Mass Spectroscopic Fragmentation Reactions, XIII:

The Behavior of Sterically Highly Hindered Porphyrins (1).

- Mass Spectra of Sterically Hindered Porphyrins -

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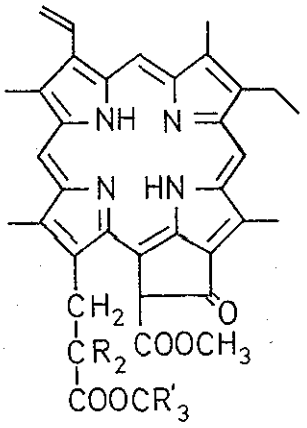
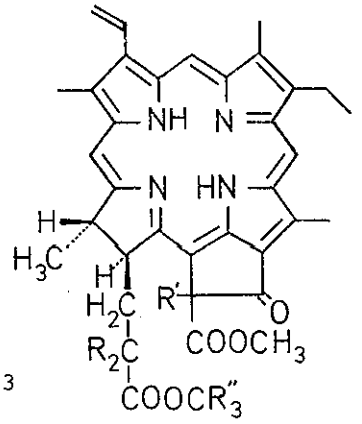
Dedicated to Dr. Ken'ichi Takeda.

It is shown that otherwise characteristic benzylic cleavage is reduced in importance as compared with complex fragmentation processes for compounds sterically hindered by 6,γ,7-substitution. Amongst these reactions are tetrahedralisation of C-γ and (in case of chlorins) formation of a 7,8-double bond, both accompanied by multiple H migrations. A rationale is given for the occasionally contradicting influence of complexed metal ions reported in literature.

Woodward (2) in the context of his chlorophyll synthesis explains the unexpected reactions of porphyrins substituted at 6-, γ- and 7-position by the steric interference of the substituents favoring strain releasing processes. This behavior is reflected also in the mass spectroscopic fragmentation: While porphyrins and chlorins lacking a γ-substituent undergo benzylic cleavage as expected for aromatic systems (3) introduction of the latter results in complex rearrangement processes as shall be demonstrated with typical examples for the four main classes, viz. pheoporphyrins, pheophorbides and 6-, γ-, 7-substituted porphyrins and chlorins without isocyclic rings.



1a: R=R'=H
1b: R=D, R'=H
1c: R=H, R'=D



2a: R =R'=R"=H
2b: R'=R"=H, R =D
2c: R =R'=H, R"=D
2d: R =R"=H, R'=CH_3

Vinylpheoporphyrin a_5 dimethyl ester (1a, Fig.1)

The spectrum of this compound has been discussed before (4,5).

The fragmentation processes suggested could essentially be corroborated by the labelled analogs (7"-CD_2, 1b, and 7"-$COOCD_3$, 1c). Loss of CH_3OH may in part be thermal, but an m^* (604 ⟶ 572) is observed. Elimination of $\cdot COOCH_3$ (m/e 545)

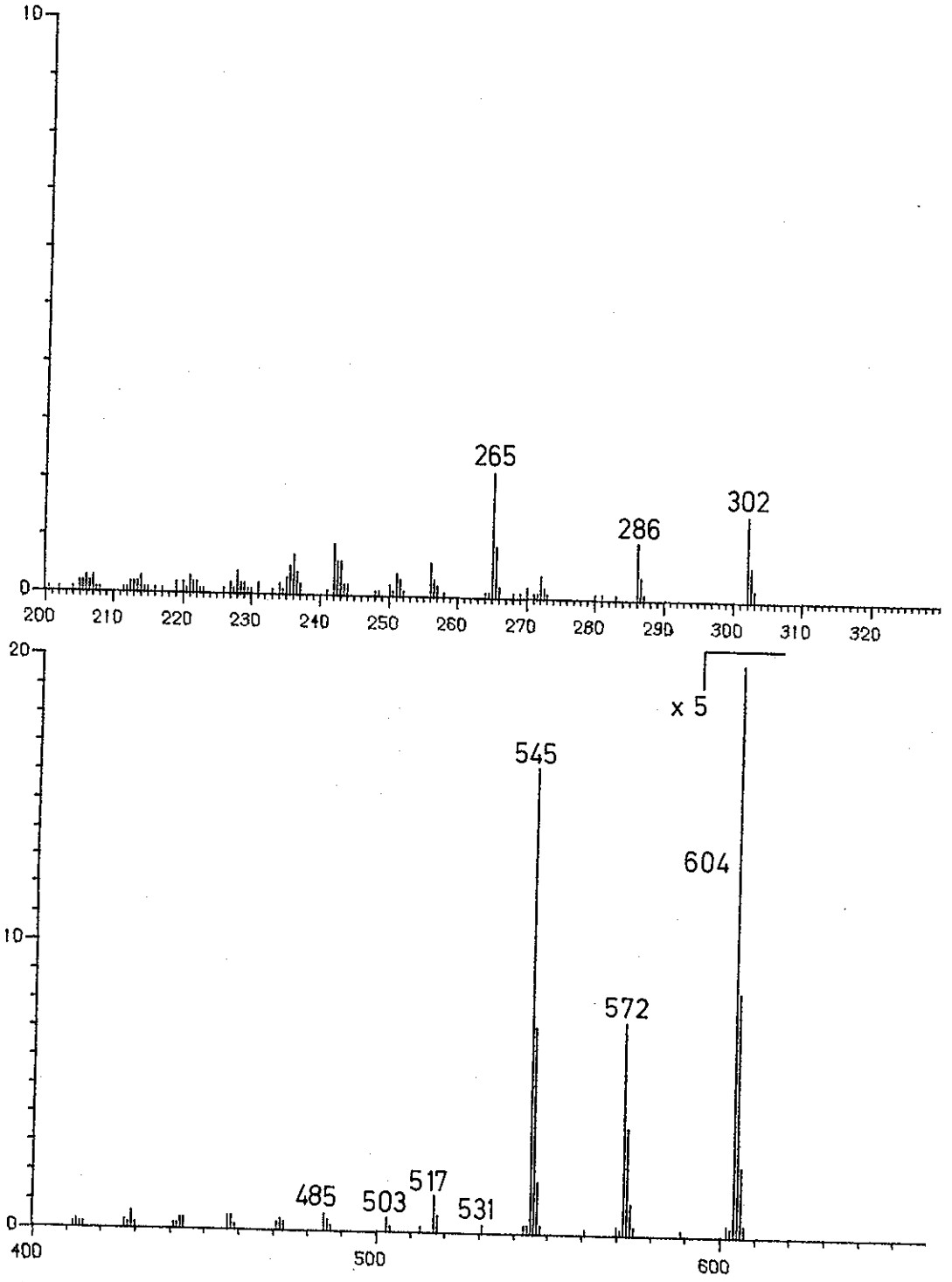
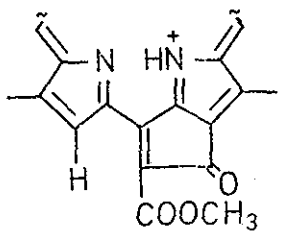


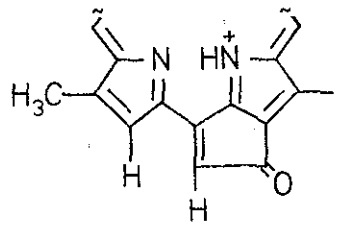
Fig.1 Mass spectrum of vinylpheoporphyrin a dimethyl ester (1a) (MAT 731, 70 eV, probe 240°, source 180°).

originates almost essentially from C-10, that of $^{\cdot}CH_2COOCH_3$ (m/e 531) from C-7 (as does $[M - {}^{\cdot}CH_2COOCH_3 + H^{\cdot}]^{++}$ (m/e 265); the origin of the additional H is unknown). As anticipated (predominance of even electron ions) (6) loss of a radical is followed by that of an even electron particle (m/e 545 - $HCOOCH_3$ ⟶ m/e 485; m/e 531 - CO ⟶ m/e 503).

