the inductive effect of the alkyl groups in stabilising the positive charge on this fragment is the controlling factor here, whereas in cleavages of types 9 and 10 hydrogen is transferred *from* the ring bearing the carbonyl substituent, and the positively charged fragment derived from this ring predominates (see above).

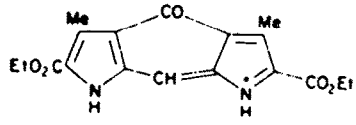
The pyrromethanes XI, XII and XIII exhibit their main fragmentations at the upper end of the spectrum, but XI for example shows ions at *m/e* 136 (xxiv), 122 (xxvi) (cleavages 12 and 11), and at *m/e* 238 (xxvii) (cleavage 12). The later presumably corresponds to ion xxvii as it is missing in the spectra of both XII and XIII, although the analogous peak (*m/e* 210) in the latter is very weak. The low abundance of these ions is probably due to the effect of the two electron-withdrawing groups in ring A which lowers the tendency to accept and stabilize a positive charge. An ion (*m/e* 123), xxviii, in the spectra of XI and XII (*m/e* 109 in XIII) may arise by hydrogen transfer from the NH group of the A-ring (cleavage 10′); in the case of the methanes (XI and XII) this ion can further fragment by loss of Me from the ethyl side-chain to give the ions observed at *m/e* 108.

The major fragments from the tetracarbethoxypyrromethane (XV) are derived by side-chain cleavages and are very similar in character to those described for XI, except for the ion *m/e* 343 which is 90% of the base peak in the spectrum. The high intensity



of the latter peak must be due to the formation of a very stable species, and this is best represented by the fully conjugated tricyclic cation xxix.





One of the ethoxycarbonyl groups is presumably lost initially, and then cyclization occurs with loss of ethanol, the latter step being confirmed by a metastable peak. This is an example of the third type of process delineated at the beginning of this section.

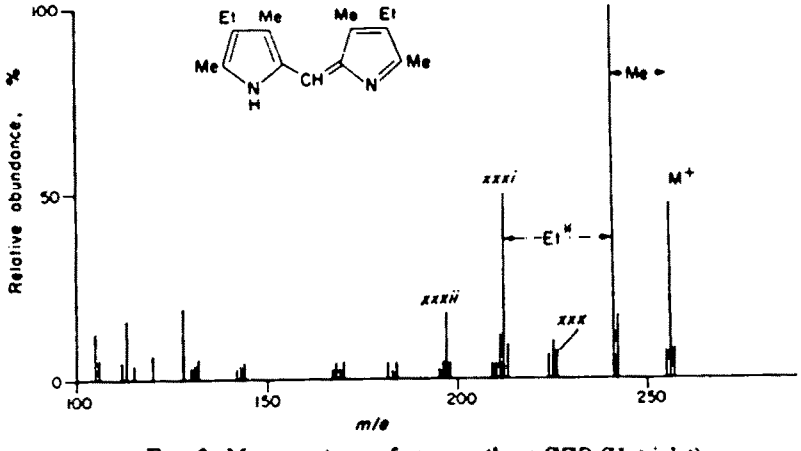
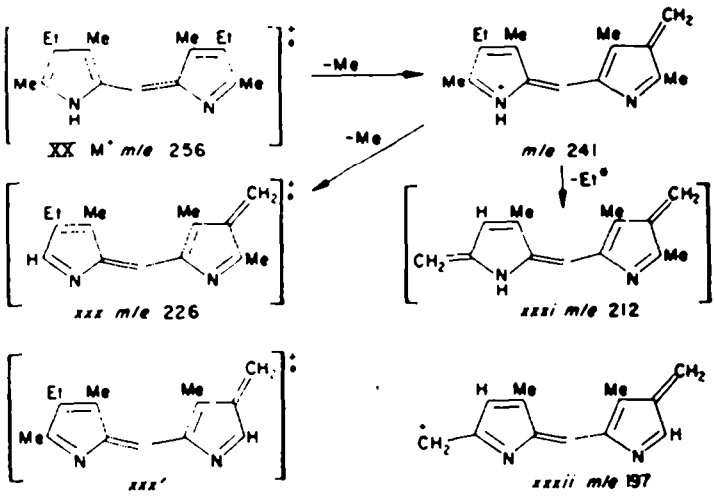


FIG. 3. Mass spectrum of pyrromethene (XX) (Hot inlet).

A further example is provided by the 3,3'-pyrromethane (XVIII) which has carboxylate ester substituents in the two α-positions flanking the methylene bridge.

Pyrromethenes

The most striking feature of pyrromethene spectra is the relatively high intensity of the molecular ion in the majority of examples studied; this clearly reflects the well known stability of the fully conjugated dipyrrolic ring system. In general, fragmentations of the side-chains predominate over cleavage at the methine bridge, e.g. cryptopyrromethene (XX; Fig. 3) exhibits a strong molecular ion, and the base peak m/e 241, is formed by loss of a Me radical from one of the Et side-chains, the next strongest peak is due to subsequent loss of Et (metastable peak at *m/e* 187·2; calc. 186·7) and may be represented by the ion xxxi, whilst the ions *m/e* 226 and 197 can be written as xxx (or xxx') and xxxii in accordance with the following scheme:



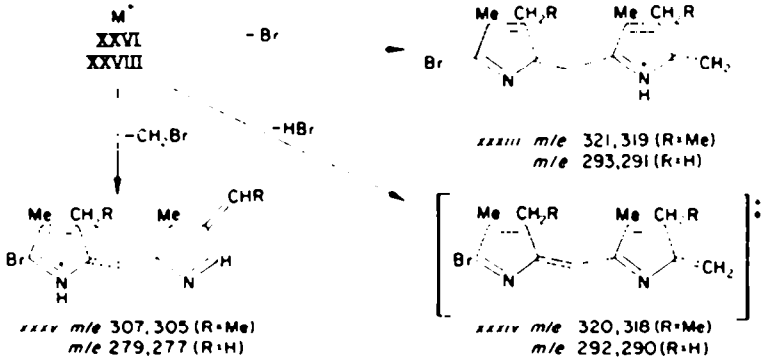
This fragmentation behaviour indicates that the generalization derived for simple pyrroles, i.e. that an even electron species does not lose an odd electron fragment,[3] does not hold for more complex systems, especially if, due to the highly aromatic character, no simple fragmentation steps are possible.

