REACTION OF 18β,19β-EPOXYLUPAN-21-ONE DERIVATIVES WITH ACIDS: A WAY TO 21,22-DISUBSTITUTED LUP-18-ENE TRITERPENOIDS+

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Dedicated to the memory of Dr Miroslav Protiva.

Depending on the conditions and the acid employed, 18β,19β-epoxy-28-hydroxy-21-oxolupan-3β-yl acetate (**2a**) and 18β,19β-epoxy-21-oxolupane-3β,28-diyl diacetate (**2b**) on treatment with acid gave three types of products: (i) 28-nor derivatives: 21-oxo-28-norlupa-16,18-dien-3β-yl acetate (**6**), 19β-hydroxy-21-oxo-28-norlup-17-en-3β-yl acetate (**7**) and 17ξ-hydroxy-21-oxo-28-norlup-18-en-3β-yl acetate (**8**), (ii) lupa-12,18-dien-21-ones **4a** and **4b**, and (iii) 22β-substituted lup-18-en-21-one derivatives of the type **5**. The formation of 22β-substituted derivatives of the type **5** probably proceeds in the enol form of epoxy ketone **2**. Opening of the epoxide ring with shift of the double bond to position 19(21) and attack by nucleophilic species at C-22 followed by elimination of water and re-formation of the 22-oxo group leads to derivatives of the type **5**.

Key words: Triterpenes; Triterpenoids; Lupane; Epoxy ketones; NMR spectroscopy, ^{1}H and ^{13}C.

Triterpenoid compounds derived from lup-18-ene and 18,19-epoxylupane are suitable starting material for the preparation of E-secolupane and des-E-lupane compounds which represent a transition to tetracyclic triterpenoids of the baccharane type and to sesterterpenoids[2–10]. In our previous paper[10], we have shown that treatment of 18β,19β-epoxy-21-oxolupane-3β,28-diyl diacetate (**2b**) with peroxyacetic acid under catalysis with strong acids (4-toluenesulfonic, sulfuric or trifluoroacetic acids) results in Baeyer–Villiger oxidation, opening of the epoxide ring and

+ Part CIX in the series Triterpenes; Part CVIII: see ref.[1]

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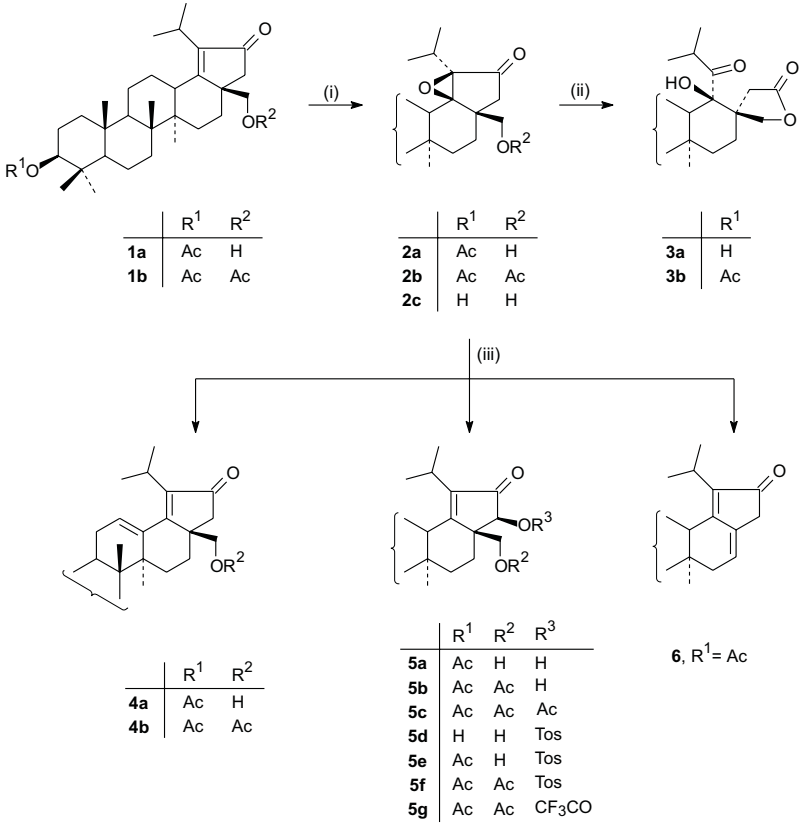
subsequent cyclization. The reaction thus leads to 19,21-secolupane compounds – spirolactones of the type **3**, which on subsequent oxidative degradation can be converted into tetranor and pentanor derivatives (des-E-compounds), similar to natural skalarane sesterterpenoids. In some cases, the mentioned reaction of epoxy ketone **2b** with peroxyacetic acid also afforded side products which in the cited paper[10] have not been identified. Now we have found that these compounds are not the products of oxidation with the peroxy acid and must therefore arise by action of acids on the epoxy ketone **2b**. For this reason, we have studied the reaction of various acids with the epoxy ketone **2b** and with the analogous epoxy ketone **2a**, containing free hydroxyl in position 28 (Scheme 1).



	R^1	R^2
1a	Ac	H
1b	Ac	Ac

	R^1	R^2
2a	Ac	H
2b	Ac	Ac
2c	H	H

	R^1
3a	H
3b	Ac

	R^1	R^2
4a	Ac	H
4b	Ac	Ac

	R^1	R^2	R^3
5a	Ac	H	H
5b	Ac	Ac	H
5c	Ac	Ac	Ac
5d	H	H	Tos
5e	Ac	H	Tos
5f	Ac	Ac	Tos
5g	Ac	Ac	CF_3CO

6, R^1 = Ac

(i) 3-chloroperoxybenzoic acid/$CHCl_3$; (ii) boric acid, air/benzene, dioxane; (iii) acid

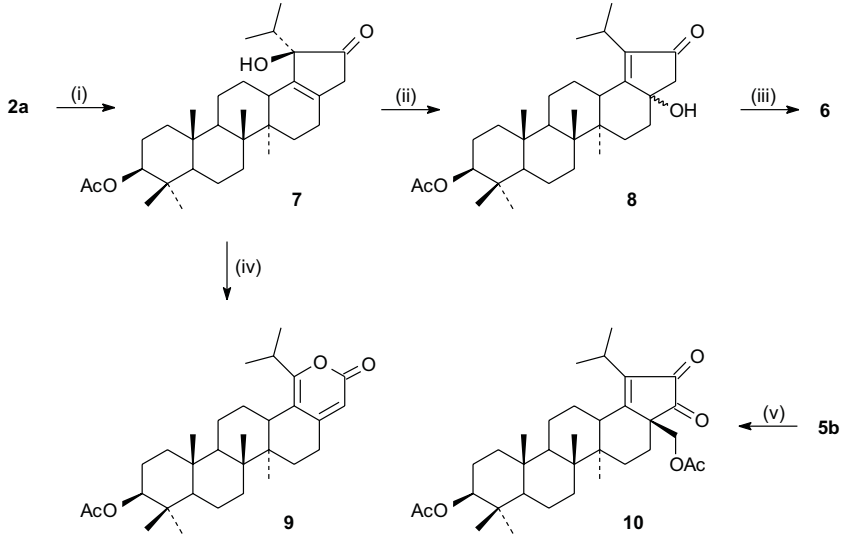
SCHEME 1

The starting 21-oxolup-18-ene-3β,28-diyl diacetate (**1b**) was prepared by oxidation of lup-18-ene-3β,28-diyl diacetate with chromium trioxide[11]; the epoxy ketone **2b** was obtained by reaction of ketone **1b** with 3-chloroperoxybenzoic acid according to the literature[10]. Mild alkaline hydrolysis of diacetate **1b** gave monoacetate **1a** with free hydroxyl in position 28. Epoxidation of the double bond in monoacetate **1a** with 3-chloroperoxybenzoic acid led to epoxy ketone **2a** which was also obtained by partial alkaline hydrolysis of diacetate **2b**; as a side product of the hydrolysis, we isolated the known[10] diol **2c**.