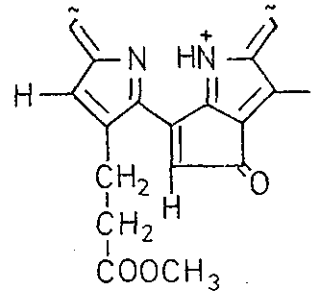
For the present topic the ion at m/e 517 ($C_{32}H_{29}N_4O_3$) is of importance. The genesis suggested (4,5) previously (M - $^{\cdot}COOCH_3$ from the C-7 side chain followed by expulsion of CO from C-9) contributes at best to a minor degree, elimination of the entire C-7 side chain (loss of the label from 1b and 1c) being the dominant process. Such a behavior (fourfold abundance as compared with the expected benzylic loss of $^{\cdot}CH_2COOCH_3$) would usually be taken as to suggest a chlorin structure. Tetrahedralisation of the trigonal C-7 (possibly by migration of the C-10 H) to release the steric strain (as pronounced (2) as typical for such systems by *Woodward*) explains this unexpected cleavage (a).



a



b



c

Methyl pheophorbide a (2a, Fig.2)

Deuterium labelling was available at 7"-CD_2 (2b) and at 7"-$COOCD_3$ (2c). Since C-10 H is exchanged in the mass spectrometer a methyl group (which does not influence the overall fragmentation behavior) had to be used instead for

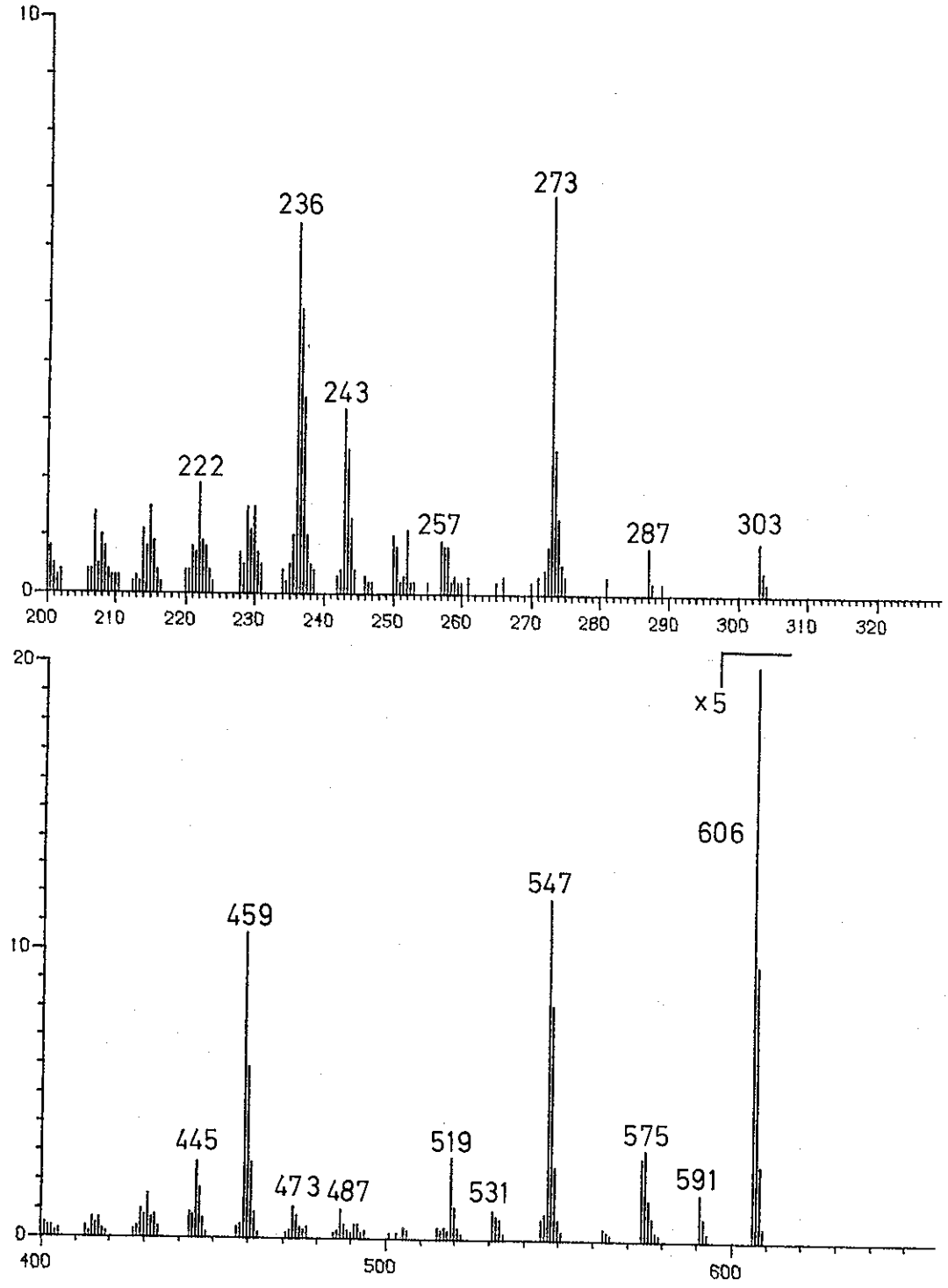


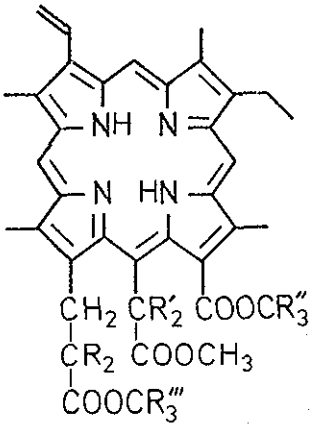
Fig.2 Mass spectrum of methyl pheophorbide a (2a) (MAT 731, 70 eV, probe 200°, source 190°).

