MASS SPECTRA OF 4,4-DIMETHYL-A-HOMOCHOLESTANE-3,5- AND 3,4a DIOLS AND THEIR DERIVATIVES*

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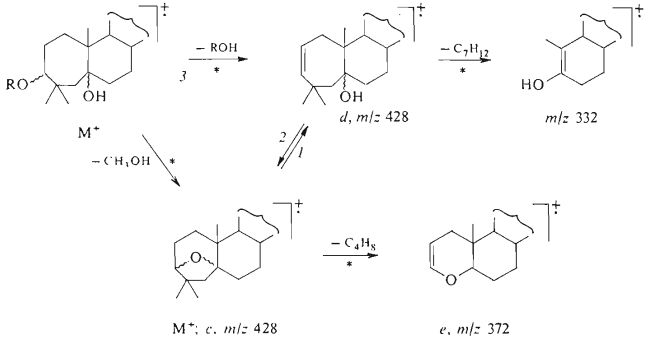
Received October 20th, 1981

Partial mass spectra of the following 4,4-dimethyl-A-homocholestane derivatives are given: 3,5-epoxides *I* and *II*, 3,5-diols *III*—*VI*, 3-methoxy-5-ols *VII*—*IX*, 3-acetoxy-5-ol *X*, 3,4a-diols *XI*—*XIV*, 3-acetoxy-4a-ols *XV*—*XVIII* and 4,4-[$^2H_6$]-dimethyl-3,4a-diol *XIX*, and their electron-impact fragmentation investigated. The mass spectra of epoxides *I* and *II*, diols *III*—*VI* and acetate *X* are very similar. Considerable differences in mass spectra of methoxy derivatives *VII*—*IX* are explained by two mechanisms of elimination of CH_3OH from M^+. The same similarity of the fragmentation processes and the mass spectra is also observed in diols *XI*—*XIV* and acetates *XV*—*XVIII*. For the formation of the characteristic ion *m/z* 288 a fragmentation scheme containing an unusual cleavage of the rings A, B, and C is proposed. On the basis of comparison with the mass spectrum of the 4,4[$^2H_6$]dimethyl analogue *XIX* it was shown that the ion *m/z* 361 in the mass spectra of diols *XI*—*XIV* is formed by elimination of the neutral fragment C_6H_{13} from A-ring of the molecular ion, the last process being accompanied by the 3-hydroxyl transfer from A-ring to the rest of the molecular ion.

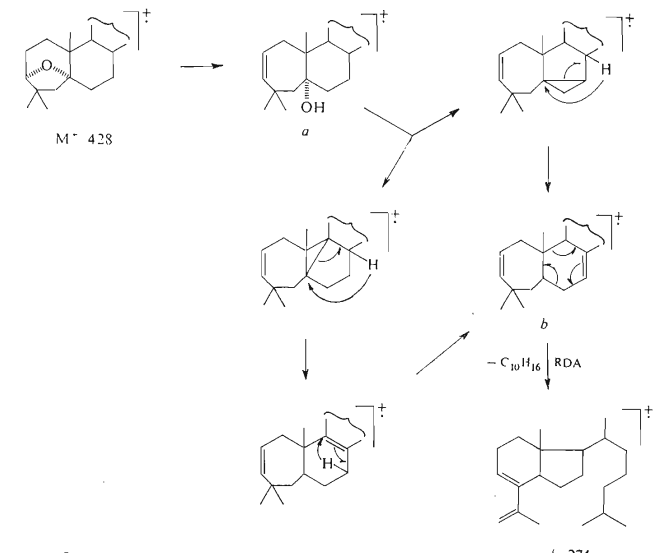
Mass spectrometric behaviour of steroidal compounds with a normal cholestane, androstane and pregnane skeleton has been summarized in several review articles[1-4]. In connection with our stereochemical studies of 4,4-dimethyl-A-homocholestane derivatives[5-7] we also analysed mass spectrometric fragmentation of these compounds with a non-classical steroidal skeleton. This paper is devoted to the electron impact fragmentation study of some 4,4-dimethyl-A-homocholestane derivatives carrying an oxygen function in positions 3,4a or 3,5.