The tetramethylpyrromethene (XIX) gives a strong M-1 peak (which is not characteristic of other pyrromethenes), and also a very intense M-15 peak due to nuclear cleavage of a Me radical. The latter kind of fragmentation is not very noticeable in simple pyrroles, but it appears to be much more common in pyrromethenes, and it also occurs quite frequently (as indicated in the previous section) in the spectra of pyrromethanes.

The fragmentation patterns of the methenes bearing nuclear carboxylic ester groups are largely dominated by cleavages of the ester groups, although nuclear alkyl cleavages are also important, e.g. in the unsymmetrical methene (XXII) the molecular ion is the base peak, intense peaks are observed for loss of nuclear Me and Et, and for fragmentation of the ester group.

The spectra of the brominated methenes (XXV–XXX) are of considerable interest since they and their analogues have been widely used in the classical Fischer-type

synthesis of porphyrins.[10] The two α-bromomethyl compounds (XXVI and XXVIII) do not give parent ions, owing to the ease with which cleavage of bromine, HBr or —CH_2Br occurs to yield ions xxxiii, xxxiv and xxxv. (Comparable cleavages of halogen have also been observed with α-halomethyl pyrroles which likewise do not give rise to molecular ions.[11]) Further fragmentations (α-cleavages) of the side-chains



then occur, but these are relatively minor compared with loss of nuclear bromine from ion xxxv, which gives rise to the base peak xxxvi in both spectra (e.g. see Fig. 4).

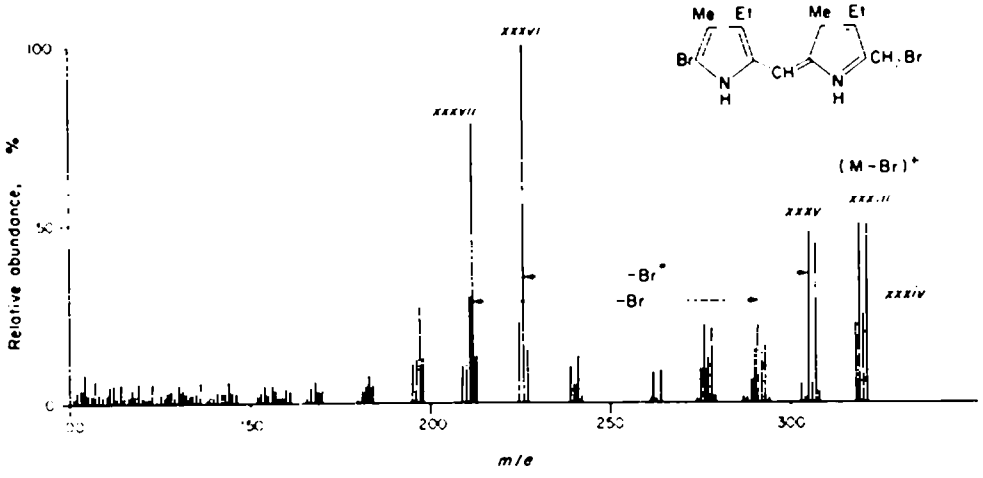
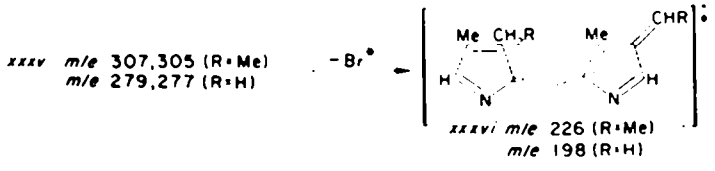


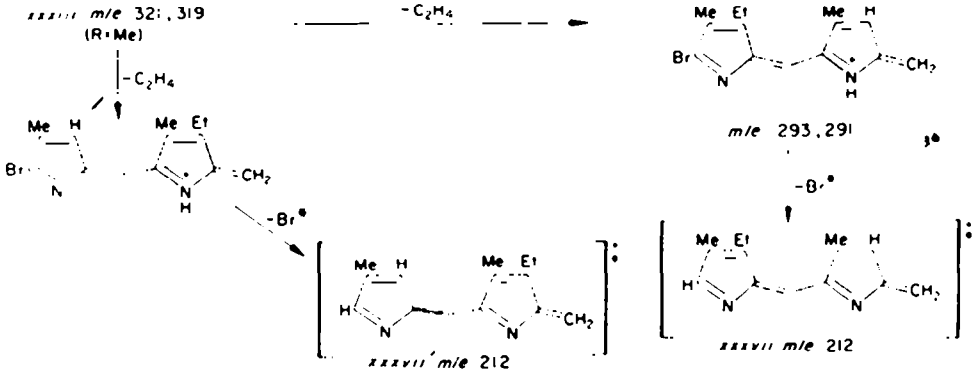
FIG. 4. Mass spectrum of pyrromethene (XXVI) (Direct inlet).

The latter cleavage is confirmed by metastable peaks in both cases. Another intense



ion (*m/e* 212) xxxvii or xxxvii′ observed in the spectrum of XXVI also arises by loss of nuclear bromine (from ions *m/e* 293 and 291) as shown by the appearance of the

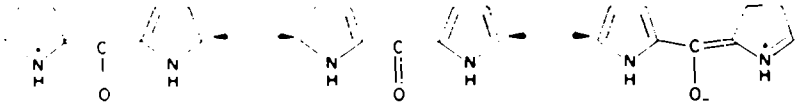
corresponding metastable peak ca. 154 (calc. 153·5 and 154·5). The ions *m/e* 293 and 291 must presumably be formed by loss of ethylene from xxxiii (R = Me), but it is not evident why ion xxxiii does not also fragment by loss of nuclear bromine as do 293 and 291.