labelling this position (2d). Except for the typical (7) loss of $^{\bullet}COOCH_3$ (m/e 547) exclusively from C-10 ($[M - {}^{\bullet}COOCH_3 - H^{\bullet}]^{++}$; m/e 273, comprises, however, 75% loss from C-10 and 25% from C-7; the origin of the additional H is unknown, not C-7" or C-10) simple cleavages resulting in elimination of one radical moiety are of minor importance (M - $^{\bullet}OCH_3$, m/e 575, only from the propionic ester chain, while M - CH_3OH stems from the C-10 carbomethoxy group; M - $^{\bullet}CH_2CH_2COOCH_3$, m/e 519, loss of the entire C-7 substituent[1]) the spectrum being governed by complex processes. The most conspicuous one results in m/e 459 ($C_{30}H_{27}N_4O$, M - 147). For this ion (for which an m* $M^{+\bullet} \longrightarrow$ m/e 459 has been observed, cf. (8) various structures and geneses have been suggested (3,4,7). An IKE spectrum indicates (besides the m* for the entire loss) two paths of formation, viz. $M^{+\bullet} \longrightarrow [M - 59]^+ \longrightarrow [M - 147]^+$ and $M^{+\bullet} \longrightarrow [M - 87]^+ \longrightarrow [M - 147]^+$. This shows (as proven by the labelled analogs) that in either sequence benzylic loss of one ester chain (C-7 or C-10) is followed by elimination of the other one plus one H of unknown origin (not from C-10). The most likely candidate is, however, C-8 since its loss results in a porphyrinic structure (b) (cf. the prefered formation of a from 1a). In the case of a loss of $[^{\bullet}CH_2CH_2COOCH_3 + H^{\bullet}]$ cis elimination would be a one-step process; a concomitant elimination of $[^{\bullet}COOCH_3 + H^{\bullet}]$ would have to be preceded by an H *migration*. This explains in either case why $H^{\bullet}$ and not the more stable $^{\bullet}CH_3$ is lost from C-8 (m/e 445 is formed by a completely different mechanism as shown by its IKE spectrum). An analogous sequence seems to lead to m/e 531 (M - 75): Loss of the C-10 - $COOCH_3$-group is followed by elimination of $^{\bullet}CH_3$ and $^{\bullet}H$ (c).

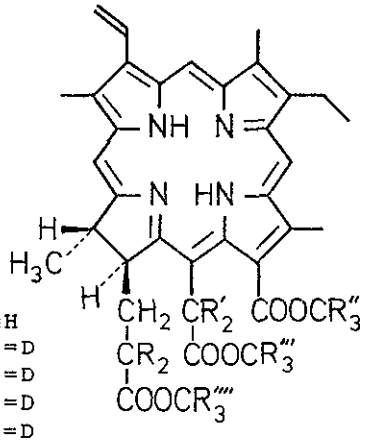
[1] Since as shall be shown below chlorins tend to fragment in a way that the 7,8-double bond is restored this ion may well suffer H *migration* from C-8 to N (cf. Cu-2a below).

m/e 487 (M - 119) is composed of $C_{32}H_{31}N_4O$ and $C_{31}H_{27}N_4O_2$ (2:3). The IKE spectrum discloses the following sequences: M - 59 - 60, M - 31 - 88, M - 87 - 32, i.e. fragmentation processes comprising the two ester groups. This is in accordance with the labelling data; due to the complex situation ion structures will, however, not be postulated. The same pertains to m/e 473 (M - 133, $C_{31}H_{29}N_5O$) for the genesis of which an IKE spectrum again indicates multiple ways of formation (the 7"-$COOCH_3$ group is lost in every instance).

m/e 243 ($[M - 120]^{++}$) results from the elimination of both carbomethoxyl groups plus 2 additional H· one of which comes from C-7". m/e 236 ($[M - 134]^{++}$) is formed by elimination of ·CH_2COOCH_3 (from C-7), ·$COOCH_3$ (from C-10) plus 2 additional H·.



3a: R =R'=R"=R'"=H
3b: R'=R"=R'"=H; R =D
3c: R =R"=R'"=H; R'=D
3d: R =R'=H; R"=R'"=D
3e: R =R'=R'"=H; R"=D



4a: R =R'=R"=R'"=R""=H
4b: R'=R"=R'"=R""=H; R =D
4c: R =R"=R'"=R""=H; R'=D
4d: R =R'=R'"=R""=H; R"=D
4e: R =R'=R'"=H; R"=R""=D
4f: R =R'=R"=H; R'"=R""=D

Chloroporphyrin e_6 trimethyl ester (3a, Fig.3)

While for 1 and 2 the steric interference of the substituents is somewhat reduced by the formation of the isocyclic ring it ought to become more obvious for 3. The mass spectrum is deceivingly simple (loss of ·$COOCH_3$; ·CH_2COOCH_3; ·OCH_3