On heating with 4-toluenesulfonic acid in benzene, the epoxy ketone **2b** afforded 22-tosyloxy derivative **5f** as the sole product. Reaction of epoxy ketone **2b** with acetic acid under catalysis with sulfuric acid gave the analogous 22-acetoxy derivative **5c** (71%), together with a small amount of side products that were not identified. In both the reactions we added to the reaction mixture a small amount of acetic anhydride to prevent the undesired hydrolysis of the acetate groups in positions 3, 28 or 22. The tosylate **5f** and acetate **5c** were identical with the side products obtained[10] in the Baeyer–Villiger oxidation of epoxy ketone **2b** with peroxyacetic acid when 4-toluenesulfonic or sulfuric acid was used as catalyst. Reaction of epoxy ketone **2b** with trifluoroacetic acid afforded mainly the 22-trifluoroacetate **5g** which was very unstable and was converted into the corresponding 22-hydroxy derivative **5b** during the work-up of the reaction mixture and chromatographic purification. In addition to these two 22-substituted compounds (**5g**, **5b**), we also isolated the dienone **4b**. Treatment of epoxy ketone **2b** with zinc iodide in boiling acetic acid resulted in predominant elimination of the epoxide oxygen atom and the unsaturated ketone **1b** was obtained as the main product. A minor amount of the 22-acetoxy derivative **5c** was also isolated.

With boron trifluoride etherate in benzene at room temperature, epoxy ketone **2b** afforded a complex mixture of products from which we were able to isolate and identify only one compound, dienone **4b**, in very low yield (10%). Similarly, reaction with sulfuric acid in boiling aqueous peroxide-free dioxane in an argon atmosphere afforded a mixture of many unidentified products neither of which predominated. However, when this reaction was performed in the presence of air oxygen, a Baeyer–Villiger-type reaction took place and we isolated from the product mixture spirolactone **3a** in 46% yield. Also, when epoxy ketone **2b** was reacted with boric acid in boiling mixture of chloroform and acetic anhydride in the presence of air, an oxidation reaction took place, spirolactone **3b** being isolated as the principal product (61%), along with the 22-acetoxy derivative **5c** (24%).

Baeyer–Villiger oxidation of the epoxy ketone **2b** and subsequent cyclization to the spirolactones **3a** and **3b** is thus extremely facile and does not require any peroxy acids. Similarly to its 28-acetate **2b**, the epoxy ketone **2a** with free hydroxyl on C-28 reacted with 4-toluenesulfonic acid under formation of 22-tosylate **5e**. The reaction also gave small amounts of tosylate **5d**, deacetylated in position 3, and of dienone **4a**. Compared with the reactions of the ketone **2b**, the epoxy ketone **2a** often underwent elimination of formaldehyde from C-17 with formation of 28-nor derivatives: its reaction with boron trifluoride etherate afforded the nordienone **6** as the sole product. Treatment with zinc iodide in boiling acetic acid also gave the nordienone **6** (29%), together with the 28-acetates – the unsaturated ketone **1b** (23%) and the dienone **4b** (11%). The nordienone **6** was also isolated in a 23% yield from the product mixture after reaction of epoxy ketone **2a** with trifluoroacetic acid which afforded dienone **4a** as the principal product (60%).



(i) boric acid/benzene, dioxane, argon; (ii) allylic rearrangement; (iii) $TosOH/CHCl_3$; (iv) $Pb(OAc)_4$, AcOH, Ac_2O/benzene; (v) CrO_3 on alumina/$CHCl_3$

SCHEME 2

Heating of the epoxy ketone **2a** with boric acid in a mixture of benzene and dioxane under argon (Scheme 2) afforded further two 28-nor derivatives: 19-hydroxy ketone **7** (66%) and 17-hydroxy ketone **8** (15%). When

the reaction was performed in the presence of air, oxidation took place (as in the case of the epoxy ketone **2b**), the spirolactone **3b** (65%) being the predominant product. The hydroxy ketones **7** and **8** are obviously intermediates in the formation of dienone **6**: a TLC and ^{1}H NMR study of reaction of hydroxy ketone **7** with 4-toluenesulfonic acid in chloroform at room temperature revealed that the 19-hydroxy ketone **7** undergoes first an allylic rearrangement to give the isomeric 17-hydroxy ketone **8** whose dehydration leads to 16,18-dien-21-one **6** as the sole product.

Hydrolysis of the acetate groups in positions 22 and 28 of the triacetate **5c** and of the 28-acetate group in diacetate **5b** is extraordinarily facile: treatment of the triacetate **5c** and diacetate **5b** with potassium hydroxide in a mixture of ethanol and benzene at room temperature (two and one equivalent, respectively) gives the 3-acetate **5a** within few minutes. Both the *O*-acetyl groups in positions 3 and 28 in the tosylate **5f** can be removed by reaction with sulfuric acid in methanol, the 22-tosyloxy group remaining intact, and the product is tosylate **5d**. The compounds without acetate groups and the partially acetylated derivatives were chemically correlated with the peracetyl derivatives by acetylation with acetic anhydride in pyridine; dienone **4a** gave dienone **4b**, compounds **5a** and **5b** afforded the triacetate **5c** and tosylates **5d** and **5e** were converted into the tosylate **5f**. The 22-hydroxy derivative **5b** was oxidized with chromium trioxide on alumina to give 21,22-diketone **10**. In the 19-hydroxy ketone **7** the presence of an α-ketol grouping was confirmed by cleavage of the C(19)–C(21) bond with lead tetraacetate; however, the expected 19-oxo-21-oic acid was obtained in the form of the enol lactone, *i.e.* the dienolide **9**. The β-configuration of the hydroxyl in the 19-hydroxy ketone **7** follows from the β-configuration of the epoxide oxygen atom[10] in the starting epoxy ketone **2a**.

Structures of the prepared compounds were confirmed by IR, UV and mass spectra (see Experimental); however, most of the evidence is based mainly on the ^{1}H and ^{13}C NMR spectra. The proton NMR data are summarized in Tables I–III, the ^{13}C NMR data in Tables IV and V. In the ^{13}C NMR spectra, the number of directly bonded hydrogen atoms was determined from APT or DEPT spectra and for compounds **4b** and **7** also from proton coupled spectra. The chemical shifts were assigned to the individual hydrogen and carbon atoms (Tables I–V) using the following two-dimensional techniques: COSY (compounds **2a**, **4b**, **5a**–**5e**, **6**, **7**, **9** and **10**), LRCOSY (**4b**, **5b** and **10**), NOESY (**5a**, **5c**–**5e** and **7**), TOCSY (**7**), HMQC or HETCOR (**5a**–**5e**, **7** and **9**) and COLOC (**5a** and **9**). By combination of the mentioned methods we have found and assigned all the hydrogen signals for compounds **5a**, **5c**–**5e** and **7**. If we assigned unequivocally also the configura-