The mass spectra of epoxides *I* and *II* are dominated by the molecular ion M^+ 428 which undergoes elimination of C_4H_8 or C_7H_{12} under formation of prominent ions *m/z* 372 and 332. Also fragment ions *m/z* 428, formed by the loss of a molecule of ROH (R = H, CH_3 or CH_3CO) from M^+ of compounds *III*—*VIII* and *X*, form ions *m/z* 372 and 332 in about the same ratio. Hence, it is evident that the fragmentation routes leading to ions *m/z* 372 and 332 in the mass spectra of compounds *I*—*VIII* and *X* originate from a common precursor — *m/z* 428 (ion *d*, Scheme 1).

* Part CCLXXVII in the series On Steroids; Part CCLXXVII: This Journal *47*, 3148 (1982).

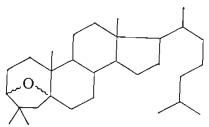


SCHEME 1



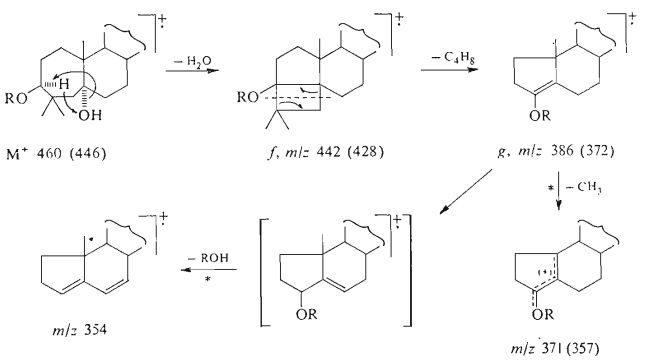
SCHEME 2

The elimination of a water molecule from M^+ of epoxides *I* and *II* has a diagnostical value. This reaction takes place after cleavage of the $C_{(4)}$—O bond as a 1,3- or 1,4-elimination[8-10] of the 5-hydroxy group. As shown by an inspection of Dreiding models the 5-hydroxy group of ion a (Scheme 2) can easily undergo 1,3-elimination with the hydrogen atom originating from carbon atom $C_{(7)}$ or $C_{(9)}$. If hydrogen rearrangement results in the formation of ion *b* (Scheme 2) with a $\Delta^{7,8}$-double bond, its decomposition proceeds by retro Diels–Alder mechanism (loss of $C_{10}H_{16}$ particle) to form the prominent ion *m/z* 274 which is characteristic of the mass spectrum of α-isomer *I*. The elimination of water from M^+ of β-epoxide *II* evidently takes place in a different way (and to a lesser extent) and it does not lead to any characteristic fragments.



I; 3α,5α
II; 3β,5β

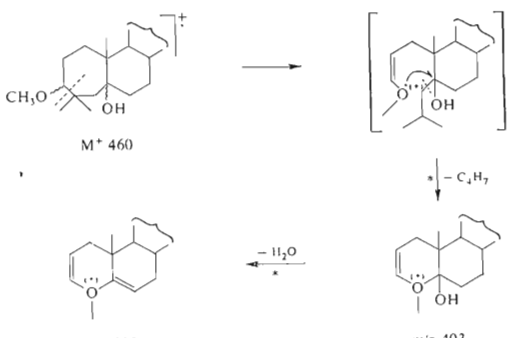
The elimination of CH_3OH from M^+ of methoxy derivatives *VII* and *VIII* (*cis* isomers) proceeds under formation of two isobaric ions of different structures: the ion *c* (Scheme 1), formed by elimination of CH_3O with the hydroxyl hydrogen (which is in *cis* position to the leaving group), can split off C_4H_8 to form ion *e*, *m/z* 372, or it can rearrange to ion *d* (Scheme 1, pathway *1*) which then splits off C_7H_{12}, affording ion *m/z* 332. It is not clear whether the ion *d* is also formed directly from M^+ by 1,2-elimination of CH_3OH. The exceptionally low stability of M^+



SCHEME 3

of compound *IX* and the different character ot its mass spectrum is connected with the fact that in this isomer conditions are fulfilled for preferential 1,4-elimination of the hydroxyl group with the hydrogen on $C_{(3)}$, in *cis* position to the hydroxyl group. The resulting ion *f* (Scheme 3) is unstable and it splits off C_4H_8 immediately, giving rise to the dominant ion *g*, *m/z* 386. The loss of CH_3 from *m/z* 386 leads to the second most abundant ion of the spectrum, *m/z* 371.