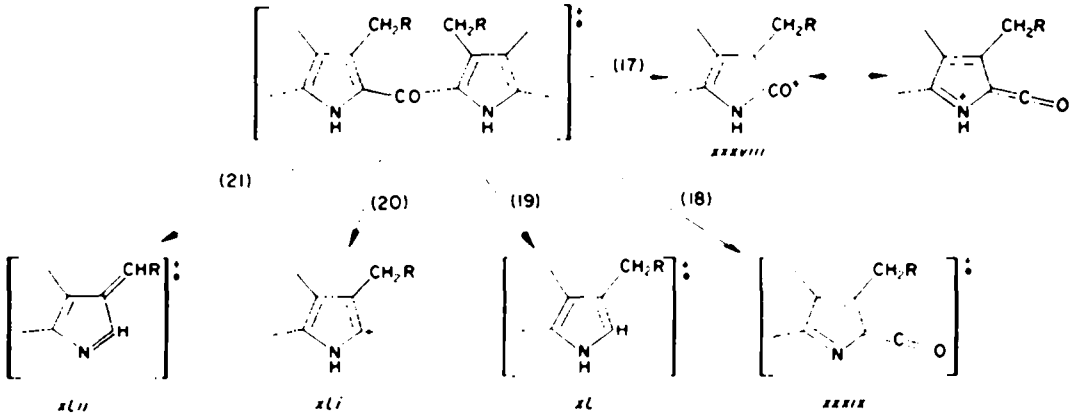
The spectra of the dipyrrolic bile pigment degradation products (XXXI, XXXII[12] and XXXIII[12]) are quite straight-forward. β-cleavage of the propionate side-chains is the predominant fragmentation and the molecular ion is quite intense (in two of the examples it is in fact the base peak). The intense peak due to loss of Me in XXXI probably arises by fission of the nuclear methoxyl substituent, since the corresponding M-15 peaks in the other spectra are relatively weak. Fragment ions corresponding to inter-nuclear cleavages are also very weak.

Pyrroketones

The fragmentation patterns of pyrroketones are much more similar to those of pyrromethanes than those of pyrromethenes as inter-nuclear cleavages readily occur in all the examples studied. Cleavage of a bond α to a carbonyl group is clearly energetically more favourable than cleavage α to a double bond (as is required for internuclear cleavage of pyrromethenes). This contrast in the behaviour of pyrroketones and pyrromethenes under electron impact is noteworthy since the carbonyl group is quite strongly polarized in pyrroketones and their structures may be described as a resonance hybrid of the following forms (two of which are methane like in character).[13]



Cleavages of side-chain substituents appear to be preferred in unsymmetrical ketones; they are generally very similar to those encountered with simple pyrroles and pyrromethanes and will therefore not be discussed in detail here. Inter-nuclear cleavages, which appear to predominate in symmetrical ketones, give rise to five main types of fragment ions by processes 17–21 as indicated below: (see also Fig. 5)
In dipyrroketone itself, for example, the molecular ion is the base peak and the only



intense ions in the spectrum at *m/e* 95, 67 and 66 can be assigned structures analogous to those represented by xxxviii, xl and xli respectively. The hydrogen transferred in the formation of ion *m/e* 67 (xl) was shown to be derived from the NH hydrogen of the other ring as the corresponding N,N-dideuterio-ketone (prepared by shaking with D_2O) gave an ion *m/e* 69. Similarly constituted ions are observed in the spectrum of the tetramethylpyrroketones (XXXV) but here the ion *m/e* 95 (xl) is the base peak, not the molecular ion. The fragmentation patterns of ketones (XXXVI; Fig. 5) and

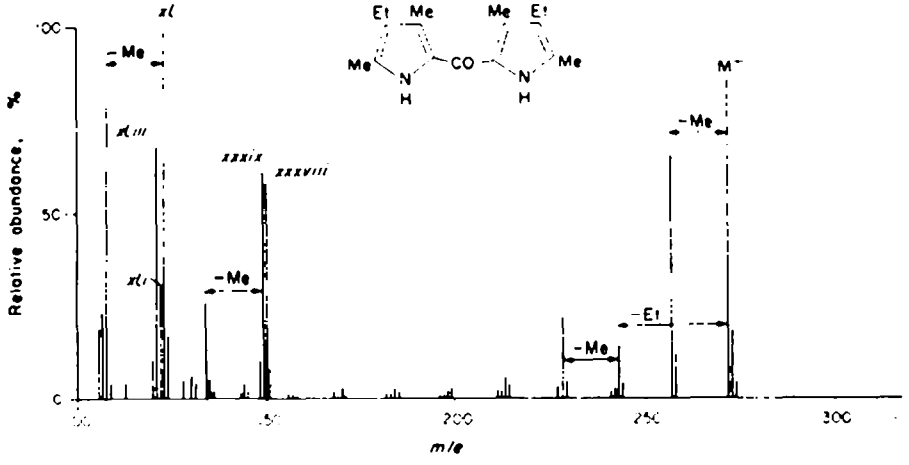
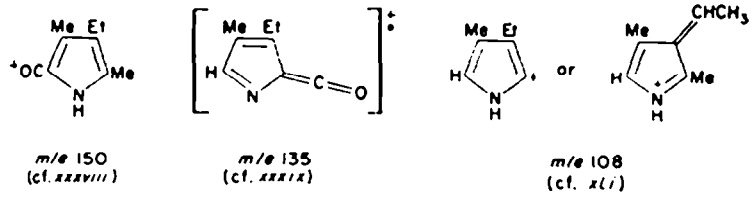


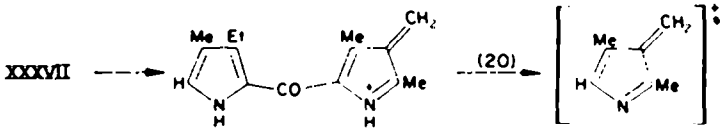
FIG. 5. Mass spectrum of pyrroketone (XXXVI) (Direct inlet).

XXXVII are somewhat more complex, e.g. in the latter ions *m/e* 150, 135 and 108

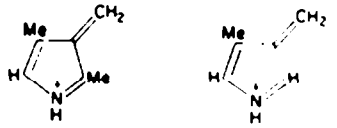


probably arise in the primary fragmentation process, and may be represented by the following structures (analogous to xxxviii, xxxix and xli respectively).

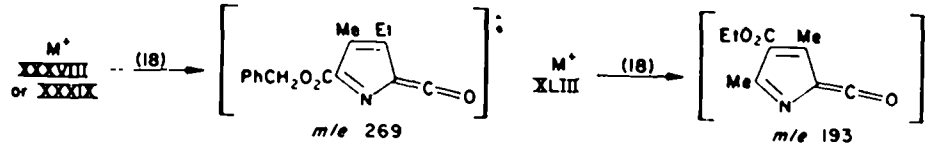
In addition the ion *m/e* 107, which is the base peak in the XXXVII spectrum, may well arise by primary cleavage of a Me group from one of the Et groups in the intact ketone, followed by a cleavage of type 20, with rearrangement of the NH hydrogen atom to the neighbouring α-position as follows:



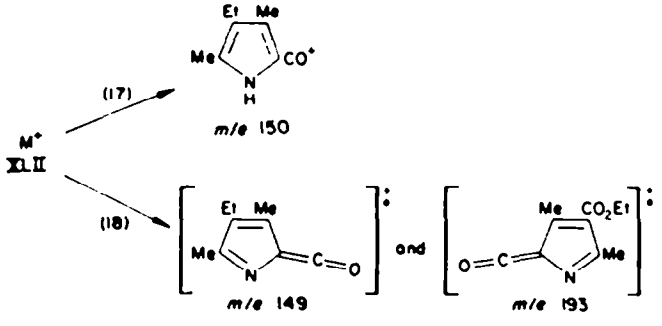
An alternative result of such primary cleavages of methyl could be that some or all of the ion *m/e* 108 has structure xliv and that the ion *m/e* 94, which is also fairly intense, has structure xlv.