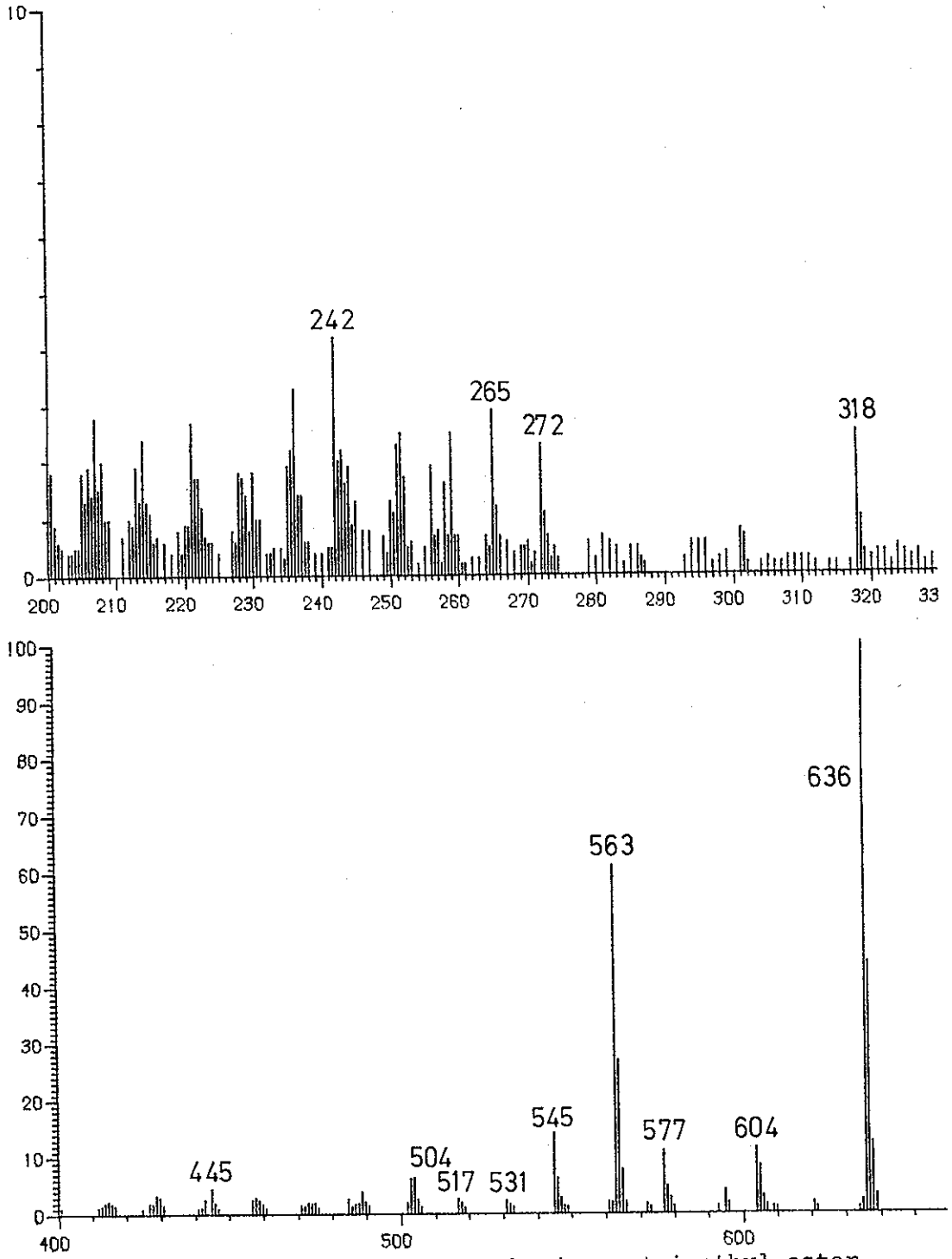


Fig.3 Mass spectrum of chloroporphyrin e_6 trimethyl ester (3a) (MAT 731, 70 eV, probe 240°, source 230°).

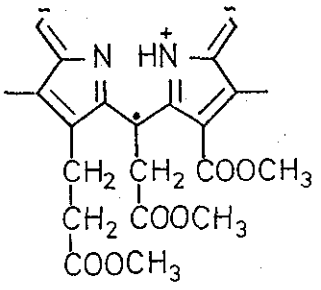
mainly from the C-7 substituent, while CH_3OH is lost from C-6 together with an H from C-γ' (50%)). The complex processes leading to fragment formation being revealed only by deuterium labelling (3b: 7",7"-CD_2; 3c: γ',γ'-CD_2; 3d: 6,7"-di-$COOCD_3$; 3e: 6-$COOCD_3$; 3f: χ,χ-d_2,6-$COOCD_3$, χ meso or NH).

$[M - {}^{\cdot}COOCH_3]^+$ (m/e 577). Only 60% of this ion are formed by the expected benzylic cleavage of the C-γ side chain, the remainder comes from C-6, a process analogous to the one leading to $[M - 87]^+$ from 1 (v. supra). That elimination of the C-6 and not (at least in addition) of the C-7 substituent is observed can be explained by the better radical stabilization (primary vs. carbonyl) in the neutral fragment. m/e 545: As shown by the IKE spectrum $^{\cdot}COOCH_3$ and CH_3OH are lost in either sequence involving the C-6 and the C-γ substituent.

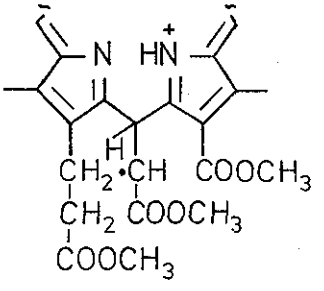
$[M - {}^{\cdot}CH_2COOCH_3]^+$ (m/e 563). This ion is not formed by the expected benzylic cleavage of the C-7 side chain but rather by elimination of the C-γ substituent in a complex rearrangement process: 1 D is lost completely from 7"-position (3b) while from the C-γ'-label (3c) 60% d_1 and 40% d_2 is retained. In addition, the χ-D from 3f is partially lost indicating scrambling of the aromatic protons. The driving force seems to be again release of strain by sp^3-hybridisation (v. supra) of a peripheral carbon atom (d ⟷ d' ⟷ d"). If the γ' ⟶ γ 1,2-H shift is a reversible reaction the ring-γ'-scrambling (resulting in the loss of χ-H and in the retention of γ'-H) can be readily explained. The γ-substituent can only be eliminated after H transfer to the γ'-radical site (d"') (otherwise there would result a carbene loss (cf. 10))which appearantly occurs from C-7" (due to the cyclic transition state involved a process with low frequency factor) probably with concomitant H-shift from C-8' or from C-7' (d"") to obtain a conjugated

system and at the same time to fill up the secondary radical site at C-7" (e).

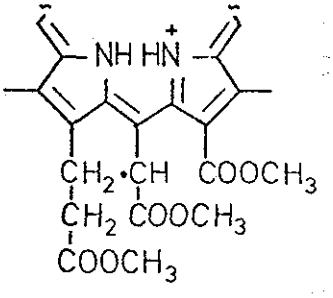
m/e 517 (M - 119) consists of a doublet, $C_{33}H_{33}N_4O_2$ (loss of 2 $^{\cdot}COOCH_3$ from C-6 and from C-γ plus an additional H$^{\cdot}$ of unknown origin), and $C_{32}H_{29}N_4O_3$ (loss of $^{\cdot}CH_2CH_2COOCH_3$ from C-7 + CH_3OH from C-6). m/e 503 (M - 133), $C_{32}H_{31}N_4O_2$ stems from the loss of $^{\cdot}CH_2COOCH_3$ from C-γ and $^{\cdot}COOCH_3$ + H$^{\cdot}$ from C-7.



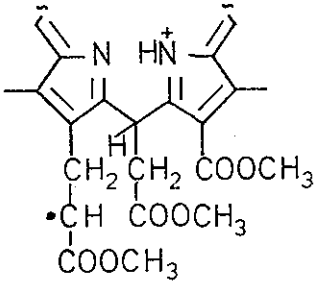
d



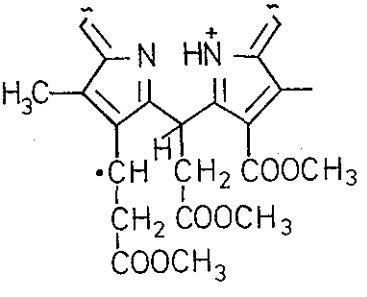
d'



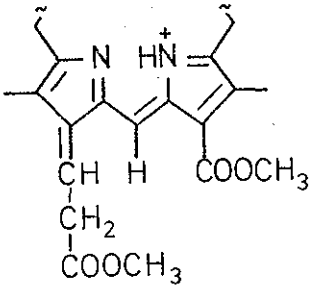
d"



d"'



d""



e

Chlorin e_6 trimethylester (4a, Fig.4)

Labelled analogs: 7",7"-CD_2 (4b), γ',γ'-CD_2 (4c), 6-$COOCD_3$ (4d), 6,7"-di-$COOCD_3$ (4e), 7",γ'-di-$COOCD_3$ (4f); cf. (3,4,8,9).