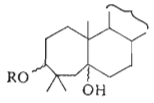
The characteristic ion *m/z* 354 is formed on elimination of CH_3OH from ion *g* (after rearrangement of the double bond). On the basis of the lower abundance of M^+ and the presence of the peaks *m/z* 386, 371 and 354 (of moderate abundance) in the spectrum of the 3,3-isomer *VIII*, it may be inferred that its molecular ion also follows this fragmentation pattern to a certain extent. An alternative decomposition path of molecular ions of methoxy alcohols *VII–IX* is started by cleavage of the $C_{(3)}$—$C_{(4)}$ bond (Scheme 4). The following elimination of the radical C_4H_7 leads to ion *m/z* 403 which loses a water molecule to give ion *m/z* 385.



SCHEME 4

The mass spectra of 3,5-diols *III–VI* do not display such dramatic differences as the spectra of their 3-methyl ethers. The presence of ion *m/z* 354 (formed by loss of water from ion *m/z* 372) in the spectrum of 3b,5α-diol *VI* indicates that the loss of water from its molecular ion is partly due to 1,4-elimination of 5-hydroxyl (according to Scheme 3). From a comparison with the mass spectrum of 3-acetoxy derivative *X* it follows that the fragmentation paths of diols and acetate are equal. This is only possible if the ion *m/z* 428, the precursor of both prominent ions *m/z* 332 and 372 in the mass spectra of acetate *X* and diols *III–VI*, has the same structure in both cases. Since the loss of CH_3COOH is known to proceed with McLafferty

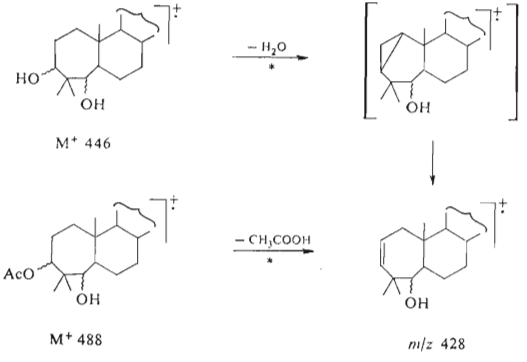
rearrangement as 1,2-elimination[11], the common structure of the ions m/z 428 is evidently *d* (Scheme 1, path *3*). The metastable peaks m^* 410·7, corresponding to the transition $M^+ \rightarrow (M-18)^+$, found in the mass spectra of diols *III*–*VI*, show that the observed 1,2-elimination of a water molecule is due to the molecular ion decomposition and not to thermal degradation of the molecule before ionization[8].



R = H: *III*; 3α,5α *IV*; 3β,5β *V*; 3α,5β *VI*; 3β,5α
R = CH_3: *VII*; 3α,5α *VIII*; 3β,5β *IX*; 3β,5α
R = CH_3CO: *X*; 3β,5α

The formation of ion m/z 372 in the mass spectra of diols *III*–*VI* and acetate *X* may be explained on the basis of a similarity with the mass spectra of epoxides *I* and *II*: On addition of the hydroxyl group to the double bond of ion *d* the structure *c* is formed (Scheme 1), which is identical with the molecular ions of epoxides *I* and *II* (this reaction, as shown elsewhere[6], also takes place in the ground state chemistry). The ion *c* further loses a molecule of isobutene to give ion m/z 372.