In the remaining pyrroketone spectra, the fragmentation patterns are considerably dependent on the effects of the nuclear carboxylate substituents which they all contain. Often where only one of the rings bears a nuclear carbonyl group the predominant cleavage is of type 18 and gives rise to the base peak e.g. XXXVIII, XXXIX and XLIII.

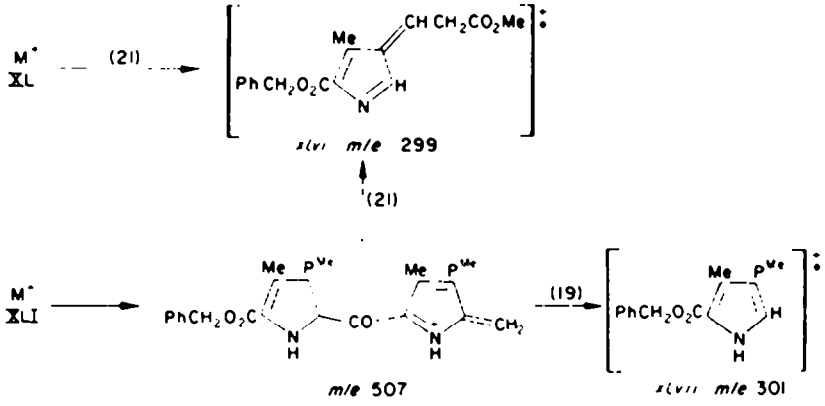


In ketone XLII, on the other hand, which is unsymmetrical and has one nuclear carbonyl substituent in a β-position, cleavage of type 17 occurs in preference and the intense ion, *m/e* 150, formed (of type xxxviii) is derived from the ring which does not

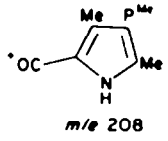


bear the carbonyl group; cleavages of type 18 do however also occur in this spectrum, and both possible ions corresponding to the two alternative modes of cleavage are observed at *m/e* 193 and 149.

The spectra of the two pyrroketones (XL and XLI) which bear propionate substituents in the same ring as the carboxylic ester substituent exhibit some unusual features. The latter does not exhibit a molecular ion owing to the ready loss of chlorine from the α-chloromethyl side-chain to give the ion *m/e* 507; this is in accord with the behaviour of the halomethyl-pyrromethenes and pyrroles discussed previously. More importantly, the major ions in both spectra however (apart from fragmentations of the benzyl esters) are not due to cleavages of type 18; instead XL gives an ion *m/e* 299, whilst XLI gives ions *m/e* 299 and 301. The structures of these ions may be written as xlvi and xlvii. the latter presumably arising by a cleavage of type 19 (and occurring in this spectrum and not the other owing to the initial loss of chlorine from the side-chain in the intact pyrroketone). Ion xlvi must arise by a new type of cleavage

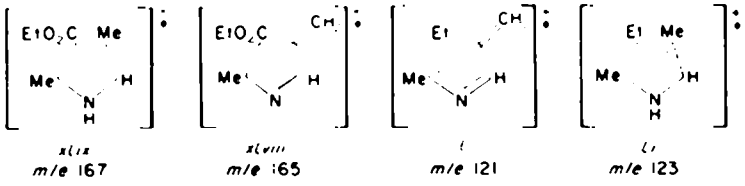


(21) in which hydrogen is transferred from either the β-alkyl side-chain or the nitrogen to the neutral fragment. The ketone XL also gives an intense ion (*m/e* 208) arising by cleavage 17, and which may be assigned the following structure (analogous to xxxviii).



m/e 208

Ketones XLII and XLIII also appear to show ions (*m/e* 165) xlviii resulting from cleavage 21, and ions (*m/e* 167) xlix (cleavage 19) as well as ions resulting from cleavages 17 and 18 which have already been discussed. In addition XLII also gives ions



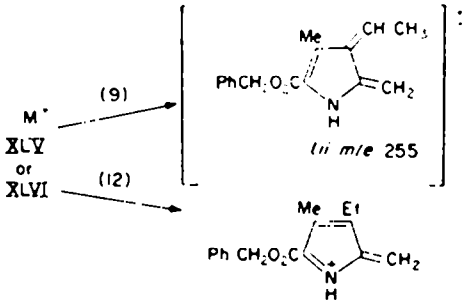
m/e 121 l and 123 li corresponding to the alternative cleavages of types 21 and 19 which can occur as this ketone is not symmetrical.

Tripyrranes and tetrapyrranes (Bilanes)

Ten examples of linear tri- and tetrapyrrolic compounds are included in this paper

in which the rings are linked by methylene or carbonyl groups. Only the more important features of their fragmentation behaviour will be discussed, in particular inter-nuclear cleavages in relation to the behaviour of similarly constituted pyrromethanes and pyrroketones.

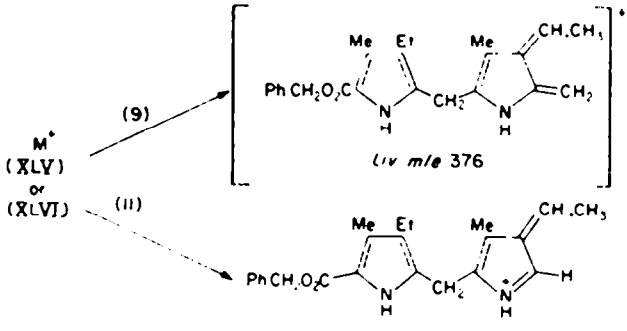
The molecular ions of these compounds are all relatively weak except for the tripyrroketone (XLVII) and the tetrapyrrole (XLVIII with a 'centrally situated' carbonyl group). By far the most abundant ion in the spectra of both XLV and XLVI *m/e* 255 arises by cleavage (9) to give the ion lii.



lii m/e 255

liii m/e 256

The alternative cleavage of the C-ring in XLV bearing the ethoxycarbonyl group is not observed, presumably due to the much greater ability of the benzyl ester group in the A-ring to assist in stabilizing the positive charge. Compound XLVI also gives an ion *m/e* 256 (lxvi) by cleavage (12). Other cleavages to give dipyrrolic fragments are very weak, but the ions *m/e* 376 and 363 in both spectra may be assigned structures liv and lv and arise by cleavages (9) and (10). Tripyrrane (XLVI) was in fact an anomal-



liv m/e 376

lv m/e 363

ous product isolated from an attempt[4] to prepare another tripyrrane (by coupling of a pyrromethane with a pyrrole), and the structure, deduced from elemental analysis and NMR spectra, was confirmed by its mass spectrum.

