Lichens and Fungi. Part 17.[1] The Synthesis and Absolute Configuration at C-20 of the (*R*)- and (*S*)-Epimers of Some 29-Substituted Lupane Derivatives and of some 30-Norlupan-20-ol Derivatives and the Crystal Structure of (20*R*)-3β-Acetoxylupan-29-ol.

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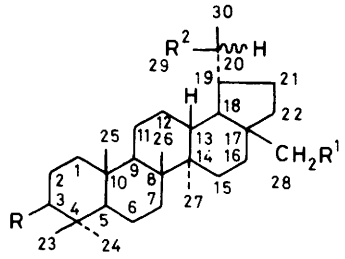
The absolute configurations at C-20 of the (*R*)- and (*S*)-aldehydes (**10a**), (**10b**), alcohols (**11a**), (**11b**), (**13a**), and (**13b**) and acids (**12a**), (**12b**), (**14a**), and (**14b**) derived from 3β-acetoxylup-20(29)-ene (**8**), *via* the epoxide (**7**), have been established by a combination of physical, spectral and *X*-ray crystallographic procedures, as have the configurations at C-20 of the (*R*)- and (*S*)-3β-acetoxy- and 3β-hydroxy-30-norlupan-20-ols (**20a**), (**20b**) and (**21a**), (**21b**). Anomalies in the literature are identified and rationalized.

Vystrcil *et al.*[2] have determined the absolute configurations at C-20 of the 29-substituted lupane derivatives (**1a**), (**1b**); (**2a**), (**2b**); (**3a**), (**3b**) and of derivatives of 30-norlupan-20-ol [*e.g.* (**4a**), (**4b**); (**5a**), (**5b**), and (**6a**), (**6b**)].[3] Absolute configurations at C-20 for the derivatives of 30-norlupane were determined by molecular rotational differences on the basis of the benzoate rule[3] and for the 29-substituted lupanes through the correlation of the aldehydes (**1a**) and (**1b**) with the corresponding 30-norlupan-20-ols (**5a**) and (**5b**) by Baeyer-Villiger oxidation.[2] Vystrcil's configurational correlations have been extended to additional derivatives of lupane unsubstituted at C-28 in order to obtain authentic specimens for comparison with a series of C-29 substituted and 30-norlupane derivatives isolated from the lichen *Pseudocyphellaria rubella*.

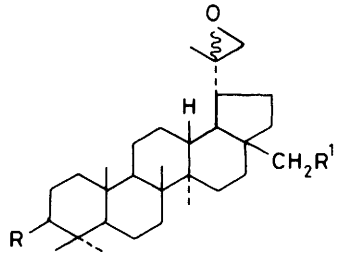
The 3β-acetoxy-20,29-epoxylupane (**7**) required for the proposed synthetic sequence (Scheme) was prepared from lupenyl acetate (**8**) by the method of Hui *et al.*[4] who did not comment on the possibility of (20*R*)- and (20*S*)-epimers. Vystrcil *et al.*[5] in a similar epoxidation reported, without evidence, a (20*RS*)-mixture of epoxides (**9a**) and (**9b**). That our product was a single epimer was apparent from the ^{1}H n.m.r. spectrum in which both 17β-methyl and 20-methyl groups appeared as single resonances, each integrating for three protons, and from the ^{13}C n.m.r. spectrum which contained 32 carbon resonances. The configuration at C-20 for the epoxide (**7**) could not be established. While the chemical shift of the 17β-methyl group (Table 1) would indicate the (20*R*)-configuration, the strong positive rotation ($[\alpha]_D^{20}$ + 21.0°) would point to the (20*S*)-configuration (Table 2).

