REACTIONS OF TRITERPENOID KETONES WITH SULFUR AND MORPHOLINE UNDER THE CONDITIONS OF WILLGERODT–KINDLER REACTION*

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19β,28-Epoxy-18α-oleanan-3-one (*I*) when heated with sulfur in morpholine gives rise to 2-oxo derivative *II*, accompanied by a small amount of the starting ketone *I*. The reaction can be controlled so that 2-oxo derivative *II* is formed almost exclusively. Derivatives *III*—*VII* with a keto group and a further functional group in the position 2 and 3 also give 2-oxo derivative *II*. In the same manner 3-oxo-18α-oleanan-28→19β-olide (*XVIII*) was converted to 2-oxo derivative *XIX*. 1-Oxo derivative *VIII* and A-nor-ketone *IX* do not react under these conditions. An addition of vicinal diamine into the reaction mixture leads to the formation of compounds *XIII*, *XV*—*XVII*, *XX* with a pyrazine cycle condensed with the ring A.

The Willgerodt reaction is known as an advantageous method for the preparation of thioamides of ω-arylalkanoic acids from aryl alkyl ketones; in the Kindler modification of this method sulfur in boiling morpholine is used and in it aryl alkyl ketones afford thiomorpholides of acids[1]. The synthetic possibilities of this reaction in the chemistry of aromatic compounds are well investigated, but their application in the field of aliphatic and alicyclic ketones is much less known (see ref.[1] and the references therein). For example in the reaction of 3-alkanones with sulfur and morpholine the formation of a mixture of 2-alkanones and thiomorpholides of acids has been observed, *i.e.* a shift of the carbonyl group by one to two carbon atoms[2]. Under similar conditions 4-heptanone and heptanal give a mixture of isomeric heptanones[3]. In the case of alicyclic ketones, when 4-methylcyclohexanone was reacted with sulfur in morpholine, the formation of a mixture of 2-, 3- and 4-methylcyclohexanone[3] was observed. A similar shift of the keto group was also observed in camphor[3].

In connection with our study of the reactivity of pentacyclic triterpenoids we applied the conditions of the Willgerodt–Kindler reaction to triterpenoid derivatives with a keto group in the ring A. As starting materials we used the following derivatives of 19β,28-epoxy-18α-oleanane and 18α-oleanan-28→19β-olide: 3-oxo derivatives *I* and *XVIII*, 2-oxo derivative *II*, 1-oxo derivative *VIII*, A-nor-ketone *IX* and ketones with a double bond or a polar substituent in the ring A, *III*—*VII*.

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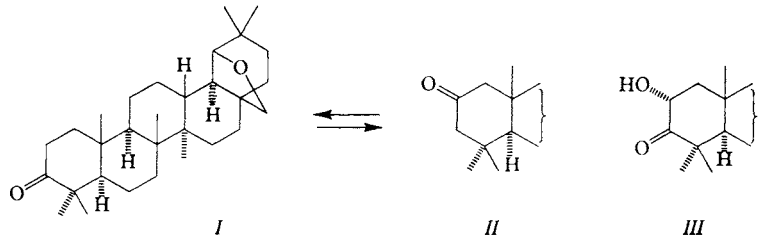
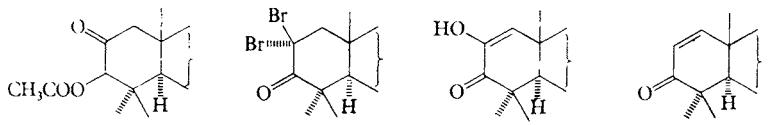
The reaction of 3-oxo derivative *I* with sulfur and morpholine lasting 16–24 h afforded 2-oxo derivative *II* as the main product, and the starting ketone *I* as contaminant. The composition of the reaction mixture depends on the ratio of the starting



I *II* *III*



IV *V* *VI* *VII*

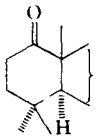
components; for the preparation of 2-oxo derivative *II* the keeping of the ratio of 30 ml of morpholine and 0·5–1·5 g of sulfur per 1 g of starting ketone *I* is an advantage. Sulfur should be added in small portions, because it sublimes from the reaction mixture and it is also consumed by side-reactions with morpholine. Under these conditions the 2-oxo derivative *II* formed is only lightly contaminated with the 3-oxo derivative *I* and by-products. If the content of ketone *I* or sulfur is decreased, polar compounds are formed as by-products. If the content of ketone *I* or sulfur is increased, the reaction mixture contains more starting ketone *I* and non-polar substances containing sulfur are formed as by-products. The reaction also can go in the opposite direction: after reaction of 2-oxo derivative *II* with sulfur in morpholine 3-oxo derivative *I* was obtained in low yield.