The mass spectra of 3,4a-diols *XI*–*XIV* and of their 3-acetoxy derivatives *XV* to *XVIII* are very similar to each other (Table I). This fact may be understood if the structure of the dominant ion m/z 428 – the parent ion of all important fragmentation processes in the spectra of diols and their 3-acetates – is assumed to be the same (Scheme 5). Therefrom it follows that in the case of diols *XIXIV* the 3-hydroxyl



SCHEME 5

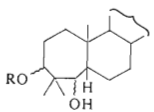
group is eliminated first; then the reaction product rearranges to the Δ^2-unsaturated ion m/z 428, formed also by the McLafferty elimination of CH_3COOH from M^+ od the acetates *XV–XVIII*.

As can be seen from further fragmentation, the decomposition of the ion m/z 428 begins almost in all instances by the allylic cleavage of the $C_{(4)}-C_{(4a)}$ bond. The

TABLE I

Partial mass spectra of compounds *XI–XVIII*

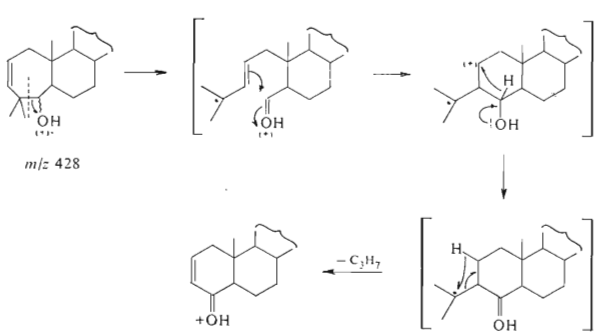
	Relative abundances								
m/z	*XI*	*XII*	*XIII*	*XIV*	*XV*	*XVI*	*XVII*	*XVIII*	elemental composition
247	11	19	19	15	10	9	8	9	$C_{18}H_{31}$
255	9	16	15	14	14	12	9	21	
273	15·5	26	25	22	19	17	15	18	$C_{19}H_{29}O$
274	13·4	14	13	17	14	10	9	15·6	$C_{19}H_{30}O$, $C_{20}H_{34}$ (1 : 1)
287	8	9	12	7·6	10	6·6	5·6	6·5	
288	20	13	14	30	14·5	9	7·4	23	$C_{20}H_{32}O$, $C_{21}H_{36}$ (4 ~ 7 : 1)
297	6·5	13	11	8	11	7	6·3	8·5	
301	6	8	7	8	7	5	4·5	5·4	
313	7·2	15	14	9	9	8	8·7	8·3	
315	31	41	36	28	40	27	22	25	
316	20	24	15	13	31	11	10	13·5	
317	59	52	24	16	45	9	11·6	9·4	$C_{23}H_{41}$
343	22	28	26	19	15	23	20	16·6	$C_{24}H_{39}O$. $C_{25}H_{43}$ (3 : 1)
345	—	—	24	—	8	—	14	—	$C_{24}H_{41}O$
361	6	20	23	11	—	—	—	—	$C_{24}H_{41}O_2$
367	3·4	8	5	3	6·2	3·7	3·5	4·6	$C_{27}H_{43}$
372	10	14	12	10	8·6	10·6	8·7	10	$C_{26}H_{44}O$
385	5	11	9	6·6	6	5·7	5·2	5	$C_{27}H_{45}O$
386	6	9	7	6·6	6·5	6·3	6·6	6	$C_{27}H_{46}O$
395	12·4	17	15	18	23	12·3	11	20	$C_{29}H_{47}$
400	—	—	—	—	7·2	—	—	—	
403	—	—	12	—	—	—	—	—	$C_{27}H_{47}O_2$
410	26	39	33	30	41·4	31	28	38	$C_{30}H_{50}$
413	19	26	25	28	19·3	18	16·6	15·6	$C_{29}H_{49}O$
428	100	100	100	100	100	100	100	100	$C_{30}H_{52}O$
446	14	5·6	7	5·7	—	—	—	—	$C_{30}H_{54}O_2$
455	—	—	—	—	—	—	—	4	
470	—	—	—	—	2·4	4	0·9	14	$C_{32}H_{54}O_2$
488	—	—	—	—	11·7	2	1·1	9·4	$C_{32}H_{56}O_3$