tion of the methylene protons, in Tables I–III the individual protons are described by stereodescriptors α and β, if the configuration is uncertain, these protons are denoted as a (highfield signal) and b (lowfield signal). In all the studied compounds, the chemical shifts of protons H-2α and H-2β differ only slightly and appear in the region δ 1.6–1.7 and their signals could not be distinguished neither in the homocorrelated nor in the heterocorrelated 2D NMR spectra. The ^{1}H NMR spectra of all the measured compounds exhibit characteristic two methyl doublets at δ 0.9–1.3 and a septet at δ 2.0–3.5 ($J \approx 7$ Hz), which correspond to an isolated isopropyl group, and further (except dienone **4b**) a doublet of doublets of H-13 in the region δ 2.6–3.2 with vicinal coupling constants J(12α,13β) = 12–13 Hz and J(12β,13β) = 3–4 Hz. The ^{1}H as well as ^{13}C NMR spectra of 22-substituted compounds of the type **5** are very similar to those of the unsaturated ketones **1a** (Tables I and IV) and **1b** (ref.[11]), except the H-22 signal which in compounds of the type **5** appears as a singlet at δ 3.7–5.1, depending on the character of substituent in position 22, and the signal of C-22 (a doublet in the region of δ 80–86). Identification of the four-spin system of protons in positions 15 and 16 is based on the COSY spectra and on the H-16β signal which is shifted downfield to $\delta \approx 2$ and forms a doublet of triplets; the found coupling constants J(16α,16β) = 13.7 Hz and J(15α,16β) ≈ J(15β,16β) ≈ 3.8 Hz correspond to an equatorial position of H-16β. In the NOESY spectra of compounds **5a** and **5c**–**5e**, the following steric contacts have been found: H-1α/H-3, H-3/H-5, H-3/H-23, H-12α/H-20, H-12β/H-20, H-13/H-15β, H-13/H-26, H-13/H-28b, H-15β/H-26, H-16α/H-22, H-16α/H-27, H-23/H-24, H-24/H-25 and H-25/H-26. The absence of cross-peaks of H-22/H-16β, H-22/H-28a, H-22/H-28b and the presence of an intense NOESY cross-peak of H-22/H-16α shows that H-22 has the α-configuration. Since these compounds were chemically correlated with other 22-substituted derivatives (**5b**, **5f**, **5g**), it is evident that in all the compounds of the type **5**, the substituent on C-22 has β-configuration.

The position of the 16(17) double bond in nordienone **6** follows from the COSY spectrum that exhibits a coupling of the olefinic proton H-16 with the two neighbouring protons on C-15, an allylic coupling of H-16 with the protons on C-22 and a homoallylic coupling of protons on C-22 with the H-15β and H-13 protons. In 19-hydroxy ketone **7**, COSY and TOCSY spectra show four isolated spin systems, three of which are due to adjacent protons on the rings A (protons in positions 1, 2, 3) and B (5, 6, 7) and in the isopropyl side chain (20, 29, 30). The fourth spin system is – thanks to the long-range couplings between the protons separated by carbon atoms of the 17(18) double bond – common to the protons on the rings C (9, 11, 12, 13),

D (15, 16) and E (22). In the NOESY spectrum we found steric contacts similar to those already mentioned for compound of the type **5**. The presence of a dienolide system in the ring E in compound **9** follows from the ^{13}C NMR spectrum and from the COLOC spectrum which confirmed the following ^{13}C-^{1}H long-range couplings: C-17/H-13, C-17/H-22, C-19/H-13, C-19/(H-29, H-30) and C-21/H-22. The spin system of protons in positions 15, 16 and 22 was identified in COSY spectra.

Mass spectra of compounds **1a**, **2a** and **4–9** exhibited very abundant peaks corresponding to fragmentation in the ring C: ions $[M - 263]^+$ for 3-*O*-acetyl derivatives and ion $[M - 221]^+$ for the 3-hydroxy derivative **5d**. Their formation can be explained by cleavage of the C(11)–C(12) and C(8)–C(14) bonds and subsequent transfer of hydrogen from the neutral fragment (rings A and B) to a charged particle involving rings D and E. The same fragmentation type has already been observed[11] in the case of unsaturated ketone **1b**. In some cases, particularly of hydroxy ketones **7** and **8**, the mentioned characteristic ions are accompanied by ions $[M - 281]^+$ that correspond to loss of water molecule from ions $[M - 263]^+$.

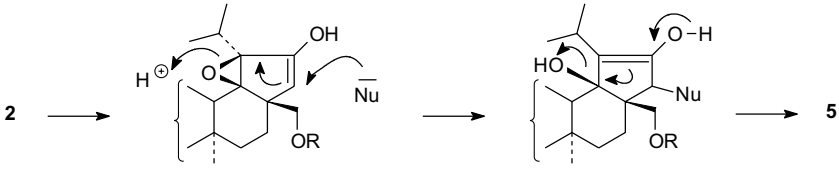
We can conclude that on treatment with the described acids 18β,19β-epoxy-21-ketones **2a** and **2b** afford three types of products:

1. 28-Nor derivatives **6**, **7** and **8** – their formation was observed only with the epoxy ketone **2a** which has free hydroxy group on the C-28 carbon atom;

2. dienones **4a** and **4b** – they are formed predominantly from the 28-hydroxy derivative **2a**, whereas in the reaction of the 28-acetoxy derivative **2b** they were found only exceptionally, in both cases only as side products;

3. 22β-substituted derivatives of the type **5** – they are typical for reactions of the 28-acetoxy derivative **2b**; in the reactions of 28-hydroxy derivative **2a**, they are more or less accompanied by dienones **4a** and **6**, depending on the conditions.

A possible explanation of the formation of 22β-substituted derivatives is given in Scheme 3. The reaction probably proceeds in the enol form by opening of the epoxide ring with shift of the double bond from position



SCHEME 3

21(22) to position 19(21) and with attack by a nucleophilic species at C-22. Elimination of water and re-formation of the 22-oxo group then leads to derivatives of the type **5**. This reaction thus represents a simple procedure for the preparation of 21,22-disubstituted lup-18-ene derivatives which may be a suitable starting material for the synthesis of E-secolupane compounds.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Optical rotation measurements at 23 °C were carried out in chloroform (*c* 0.3–0.5) on an automatic polarimeter ETL-NPL (Bendix–Ericsson), accuracy ±2°; they are given in 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded in chloroform on a PE 684 (Perkin–Elmer) spectrometer, wavenumbers are given in cm^{-1}. UV spectra were measured on a Unicam SP-700 instrument. ^{1}H and ^{13}C NMR spectra were taken on a Varian UNITY-INOVA 400 FT spectrometer (^{1}H at 400 MHz, ^{13}C at 100.58 MHz) in deuteriochloroform with tetramethylsilane as internal standard (for the ^{13}C NMR data δ ($CDCl_3$) 77.00 ppm). The chemical shift values (δ-scale, ppm) and coupling constants (Hz) in the ^{1}H NMR spectra were obtained by first-order analysis. Electron impact mass spectra were measured on an INCOS 50 (Finnigan MAT) instrument; ionizing electron energy 70 eV.

Column chromatography was carried out on silica gel Silpearl (Kavalier, Votice, Czech Republic). The purity of the samples was checked by thin-layer chromatography (TLC) on DC-Alufolien Kieselgel 60 F_{254} (Merck) plates. Spots were detected by spraying with 10% sulfuric acid and subsequent heating. Preparative TLC was performed on silica gel 60 G (Merck); compounds were detected by UV light (254 nm) after spraying with 0.3% solution of morin in methanol. The identity of samples prepared by different procedures was verified by TLC, IR and ^{1}H NMR spectra. Analytical samples were dried over phosphorus pentoxide at 100 °C under diminished pressure.

The usual work-up denotes dilution of the reaction mixture with water, extraction of the products with ether, successive washing of the ethereal layer with dilute (1 : 4) hydrochloric acid (if necessary), sodium hydrogencarbonate solution and with water, drying over sodium sulfate and evaporation of the solvent. The hydroxy derivatives were acetylated with a mixture of acetic anhydride and pyridine (1 : 1) at room temperature for 12–18 h and the reaction mixture was worked up in the usual manner. After crystallization, the acetyl derivatives were obtained in 70–90% yield.

