# ETHYLENE DITHIOKETALS IN RING A OF 19β,28-EPOXY-18α--OLEANANE; MASS SPECTRA AND REDUCTION WITH DEUTERATED RANEY-NICKEL*

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Ethylene dithioketals in positions 1, 2 and 3 of 19β,28-epoxy-18α-oleanane were prepared and reduced with deuterated Raney-nickel. The mass spectra of dithioketals and corresponding 1,1-, 2,2- and 3,3-dideuterio derivatives were studied and discussed with the possibility of localizing the functional group in the A ring.

Ethylene dithioketals display characteristic mass spectra and fragmentation. This is made use of mainly in the chemistry of steroids, where the position of the original keto group on the skeleton may be determined by means of the mass spectra of ethylene dithioketals[1-5]. A similar fragmentation is also displayed by steroidal ketals[5,6]. In contrast to this, in the field of pentacyclic triterpenoids ethylene dithioketals were used only seldom (*cf.*[7,8]). Therefore, we prepared ethylene dithioketals *II*, *V*, *VIII* and *XI* in ring A of 19β,28-epoxy-18α-oleanane (*XII*) in order to study their mass spectra and compare them with steroidal analogues. On their reduction with deuterated Raney-nickel corresponding dideuterio derivatives *III*, *VI* and *IX* were obtained for the study of fragmentation behaviour.

For the preparation of ethylene dithioketals *II*, *V*, *VIII* and *XI* corresponding oxo derivatives *I* (ref.[9]), *IV* (ref.[10]), *VII* (ref.[11]) and *X* (ref.[12]) were used as starting compounds. When reacted with ethane dithiol and using boron trifluoride etherate as condensing agent[13] they gave the required ethylene dithioketals. Condensations were carried out without solvents. Thus, high yields were achieved, while when acetic acid was used as solvent[13] the yields did not exceed 50%. In derivatives *I*, *IV* and *VII* the reaction with ethane dithiol took place quantitatively after 15 min, while in the case of the sterically more requiring 2-methyl ketone *X* it took 2 h.

The mass spectromeric fragmentation behaviour of ethylene dithioketals *II*, *V*, *VIII* and *XI* is different from the characteristic fragmentation of steroidal analogues[1-4]. It is also different from 4,4-dimethylsteroidal analogues[5] and it depends on the position of the dithioketal function and the possibilities of the mechanism of its elimination.

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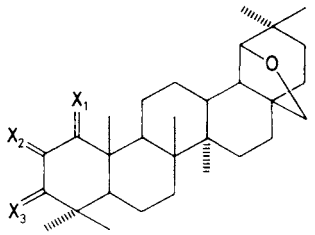
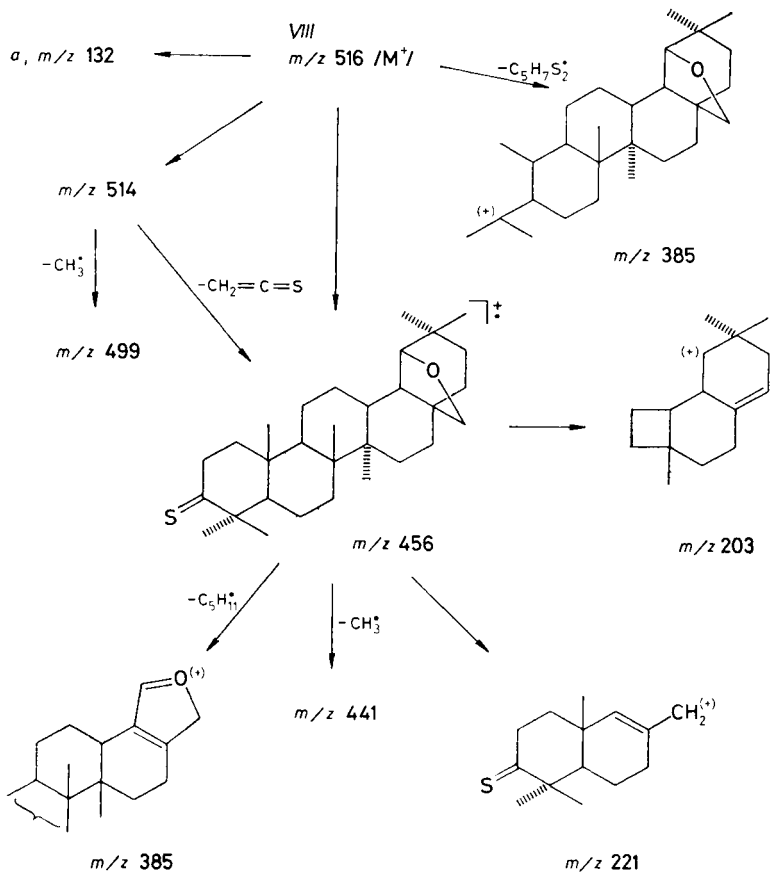
The mass spectrum of derivative *VIII* with the dithioketal function in position 3 is the most distinct (Scheme 1). The molecular ion of $m/z$ 516 is of negligible intensity. The ion M − 2 ($m/z$ 514) is more abundant. The main ionic species are formed from both these ions. The results from the steroid field indicate as the most abundant ion in 3-ethylene dithioketals the ion with $m/z$ 131 ($C_5H_7S_2$) (ref.[1,5]), with a quite logical mechanism of formation, even in the case of 4,4-dimethyl derivatives.