3β-Acetoxy-20,29-epoxylupane (**7**) was rearranged with BF_3–Et_2O to (20*RS*)-3β-acetoxylupan-29-al (**10a**), (**10b**) in quantitative yield (δ 9.60, s, 9.85, d, *J* 2.0 Hz, CHO) (3:2). Reduction of the epimeric mixture of aldehydes (**10a**) and (**10b**) with sodium borohydride gave the epimeric alcohols (**11a**) and (**11b**) which were separated by multiple (× 4) p.l.c. on silica gel with ether–benzene (7:93). The faster moving epimer was identified as (20*S*)-3β-acetoxylupan-29-ol (**11b**) by the identity of the signal produced by the C-29 protons (δ 3.40, d, *J* 6.9 Hz) and that produced by the C-20 methyl group (δ 0.81, d, *J* 6.5 Hz) with the corresponding signals reported for the (20*S*)-epimer (**2b**).[2] The slower moving (20*R*)-epimer was identified by a similar comparison of characteristic ^{1}H n.m.r. signals.[2] It is noteworthy that the elution order of the epimers (**11a**) and (**11b**) was the reverse of that reported for the epimers (**2a**) and (**2b**).[2] This is probably a solvent effect and may be due to the very much greater solubility of the (20*S*)-epimer (**11b**) in ether compared

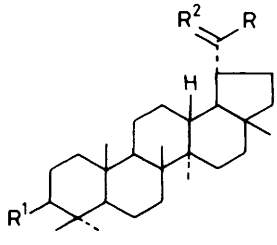


(**a**) 20*R* (**b**) 20*S*

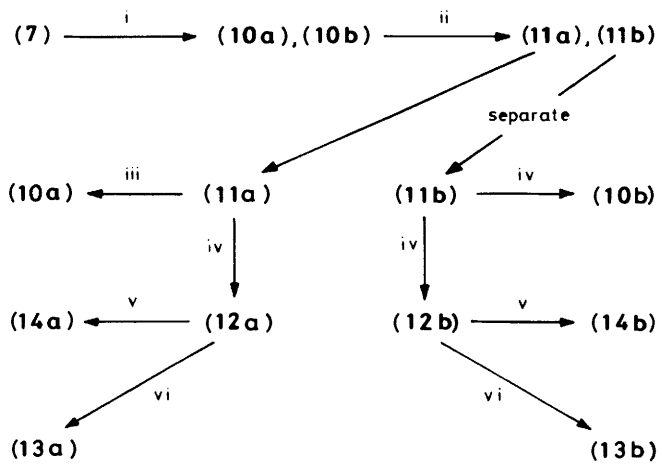
	R	R^1	R^2
(**1**)	OAc	OAc	CHO
(**2**)	OAc	OAc	CH_2OH
(**3**)	OAc	OAc	CO_2H
(**4**)	H	H	OH
(**5**)	OAc	OAc	OH
(**6**)	OAc	OAc	OAc
(**10**)	OAc	H	CHO
(**11**)	OAc	H	CH_2OH
(**12**)	OAc	H	CO_2H
(**13**)	OH	H	CH_2OH
(**14**)	OH	H	CO_2H
(**18**)	OAc	H	$CH(OMe)_2$
(**20**)	OAc	H	OH
(**21**)	OH	H	OH
(**24**)	OH	H	Me



	R	R^1
(**7**)	OAc	H
(**9**)	OAc	OAc
(**17**)	OH	H



	R	R^1	R^2
(**8**)	Me	OAc	CH_2
(**15**)	CH_2OH	OH	CH_2
(**16**)	CHO	OAc	CH_2
(**19**)	CH_2OH	OAc	CH_2
(**22**)	Me	OAc	O
(**23**)	Me	OH	O



Scheme. *Reagents:* i, BF_3–Et_2O; ii, $NaBH_4$; iii, CrO_3–pyridine; iv, Jones Reagent; v, KOH–ethanol; vi, LAH.

with the (20*R*)-epimer (**11a**). With the (20*R*)- and (20*S*)-3β-acetoxylupan-29-ols (**11a**) and (**11b**) characterized it was a comparatively straightforward matter to convert them unequivocally into the pure (20*R*)- and (20*S*)-epimers listed in Scheme. Oxidation of each alcohol epimer with Vystrcil's[2] modified Collin's reagent gave the corresponding aldehyde epimer. (20*R*)-3β-Acetoxylupan-29-al (**10a**) had m.p. 198—201 °C [δ 9.85, d, *J* 2.0 Hz (CHO)] and (20*S*)-3β-acetoxylupan-29-al (**10b**) had m.p. 194—197 °C (δ 9.60, s, CHO).