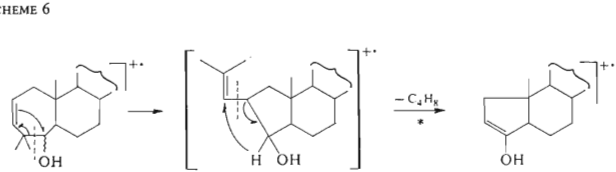
R = H: *XI*; 3α,4aα *XII*; 3β,4aβ *XIII*; 3α,4aβ *XIV*, 3β,4aα

R = CH_3CO: *XV*, 3α,4aα *XVI*; 3β,4aβ *XVII*; 3α,4aβ *XVIII*; 3β,4aα

subsequent contraction of A-ring to a 6-membered ring followed by the loss of C_3H_6 leads to the formation of ion *m/z* 385 (Scheme 6), while the contraction to a five--membered ring with the loss of an isobutene molecule, gives rise to ion *m/z* 372 (Scheme 7). Similarly, the prominent ion *m/z* 343 is formed from ion *m/z* 428 by cleavage



SCHEME 6

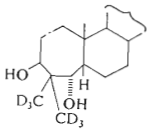


SCHEME 7

of the $C_{(4)}$—$C_{(4a)}$ and $C_{(1)}$—$C_{(10)}$ bonds. Its further decomposition (by loss of a CO molecule) leads to the prominent ion *m/z* 315. On the other hand, the ions *m/z* 316 and 317 result from the cleavage of $C_{(4a)}$—$C_{(5)}$ and $C_{(1)}$—$C_{(10)}$ bonds of the ion *m/z* 428. The origin of the leaving species C_3H_7 and C_4H_8 (in agreement with Schemes 6

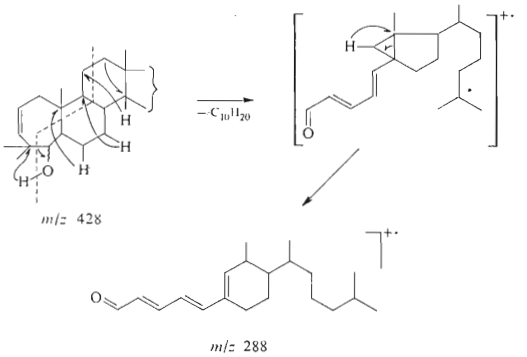
and 7) is confirmed by the observation that the peaks m/z 385 and 372 in the mass spectrum of compound *XIX* are not shifted, the same as the peaks m/z 343, 315, 316, and 317.

The mechanism of formation of the prominent ion m/z 288, present in the mass spectra of diols *XI*–*XIV* and their 3-acetoxy derivatives *XV*–*XVIII* proved to be very complex and unusual. The elemental composition of the ion m/z 288 corresponds to an elimination of a molecule $C_{10}H_{20}$ from the ion m/z 428. In the mass spectrum of hexadeuterio analogue *XIX* the ion m/z 288 is not shifted. It follows that the carbon atom $C_{(4)}$ with both methyl groups is lost by formation of ion m/z 288.



XIX

Hence, it cannot arise from a simple D-ring cleavage of the ion m/z 428, as originally assumed (the D-ring cleavage in the ion m/z 428 proceeds with a loss of a species $C_{11}H_{23}$ leading to an ion m/z 273). As evident from Scheme 8, the formation of ion m/z 288 requires a cleavage of the rings A, B, and C, and a transfer of four hydrogen atoms onto the leaving neutral fragment. Although this process seems unlikely at the first sight, it may be forced by an energy release, resulting from the extensive charge delocalization along the conjugated system in the ion formed.