*I*, $X_1 = O$; $X_2 = X_3 = H$
*II*, $X_1 = \langle S \rangle$; $X_2 = X_3 = H_2$
*III*, $X_1 = {}^2H_2$; $X_2 = X_3 = H_2$
*IV*, $X_1 = X_3 = H_2$; $X_2 = O$
*V*, $X_1 = X_3 = H_2$; $X_2 = \langle S \rangle$
*VI*, $X_1 = X_3 = H_2$; $X_2 = {}^2H_2$
*VII*, $X_1 = X_2 = H_2$; $X_3 = O$
*VIII*, $X_1 = X_2 = H_2$; $X_3 = \langle S \rangle$
*IX*, $X_1 = X_2 = H_2$; $X_3 = {}^2H_2$
*X*, $X_1 = H_2$; $X_2 = \alpha CH_3, \beta H$; $X_3 = O$
*XI*, $X_1 = H_2$; $X_2 = \xi CH_3, \xi H$; $X_3 = \langle S \rangle$
*XII*, $X_1 = X_2 = X_3 = H_2$

In contrast to this, in derivative *VIII* the most abundant ion radical has $m/z$ 132 ($C_5H_8S_2$, 100%), to which the ion $m/z$ 146 ($C_6H_{10}S_2$, 100%) corresponds in the case of 2-methyl derivative *XI*. For their formation we propose a mechanism which is based on the homolytic cleavage of the 3−4 bond, followed by simple cleavage of the 1−10 bond. In this mechanism the hydrogen transfer typical in steroidal analogues is lacking. The proposal of the formation of ions $m/z$ 132 and 146 is shown in Scheme 2. The ions $m/z$ 131 and $m/z$ 145 are of low intensity. Further important ionic species (Scheme 1) are connected either with the fragmentation of the ketal function − the ion $m/z$ 456 formed by loss of thioketene from ion $m/z$ 514 and the ion $m/z$ 385 formed from the molecular ion by loss of the radical $C_5H_7S_2$ − or they depend on the known fragmentation of the derivatives of 19β,28-epoxy-18α--oleanane[14].

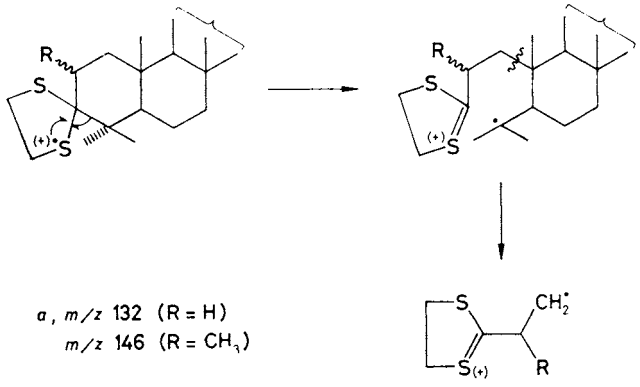



SCHEME 1

The mass spectrum of derivative *V* with the dithioketal function in position 2 is indistinct; in the region of higher or medium masses it contains no important ions. The expected analogues of the ions typical of ethylene dithioketal function are not present, while in the steroidal analogues the ion *m/z* 131 is again dominant[1].