28-Hydroxy-21-oxolup-18-en-3β-yl Acetate (**1a**)

A solution of potassium hydroxide (0.5 g, 8.9 mmol) in ethanol (40 ml) was added to a solution of diacetate **1b** (4.0 g, 7.4 mmol, ref.[11]) in benzene (40 ml), the mixture was set aside for 8 h at room temperature and then worked up in the usual manner. Repeated crystallization from chloroform–methanol afforded monoacetate **1a** (2.4 g, 65%), m.p. 292–294 °C, $[\alpha]_D$ –69. IR: 3 621, 1 719, 1 687, 1 602, 1 254. MS, *m/z* (%): 498 (M^+, 8), 438 (5), 395 (12), 259 (5), 235 (70), 189 (24), 43 (100). For $C_{32}H_{50}O_4$ (498.7) calculated: 77.06% C, 10.11% H; found: 76.84% C, 9.88% H.

18β,19β-Epoxy-28-hydroxy-21-oxolupan-3β-yl Acetate (**2a**)

Method A) By epoxidation of ketone **1a**: A solution of the ketone **1a** (3.0 g, 6.02 mmol) and 3-chloroperoxybenzoic acid (70%, 3.0 g, 12.2 mmol) in chloroform (30 ml) was allowed to stand at room temperature. After 8 days, it was diluted with chloroform (30 ml) and washed successively with 5% solution of sodium iodide, saturated solution of sodium sulfite, saturated solution of sodium hydrogencarbonate and water, and dried over sodium sulfate. Crystallization from chloroform–methanol afforded the epoxy ketone **2a** (2.5 g, 81%), m.p. 253–255 °C, $[\alpha]_D$ +36. IR: 3 620, 1 734, 1 255. MS, *m/z* (%): 514 (M^+, 3), 496 (2), 484 (3), 483 (3), 441 (2), 383 (25), 251 (74), 203 (36), 189 (55), 43 (100). For $C_{32}H_{50}O_5$ (514.7) calculated: 74.67% C, 9.79% H; found: 74.86% C, 10.01% H.

Method B) By hydrolysis of diacetate **2b**: A solution of potassium hydroxide (0.2 g, 3.6 mmol) in ethanol (20 ml) was added to a solution of diacetate **2b** (1.7 g, 3.1 mmol, ref.[10]) in benzene (20 ml) and the mixture was set aside at room temperature for 8 h. After the usual work-up, the mixture of products was separated on a column of silica gel (40 g). Light petroleum–ether (4 : 1) eluted successively the starting diacetate **2b** (0.2 g, 12%) and monoacetate **2a** (0.9 g, 57%); light petroleum–ether (1 : 1) eluted the diol **2c** (0.3 g, 21%), m.p. 182–183 °C (chloroform–methanol) (reported[10] m.p. 182–183 °C).

Reaction of 18β,19β-Epoxy-28-hydroxy-21-oxolupan-3β-yl Acetate (**2a**)

Method A) With 4-toluenesulfonic acid: A solution of epoxy ketone **2a** (120 mg, 0.23 mmol) and 4-toluenesulfonic acid monohydrate (50 mg, 0.26 mmol) in chloroform (5 ml) was heated at 50 °C for 6 h. After cooling, the reaction mixture was worked up as usual and subjected to preparative TLC on silica gel in benzene–ether (3 : 2) which afforded tosylate **5e** (110 mg, 71%), dienone **4a** (10 mg, 9%) and tosylate **5d** (8 mg, 5%).

Method B) With trifluoroacetic acid: A solution of epoxy ketone **2a** (200 mg, 0.39 mmol) in trifluoroacetic acid (4 ml, 52 mmol) was set aside for 12 h at room temperature, diluted with ether, poured into a solution of sodium hydrogencarbonate and worked up in the usual manner. Chromatography on a column of silica gel (25 g) in benzene–ether (5 : 1) afforded nordienone **6** (42 mg, 23%) and dienone **4a** (115 mg, 60%).

Method C) With boron trifluoride etherate: Boron trifluoride etherate (0.2 ml, 1.6 mmol) was added to a solution of epoxy ketone **2a** (100 mg, 0.19 mmol) in benzene (6 ml) and the reaction mixture was set aside at room temperature for 5 h. Methanol (5 ml) was added and the mixture was worked up in the usual manner. Crystallization from chloroform–methanol afforded nordienone **6** (82 mg, 90%).

Method D) With boric acid: Boric acid (210 mg, 3.40 mmol) was added to a solution of epoxy ketone **2a** (210 mg, 0.41 mmol) in a mixture of anhydrous benzene (10 ml) and anhydrous dioxane (10 ml) and the reaction mixture was refluxed under argon for 60 h. The usual work-up and preparative TLC on silica gel in light petroleum–ether (1 : 1) afforded hydroxy ketone **7** (130 mg, 66%) and hydroxy ketone **8** (30 mg, 15%). Performing the reaction under the same conditions but without the inert atmosphere afforded the hydroxy ketone **7** (10%) and the spirolactone **3b** (65%), m.p. 336–340 °C (chloroform–methanol), identical with a sample obtained according to the literature[10] (reported[10] m.p. 342–346 °C).

Method E) With zinc iodide: A solution of epoxy ketone **2a** (100 mg, 0.19 mmol) and zinc iodide (250 mg, 0.78 mmol) in acetic acid (10 ml) was refluxed for 4 h and then the mixture was worked up in the usual manner. Preparative TLC on silica gel in light petroleum–ether

(1 : 1) afforded nordienone **6** (26 mg, 29%), dienone **4b** (11 mg, 11%) and the unsaturated ketone **1b** (24 mg, 23%).

Reaction of 18β,19β-Epoxy-21-oxolupane-3β,28-diyl Diacetate (**2b**)

Method A) With acetic acid under catalysis with sulfuric acid: Acetic acid (15 ml), acetic anhydride (0.5 ml) and sulfuric acid (0.5 ml) were added to a solution of epoxy ketone **2b** (500 mg, 0.90 mmol, ref.[10]) in chloroform (5 ml). The mixture was allowed to stand for 5 days at room temperature and then warmed for 2 h at 40 °C. After cooling and dilution with chloroform, the solution was worked up in the usual manner. Crystallization from chloroform–methanol gave triacetate **5c** (380 mg, 71%).

Method B) With 4-toluenesulfonic acid: A solution of epoxy ketone **2b** (200 mg, 0.36 mmol), 4-toluenesulfonic acid monohydrate (90 mg, 0.47 mmol) and a small amount of acetic anhydride (0.1 ml) in benzene (8 ml) was refluxed for 8 h. After cooling, the reaction mixture was diluted with ether and worked up in the usual manner. Crystallization from ethyl acetate–methanol gave tosylate **5f** (240 mg, 94%).

Method C) With trifluoroacetic acid: A solution of epoxy ketone **2b** (230 mg, 0.41 mmol) in a mixture of benzene (4 ml) and trifluoroacetic acid (4 ml, 52 mmol) was refluxed for 3 h and then about half of the volume was distilled off. The reaction mixture was cooled, diluted with benzene and stirred with solid sodium hydrogencarbonate. After the carbon dioxide evolution ceased, the solution was filtered through a column of alumina (5 g). The benzene eluate (80 mg) was twice extracted with boiling ether; the ether-insoluble portion was trifluoroacetate **5g** (56 mg, 21%). Ether eluted from the column a mixture of products which were combined with the ethereal extract from the trifluoroacetate and separated by preparative TLC on silica gel in light petroleum–ether (2 : 3), affording dienone **4b** (35 mg, 16%), 22-hydroxy derivative **5b** (94 mg, 41%) and a mixture of other compounds (30 mg) which were not identified.