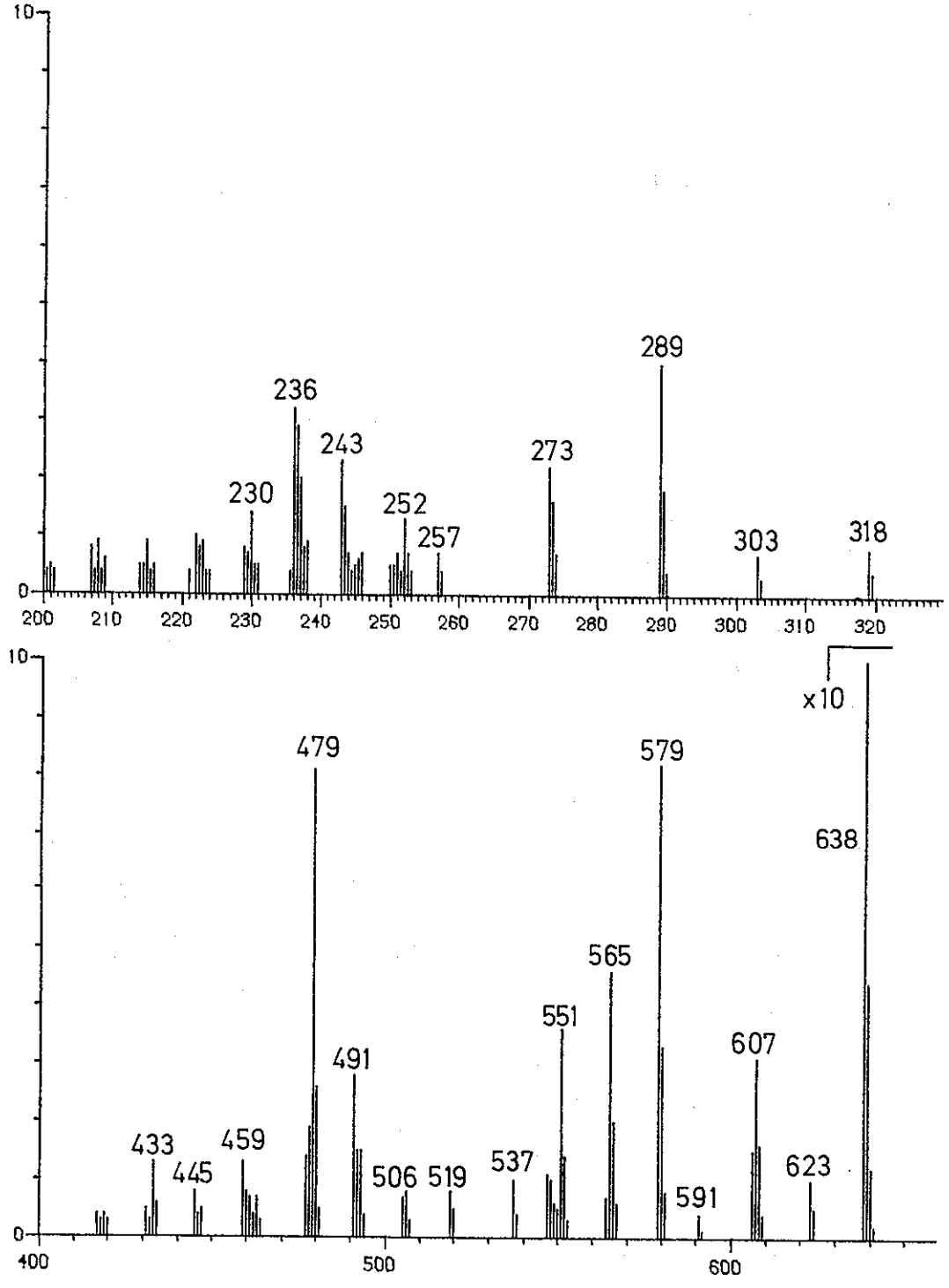
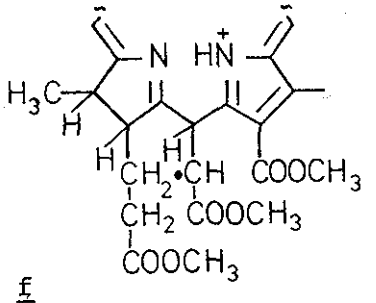


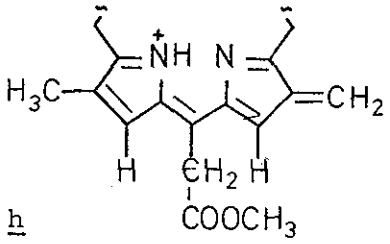
Fig.4 Mass spectrum of chlorin e_6 trimethyl ester (4a) (MAT 731, 70 eV, probe 200°, source 170°).

$[M - {}^{\cdot}COOCH_3]^+$ (m/e 579). 80% stem from benzylic cleavage of the C-γ chain, 20% from elimination of the C-6 ester group. The lower percentage of this "direct ring cleavage" as compared with 3a reflects the reduced steric strain due to the sp^3-hybridized C-8. $[M - {}^{\cdot}COOCH_3 - H^{\cdot}]^{++}$ (m/e 289) involves elimination of 60% from C-γ' and 40% from C-6 with an additional H· which neither comes from C-γ' nor from C-7". m/e 547 (M - 91, i.e. $[M - {}^{\cdot}COOCH_3 - CH_3OH]$) involves the C-6 and C-γ, but not the C-7 substituent (*cf.* 3a). $[M - {}^{\cdot}CH_2CH_2COOCH_3]^+$, m/e 551 reflects exclusively the loss of the C-7 chain.

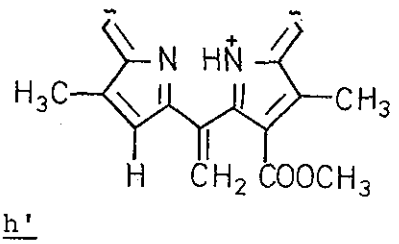
$[M - {}^{\cdot}CH_2COOCH_3]^+$ (m/e 565). As observed with 3a the C-γ side chain is lost accompanied by complex H *migrations*: From 4b is retained about 10% d_o, 30% d_1 and 60% d_2, from 4c about 40% d_o, 40% d_1 and 20% d_2. From these data it can be concluded that H-*scrambling* is of minor importance here since only ~20% d_2 are retained from C-γ'-d_2. H-transfer from C-γ' to C-γ and from C-7" to C-γ' (cf. d ↔ d' ↔ e) may be responsible for about 30% of this ion. It is possible that due to the altered steric relationship as compared with d the γ'-radical site in f may pick up an H not only from C-7" but also from C-7 or C-7' which would account for the remaining 10% loss of one C-γ' H. For 40% an H atom from some other source has to be transfered to C-γ to obtain sp^3-hybridisation which results in the loss of the C-γ side chain together with both C-γ' D-atoms. In any case release of steric strain by turning the γ-substituent out of the ring plane is reached by several competing processes though the driving force is the same.