The conversion of 3-oxo derivative *I* to 2-oxo derivative *II* requires the presence of both sulfur and morpholine. If toluene or diisopropylamine is used instead of morpholine, the reaction does not take place. When morpholine is substituted by piperidine the reaction proceeds very slowly, and after 80 h only traces of 2-oxo derivative *II* are formed.

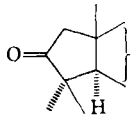
The compounds containing in the position 2 and 3 a keto group and a further functional group, such as hydroxy ketone *III*, acetoxy ketone *IV*, dibromo ketone *V*, diketone *VI* or α, β-unsaturated ketone *VII* react with sulfur in morpholine similarly as unsubstituted ketones *I* and *II*, giving after 8–16 h of heating 2-oxo derivative *II*, accompanied by a small amount of 3-oxo derivative *I*. Hence, in all these compounds

reduction of the double bond or reductive elimination of the functional group take place at some stage of the reaction. In the case of hydroxy ketone *III*, heated for 2 h, a mixture of 3-oxo and 2-oxo derivative, *I* and *II*, was obtained in a 1 : 1 ratio which on prolongation of the reaction time was converted to 2-oxo derivative *II*. Hence, in this case the reduction step precedes the carbonyl group shift from position 3 to position 2. Diketone *VI* gives 2-oxo derivative *II* only in low yield; a considerable proportion of polar substances appears in the reaction mixture.

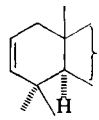
Since under the conditions of Willgerodt reaction olefins, alcohols and further derivatives[1] also react, we tried to carry out the reaction with the unsaturated derivative *X*, 3β-hydroxy derivative *XI* and acetate *XII*. However, these compounds do not react with sulfur and morpholine even on prolongation of the reaction time to 40 h. Thus the unsaturated derivative *X* cannot be an intermediate of the carbonyl group shift from the position 3 to the position 2, as might be expected on the basis of one of the mechanisms proposed for Willgerodt reaction[1] in the case of aryl alkyl ketones.



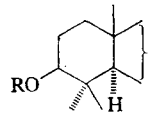
VIII



IX



X

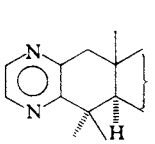


XI, R = H
XII, R = $COCH_3$

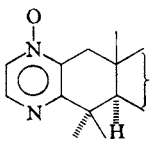
In contrast to ketones *I* and *II* 1-oxo derivative *VIII* or ketone *IX* with a five, membered ring A do not react on prolongation of the reaction time to 80 h either. Neither is 30-nor-lupan-20-one – a triterpenoid aliphatic ketone with a keto group in the side chain – changed by heating with sulfur and morpholine after this time. According to thin-layer chromatography 5α-cholestan-3-one when heated for 8 h gives only traces of 5α-cholestan-2-one and the starting ketone; the predominant part of the material is converted to a complex mixture of polar substances, which according to ^{1}H NMR spectroscopy contain the morpholine system in the molecule.

The preceding reactions of ketones with sulfur were carried out in morpholine purified by rectification. If commercial morpholine is used for the reaction of 3-oxo derivative *I*, a by-product is formed in addition to the 2-oxo derivative *II*; according to its high-resolution mass spectrum (M^+ *m/z* 476, $C_{32}H_{48}N_2O$) it contains two carbon atoms more than the original triterpenoid skeleton, further two nitrogen atoms and four additional unsaturations. In the ^{1}H NMR spectrum it displays two signals of aromatic hydrogens (8·26 and 8·39 ppm) forming an AB system; their coupling constant (2·0 Hz) corresponds to the value of $J_{2,3}$ (1·8 Hz) found in pyrazine[4]. The UV spectrum is also similar to the spectra of pyrazine and its derivatives, but it differs somewhat from the spectra of other nitrogen heterocycles[5]. On the basis

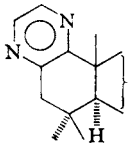
of these facts we assign the by-product the structure *XIII* with a pyrazine ring fused with the A ring in the position 2(3). In agreement with this structure the ^{1}H NMR spectrum also indicates an AB system of protons at $C_{(1)}$ where the chemical shifts (2·50 and 3·08 ppm) and the geminal coupling constant ($J_{1,1}$ = 17·1 Hz) correspond to the presence of an aromatic ring in the neighbourhood of $C_{(1)}$. The signals of the two methyl groups are also considerably shifted downfield in comparison with 19β,28-epoxy-18α-oleanane[6], *i.e.* to 1·30 ppm.