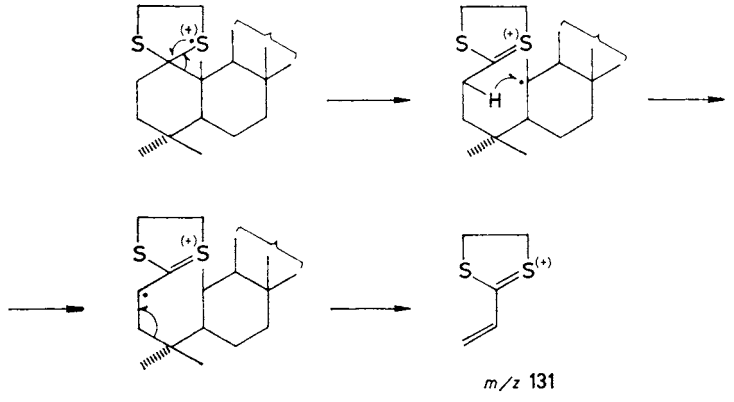
In contrast to this the mass spectrum of derivative *II* has two characteristic ions (of almost identical abundance), indicating the ethylene dithioketal function in position 1 – *m/z* 131 and *m/z* 132. The formation of the first is assumed to be based on the homolytic cleavage of the 1–10 bond, connected with a hydrogen transfer from position 2 and subsequent cleavage of the 3–4 bond (see Scheme 3). The ion *m/z* 132 is formed by the same mechanism, but without hydrogen transfer. Further characteristic ions in the region of higher and medium masses are analogous to the ions in the spectra of *VIII* and *XI*. In addition to this there are also two distinct

hydrocarbon ions with $m/z$ 177 and $m/z$ 191, which belong to the central rings of the skeleton.




SCHEME 2

The ethylene dithioketals *II*, *V* and *VIII* were desulfurated with deuterated Raney-nickel (according to ref.[13]), with the aim of obtaining corresponding dideuterio derivatives *III*, *VI* and *IX*. This method of introduction leads to a considerable scattering of the isotope; in all three instances the content of $^2H_2$ did not exceed 60%. The values of scattering are comparable with the values given for the steroidal skeleton labelled in the same positions and in the same manner[15].




SCHEME 3

The fragmentation of the allobetulin skeleton was sufficiently investigated in dependence on substitution[14]. Nonetheless, the mass spectra of deuterated deriva-

tives *III*, *VI* and *IX* show new interesting facts. Their comparison with the spectrum of 19β,28-epoxy-18α-oleanane (*XII*)[16] permits the identification of the ions belonging to ring A, Table I. From this it is evident that the important ion with *m/z* 203 ($C_{15}H_{23}$), which was localized[14] in rings D and E, is a doublet to which the fragments of the rings D, E and A, B contribute to a comparable extent. The ion *m/z* 203, belonging to the rings A, B is formed by cleavage of the 8–14 and 12–13 bonds in the ring C, connected with the loss of the methyl radical. The molecule of ethylene which is the first neutral loss from the molecular ion (ion *m/z* 383 in derivative *XII*) of lupane skeleton[17], ursane and oleanane skeleton[18], does not originate from the ring A.

It may be concluded that the mass spectra may serve for the localization of the ethylene dithioketal function in the A ring of the triterpenoid skeleton. Ethylene dithioketals in positions 1 and 3 differ distinctly according to the surroundings of the functional group, while position 2 does not enable a specific fragmentation.