Method D) With zinc iodide: A solution of epoxy ketone **2b** (100 mg, 0.18 mmol) and zinc iodide (350 mg, 1.1 mmol) in acetic acid (10 ml) was refluxed for 20 h and then the reaction mixture was worked up in the usual manner. Preparative TLC on silica gel in light petroleum–ether (1 : 1) afforded the unsaturated ketone **1b** (60 mg, 62%) identical with the sample described in the literature[11]. M.p. 235–238 °C (chloroform–heptane) or 150–152 °C and after resolidification 199–201 °C (chloroform–methanol). (Reported[11] m.p. 198–201 °C with change of modification at 150 °C (chloroform–methanol)). The TLC gave further the triacetate **5c** (29 mg, 27%).

Method E) With boric acid: A solution of epoxy ketone **2b** (100 mg, 0.18 mmol) in a mixture of chloroform (4 ml) and acetic anhydride (4 ml) was refluxed with boric acid (100 mg, 1.6 mmol) for 6 h and the mixture was worked up in the usual manner. Preparative TLC on silica gel in light petroleum–ether (1 : 1) afforded triacetate **5c** (26 mg, 24%) and spirolactone **3b** (58 mg, 61%). Using conditions described for the reaction of the epoxy ketone **2a** under method *D*), no reaction of epoxy ketone **2b** with boric acid was observed.

Method F) With sulfuric acid in dioxane: Sulfuric acid (0.1 ml) was added to a solution of epoxy ketone **2b** (100 mg, 0.18 mmol) in a mixture of dioxane (5 ml) and water (1 ml) and the mixture was refluxed for 4 h. After the usual work-up, the product mixture was subjected to preparative TLC on silica gel in light petroleum–acetone (5 : 2) to give spirolactone **3a** (40 mg, 46%), m.p. 353–358 °C (reported[10] m.p. 356–361 °C) and epoxy ketone **2c** (15 mg, 18%), m.p. 184–186 °C (reported[10] m.p. 182–183 °C). When the reaction was performed in

an argon atmosphere and with dioxane freshly distilled from lithium aluminium hydride, but under otherwise the same conditions, a complex mixture of unidentified products was obtained.

28-Hydroxy-21-oxolupa-12,18-dien-3β-yl Acetate (**4a**)

The compound was obtained in the reactions of epoxy ketone **2a** described under *A*) and *B*). M.p. 238–239 °C (ether–heptane), $[\alpha]_D$ +331. IR: 3 620, 1 723, 1 686, 1 648, 1 605, 1 254. UV (methanol): λ_{max}, nm (log ε): 277 (4.15). MS, *m/z* (%): 496 (M^+, 43), 481 (56), 436 (4), 421 (8), 233 (100), 215 (21), 189 (15), 43 (64). For $C_{32}H_{48}O_4$ (496.7) calculated: 77.37% C, 9.74% H; found: 77.52% C, 9.60% H.

21-Oxolupa-12,18-diene-3β,28-diyl Diacetate (**4b**)

The compound was obtained in the reactions of epoxy ketone **2a**, described under *E*), and of epoxy ketone **2b**, described under *C*), and also by acetylation of dienone **4a**. M.p. 191–192 °C (chloroform–heptane), $[\alpha]_D$ +349. IR: 1 725, 1 689, 1 648, 1 606, 1 253. MS, *m/z* (%): 538 (M^+, 4), 523 (3), 478 (1), 463 (1), 435 (1), 275 (58), 215 (18), 189 (16), 43 (100). For $C_{34}H_{50}O_5$ (538.7) calculated: 75.80% C, 9.36% H; found: 75.62% C, 9.45% H.

22β,28-Dihydroxy-21-oxolup-18-en-3β-yl Acetate (**5a**)

Method A) By hydrolysis of triacetate **5c**: A solution of triacetate **5c** (50 mg, 0.08 mmol) and potassium hydroxide (9.5 mg, 0.17 mmol) in a mixture of benzene (2 ml) and ethanol (1.8 ml) was set aside for 15 min at room temperature and was worked up in the usual manner. Purification by TLC on silica gel in chloroform–ethyl acetate (1 : 1) afforded diol **5a** (33 mg, 77%), m.p. 205–215 °C (decomp.)(ether). IR: 3 536, 1 720, 1 702, 1 589, 1 255. MS, *m/z* (%): 514 (M^+, 2), 496 (0.5), 484 (2), 466 (0.5), 406 (0.2), 264 (63), 251 (48), 189 (11), 43 (100). For $C_{32}H_{50}O_5$ (514.7) calculated: 74.67% C, 9.79% H; found: 74.82% C, 9.55% H.

Method B) By hydrolysis of diacetate **5b**: A solution of potassium hydroxide (3.2 mg, 0.06 mmol) in ethanol (0.5 ml) was added to a solution of diacetate **5b** (30 mg, 0.05 mmol) in benzene (0.5 ml). After standing for 5 min at room temperature, the reaction mixture was worked up as usual and purified as described under *A*) to give diol **5a** (16 mg, 58%).

22β-Hydroxy-21-oxolup-18-ene-3β,28-diyl Diacetate (**5b**)

The compound was obtained in the reaction of epoxy ketone **2b** described under *C*). M.p. 213–214 °C (ether–heptane), $[\alpha]_D$ +12. IR: 3 552, 3 413, 1 728, 1 709, 1 593, 1 255. MS, *m/z* (%): 556 (M^+, 2), 496 (2.5), 453 (0.6), 293 (36), 189 (18), 43 (100). For $C_{34}H_{52}O_6$ (556.8) calculated: 73.34% C, 9.41% H; found: 73.36% C, 9.57% H.

21-Oxolup-18-ene-3β,22β,28-triyl Triacetate (**5c**)

The compound was obtained in the reactions of epoxy ketone **2b** described under *A*), *D*) and *E*), and also by acetylation of compounds **5a** and **5b**. M.p. 291–293 °C, $[\alpha]_D$ +3. IR: 1 737, 1 720, 1 598, 1 254. UV (methanol): λ_{max}, nm (log ε): 244 (4.15). MS, *m/z* (%): 598 (M^+, 3), 538 (1), 495 (2), 335 (62), 293 (26), 189 (25), 43 (100). For $C_{36}H_{54}O_7$ (598.8) calculated: 72.21% C, 9.09% H; found: 72.37% C, 8.87% H.

3β,28-Dihydroxy-21-oxolup-18-en-22β-yl 4-Toluenesulfonate (**5d**)

Sulfuric acid (0.3 ml) was added to a solution of tosylate **5f** (100 mg, 0.14 mmol) in chloroform (1 ml) and methanol (2 ml) and the mixture was refluxed for 2 h. The usual work-up followed by purification by TLC on silica gel in chloroform–ethyl acetate (1 : 1) afforded tosylate **5d** (75 mg, 85%), m.p. 138–141 °C (ether–heptane), $[\alpha]_D$ –44. IR: 3 614, 1 716, 1 598, 1 023, 871. MS, *m/z* (%): 626 (M^+, 2), 456 (9), 454 (7), 424 (100), 405 (27), 190 (35), 189 (28), 91 (42). For $C_{37}H_{54}O_6S$ (626.9) calculated: 70.89% C, 8.68% H; found: 70.56% C, 8.81% H.

The tosylate **5d** was also obtained in the reaction of epoxy ketone **2a** described under *A*).

28-Hydroxy-21-oxolup-18-ene-3β,22β-diyl 3-Acetate 22-(4-Toluenesulfonate) (**5e**)

The compound was obtained in the reaction of epoxy ketone **2a** described under *A*). M.p. 188–190 °C (chloroform–heptane), $[\alpha]_D$ –27. IR: 3 607, 1 716, 1 598, 1 255. MS, *m/z* (%): 668 (M^+, 0.2), 498 (1), 496 (2), 466 (67), 405 (27), 235 (17), 217 (46), 203 (53), 204 (53), 190 (89), 43 (100). For $C_{39}H_{56}O_7S$ (668.9) calculated: 70.02% C, 8.44% H; found: 70.13% C, 8.61% H.