XIII

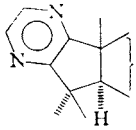


XIV

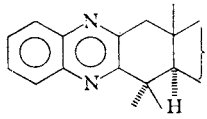


XV

The pyrazine system of derivative *XIII* shows only a weak reactivity: it is not reduced with lithium aluminum hydride in boiling dioxane or with sodium in 1--propanol and it does not yield any products in an attempt at radical bromination with bromine in the presence of dibenzoyl peroxide. On reaction with peracetic acid it very reluctantly yields an N-oxide. Of the two possible variants for the position of the oxygen atom we assign this product the structure of 1'-oxide *XIV* on the basis of its ^{1}H NMR spectrum; the chemical shift of the protons in the position 1 (2·12 and 3·43 ppm) differs considerably from the shifts found in pyrazine derivative *XIII*, which indicates a change in the proximity of $C_{(1)}$. On the contrary, the chemical shifts of the methyl groups in compounds *XIII* and *XIV* are practically the same; in the case of the isomeric 4'-oxide an affecting of the chemical shifts of the methyl groups in the position 4 could be expected.



XVI

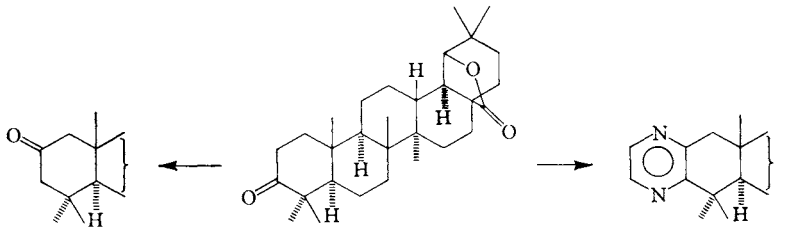


XVII

On heating 3-oxo derivative *I* with sulfur, morpholine and ethylenediamine for for 1–2 h pyrazine derivative *XIII* was obtained as the sole reaction product. All substituted ketones *III*–*VII* also give derivative *XIII* in high yield under these conditions. Derivative *XIII* was also obtained as the only product from 2-oxo derivative *II*; the isomeric derivative *XV* with a pyrazine cycle condensed to A ring in position 1(2) could not be detected in the reaction mixture. In the presence of ethylenediamine 1-oxo derivative *VIII* and A-nor-ketone *IX* also react with sulfur in mor-

pholine, but less willingly than the preceding ketones. When the reaction time was prolonged to 24–40 h, compounds *XV* or *XVI* were obtained, the ^{1}H NMR spectra and UV spectra of which show that they are again derivatives with a fused pyrazine ring. Again, compounds *X*–*XII* did not give any product. The reactions mentioned include at some stage a condensation and dehydrogenation step and they seem to be typical of vicinal diamines. Urea and biacetyl dioxime do not take part in the reaction of 3-oxo derivative *I* with sulfur in morpholine and only 2-oxo derivative *II* is formed. On the contrary, when ketone *I* reacts in the presence of *o*-phenylenediamine, quinoxaline derivative *XVII* was obtained, characterized by its typical ultraviolet and ^{1}H NMR spectrum; this compound was prepared earlier[7,8] in a different manner.

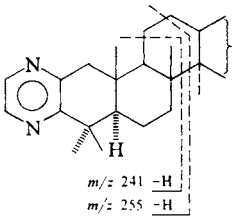
3-Oxo-18α-oleanan-28→19β-olide (*XVIII*) reacted with sulfur in morpholine to give 2-oxo derivative *XIX*; in the presence of ethylenediamine it gave the pyrazine derivative *XX*. In both cases the lactone ring remained unchanged.