The tripyrroketone (XLVII) exhibits a much more complex fragmentation pattern than the other two tripyrranes; the molecular ion is the base peak, and substantial fragment ions corresponding to a number of different modes of inter-nuclear cleavage are observed. This markedly different behaviour must be attributed to the stabilizing effect of the ketonic carbonyl group.

The tetrapyrroketone (XLVIII; Fig. 6) which also exhibits an intense molecular ion behaves in a different fashion to the foregoing tripyrroketone, largely perhaps

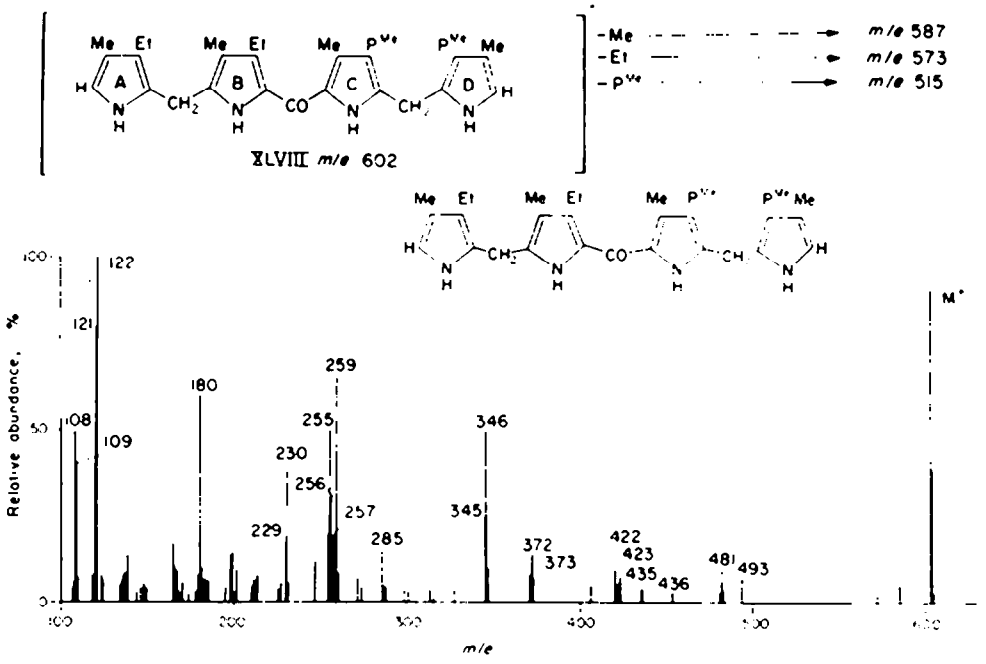
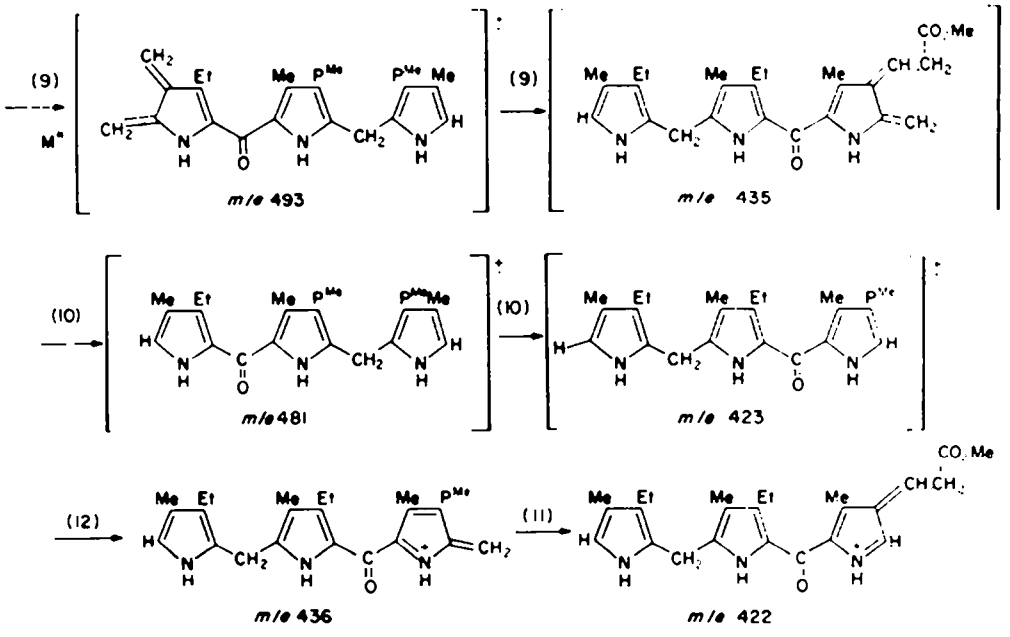
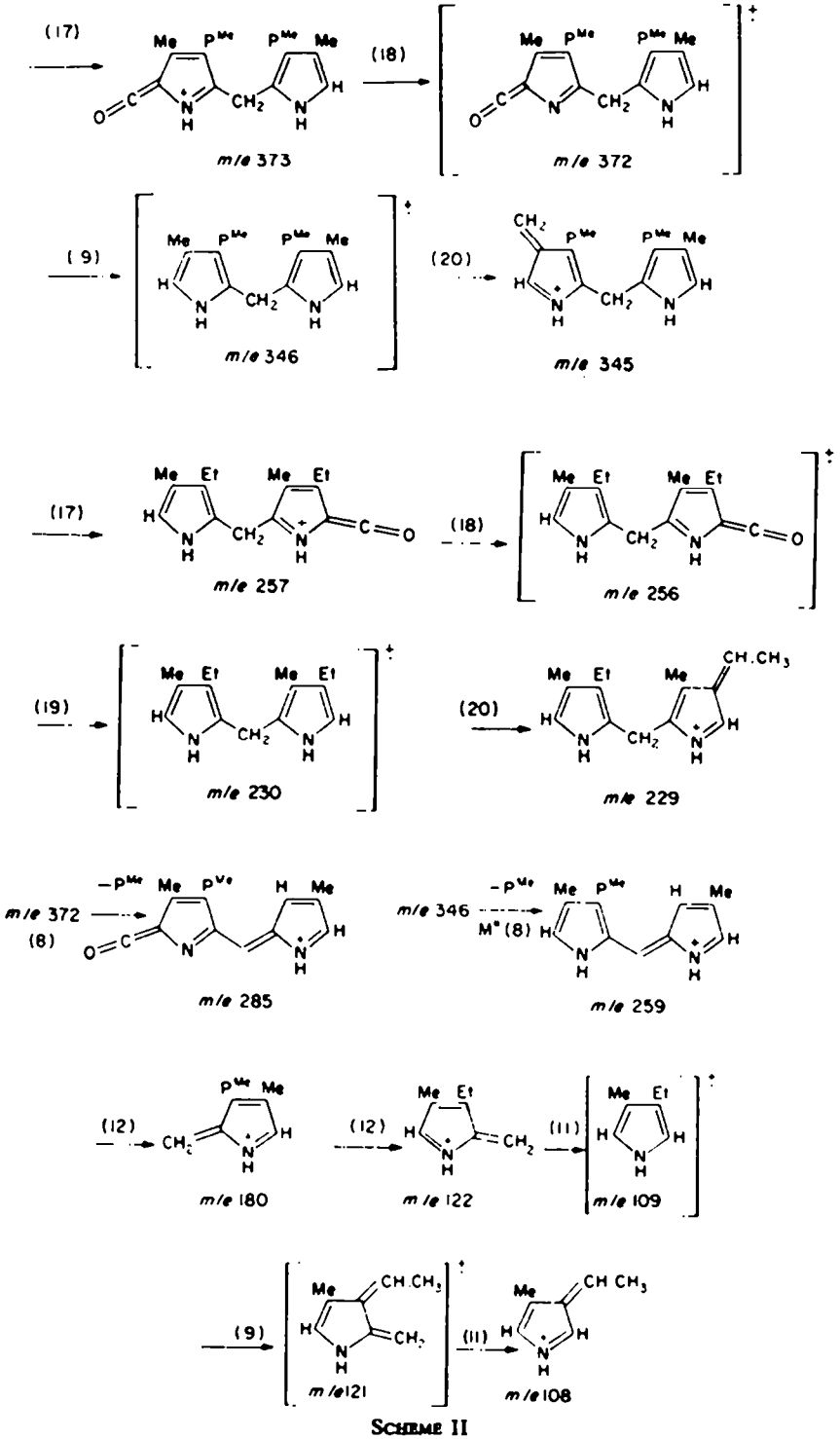