f



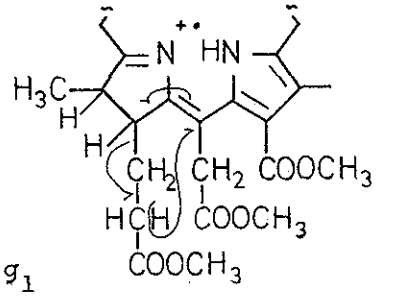
h



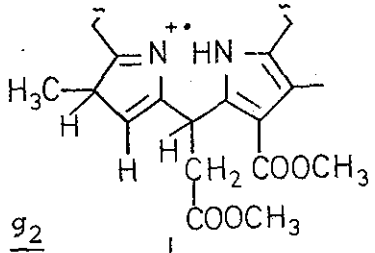
h'

m/e 479 (M - 159, $C_{30}H_{31}N_4O_2$) is the most important species exhibiting an m* for the entire loss from $M^{+\cdot}$ (8). Since the label from 4f is lost during this process the following sequence has been suggested yielding g (8) (the IKE spectrum demonstrates also the steps $M^{+\cdot} \longrightarrow$ m/e 552 $\longrightarrow$ m/e 479).

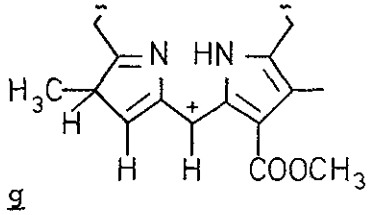
From 4b can be seen one D is lost only partially indicating that the process leading to g can be responsible at the most for 20% of m/e 479. The major part seems to be associated intimately with the elimination of C-γ CH_2COOCH_3 discussed above the amounts of loss of the C-γ' label being about the same here (loss of d_1 and d_2 ~1:1). Since about 80% of d_2 from C-7" is lost (possibly multiple) H-shifts either to C-γ or to C-γ' (f) must occur from sites which have not been labelled. The final ion way well be g in every case.



g1



g2



g

m/e 537 (M - 101, $C_{32}H_{33}N_4O_4$). An IKE spectrum suggests the sequence $M^{+\cdot} \longrightarrow [M - 86]^{+\cdot} \longrightarrow [M - 101]$ (cf. m/e 479). The elemental composition and the labelling data indicate loss of the C-7 side chain (from C-7" d_1 and d_2 is lost at about equal amounts) with back rearrangement of 1H and in analogy to the formation of m/e 479 concomitant radical elimination (probably C-8 CH_3 group). m/e 519 (M - 119, $C_{32}H_{31}N_4O_3$) is formed by the loss of the entire C-7 side chain, $^{\cdot}OCH_3$ in equal amounts from C-γ and C-6 ester group and an additional H$^{\cdot}$ (not from C-γ'). m/e 491 (M - 147, $C_{31}H_{31}N_4O_2$). Loss of 147 u is the dominating process for 2a. In contrast, however, to the rather straightforward situation in the case of the latter the IKE spectrums suggests for 4a multiple paths of formation (from m/e 506, 519, 551, 565, and directly from M^+). Labelling reveals that at least $^{\cdot}CH_2COOCH_3$ is lost from the C-7 substituent, that the C-γ'-label is retained completely and that $^{\cdot}OCH_3$ is lost from the C-6 and C-γ ester groups in equal amounts. Structures as h and h' are likely candidates.

Cu methyl pheophorbide a (Cu-2a, Fig.5)

Labelled analogs available Cu-2c and Cu-2d. The metal complexes shed some further light on the fragmentation processes of highly substituted chlorins. Most conspicuously $[M - 87]^+$ (loss of the C-7 ester chain) is absent. This observation falls into the pattern of the tendency of chlorins to restore the porphyrinic 7,8-double bond (b, c). In the case of uncomplexed 2a this can be achieved by migration of C-8 H to one of the central N atoms after the loss of the C-7 substituent (hence $[M - 87]^+$ is observed). Such an H shift is not possible if the N atoms are occupied by the complexing metal ion; hence double bond formation is possible only by further radical losses (M - 147, b). Similarly, $[M - 75]^+$ is enhanced in abun-

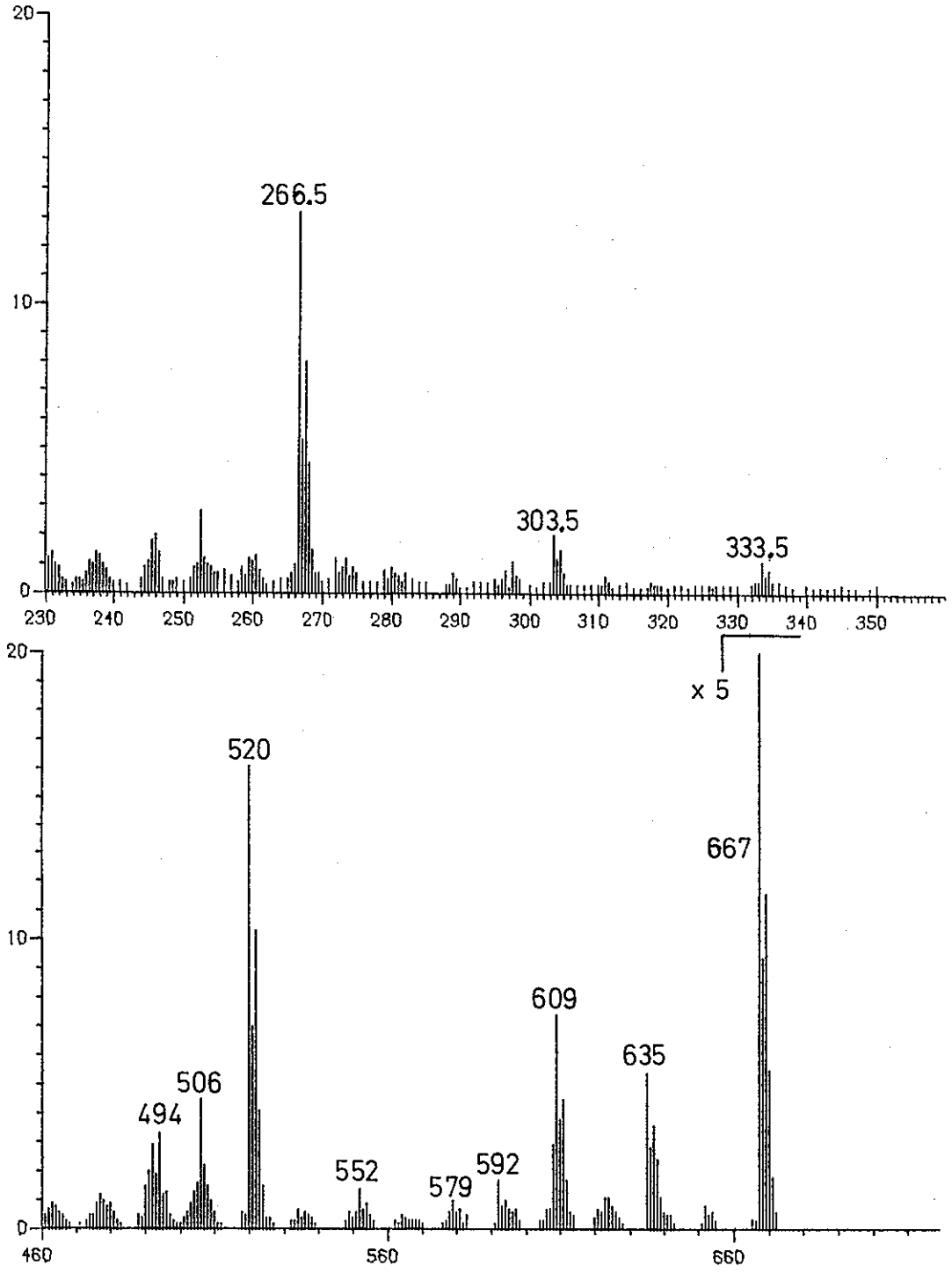
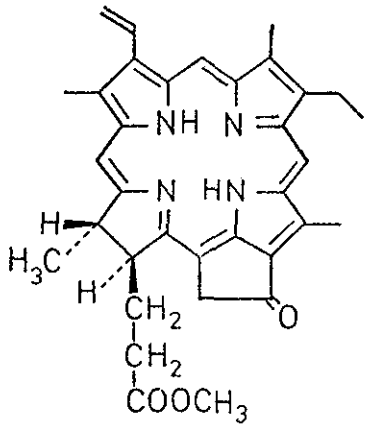