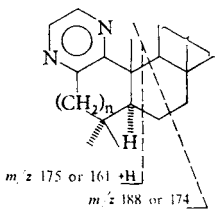
XIX *XVIII* *XX*

The compounds with the pyrazine ring display in their mass spectra in addition to the usual fragmentations typical of derivatives of 19β,28-epoxy-18α-oleanane (ref.[9]) also a characteristic fragmentation which depends on the position of the pyrazine ring. In derivatives of type *XXI* with the pyrazine ring in the position 2(3), the most abundant fragment ions comprize the pyrazine ring and the A and B rings, and they correspond to the cleavage of the C ring, as indicated in formula *XXI* (*m*/*z* 255). The skeletal fragmentation is accompanied by a hydrogen atom transfer to the neutral fragment. This fragmentation also appears in N-oxide *XIV* after the loss of an oxygen atom. The ions formed by the fragmentation common in triterpenoids[10] (*XXI*, *m*/*z* 241) are less abundant. On the other hand the derivatives of the type *XXII* with a pyrazine cycle in the position 1(2) are cleaved predominantly in B ring. As the most abundant ions the ions *m*/*z* 175 (in compound *XV*) or 161 (in compound *XVI*) are formed by hydrogen transfer from the neutral fragment; the ions *m*/*z* 188 or 174 (see formula *XXII*) are less abundant.

The mentioned reactions of the triterpenoid ketones with sulfur and morpholine represent an advantageous method for the shift of the keto group from position 3 to position 2 in one reaction step; the methods known so far include multistep procedures[11,12]. This method can be also used for the conversion of substituted 2-oxo



XXI



XXII
n = 1 or 0

and 3-oxo derivatives to unsubstituted 2-oxo derivatives. The reaction with vicinal diamines is suitable for the preparation of triterpenoids with a pyrazine cycle condensed to A ring.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Optical rotations were measured on an ETL-NPL polarimeter (Bendix-Ericsson) in chloroform solution (*c* 0·5 to 1·3) with a $\pm 2°$ accuracy. The infrared spectra were measured on a PE 684 (Perkin–-Elmer) instrument in chloroform. The 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 200°C, temperature of the direct inlet system 105—140°C. The ^{1}H NMR spectra were measured in deuteriochloroform solution on a Tesla BS 487 A instrument at 80 MHz, using hexamethyldisiloxane as internal reference. The chemical shifts were referred to tetramethyl silane and they are given in δ-scale (in ppm). The ultraviolet spectra were measured on a Unicam SP 700 spectrophotometer in cyclohexane solution. The identity of the samples prepared in various ways was checked by thin-layer chromatography, infrared and ^{1}H NMR spectra. The course of the reactions was checked by thin-layer chromatography on silica gel G (Merck), detection was done by spraying the plates with a 10% sulfuric acid solution and heating. The same silica gel was used for preparative thin-layer chromatography. For column chromatography silica gel Silpearl (Kavalier, Votice) was used. The samples for analysis were dried in a vacuum at 100°C, over phosphorus pentoxide.

The morpholine used for the reactions was purified by rectification on a 80 cm column packed with helices and the fraction boiling between 127 and 128°C was collected. The reaction mixtures containing morpholine and sulfur were worked up in the following manner: The hot mixture was poured into a 5-fold amount of 5% sodium sulfide and the precipitate formed was filtered off under suction. After drying it was put on a small column of 2—5 g of silica gel, eluted with chloroform and the eluate evaporated to dryness. The starting compounds *I*, *V* and *VII* are described in ref.[13], *II* in ref.[14], *III* and *IV* in ref.[15], *VIII* in ref.[16], *IX* in ref.[17], *X* in ref.[18], *XI* and *XII* in ref.[19] and *XVIII* in ref.[20].