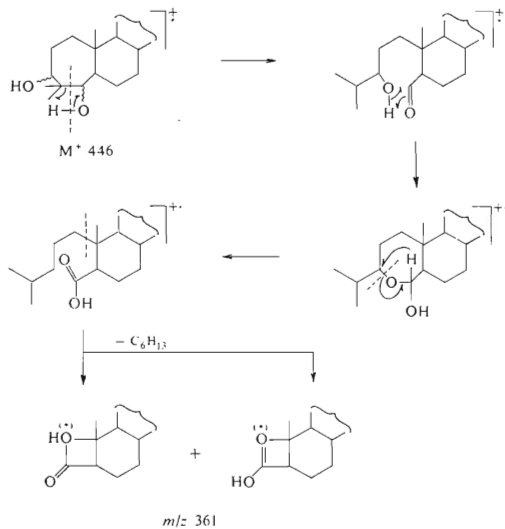


m/z 428

m/z 288

SCHEME 8

In the mass spectra of diols *XI*–*XIV* a fairly abundant but very interesting ion m/z 361 ($C_{24}H_{41}O_2$) was also observed. It has been found to arise from the molecular ions by a loss of C_6H_{13}. As this ion in the mass spectrum of the hexadeuterio-analogue *XIX* was not shifted, a splitting of the ring A with a loss of $C_{(4)}$ atom must be involved. This is only possible after the transfer of the 3-hydroxy group to the neutral fragment (Scheme 9), similarly as observed in the mass spectra of 3-hydroxy-4,4-dimethyl-A-homo-5β-cholestan-4a-one[5]. After the cleavage of the $C_{(4)}$—$C_{(4a)}$ bond a recombination of the seven-membered A-ring may take place by addition of the electron pair of the oxygen atom in the position 3 onto the electron-deficient carbon atom $C_{(4a)}$. The hydroxyl rearrangement is completed by cleavage of the $C_{(3)}$—O bond. Subsequent elimination of C_6H_{13} brings about the formation of the oxonium ion m/z 361.



SCHEME 9

It is evident that without prior understanding of this rearrangement any attempt to interpret the formation of the ion m/z 361 would be quite misleading in structure considerations.

EXPERIMENTAL

The mass spectra were measured on a double focussing mass spectrometer AEI MS 902 (Associated Electric Industries, Manchester, G.B.). The samples were introduced by direct inlet into the ion source heated at 140—170°C. The low-resolution mass spectra were recorded at resolving power of 1 000 and an electron energy of 70 eV. The high-resolution measurements were carried out using the resolving power $m_1/(m_1 - m_2) = 10\,000$. The accurate masses found are within ±3 ppm of the theoretical values. The syntheses of compounds *I*—*XVIII* were described earlier[5-7]. 4,4-[$^2H_6$]-Dimethyl-A-homo-5β-cholestane-3β,4aα-diol (*XIX*) was prepared from 3β-hydroxy-4,4-[$^2H_6$]-dimethyl-A-homo-5β-cholestan-4a-one[5] by reduction with lithium aluminum hydride.

Partial mass spectra (most important peaks from the upper part of the spectrum) of compounds *I*—*X* and *XIX* are presented. The masses and the corresponding relative abundances (percent of base peak, in brackets) are given. The elemental composition corresponding to the accurate mass found (if determined) follows the values of relative abundance in brackets. For the mass spectra of compounds *XI*—*XVIII* see Table I.