Fig.5 Mass spectrum of Cu methyl pheophorbide a (Cu-2a) (MAT 731, 70 eV, probe 240°, source 170°).

dance. That the transition chlorin ⟶ porphyrin is an energy gaining and, therefore, favorable process becomes evident from the spectrum of Ni pyromethylpheophorbide a Ni-5 (4,11) where again loss of $^{\cdot}CH_2CH_2COOCH_3$ (M - 87) per se (which is the main process for the uncomplexed compound) becomes negligible while combined elimination with CO (M - 115) is raised in importance to give the most abundant fragment (35% rel. int.). Formation of, e.g., i could explain this behavior.



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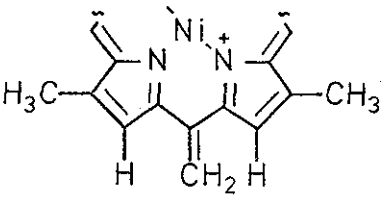


i

Cu chlorin e_6 trimethyl ester (Cu-4a, Fig.6)

Labelled analogs available Cu-4b, Cu-4c, Cu-4d. The most striking differences in comparison with uncomplexed 4a are drastic reduction in abundance of single radical losses (M - 73 without appearant H *migrations*), no $[M - 159]^+$; $[M - 147]^+$ (labelled analogs suggest formation as from the uncomplexed 4a with a slight preference of elimination from C-6, viz. 60%) and $[M - 160]^{+\cdot}$ are the prevailing fragment ions, the latter again without appearant H-shifts. $[M - 160]^{+\cdot}$ (m/e 539) is formed by elimination of the C-γ + C-7 substituents. The differing behavior of uncomplexed and complexed 4a finds it's

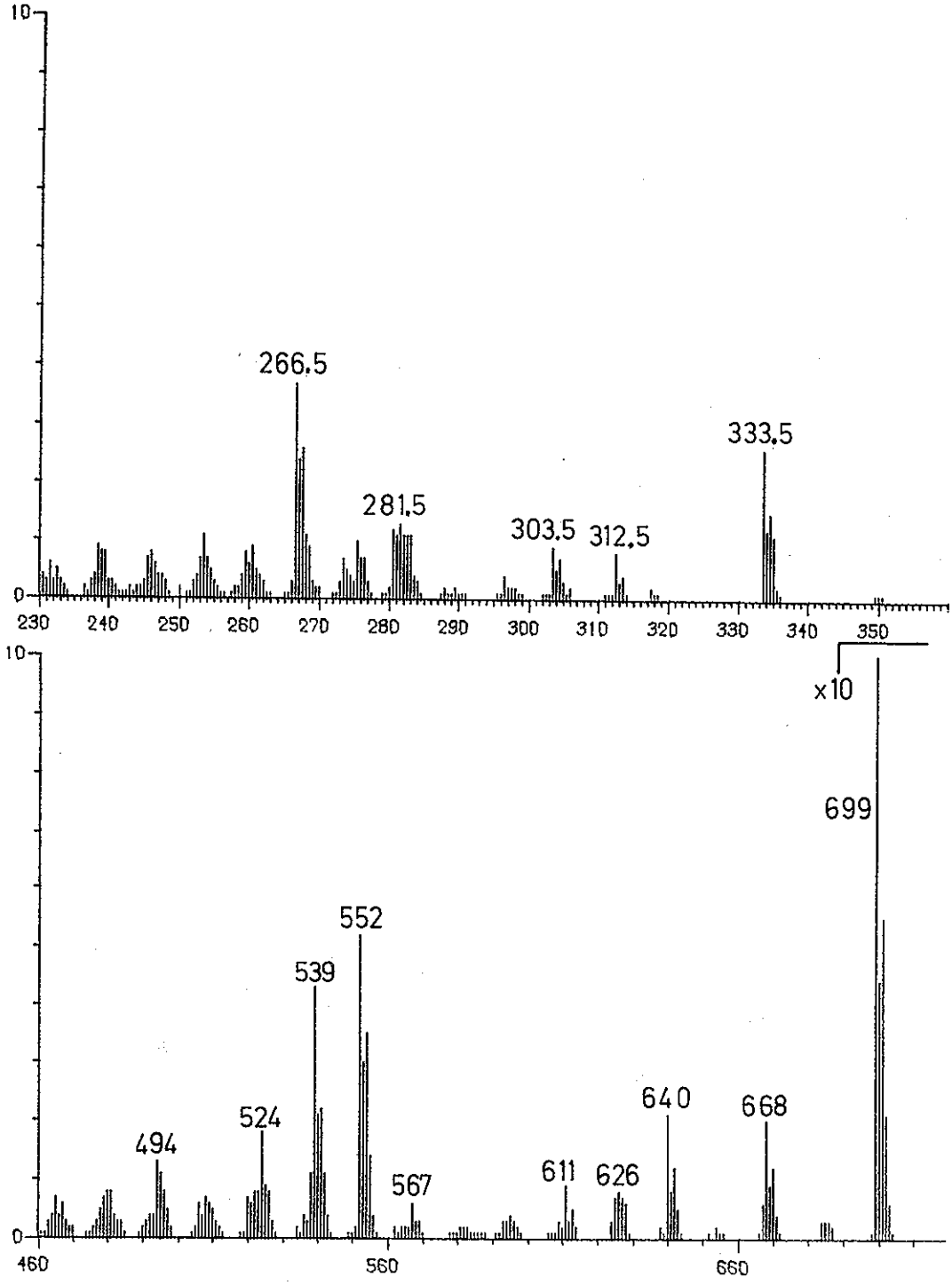
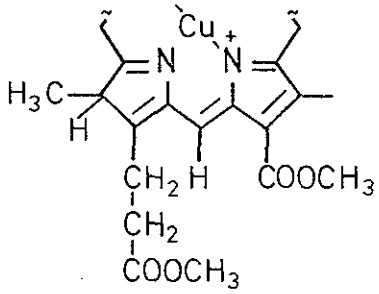
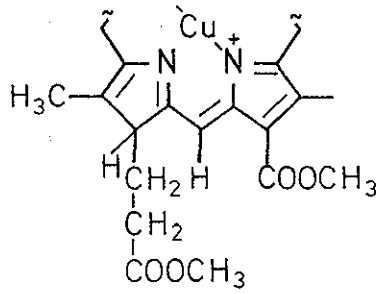