FIG. 6. Mass spectrum of tetrapyrrane (XLVIII) (Direct inlet) cf. Scheme II.

because it lacks any nuclear carbonyl substituents other than the ketone group itself. Structures for most of the principal fragments are given in the following scheme together with an indication of the probable modes of cleavage involved in their formation:



SCHEME II



SCHEME II

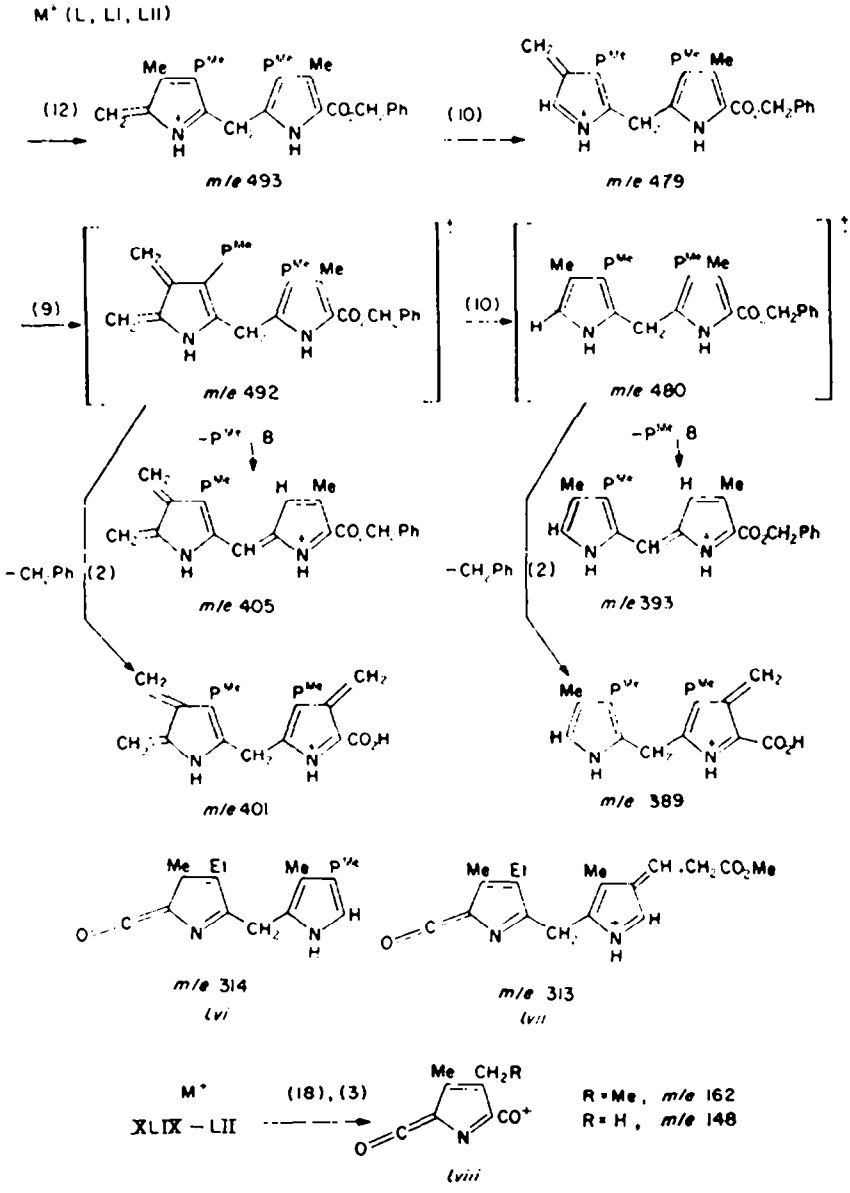
It will be seen from Fig. 6 that tripyrrolic fragments are relatively very weak compared to mono- and di-pyrrolic fragments, and that dipyrrolic fragments arising from the two central rings are *not* formed; thus cleavage at the central ketonic linkage appears to be favoured over cleavage at either of the two methylene bridges. Complete cleavages of β-substituents (type 8) are more marked in the spectrum of this tetrapyrrole than in the preceding tripyrroketone (XLVII) presumably because the hydrogen transfer processes from the methylene bridges, which accompany them to give stable methene-salt-like species (see page 4) are facilitated by the absence of electron-withdrawing substituents in the terminal rings of the tetrapyrrole. One such cleavage, from a dipyrrolic fragment, is marked by a strong metastable peak, i.e. 346 → 259 (cleavage of $CH_2CH_2CO_2Me$), m*, obs. 194; calc. 294.