21-Oxolup-18-ene-3β,22β,28-triyl 3,28-Diacetate 22-(4-Toluenesulfonate) (**5f**)

The compound was obtained in the reaction of epoxy ketone **2b** described under *B*), and also by acetylation of compounds **5d** and **5e**. M.p. 128–130 °C (ethyl acetate–methanol), 204–207 °C (chloroform–heptane), $[\alpha]_D$ +8. IR: 1 728, 1 715, 1 256, 1 177, 874. MS, *m/z* (%): 710 (M^+, 10), 650 (10), 607 (3), 538 (5), 496 (2), 484 (12), 465 (10), 447 (100), 433 (10), 405 (14), 277 (53), 189 (32). For $C_{41}H_{58}O_8S$ (710.9) calculated: 69.26% C, 8.22% H; found: 69.35% C, 8.40% H.

21-Oxolup-18-ene-3β,22β,28-triyl 3,28-Diacetate 22-Trifluoroacetate (**5g**)

The compound was obtained by reaction of epoxy ketone **2b** as described under *C*). M.p. 243–248 °C, $[\alpha]_D$ –14. IR: 1 791, 1 720, 1 593, 1 254. MS, *m/z* (%): 652 (M^+, 0.4), 592 (1), 549 (1), 478 (1), 389 (13), 375 (1), 189 (22), 43 (100). The trifluoroacetate **5g** was converted into the 22-hydroxy derivative **5b** on stirring its ethereal solution with an aqueous solution of sodium hydrogencarbonate or on chromatography on silica gel or on standing of its chloroform solution after NMR measurements.

21-Oxo-28-norlupa-16,18-dien-3β-yl Acetate (**6**)

The compound was obtained in the reactions of epoxy ketone **2a** described under *B*), *C*) and *E*). M.p. 280–282 °C (chloroform–methanol), $[\alpha]_D$ +28. IR: 1 720, 1 687, 1 561, 1 254. UV (methanol): λ_{max}, nm (log ε): 218 (3.94), 290 (4.12). MS, *m/z* (%): 466 (M^+, 9), 406 (2), 391 (4), 363 (2), 203 (82), 189 (28), 43 (100). For $C_{31}H_{46}O_3$ (466.7) calculated: 79.78% C, 9.94% H; found: 80.01% C, 10.06% H.

Nordienone **6** was also obtained as the sole product by reaction of hydroxy ketones **7** and **8** with 0.5% solution of 4-toluenesulfonic acid in chloroform for 4 days at room temperature.

TABLE I

Proton NMR data of compounds **1a**, **2a**, **4b**, **5f** and **5g**. Chemical shift values marked with tilde (~) were obtained from 2D spectra

Proton	Chemical shifts/*Coupling constants*				
	1a	**2a**[a]	**4b**[b]	**5f**[c]	**5g**
1α	1.06 td *~13;13;5*	1.03 td *~13;13;5*	~1.14	1.03 td *~13;13;5*	1.05 td *12.5;12.5;4.9*
1β	1.76 dt *13.1;3.7;3.7*	~1.72	1.73 dt *13.2;3.5;3.5*	[d]	[d]
3α	4.49 dd *11.0;5.5*	4.47 dd *11.0;5.5*	4.51 dd *11.0;5.5*	4.48 dd *10.7;5.7*	4.49 dd *10.9;5.6*
5α	0.82 m	0.80 m	[d]	0.82 m	0.83 m
13β	2.78 dd *12.5;3.4*	2.62 dd *~12;4*	–	2.90 dd *12.6;3.1*	2.90 dd *12.6;3.3*
20	3.19 septet *6.9*	2.06 septet *6.9*	2.79 septet *7.0*	3.19 septet *6.9*	3.24 septet *6.9*
22a	1.92 d *18.6*	1.71 d *18.6*	2.02 d *18.4*	4.57 s	5.06 s
22b	2.44 d *18.6*	2.61 d *18.6*	2.42 d *18.4*	–	–
23	0.857 s	0.850 s	0.879 s	0.858 s	0.862 s
24	0.849 s	0.843 s	0.884 s	0.847 s	0.852 s
25	0.926 s	0.899 s	1.024 s[e]	0.917 s	0.927 s
26	1.134 s	1.108 s	1.069 s[e]	1.122 s	1.131 s
27	0.947 s	1.078 s	1.012 s[e]	0.946 s	0.990 s
28a	3.67 d *10.7*	3.73 d *10.7*	3.91 d *11.0*	4.00 d *11.3*	4.08 d *11.5*
28b	3.72 d *10.7*	4.03 d *10.7*	4.10 d *11.0*	4.62 d *11.3*	4.39 d *11.5*
29	1.214 d *6.9*	1.287 d *6.9*	1.200 d *7.0*	1.140 d *6.9*	1.192 d *7.0*
30	1.194 d *6.9*	1.210 d *6.9*	1.159 d *7.0*	1.128 d *6.9*	1.192 d *7.0*
3β-OAc	2.052 s	2.046 s	2.056 s	2.055 s	2.061 s
28-OAc	–	–	2.006 s	1.869 s	1.930 s

[a] H-2α, H-2β: 1.62–1.70; H-6a: ~1.38; H-6b: ~1.54. [b] H-2α, H-2β: 1.60–1.70; H-11α, H-11β: ~2.05; H-12: 5.57 bt, J = 3.9, 3.9; H-15a: ~1.22; H-16α: ~1.54; H-16β: ~2.00. [c] OTos: 2.45 s (CH_3); 7.36 d, J = 8.2 (H-3′, H-5′); 7.90 d, J = 8.2 (H-2′, H-6′). [d] Signal was not identified. [e] Signals may be mutually interchanged.

TABLE II

Proton NMR data of compounds **5a**–**5e**. Chemical shift values marked with tilde (~) were obtained from 2D spectra