Reactions of Ketones *I*, *II* and *XVIII* with Sulfur and Morpholine

a) A solution of 19β,28-epoxy-18α-oleanan-3-one (*I*, 1 g) and sulfur (0·2 g) in morpholine (30 ml) was refluxed for 24 h. After every 8 h 0·2 g sulfur were added. After working up the product was purified by chromatography on 10 g of silica gel, using light petroleum and ether (6 : 1) for elution. Crystallization from a mixture of benzene and ethanol gave 780 mg (78%)

of 19β,28-epoxy-18α-oleanan-2-one (*II*), m.p. 245–247°C, $[\alpha]_D$ +74°. Lit.[14] gives m.p. 245 to 247°C, $[\alpha]_D$ +74°. ^{1}H NMR spectrum: 0·80, 0·87, 0·88, 0·93, 0·96, 0·99 and 1·05 (7 × CH_3), 1·93 d (1αH), 2·42 dd (1βH), 2·26 d (3αH), 2·17 dd (3βH), $J_{1\alpha,1\beta}$ = 12·6 Hz, $J_{3\alpha,3\beta}$ = 13·9 Hz, $J_{1\beta,3\beta} \approx$ 1·5 Hz, 3·44 d and 3·77 d (J = 8 Hz, $C_{(28)}H_2$), 3·53 s ($C_{(19)}H$). The substance *II* obtained is identical with an authentic sample[14].

b) A solution of 3-oxo derivative *I* (2 g) and sulfur (2·5 g) in morpholine (20 ml) was refluxed for 16 h and then worked up. Chromatography of the residue on a column of silica gel (100 g) with light petroleum–ether mixture 15 : 1 gave gradually 0·15 g of a mixture of non-polar sulfur-containing compounds, then 0·2 g (10%) of 3-oxo derivative *I* and 1·3 g (65%) of 2-oxo derivative *II*.

c) A solution of 2-oxo derivative *II* (0·1 g) and sulfur (0·1 g) in morpholine (2 ml) was refluxed for 24 h and then worked up. Chromatography of the reaction mixture on a plate with 10 g of silica gel using light petroleum–ether 3 : 1 for development gave 76 mg (76%) of the starting 2-oxo derivative *II* and 7 mg (7%) of 3-oxo derivative *I*.

d) A mixture of 3-oxo-18α-oleanan-28→19β-olide (*XVIII*, 0·45 g), sulfur (0·5 g) and morpholine (10 ml) was refluxed for 24 h and worked up. Repeated crystallization of the residue from a mixture of chloroform and methanol gave 320 mg (71%) of 2-oxo-18α-oleanan-28→19β-olide (*XIX*), m.p. 339–341°C (sublimates at 290°C), $[\alpha]_D$ +82°. Infrared spectrum: 1 763 (lactone ring), 1 700 (six-membered cyclic ketone), 1 121, 968, 922 cm^{-1}. ^{1}H NMR spectrum: 0·88 (2 × × CH_3), 0·92 (2 × CH_3), 0·96, 1·03 and 1·04 (3 × CH_3), 1·92 d and 2·41 bd (J = 13 Hz, $C_{(1)}H_2$), 2·17 bd and 2·27 d (J = 14 Hz, $C_{(3)}H_2$), 3·94 s ($C_{(19)}H$). For $C_{30}H_{46}O_3$ (454·7) calculated: 79·24% C, 10·20% H; found: 79·11% C, 10·24% H.

Reaction of Derivatives *III*–*XII* with Morpholine and Sulphur

For the subsequent reactions the following general procedure was used: A solution of 100 mg of compound and 150 mg of sulfur in 2 ml of morpholine was refluxed for the indicated time and then worked up.

a) 2α-Hydroxy-3-oxo derivative *III* gives a mixture after 2 h, from which 40 mg (40%) of 3-oxo-derivative *I* and 40 mg (40%) of 2-oxo derivative *II* were obtained by thin-layer chromatography. On prolonging the reaction time to 10 h 2-oxo derivative *II* is formed, which was isolated by crystallization from ethanol in a 70% yield.

b) 3β-Acetoxy-2-oxo derivative *IV* was reacted for 4 h, affording 2-oxo derivative *II*, which was isolated by crystallization from ethanol in a 63% yield.

c) Dibromo ketone *V* afforded 2-oxo derivative *II* after 16 h refluxing, and it was isolated by crystallization from ethanol in a 60% yield.

d) Diketone *VI* was refluxed for 8 h, giving a mixture from which 43% of 2-oxo derivative *II* were isolated by chromatography on a column of silica gel (10 g) with light petroleum and ether in a 8 : 1 ratio. Further fractions contained very polar substances.

e) α,β-Unsaturated ketone *VII* was refluxed for 14 h, affording 2-oxo derivative *II* which was isolated from the mixture by crystallization from a mixture of chloroform and ethanol in a 77% yield.

f) Unsaturated derivative *X*, hydroxy derivative *XI* and acetoxy derivative *XII* would not react even after 40 h refluxing, 1-oxo derivative *VIII* and A-nor-ketone *IX* did not react even after 80 h refluxing and the major part of the starting material was recovered.