The remaining tetrapyrranes, prepared in the course of our synthetic studies in porphyrins,[cf.5] present an interesting series for comparison of the effects of minor structural variations on the observed fragmentation patterns. The first point to notice is that although the spectra were all determined on the same spectrometer (MS9), under as similar conditions as possible, the intensities of the various ions very considerably from one spectra to another even though a large number of the ions are common to all the spectra; clearly the intensities (i.e. the extent of fragmentation) are very dependent on the precise running conditions.* As with the tetrapyrroketone already discussed, the molecular ions and tripyrrolic fragments are usually rather weak. Dipyrrolic and monopyrrolic fragments are much more intense, but, although reasonable structures can be written for most of the observed ions, these will not be discussed in detail, but rather the more important differences between the spectra which might be used in distinguishing between the compounds.

Ions *m/e* 493, 492, 480 and 479 arise from L, LI, and LII but not from XLIX, and they are therefore clearly characteristic of the C and D rings in the former compounds, and may be represented by the structures on the following page. Ions *m/e* 405 and 401 are methene like species observed in the spectra of L, LI and LII and formed by cleavage of the propionate and benzyl ester side-chains. The intense ions *m/e* 389 and 393 in the same spectra are also derived from the C and D rings probably by cleavage of the benzyl ester or propionate groups, either preceding or following internuclear cleavage of the tetrapyrroles. Ions *m/e* 314 and 313 are also observed in the spectra of L, LI and LII as would be expected. However the ions *m/e* 314 and 313 in the spectrum of XLIX cannot be due to the same species, but must be due to alternatives lvi and lvii arising from rings B and C. (It seems unlikely that the latter species are very important in contributing to the ions *m/e* 314 and 313 in L and LI since LII cannot give rise to them).

Other distinguishing features in the spectra are the ions *m/e* 162 and 148; the former occurs in the spectra of XLIX, L and LII only, and the latter in the spectrum of LII. These ions may be attributed to fragments lviii arising from the A-ring by cleavage at the carbonyl group (18) and loss of benzyloxy (3), or *vice-versa*.

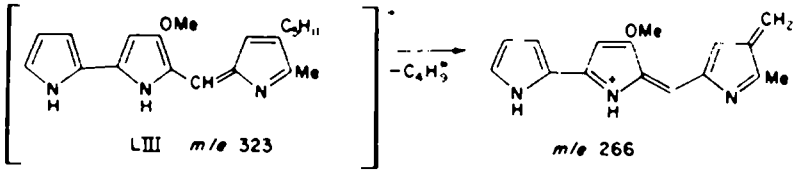
* We have found, for example, that the overall fragmentation pattern is very dependent on the time the sample is heated in the direct inlet and it is obvious that some thermal degradation must occur.



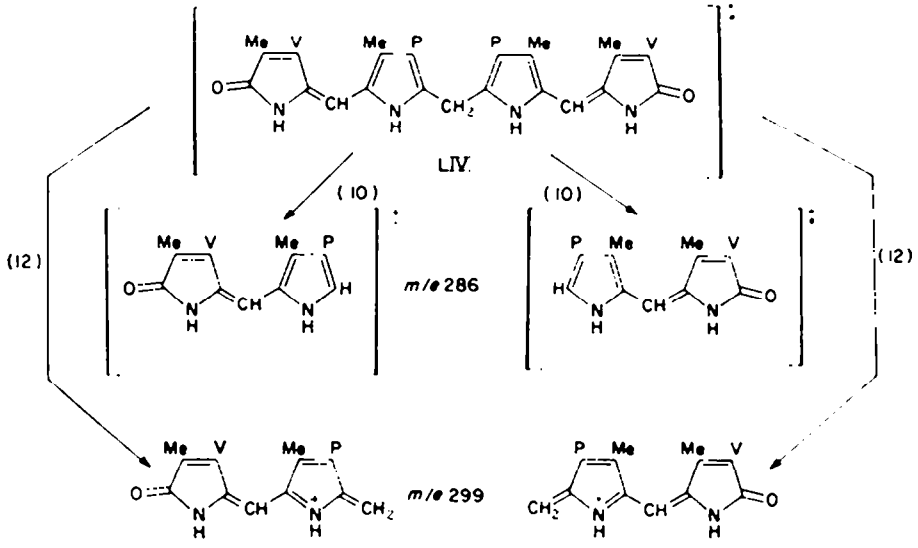
Natural products

The spectra of three linear polypyrroles have been determined, prodigiosin, bilirubin and d-urobilin. The spectrum of prodigiosin (LIII) is extremely simple; the parent ion is the base peak, as expected in view of the stability of pyrromethene linkages under electron impact (already discussed), and clearly the direct pyrrole-pyrrole linkage is equally (if not more) stable, for the only other intense ion produced results from β-cleavage of the alkyl side-chain (metastable peak at 219). (A weak ion is also observed for the loss of 15 mass units from the parent ion, and this may be derived either by cleavage of the terminal methyl group of the alkyl side-chain or by cleavage

of methyl from the methoxyl group). The identification of alkyl homologues of prodigiosin, such as those recently discovered,[14] by mass spectrometry should thus be relatively easy.