Proton	Chemical shifts/*Coupling constants*				
	5a	**5b**[a]	**5c**	**5d**[b]	**5e**[b]
1α	1.05 td *~12.5;12.5;5.4*	~1.04	1.05 td *~13;13;5*	~0.96	1.04 td *12.8;12.8;5.0*
1β	1.75 dt *~13.0;3.5;3.5*	~1.77	~1.75	~1.74	~1.73
2α,2β	1.60–1.68	1.60–1.68	1.62–1.70	1.58–1.68	1.60–1.66
3α	4.49 dd *10.7;5.8*	4.49 dd *10.7;5.7*	4.49 dd *11.0;5.5*	3.21 dd *11.3;5.2*	4.48 dd *10.8;5.6*
5α	0.82 m	0.82 m	0.82 m	~0.70	0.81 m
6a	~1.42	[c]	~1.36	~1.34	~1.36
6b	~1.52	[c]	~1.54	~1.54	~1.54
7a	~1.36	[c]	~1.38	~1.35	~1.36
7b	~1.50	[c]	~1.50	~1.49	~1.50
9α	~1.35	~1.30	~1.34	~1.28	~1.31
11a	~1.28	[c]	~1.32	~1.28	~1.30
11b	~1.62	~1.58	~1.62	~1.54	~1.62
12α	~1.84	~1.80	~1.84	~1.83	~1.84
12β	2.03 m	1.99 m	2.03 m	2.05 m	2.05 m
13β	2.78 dd *12.8;3.1*	2.92 bdd *12.8;3.5*	2.87 dd *12.7;3.5*	2.85 dd *12.8;3.4*	2.85 dd *12.6;3.0*
15α	~1.27	~1.28	~1.28	~1.26	~1.26
15β	~1.85	~1.77	~1.76	~1.76	~1.76
16α	~1.50	~1.66	~1.77	~1.57	~1.58
16β	2.21 dt *13.7;3.8;3.8*	~1.92	~1.86	1.98 dt *13.7;3.8;3.8*	1.99 dt *13.6;3.8;3.8*
20	3.22 septet *6.9*	3.20 septet *6.9*	3.22 septet *6.9*	3.22 septet *7.0*	3.22 septet *7.0*
22α	3.69 s	3.70 bd *4.8*	4.98 s	4.52 s	4.52 s
23	0.859 s	0.861 s	0.859 s	0.971 s	0.857 s
24	0.849 s	0.850 s	0.848 s	0.765 s	0.847 s
25	0.918 s	0.925 s	0.922 s	0.882 s	0.915 s
26	1.108 s	1.135 s	1.120 s	1.090 s	1.098 s
27	0.957 s	0.953 s	0.974 s	0.955 s	0.955 s
28a	3.62 d *11.0*	3.97 d *10.7*	4.02 d *11.3*	3.81 d *12.0*	3.81 d *11.8*
28b	3.82 d *11.0*	4.68 d *10.7*	4.35 d *11.3*	3.83 d *12.0*	3.83 d *11.8*
29	1.208 d *6.9*	1.185 d *6.9*	1.198 d *6.8*	1.172 d *6.8*	1.175 d *7.0*
30	1.178 d *6.9*	1.181 d *6.9*	1.189 d *6.8*	1.118 d *6.8*	1.131 d *7.0*
3β-OAc	2.057 s	2.056 s	2.056 s	–	2.051 s
22β-OAc	–	–	2.169 s	–	–
28-OAc	–	1.884 s	1.933 s	–	–

[a] OH: 2.66 d, J = 4.8. [b] OTos: 2.45 s (CH_3); 7.36 d, J = 8.2 (H-3′, H-5′); 7.91 d, J = 8.2 (H-2′, H-6′). [c] Signal was not identified.

TABLE III

Proton NMR data of compounds **6**–**10**. Chemical shift values marked with tilde (~) were obtained from 2D spectra

Proton	Chemical shifts/*Coupling constants*				
	6[a]	**7**[b]	**8**	**9**	**10**[c]
1α	1.07 td *~13;13;5*	1.03 td *~13;13;6*	[d]	1.05 td *~12;12;4.6*	1.07 td *~13.5;13.5;5.5*
1β	1.74 dt *13.2;3.6;3.6*	1.74 dt *13.1;3.6;3.6*	[d]	[d]	~1.75
3α	4.50 dd *11.2;5.2*	4.50 dd *10.6;5.8*	4.49 dd *10.6;5.7*	4.49 dd *11.2;5.3*	4.50 dd *11.0;5.5*
5α	0.84 m	0.84 m	[d]	0.83 m	0.82 m
13β	2.92 dd *12.4;4.2*	2.59 bm	3.18 dd *12.5;3.7*	2.78 dd *12.8;3.1*	3.13 dd *12.4;3.6*
15α	1.85 dd *17.8;6.4*	~1.46	[d]	0.94 dt 14.0;8.2;8.2	[d]
15β	2.41 bd *17.8*	~1.62	[d]	2.01 dt *14.0;5.3;5.3*	[d]
16α	5.69 m *6.2;2.6;1.2;1.2*	2.20 bm	[d]	2.46 bdd *8.2;5.3*	[d]
16β	–	1.99 bdd *~18.2;6.0*	[d]	2.46 bdd *8.2;5.3*	[d]
20	3.18 septet *7.0*	2.22 septet *~7.0*	3.13 septet *6.9*	3.22 septet *6.8*	3.37 septet *7.0*
22a	2.78 bs	2.54 dd *~21;3.7*	2.37 d *18.7*	5.90 t *~1.2;1.2*	–
22b	2.78 bs	2.89 bdd *~21;4*	2.40 d *18.7*	–	–
23	0.870 s	0.863 s	0.860 s	0.863 s	0.864 s
24	0.860 s	0.852 s	0.851 s	0.863 s	0.857 s
25	0.919 d[e]	0.887 s	0.911 s[f]	0.863 s	0.972 s[f]
26	1.075 s	1.032 s[f]	1.163 s	1.076 s	1.182 s
27	0.948 s	1.004 s[f]	0.932 s[f]	0.896 s	0.946 s[f]
29	1.248 d *7.0*	0.982 d *6.7*	1.206 d *6.9*	1.243 d *6.8*	1.267 d[f] *7.0*
30	1.206 d *7.0*	0.883 d *7.2*	1.187 d *6.9*	1.227 d *6.8*	1.244 d *7.0*
3β-OAc	2.050 s	2.055 s	2.056 s	2.057 s	2.059 s

[a] H-2α, H-2β: 1.60–1.70; H-6a: ~1.42; H-6b: ~1.56; H-12α: ~1.65; H-12β: 2.46 m. [b] H-2α, H-2β: 1.60–1.70; H-6a: ~1.42; H-6b: ~1.55; H-7a: ~1.40; H-7b: ~1.51; H-9: ~1.43; H-11a: ~1.31; H-11b: ~1.54; H-12α: ~1.32; H-12β: 2.11bm; OH: 2.67 bs. [c] H-2α, H-2β: 1.62–1.67; H-6a: ~1.38; H-6b: ~1.55; H-28a: 4.03 d, J = 11.0; H-28b: 4.85 d, J = 11.0; 28-OAc: 1.915 s. [d] Signal was not identified. [e] J = 0.8. [f] Signals may be mutually interchanged.

TABLE IV
^{13}C chemical shifts of compounds **1a**, **2a**, **4b**, **6, 7**, **9** and **10**

Carbon	**1a**	**2a**	**4b**	**6**	**7**	**9**	**10**
1	38.53	38.50	38.65	38.37	38.52	38.36	38.59
2	23.59	23.55	23.57	23.59	23.65	23.60	23.59
3	80.72	80.70	80.64	80.74	80.82	80.64	80.63
4	37.76	37.76	37.73	37.76	37.81	37.77	37.78
5	55.37	55.45	55.43	55.28	55.65	55.56	55.40
6	18.09	18.05	18.11	18.02	18.12	17.91	18.09
7	34.78	34.10	34.17	34.25	33.91	33.98	34.62
8	41.39	41.19	38.96	40.45	40.44[a]	41.64[a]	41.62
9	50.93	51.24	47.24	49.71	51.00	51.06	50.92
10	37.10	37.14	36.87	36.96	37.14	37.02	37.16
11	21.23	21.25	23.39	20.59	21.20	21.60	21.16
12	27.79[a]	29.71	127.72	25.85	25.03	27.37	27.92[a]
13	42.43	37.79	136.11	40.83	38.67	38.36	43.57
14	45.67	42.23	44.95[a]	43.17	40.63[a]	41.80[a]	45.69
15	27.35[a]	23.58[a]	26.28	32.75	27.99	30.40	27.23[a]
16	32.24	26.47[a]	30.81	121.66	24.60	29.85	26.49[a]
17	47.27	43.33	45.18[a]	134.20	134.04	115.68	49.58
18	172.98	79.39[b]	169.57	164.23	139.89	161.54	170.17
19	146.95	72.16[b]	145.58	147.03	85.84	165.20	152.36
20	25.21	26.34	25.32	26.25	35.12	29.75	25.87
21	208.49	210.49	206.98	206.42	216.96	163.05	189.41[b]
22	47.38	43.54	47.24	38.91	45.09	108.44	200.90[b]
23	27.90	27.92	28.09	27.91	27.87	27.84	27.92
24	16.51	16.48	16.12[b]	16.52	16.46	16.48[b]	16.53
25	16.86	16.76[c]	16.80[b]	16.38[a]	16.58	16.45[b]	16.87[c]
26	16.76	16.68[c]	20.89[c]	17.10[a]	14.34	19.91	16.93[c]
27	15.90	16.35[c]	17.68[c]	15.79[a]	15.68	15.74	16.03
28	65.85	64.27	66.56	–	–	–	64.17
29	20.64	18.32	22.93[c]	20.81	15.31	20.83	20.30
30	20.17	17.45	20.07[c]	20.07	17.97	20.83	19.65
3β-OAc	21.32	21.30	21.30	21.28	21.32	21.29	21.31
	171.05	171.01	170.97	171.02	171.03	170.99	171.04
28-OAc	–	–	20.73	–	–	–	20.37
	–	–	170.82	–	–	–	171.00

[a, b, c] Signals with identical symbols may be interchanged.