19β,28-Epoxy-18α-olean-2-eno[2,3-*b*]pyrazine (*XIII*)

A mixture of 3·1 g of 3-oxo derivative *I*, 2 g of sulfur, 2 ml of ethylenediamine and 20 ml of morpholine was refluxed for 2 h and then worked up. Crystallization of the residue from a mixture of chloroform and ethanol gave 2·95 g (88%) of compound *XIII*, m.p. 264–265°C (sublimates at 240–250°C), $[\alpha]_D$ +38°. Infrared spectrum: 1 404, 1 109, 1 033 (C—O—C) cm^{-1}. ^1H NMR spectrum: 0·82, 0·83, 0·94, 0·97, 1·06, 1·30, 1·31 (7 × CH_3), 2·50 bd and 3·08 d (J = 17·1 Hz, $C_{(1)}H_2$), 3·45 d and 3·80 d (J = 8·0 Hz, $C_{(28)}H_2$), 3·57 s ($C_{(19)}H$), 8·26 d and 8·39 bd (J = = 2·0 Hz, pyrazine ring). Mass spectrum, *m/z* (%): 476 (100, M^+, $C_{32}H_{48}N_2O$), 461 (48), 445 (13), 431 (9), 405 (35, $C_{27}H_{37}N_2O$), 255 (55, $C_{17}H_{23}N_2$), 241 (12, $C_{16}H_{21}N_2$), 187 (28), 159 (27). UV spectrum, λ_{max} (ε): 270 (8 700), 277 (7 800), 315 (930), 320 (1 030), 326 nm (830). For $C_{32}H_{48}N_2O$ (476·7) calculated: 80·62% C, 10·15% H, 5·88% N; found: 80·43% C, 10·27% H, 6·03% N.

After 1–2 h refluxing under the same conditions ketone *II*, acetoxy ketone *IV*, hydroxy ketone *III*, dibromo ketone *V*, diketone *VI* and α,β-unsaturated ketone *VII* give pyrazine derivative *XIII* as the sole product isolated by crystallization in 80–90% yield. The unsaturated derivative *X*, hydroxy derivative *XI* and acetate *XII* do not give any product even after 24 h refluxing, so that the major part of the starting compound could be recovered unreacted.

19β,28-Epoxy-18α-olean-2-eno[2,3-*b*]pyrazine-1′-oxide (*XIV*)

A solution of the pyrazine derivative *XIII* (120 mg) in 30% peracetic acid (5 ml) was allowed to stand at room temperature for 3 weeks. After dilution with water the products were extracted with ether and the ethereal extract washed consecutively with a 5% solution of potassium iodide, 5% solution of sodium sulfite, water, a saturated solution of sodium hydrogen carbonate and water, and dried over sodium sulfate and evaporated to dryness. Chromatography of the residue on a silica gel column (10 g) with a mixture of light petroleum and ether 6 : 1 gave 40 mg of the starting derivative *XIII* and 70 mg (56%) of oxide *XIV*, crystallized from acetone. M.p. 255 to 258°C, under decomp. (sublimates at 245–250°C), $[\alpha]_D$ +70°. Infrared spectrum: 1 579, 1 429, 1 140, 1 032 (C—O—C) cm^{-1}. ^1H NMR spectrum: 0·82 and 0·84 (2 × CH_3), 0·95 (2 × CH_3), 1·05, 1·30 and 1·33 (3 × CH_3), 2·12 bd and 3·43 d (J = 18·7 Hz, $C_{(1)}H_2$), 3·45 d and 3·78 d (J = 8·0 Hz, $C_{(28)}H_2$), 3·56 s ($C_{(19)}H$), 7·98 and 8·31 bd (J = 3·8 Hz, pyrazine ring). Mass spectrum, *m/z* (%): 492 (27, M^+), 477 (48), 476 (100), 475 (24), 461 (63), 421 (14), 405 (39), 255 (70), 187 (38). UV spectrum, λ_{max} (ε): 229 (34 000), 234 (35 000), 272 nm (16 000). For $C_{32}H_{48}N_2O_2$ (492·7) calculated: 78·00% C, 9·82% H, 5·69% N; found: 78·12% C, 9·93% H, 5·60% N.