I: 274 (22); 315 (14); 332 (50); 357 (7); 359 (6); 372 (25); 395 (7); 410 (12); 413 (15); M^+ 428 (100).
II: 301 (5); 315 (17, $C_{22}H_{35}O + C_{23}H_{39}$. 1 : 1); 328 (5); 332 (50, $C_{23}H_{40}O$); 357 (6·4); 359 (8·3, $C_{25}H_{43}O$); 372 (22, $C_{26}H_{44}O$); 410 (4·2); 413 (10); M^+ 428 (100, $C_{30}H_{52}O$).
III: 193 (35); 247 (13·4); 315 (30); 317 (16); 328 (15); 332 (100); 357 (18); 359 (19); 367 (6·7); 372 (52); 383 (6·5); 385 (10); 395 (10); 410 (27); 313 (24); 428 (98); M^+ 446 (33).
IV: 247 (20); 261 (14); 275 (17); 287 (11); 301 (15); 317 (17); 328 (16·7); 332 (81); 343 (15); 354 (13); 355 (11); 357 (25); 359 (19); 372 (52); 385 (17); 395 (13); 403 (9·5); 410 (27); 413 (29); 428 (100); M^+ 446 (14·3).
V: 247 (6); 301 (7); 315 (20); 328 (10); 332 (54); 357 (9); 359 (9·5); 367 (10); 372 (31); 385 (4); 395 (4·4); 410 (15); 413 (14); 428 (100); M^+ 446 (8).
VI: 247 (27); 259 (15); 261 (14); 287 (13); 301 (10); 315 (26); 329 (17); 332 (68, $C_{23}H_{40}O$); 343 (22, $C_{25}H_{43}$); 354 (18, $C_{26}H_{42}$); 357 (34, $C_{25}H_{41}O$); 359 (18, $C_{25}H_{43}O$); 372 (86, $C_{26}H_{44}O$); 383 (11, $C_{28}H_{47} + C_{27}H_{43}O$, 4 : 1); 385 (11, $C_{28}H_{49} + C_{27}H_{45}O$, 1 : 1); 395 (6); 403 (12); 410 (9); 413 (16); 428 (100); M^+ 446 (36).
VII: 247 (8); 261 (9); 315 (18); 317 (10, $C_{22}H_{37}O$); 332 (100, $C_{23}H_{40}O$); 341 (8); 342 (17, $C_{25}H_{42}$); 357 (14, $C_{25}H_{41}O$); 359 (22, $C_{25}H_{43}O$); 371 (6); 372 (37, $C_{26}H_{44}O$); 385 (6); 386 (3·5); 395 (3·2); 403 (36, $C_{27}H_{47}O_2$); 410 (10); 413 (8); 428 (75, $C_{30}H_{52}O$); 442 (6·3); M^+ 460 (74, $C_{31}H_{56}O_2$).
VIII: 247 (19); 261 (21, $C_{19}H_{33}$); 315 (25, $C_{23}H_{39} + C_{22}H_{35}O$, 3 : 1); 317 (23, $C_{22}H_{37}O$ + + $C_{23}H_{41}$, 4 : 3); 332 (100, $C_{23}H_{40}O$); 341 (23, $C_{25}H_{41}$); 342 (14, $C_{25}H_{42}$); 357 (14, $C_{25}H_{41}O$); 359 (28, $C_{25}H_{43}O$); 371 (38, $C_{26}H_{43}O$); 372 (44, $C_{26}H_{44}O$); 386 (21, $C_{27}H_{46}O$); 395 (7); 403 (26, $C_{27}H_{47}O_2$); 410 (17); 413 (16); 428 (65, $C_{30}H_{52}O$); 442 (8); 445 (4); M^+ 460 (30, $C_{31}H_{56}O_2$).
IX: 315 (6); 317 (4); 328 (4); 332 (11); 354 (16, $C_{26}H_{42}$); 355 (10, $C_{26}H_{43}$); 371 (72, $C_{26}H_{43}O$); 386 (100, $C_{27}H_{46}O$); 395 (3·3); 403 (3·3); 410 (5); 413 (2·2); 428 (10); 442 (3); M^+ 460 (4·4, $C_{31}H_{56}O_2$).
X: 247 (12); 274 (23); 315 (20); 328 (6·4); 332 (67); 341 (6·4); 357 (11); 359 (10); 372 (31); 383 (23); 395 (11); 401 (5); 410 (26); 413 (13); 428 (100); 446 (3); 455 (2); 470 (7·4); M^+ 488 (3·5).
XIX: 247 (16); 261 (16); 274 (10); 279 (16·1); 280 (9); 287 (6·8); 288 (30); 294 (4·4); 297 (4·5); 301 (7·7); 302 (5·7); 303 (6·6); 313 (8·4); 315 (16·3); 316 (14); 317 (25); 321 (11); 343 (14·8); 361 (11·6); 367 (3·4); 372 (10·2); 385 (5·2); 386 (2·5); 387 (5); 401 (11); 416 (22); 419 (18); 434 (100); M^+ 452 (9·8).

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Translated by Ž. Procházka.