Fig.6 Mass spectrum of Cu chlorin e_6 trimethyl ester (Cu-4a) (MAT 731, 70 eV, probe 210°, source 180°).

explanation in the stabilisation of the odd-electron $M^{+\cdot}$ by absorption of the unpaired electron by the metal (11). Hence, typical radical processes as the H-shifts during the formation of $[M - 73]^+$ and $[M - 159]^+$ which comprise temporary radical sites in the side chains are suppressed. However, since steric strain can only be alleviated by sp^3-hybridisation of C-γ this has to be achieved by a shift of the C-7 and C-8 H with subsequent loss of the $\cdot CH_2COOCH_3$ group (k,k'). Elimination of $\cdot CH_2CH_2COOCH_3$ (M - 160) or of $\cdot CH_3$ (M - 88) restores the porphyrinic structure. The role of the central Cu in radical stabilisation is further demonstrated by the high number of ions formed by the loss of an even electron neutral (m/e 626, 552, 524, 494).



k



k'

The spectra both of Cu-2a and Cu-4a exhibit an abundant ion at m/e 266.5. From Cu-2a it is formed by the loss of $\cdot COOCH_3$ from C-10 and of $\cdot CH_2COOCH_3$ from C-7', in the case of Cu-4a by additional loss of CH_3OH (C-γ' H is partially involved).

Summarizing the following generalisations are possible for porphyrins and chlorins substituted in 6-, γ- and 7-position:

1) Benzylic cleavage is still a favored process which may, however, be imbedded in more complex fragmentations.

2) Release of steric strain is achieved by sp^3-hybridisa-

tion of one of the peripheral C by H *migration*. The primary step which may comprise H transfer from various loci of origin (resulting occasionally in a typical scrambling) can entail subsequent H *migration* to compensate for newly formed radical sites. The macrocyclic conjugation if interrupted by such tautomerisation is restored by elimination of a substituent. Despite of the various paths leading to it an ion may well finally have an unique structure.

3) Chlorins in addition to the release of strain by process 2) tend to restore the 7,8-double bond. This can be achieved either by H *migration* after loss of especially the C-7 substituent or by the (formal) loss of 3 radicals. Hence, abundant ions due to combined eliminations are observed. For those in addition to metastable transitions for the single steps an m^* for the entire elimination starting from $M^{+\cdot}$ is observed indicating a triggering function of the first process if not (within the time scale of a mass spectrometer) concertedness of the overall fragmentation.

4) Hydrogen migrations are suppressed in metal complexes when they result in the intermediate formation of radical sites outside of the macrocyclic system. Therefore, loss of the entire γ-substituent per se is reduced in abundance and not any more accompanied by partial retentions of the C-γ' label and by H-transfer from the C-7 side chain. In addition, tautomerisation involving N as an H acceptor is no more possible. Since such a process seems to restore the 7,8-double bond after elimination of the C-7 substituent from a chlorin, loss of the latter per se is also drastically reduced in abundance. However, H *migrations* along the periphery (e.g., C-7 $\longrightarrow$ C-γ) seem to be feasible releasing the steric strain by sp^3-hybridisation of C-γ followed by the loss of its substituent and subsequent elimination of one of the substituents from ring D to form the 7,8-double bond.

5) The observations discussed above shed also some light on the somewhat enigmatic influence of the complexing metal upon the fragmentation (for a literature compilation see (12)). *Meot-Ner* (13,14) had observed that unsubstituted porphin as well as meso-tetraphenylporphin preferentially lose odd numbers of radicals ($H^{\bullet}$, $Ph^{\bullet}$) in accordance with the known stability of even electron systems (6), while their metal complexes eliminate even numbers of radicals irrespective whether the metal may exist in a lower valency state or not; cf. (11). All porphyrinic systems, however, carrying aliphatic substituents, cf. (11,12) (for those with steric interference of their side chain v. infra) do not show such a change in behavior if complexed. The explanation offered by *Meot-Ner* (13,14) is that porphin or meso-tetraphenyl porphin necessarily loses an electron from the Π-system during ionisation and loss of an odd number of substituents would restore even-electronicity, loss of 3 radicals even a new *Hückel* system (providing electron counting to comply with the 4n + 2 formula means anything in the complex porphin Π-system!). In a metal complex of one of the unsubstituted aromatic systems ionisation will occur at the metal and hence even-electronicity of the macrocycle is retained by the loss of an even number of radicals (in which way, e.g., Mg^{++} should lose a further electron has not been discussed, possibly from one of the common Mg-N orbitals). For aliphatically substituted systems the radical site formed during ionisation is assumed to be located outside the ring system and hence there is no different behavior of complexed and uncomplexed compounds.

The last argument is not quite convincing since ionisation and radical localisation outside the Π-system would not be compatible with the low IP, and especially with the normal behavior of alkyl substituted porphyrins (11,13) and the high stability of benzylic ions which demands charge delocalisa-

tion. The answer seems rather to rest on product stabilisation. An ion formed by benzylic cleavage is so well resonance stabilised (participation of non-bonding electrons from N, cf. (15), possibly ring expansion analogous to benzyl ⟷ tropylium) that even contribution of an electron from a metal atom will not render a different process more favorable. Hence there is no apprecible influence of the complexing metal upon the fragmentation behavior, while for unsubstituted species where benzylic cleavage cannot occur radical stabilisation by the metal plays a dominating role (v. supra). Radical stabilisation by the complexing metal becomes evident also for highly substituted compounds where benzylic cleavage by itself does not bring the necessary release of steric strain. 1,2-H shifts (e.g., C-γ' ⟶ C-γ) removing the radical site temporarily from the π-system would need additional activation energy making these processes less likely. H *migration* on the periphery followed by substituent elimination, loss of even electron species or of two radicals etc. determine now the appearance of the spectrum which is not any more dominated by the - otherwise - overwhelmingly favorable benzylic cleavage (16).

Acknowledgement

Financial support by *Deutsche Forschungsgemeinschaft* and by *Fonds der Chemischen Industrie* is gratefully acknowledged.

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Received, 26th July, 1976