## EXPERIMENTAL

The melting points were measured on a Kofler block and they are not corrected. Optical rotations were measured on an automatic polarimeter (ETL-NPL, Bendix–Ericsson) in chloroform, with a ±2% accuracy. The $^1$H NMR spectrum was measured on a Tesla BS 487 A instrument at 80 MHz, in deuteriochloroform with hexamethyl disiloxane as internal reference. The chemical shifts were calculated with respect to tetramethylsilane and they are given in ppm (δ-scale). The

TABLE I

Comparison of the mass spectrum of *XII* with dideuterio analogues *III*, *VI*, and *IX*

| Compound | Important ions[a], *m/z* | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *XII* | 426 (25) | 411 (10) | 395 (17) | 383 (5) | 355 (10) | 257 (8) | 247 (7) | 231 (9) | 220 (12) | 217 (11) | 203 (35) | 191 (100) | 177 (30) |
| *III* | 428 (20) | 413 (14) | 397 (21) | 385 (6) | 357 (11) | 257 (9) | 247 (9) | 231 (9) | 220 (14) | 217 (10) | 203 (45) 205 (43) | 193 (100) | 177 (31) |
| *VI* | 428 (24) | 413 (15) | 397 (18) | 385 (7) | 357 (10) | 257 (10) | 247 (7) | 231 (8) | 220 (11) | 217 (10) | 203 (42) 205 (38) | 193 (100) | 177 (32) |
| *IX* | 428 (19) | 413 (12) | 397 (20) | 385 (5) | 357 (12) | 257 (9) | 247 (7) | 231 (10) | 220 (12) | 217 (10) | 203 (48) 205 (43) | 193 (100) | 177 (31) |

[a] The number in brackets means the relative abundance of the ions.

mass spectra were measured on a Varian MAT 311 instrument. The energy of the ionizing electrons was 70 eV, the ionizing current 1 mA, temperature of the ion source was 200°C and the temperature of the direct inlet system was 90–140°C. The composition of the ions (where mentioned) was checked by means of high resolution measurements, with an error lower than 5 ppm. The mentioned geneses of the ions were confirmed by the direct analysis of daughter ions technique. For preparative chromatographies on thin layers silica gel G according to Stahl (Merck) were used.

19β,28-Epoxy-1,1-ethylenedithio-18α-oleanane (*II*)

1-Oxo derivative *I* (30 mg) was dissolved in ethane dithiol (0·1 ml) and boron trifluoride etherate (0·1 ml) and after standing for 15 min at room temperature the mixture was diluted with ether (20 ml) and repeatedly extracted with a sodium hydroxide solution (1 mol $l^{-1}$) until ethane dithiol was eliminated. The organic phase was washed with water, dried over sodium sulfate and evaporated. Dithioketal *II* was isolated by preparative thin-layer chromatography on silica gel (elution with light petroleum–ether 9 : 1). Yield, 23 mg (66%) of dithioketal *II*, m.p. 175 to 178°C (ether–light petroleum), $[\alpha]_D$ +55° (*c* 0·5). Mass spectrum, *m/z* (composition, %): 516 ($M^+$, $C_{32}H_{52}OS_2$, 8), 514 ($C_{32}H_{50}OS_2$, 26), 501 (2), 499 (2), 456 ($C_{30}H_{48}OS$, 11), 426 (14), 395 (10), 385 ($C_{27}H_{45}O$, 16), 221 ($C_{14}H_{21}S$, 14), 203 ($C_{15}H_{23}$, 33), 191 ($C_{14}H_{23}$, 81), 177 ($C_{13}H_{21}$, 71), 132 ($C_5H_8S_2$, 70), 131 ($C_5H_7S_2$, 71), 95 (100).

19β,28-Epoxy-2,2-ethylenedithio-18α-oleanane (*V*)

2-Oxo derivative *IV* (30 mg) was processed using the same procedure as for *I*. Yield, 27 mg (77%) of dithioketal *V*, m.p. 170–174°C (ether–light petroleum), $[\alpha]_D$ +46° (*c* 0·5). Mass spectrum, *m/z* (%): 516 ($M^+$, $C_{32}H_{52}OS_2$, 8), 501 (5), 456 (7), 441 (8), 423 (4), 221 (8), 203 (10), 189 (11), 95 (49), 41 (100).