19β,28-Epoxy-18α-olean-1-eno[1,2-*b*]pyrazine (*XV*)

A mixture of 19β,28-epoxy-18α-oleanan-1-one (*VIII*, 150 mg), sulfur (100 mg), ethylenediamine (1 ml) and morpholine (5 ml) was refluxed for 16 h and then an additional 100 mg of sulfur were added to it and the mixture was refluxed for another 24 h and worked up. A precipitate was formed during the reaction. The reaction product was purified by preparative thin-layer chromatography on 10 g of silica gel, using a mixture of light petroleum and ether 3 : 1 for development. Crystallization from a mixture of chloroform and methanol gave 68 mg (42%) of pyrazine derivative *XV*, m.p. 244–246°C (sublimates about 220°C), $[\alpha]_D$ +80°. Infrared spectrum: 1 531, 1 392, 1 034 (C—O—C) cm^{-1}. ^1H NMR spectrum: 0·83, 0·92, 0·95, 0·96, 1·14, 1·15 and 1·24 (7 × CH_3), 2·40 m (2 H), 2·82 d and 3·07 bd (J = 17·0 Hz, $C_{(3)}H_2$), 3·46 d and 3·83 d (J = 8·0 Hz, $C_{(28)}H_2$), 3·61 s ($C_{(19)}H$), 8·25 bs (2 H, pyrazine ring). Mass spectrum, *m/z* (%): 476 (40), 461 (38), 405 (2), 255 (8), 241 (8), 188 (23), 175 (100). UV spectrum, λ_{max} (ε): 268

(9 400), 273 (7 700), 313 nm (760). For $C_{32}H_{48}N_2O$ (476·7) calculated: 80·62% C, 10·15% H, 5·88% N; found: 80·47% C, 9·98% H, 5·67% N.

19β,28-Epoxy-A-nor-18α-olean-1-eno[1,2-*b*]pyrazine (*XVI*)

A mixture of 19β,28-epoxy-A-nor-18α-oleanan-2-one (*IX*, 200 mg), sulfur (250 mg), ethylenediamine (1 ml) and morpholine (10 ml) was refluxed for 24 h and then worked up. During the reaction a precipitate was formed. Chromatography of the residue on 30 g of silica gel with a 6 : 1 light petroleum ether mixture and crystallization from methanol gave 160 mg (74%) of derivative *XVI*, m.p. 233—235°C (sublimates at 180—190°C), $[\alpha]_D$ +4°. Infrared spectrum: 1 032 cm^{-1} (C—O—C). ^1H NMR spectrum: 0·80, 0·95 and 0·96 (3 × CH_3), 1·13 (2 × CH_3), 1·18 and 1·32 (2 × CH_3), 2·23 m (1 H, $W_{1/2}$ = 20 Hz), 2·79 m (1 H, $W_{1/2}$ = 22 Hz), 3·47 d and 3·82 d (J = 8·0 Hz, $C_{(28)}H_2$), 3·57 s ($C_{(19)}H$), 8·10 d and 8·30 d (J = 2·5 Hz, pyrazine ring). Mass spectrum, m/z (%): 462 (74, M^+), 447 (36), 432 (8), 391 (13), 241 (22), 229 (22), 227 (25), 174 (53), 161 (100). UV spectrum, λ_{max} (ε): 273 (8 500), 279 (7 100), 327 nm (1 100). For $C_{31}H_{46}N_2O$ (462·7) calculated: 80·47% C, 10·02% H, 6·06% N; found: 80·23% C, 10·07% H, 5·90% N.

19β,28-Epoxy-18α-oleana-2-eno[2,3-*b*]quinoxaline (*XVII*)