3β-Acetoxylupan-29-al (**10**) of unspecified stereochemistry has been reported by Hui *et al.*[4-6] and by Ruzicka *et al.*[7] Hui *et al.* isolated the aldehyde from the stems of *Lithocarpus polystachya*,[4] m.p. 227—119 °C; (δ 9.60, s, CHO), and synthesized it by the rearrangement of the epoxide (**7**) with $CHCl_3$–CH_3OH–conc. HCl (m.p. 225—228 °C)[4]; by isomerization of lup-20(29)-ene-3β,30-diol (**15**) with CH_3CO_2H–conc. HCl (m.p. 227—228 °C)[6] and by the hydrogenation of 3β-acetoxylup-20(29)-en-30-al (**16**) (m.p. 228—230 °C).[6] Ruzicka *et al.*[7] reported m.p. 223—226 °C for the aldehyde prepared by the rearrangement of lupeol epoxide (**17**) and acetylation of the product. In our hands when 3β-acetoxy-20,29-epoxylupane (**7**) was treated with $CHCl_3$–CH_3OH–conc. HCl the product was (20*RS*)-3β-acetoxylupan-29-al dimethyl acetal (**18**). Hydrolysis of the acetal (**18**) in dioxane 25% 2M-H_2SO_4 for 24 h gave (20*RS*)-3β-acetoxylupan-29-al (**10a**) and (**10b**), m.p. 175—180 °C; [δ 9.60, s; 9.85, d, *J* 2.0 Hz, CHO) (*ca.* 3:2)]. There was no apparent hydrolysis of the acetal after 1 h with dioxane–10% 2M-H_2SO_4. An almost identical mixture of epimeric aldehydes (**10**) (m.p. 175—180 °C) was obtained from the isomerization of the unsaturated alcohol (**19**) with $CHCl_3$–CH_3CO_2H–conc. HCl. It would appear from the specific rotations reported by Ruzicka *et al.*[7] (+14.4°) and by Hui *et al.*[4-6] (+10.8°) that they in fact had a (20*RS*)- mixture of aldehydes (see Table 2). It is suggested that the higher m.p. reported by earlier workers[4,6,7] may be due to the presence of the (20*RS*)-3β-acetoxylupan-29-oic acids (**12a**), (**12b**) [(20*R*)-epimer, m.p. 273—276 °C; (20*S*)-epimer, m.p. 287—290 °C)]. The (20*R*)- and (20*S*)-aldehydes (**10a**), (**10b**) are oxidized extremely rapidly by air when moist with solvent to give the corresponding acids. It was necessary to exercise great care when crystallizing the aldehydes to avoid the formation of appreciable quantities of acid. Invariably a second crop of crystals contained 20—50% of acid (t.l.c., i.r.). A specimen of (20*S*)-3β-acetoxylupan-29-al (**10b**) containing *ca.* 40% of the corresponding acid had m.p. 226—236 °C. It is noteworthy that Ruzicka *et al.*[8] reported m.p. 248—253 °C for (**1**), some 40 °C higher than that reported by Vystrcil *et al.*[5] for a (20*RS*)-mixture of epimers (**1a**), (**1b**) and for the individual epimers.[2]