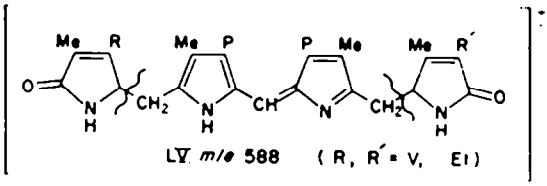
Bilirubin, which has an ac-biladiene (or methylene bispyrromethene) structure LIV also fragments largely as expected. The parent ion is quite strong (*m/e* 584) but the two principal ions in the spectrum arise from cleavages occurring at the weak point, the central methylene bridge. Most of the other minor peaks may be derived by side-chain cleavages of these two fragments, but the origin of the ion *m/e* 110 is obscure. Two alternative structures for each of these ions may be written, as shown,



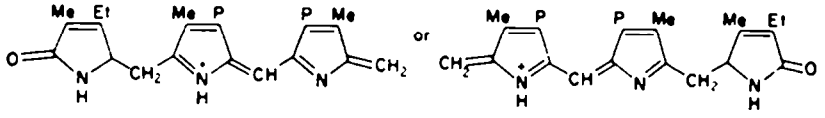
depending on which way the cleavage occurs, and there seems no reason to suppose that one may be favoured rather than the other.

The structure of the bile pigment, d-urobilin, which is a metabolite of bilirubin is still uncertain, but there seems to be general agreement[15] that it is best represented as one or other of the two tetrahydro-analogues of bilirubin (LVa or LVb). The mass spectrometric results support this contention, for the molecular ion is at *m/e* 588 (10% of the base peak) and an ion *m/e* 466 (absent in the spectrum of bilirubin) is presumably derived by fission of either one of the terminal rings (i.e. that one which still bears a vinyl substituent). For simplicity in the further discussion only one of these possibilities will be described, but it should be remembered that the mass spectrometric results do not allow of a distinction between them. Ions *m/e* 288 and 301 are

possibly the ethyl analogues of the vinyl substituted ions *m/e* 286 and 299 observed in the bilirubin spectrum, but the precise structure of the other intense dipyrrolic fragment *m/e* 302 is somewhat less certain. It is clear that the ion *m/e* 466 can be accounted for by a cleavage of a relatively weak methane linkage, but the formation of the dipyrrolic ions just mentioned must involve either fission of the much stronger central methene linkage, or alternatively extensive hydrogen rearrangements. It is perhaps significant in this respect that monopyrrolic fragments *m/e* 181, 180, 167, 166, 125, 122, 110, 108 etc. are much more intense than in bilirubin, and that fragments corresponding to the central two rings (which are joined by a methine bridge and which might therefore be expected to be relatively stable) are virtually non-existent.



LV *m/e* 588 (R, R' = V, Et)



m/e 466

EXPERIMENTAL

Mass spectra were determined with three different spectrometers, a C.E.C. No. 21-103C, and Atlas CH4 at Stanford, and an A.E.I. MS9 at Liverpool. In general, there were no significant differences between the results with different spectrometers. Heated inlet systems (200°) were used in the earlier experiments with the lower mol. wt. compounds, but with the tetrapyrranes it was essential to use "direct" inlet systems heated to 200-250°. The ionizing voltage was kept at 70 eV and the ionizing current at 50 μA.

Most of the compounds used in this work were prepared in the course of our studies at Liverpool aimed at the stepwise synthesis of porphyrins and some are also described by Fischer and Orth.[8,10] The preparation of XII and XIII is described below: XXI, XXXI–XXXIII and LV were supplied by Professor C. H. Gray and Dr. D. C. Nicholson, XXXIV by Professor H. Rapoport, LIV by Dr. R. J. S. Beer and Professor H. Rapoport, and LVI by Dr. A. Moscowitz. The structures of all the compounds prepared in Liverpool were confirmed by NMR spectra.

Dimethyl 4'-ethyl-3',4,5'-trimethylpyrromethane-3,5-dicarboxylate (XII) (with Mr. D. J. NEWMAN)

(a) Sulphuryl chloride (2·1 ml) in glacial AcOH (5 ml) was added dropwise with swirling to a hot (50°) solution of dimethyl 3,5-dimethylpyrrole-2 4-dicarboxylate[9] (5·2 g) in glacial AcOH (100 ml). The mixture was stirred at 70° for 1 hr and then allowed to cool overnight to room temp. The 5-*chloromethylpyrrole* (2·35 g 40%, m.p. 162°) which had crystallized out was filtered off and washed with light petroleum (b.p. 40–60°). On recrystallization from glacial AcOH the m.p. was raised to 167–168°. (Found: C, 48·8; H, 4·9; N, 5·9. $C_{16}H_{18}ClNO_4$ requires: C, 48·9; H, 4·9; N, 5·7%.)

(b) Benzyl 3,5-dimethylpyrrole-4-ethylpyrrole-2-carboxylate (4·0 g) in ether (170 ml) was hydrogenated at 1 atm and 20° over Pa–C (0·25 g g, 10%) After removal of catalyst and solvent the corresponding carboxylic acid was obtained as a pale pink crystalline solid

(c) The Li salt of the foregoing acid (prepared from 0·67 g acid and 0·15 g MeOLi) in 50% aqueous MeOH (10 ml) was added to a solution of the pyridinium salt of the above chloromethylpyrrole

(prepared from 0·92 g pyrrole and 2 ml pyridine) in 50% aqueous MeOH (20 ml). The mixture was kept at 40° for 40 hr (under N_2), and the reaction product filtered off and recrystallized from EtOH. The required *pyrromethane* (0·66 g 60%) had m.p. 143–144°. (Found: C, 65·2; H, 7·2; N, 8·3. $C_{16}H_{24}N_2O_4$ requires: C 65·0; H, 7·3; N 8·4%.)

Dimethyl 3,4,4',5'-tetramethylpyrromethane-3,5-dicarboxylate (XIII) (with Mr. D. J. NEWMAN)

This preparation was carried out in the same manner as XII but using benzyl 3,4,5-trimethylpyrrole-2-carboxylate instead of benzyl 4-ethyl-3,5-dimethyl-2-carboxylate. The required *pyrromethane* was obtained in 70% yield and had m.p. 179–181° (from MeOH). (Found: C 64·1; H, 6·9; N 8·7. $C_{17}H_{22}N_2O_4$ requires: C 64·1; H 7·0; N 8·8%.)

Acknowledgements—We thank the National Institutes of Health of the U.S. Public Health Service and the Nuffield Foundation for financial support. The purchase of the Atlas CH4 mass spectrometer was made possible through the National Aeronautics and Space Agency (Grant No. NsG 81-60). We are also grateful to Dr. R. J. S. Beer (Liverpool), Professor C. H. Gray and Dr. D. C. Nicholson (London), Dr. A. Moscowitz (Minneapolis) and Professor H. Rapoport (Berkeley) for several samples. We thank Mr K. M. Smith for assistance in determining some of the mass spectra.