A mixture of 3-oxo derivative *I* (200 mg), sulfur (100 mg), *o*-phenylenediamine (100 mg) and morpholine (1 ml) was refluxed for 1 h and then worked up. Crystallization from a mixture of chloroform and methanol gave 180 mg (75%) of derivative *XVII*, m.p. 277—279°C (sublimates at 230°C), $[\alpha]_D$ +66°. Lit.[7] gives m.p. 276—277°C, lit.[8] gives m.p. 269—273°C. Infrared spectrum: 1 565, 1 486, 1 078, 1 032 (C—O—C) cm^{-1}. ^1H NMR spectrum: 0·83, 0·86, 0·95, 0·98, 1·08 (5 × CH_3), 1·43 (2 × CH_3), 2·64 d and 3·35 d (J = 17·0 Hz, $C_{(1)}H_2$), 3·46 d and 3·81 d (J = = 8·0 Hz, $C_{(28)}H_2$), 3·57 s ($C_{(19)}H$), 7·60 m (2 H), 7·95 m (2 H). UV spectrum, λ_{max} (ε): 232 (26 000), 236 (34 000), 240 (30 000), 310 (8 300), 321 (9 800). For $C_{36}H_{50}N_2O$ (526·8) calculated: 82·08% C, 9·57% H, 5·32% N; found: 82·23% C, 9·43% H, 5·27% N.

18α-Olean-2-eno[2,3-*b*]pyrazin-28→19β-olide (*XX*)

A mixture of ketolactone *XVIII* (150 mg), sulfur (100 mg), ethylenediamine (0·1 ml) and morpholine (1 ml) was refluxed for 1 h and worked up. Crystallization from chloroform gave 120 mg (75%) of derivative *XX*, sublimating at 310°C but not melting till 360°C, $[\alpha]_D$ +24°. Infrared spectrum: 1 763 (five-membered lactone), 1 405, 1 108 cm^{-1}. ^1H NMR spectrum: 0·84, 0·92, 0·98, 1·00, 1·04, 1·29 and 1·30 (7 × CH_3), 2·49 bd and 3·07 d (J = 17 Hz, $C_{(1)}H_2$), 3·96 s ($C_{(19)}H$), 8·26 d and 8·40 bd (J = 2 Hz, pyrazine ring). Mass spectrum, m/z (%): 490 (95, M^+, $C_{32}H_{46}N_2O_2$), 475 (60), 445 (6), 431 (6), 258 (54, $C_{17}H_{26}N_2$), 255 (100, $C_{17}H_{23}N_2$), 243 (19), 241 (29), 187 (32). UV spectrum, λ_{max} (ε): 270 (8 700), 276 (7 700), 315 (910), 321 nm (1 020). For $C_{32}H_{46}N_2O_2$ (490·7) calculated: 78·32% C, 9·45% H, 5·71% N; found: 78·09% (C, 9·37% H, 5·55% N.

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REFERENCES

1. Brown E. V.: Synthesis *1975*, 358.
2. Bible R. H. jr: J. Amer. Chem. Soc. *79*, 3924 (1957).
3. Behforouz M.: *Thesis*. University of Indiana 1965.
4. Tori K., Ogata M.: Chem. Pharm. Bull. *12*, 272 (1964).

5. Jaffe H. H., Orchin M.: *Theory and Applications of Ultraviolet Spectroscopy*, p. 361. Wiley, New York 1962.
6. Lehn J. M., Vystrčil A.: Tetrahedron *19*, 1733 (1963).
7. Huneck S.: Chem. Ber. *98*, 1837 (1965).
8. Dischendorfer O., Polak O.: Monatsh. Chem. *51*, 43 (1929).
9. Schmidt J., Huneck S.: Org. Mass Spectrom. *14*, 646 (1979).
10. Budzikiewicz H., Wilson J. M., Djerassi C.: J. Amer. Chem. Soc. *85*, 3688 (1963).
11. Morris D. G.: Chem. Soc. Rev. *11*, 397 (1982).
12. Kane V. V., Singh W., Martin A., Doyle D. L.: Tetrahedron *39*, 345 (1983).
13. Klinot J., Vystrčil A.: This Journal *31*, 1079 (1966).
14. Klinot J., Waisser K., Streinz L., Vystrčil A.: This Journal *35*, 3610 (1970).
15. Sejbal J., Klinot J., Vystrčil A.: This Journal, in press.
16. Huneck S.: Chem. Ber. *98*, 2291 (1965).
17. Klinot J., Vystrčil A.: This Journal *27*, 377 (1962).
18. Klinot J., Vystrčil A.: This Journal *29*, 516 (1964).
19. Schulze H., Pieroh K.: Chem. Ber. *55*, 2332 (1922).
20. Vystrčil A., Stejskalová-Vondrášková E., Černý J.: This Journal *24*, 3279 (1959).

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