TABLE V
^{13}C chemical shifts of 22β-substituted derivatives **5a**–**5g**

Carbon	**5a**	**5b**	**5c**	**5d**[a]	**5e**[a]	**5f**[b]	**5g**[c]
1	38.55	38.60	38.56	38.87	38.56	38.50	38.55
2	23.59	23.62	23.60	27.26	23.58	23.54	23.57
3	80.73	80.72	80.69	78.83	80.69	80.62	80.69
4	37.76	37.79	37.77	38.82	37.76	37.71	37.76
5	55.42	55.48	55.43	55.34	55.43	55.38	55.42
6	18.06	18.08	18.04	18.14	18.04	17.97	18.02
7	34.47	34.51	34.53	34.60	34.52	34.56	34.48
8	41.27	41.25	41.26	41.27	41.29	41.20	41.29
9	50.94	51.01	50.92	50.98	50.90	50.86	50.87
10	37.08	37.13	37.10	37.15	37.08	37.03	37.09
11	21.15	21.24	21.20	21.08	21.11	21.11	21.14
12	27.75	27.66	27.79	27.86	27.79	27.70	27.67
13	43.13	43.03	42.99	43.21	43.16	43.12	43.10
14	45.03	44.56	44.78	44.90	44.89	44.57	44.81
15	27.35	27.84	27.66	27.53	27.51	27.56	27.50
16	29.96	30.51	30.72	30.04	30.01	29.97	30.60
17	51.09	49.79	48.66	50.54	50.53	48.65	48.46
18	170.48	166.37	166.76	169.19	169.03	166.80	167.42
19	144.22	144.38	145.38	145.36	145.38	145.01	145.45
20	25.36	25.47	25.53	25.50	25.49	25.40	25.53
21	208.24	207.20	201.43	199.26	199.21	198.39	198.35
22	82.15	81.69	80.08	85.93	85.94	85.06	82.53
23	27.87	27.90	27.89	27.91	27.87	27.84	27.87
24	16.50[d]	16.52	16.52[d]	15.37	16.49	16.46	16.50
25	16.86	16.87	16.87	16.78[d]	16.84	16.81	16.85
26	16.66	16.80	16.78	16.72[d]	16.70[d]	16.75[d]	16.75[d]
27	16.52[d]	16.70	16.56[d]	16.68[d]	16.62[d]	16.62[d]	16.61[d]
28	64.62	63.47	62.88	63.07	63.00	62.47	62.66
29	21.39	21.56	21.24	21.04	21.05	21.05	21.16
30	19.70	19.48	19.43	19.61	19.61	19.33	19.37
3β-OAc	21.30	21.31	21.31	–	21.27	21.27	21.30
	171.07	171.01	171.02	–	171.01	170.97	171.11
22β-OAc	–	–	20.74	–	–	–	–
	–	–	170.75	–	–	–	–
28-OAc	–	20.57	20.63	–	–	20.53	20.33
	–	170.25	170.48	–	–	170.34	170.29

[a] OTos: 21.71 (CH_3), 133.10 (C-1′), 128.13 (C-2′, C-6′), 129.84 (C-3′, C-5′), 145.15 (C-4′). [b] OTos: 21.67 (CH_3), 133.31 (C-1′), 128.01 (C-2′, C-6′), 129.70 (C-3′, C-5′), 144.87 (C-4′). [c] $OCOCF_3$: 157.24 J(C,F) = 46 (CO), signal CF_3 was not found. [d] Signals may be mutually interchanged.

19β-Hydroxy-21-oxo-28-norlup-17-en-3β-yl Acetate (**7**)

The compound was obtained in the reaction of epoxy ketone **2a** described under *D*). M.p. 217–220 °C (decomp.) (chloroform–heptane), $[\alpha]_D$ +31. IR: 3 562, 1 745, 1 718, 1 651, 1 255. MS, *m/z* (%): 484 (M^+, 5), 466 (8), 456 (4), 441 (95), 203 (38), 43 (100). For $C_{31}H_{48}O_4$ (484.7) calculated: 76.81% C, 9.98% H; found: 76.53% C, 10.11% H.

17ξ-Hydroxy-21-oxo-28-norlup-18-en-3β-yl Acetate (**8**)

The compound was obtained in the reaction of epoxy ketone **2a** described under *D*). M.p. 218–220 °C (decomp.) (methanol). IR: 3 599, 1 720, 1 697, 1 610, 1 254. MS, *m/z* (%): 484 (M^+,14), 466 (12), 424 (9), 406 (9), 391 (8), 221 (18), 203 (20), 189 (35), 43 (100).

3β-Acetoxy-19,21-seco-28-norlupa-17(22),18-dien-21,19-olide (**9**)

Hydroxy ketone **7** (90 mg, 0.19 mmol) and lead tetraacetate (270 mg, 0.61 mmol) were dissolved in a mixture of anhydrous benzene (3 ml), acetic acid (3 ml) and acetic anhydride (0.5 ml) and the solution was refluxed for 7 h. After the usual work-up, the product was subjected to preparative TLC in light petroleum–ether (2 : 3) which afforded the starting hydroxy ketone **7** (25 mg, 28%) and dienolide **9** (60 mg, 67%), m.p. 232–235 °C (chloroform–heptane), $[\alpha]_D$ –26. UV (cyclohexane):λ_{max}, nm (log ε): 303 (3.75). IR: 1 732 sh, 1 705, 1 632, 1 556, 1 522, 1 248. MS, *m/z* (%): 482 (M^+, 11), 454 (3), 439 (2), 407 (2), 379 (1), 219 (21), 203 (32), 191 (50), 43 (100). For $C_{31}H_{46}O_4$ (482.7) calculated: 77.13% C, 9.61% H; found: 76.96% C, 9.80% H.

21,22-Dioxolup-18-ene-3β,28-diyl Diacetate (**10**)

A solution of hydroxy ketone **5b** (60 mg, 0.11 mmol) in chloroform (2 ml) was adsorbed on alumina (1 g) with chromium trioxide (40 mg, 0.40 mmol). After standing for 24 h at room temperature, the product was eluted with a chloroform–methanol mixture. The solvents were evaporated, the residue was dissolved in chloroform and the solution was filtered through a layer of silica gel to give diketone **10** (49 mg, 82%), m.p. 269–271 °C (chloroform–methanol), $[\alpha]_D$ –135. IR: 1 761, 1 731, 1 710, 1 575, 1 258. UV (cyclohexane): λ_{max}, nm (log ε): 199 (4.0), 288 (3.71). MS, *m/z* (%): 554 (M^+, 5), 484 (28), 424 (3), 409 (2), 381 (3), 220 (6), 203 (7), 190 (18), 189 (14), 43 (100). For $C_{34}H_{50}O_6$ (554.7) calculated: 73.61% C, 9.09% H; found: 73.39% C, 9.05% H.

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