19β,28-Epoxy-3,3-ethylenedithio-18α-oleanane (*VIII*)

3-Oxo derivative *VII* (150 mg) was worked up using the same procedure as for *I*. Yield, 130 mg (74%) of dithioketal *VIII*, m.p. 173–176°C (ether–light petroleum), $[\alpha]_D$ +35° (*c* 0·4). Mass spectrum, *m/z* (composition, %): 516 ($M^+$, 2), 514 ($C_{32}H_{50}OS_2$, 18), 499 (2), 456 ($C_{30}H_{48}OS$, 20), 441 (2), 385 (doublet 3 : 1, $C_{27}H_{45}O$, $C_{25}H_{37}OS$, 35), 247 (17), 221 ($C_{14}H_{21}S$, 12), 203 ($C_{15}H_{23}$, 15), 191 ($C_{14}H_{23}$, 16), 177 ($C_{13}H_{21}$, 16), 165 (20), 132 ($C_5H_8S_2$, 100), 131 ($C_5H_7S_2$, 20). $^1H$ NMR spectrum: 0·79 s ($CH_3$), 0·895 s ($CH_3$), 0·93 s (2 $CH_3$), 0·97 s ($CH_3$), 1·02 s ($CH_3$), 1·15 s ($CH_3$), 2·99 dd ($J_1$ = 13 Hz, $J_2$ = 3 Hz), 3·2 bs (4 H), 3·42 d and 3·77 d, $J$ = 8 Hz (28-$H_2$), 3·52 s (19-H).

19β,28-Epoxy-3,3-ethylenedithio-2ξ-methyl-18α-oleanane (*XI*)

3-Oxo derivative *X* (30 mg) was worked up using the same procedure as for *I*, but the reaction time was prolonged to 2 h. Yield, 18 mg (51%) of dithioketal *XI*, m.p. 184–187°C (ether–light petroleum), $[\alpha]_D$ +43° (*c* 0·7). Mass spectrum, *m/z* (composition, %): 530 ($M^+$, 0·5), 528 ($C_{33}H_{52}OS_2$, 2), 470 ($C_{31}H_{50}OS$, 7), 385 ($C_{27}H_{45}O$, 12), 247 (9), 203 (6), 191 (6), 177 (9), 165 (14), 146 ($C_6H_{10}S_2$, 100), 145 ($C_6H_9S_2$, 26).

Dideuterio Derivatives *III*, *VI* and *IX*

Preparation of deuterated Raney-nickel: Sodium (190 mg) was dissolved in deuterium oxide (3 ml, 99·9%). Raney-nickel (250 mg) was added to the solution over 5 min under stirring and

heating at 50°C. Then the solution was eliminated by decantation and the sediment washed with deuterium oxide (3 × 2 ml) and deuteriomethanol ($CH_3O^2H$, 2 × 1 ml). The catalyst was used immediately. The Raney-nickel prepared in this way was refluxed with dithioketal *II* (21 mg) dissolved in 2 ml of deuteriomethanol and 2 ml of hexadeuteriobenzene. After 1 h refluxing the mixture was cooled and filtered through a small column of silica gel. Crystallization from light petroleum–ether mixture 15 mg of (1,1-$^2H_2$)-19β,28-epoxy-18α-oleanane (*III*) (60%) were obtained, with m.p. 228–230°C, $[\alpha]_D$ +58° (*c* 0·1). Ref.[16] *XII*: m.p. 230–231·5°C, $[\alpha]_D$ +53°. (2,2-$^2H_2$)-19β,28-Epoxy-18α-oleanane (*VI*), m.p. 228–230°C, $[\alpha]_D$ +55° (*c* 0·3) and (3,3-$^2H_2$)-19β,28-epoxy-18α-oleanane (*IX*), m.p. 225–230°C, $[\alpha]_D$ +55° (*c* 0·3) were prepared in the same manner as *III*. Deuterium distribution (%) – *III*: $d_0$ = 11, $d_1$ = 20, $d_2$ = 51, $d_3$ = 13, $d_4$ = 5; *VI*: $d_0$ = 10, $d_1$ = 18, $d_2$ = 58, $d_3$ = 10, $d_4$ = 4; *IX*: $d_0$ = 9, $d_1$ = 20, $d_2$ = 56, $d_3$ = 13, $d_4$ = 2.

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