Vystrcil *et al.*[2] reported that the (20*RS*) mixture of aldehydes (**1a**) and (**1b**) could not be separated on silica gel or alumina because of oxidation and isomerization. We found that a complete separation of the epimers (**10a**) and (**10b**) could not be achieved by p.l.c. with ether–hexane but the faster moving less polar (20*R*)-epimer (**10a**) was concentrated in the front half of the band and the more polar, (20*S*)-epimer in the rear half. Significant oxidation or isomerization did not occur. A mixture of the epimers (**10a**) and (**10b**) was recovered unchanged after equilibration for 24 h with CF_3CO_2H–$CHCl_3$ and no apparent conversion to the more stable epimer was achieved by chromatography on alumina (Merck neutral grade 2—3).

(20*R*)-3β-Acetoxy-30-norlupan-20-ol (**20a**) has been reported.[3] We have now prepared the (20*S*)-epimer (**20b**). The configuration of the noracetoxyalcohols (**20a**) and (**20b**) was confirmed by a comparison of the ^{13}C n.m.r. spectra of the derived nordiols (**21a**) and (**21b**) with those reported by Wenkert *et al.*[9] for the (20*RS*)-noralcohols (**4a**) and (**4b**). Because of the proximity of the C-12 protons, the side chains of the noralcohols were considered[9] to be locked into conformations in which the C-20 methyl and hydroxy groups occupied positions equatorially and axially inclined with respect to the pentacyclic ring system (Figure 1). Thus the C-20 epimers were distinguished by the occurrence[9] of the C-29 signals of the noralcohols at δ 23.0 in the (20*R*)-epimer, and at δ 17.0 in the (20*S*)-epimer. The C-29 signals of the (20*RS*)-nordiols (**21a**) and (**21b**) occurred at δ 23.1 and δ 17.2 respectively (Table 3).

Table 1. ^1H N.m.r. Chemical shifts (δ) of methyl groups

	4β	4α	8β	10β	14α	17β		20*	
						20*R* a	20*S* b	20*R* a	20*S* b
(7)	0.85	0.85	1.03	0.87	0.93	0.74		1.24	
(**10a**)	0.84	0.84	1.04	0.86	0.91	0.75		1.075 d	
(**10b**)	0.84	0.84	1.04	0.87	0.93		0.79		1.024 d
(**11a**)	0.85	0.85	1.04	0.87	0.93	0.73		0.95 d	
(**11b**)	0.85	0.85	1.05	0.86	0.93		0.77		0.81 d
(**12a**)	0.85	0.85	1.04	0.87	0.92	0.75		1.145 d	
(**12b**)	0.85	0.85	1.04	0.87	0.92		0.78		1.05 d
(**13a**)	0.77	0.97	1.04	0.84	0.93	0.73		0.96 d	
(**13b**)	0.78	0.98	1.04	0.86	0.93		0.78		0.82 d
(**14a**)	0.77	0.97	1.03	0.84	0.92	0.74		1.147 d	
(**14b**)	0.77	0.97	1.04	0.84	0.93		0.77		1.05 d
(**20a**)	0.84	0.84	1.04	0.86	0.92	0.75		1.12 d	
(**20b**)	0.84	0.84	1.03	0.86	0.95		0.77		1.07 d
(**21a**)	0.78	0.98	1.06	0.85	0.96	0.78		1.13 d	
(**21b**)	0.78	0.98	1.05	0.86	0.91		0.78		1.08 d
(**18**)	0.85	0.85	1.03	0.87	0.93	0.73	0.76		

* All C-20 methyl doublets had *J ca.* 6.5 Hz.

Table 2. Specific rotations $[\alpha]_D^{20}$ of C-20 epimers

Compound	20*R* (a)	20*S* (b)	Δ(*R* → *S*)
3β-Acetoxylupan-29-al (**10**)	−24.12°	+22.00°	+46.12°
3β-Acetoxylupan-29-ol (**11**)	−6.00°	+2.58°	+8.58°
3β-Acetoxylupan-29-oic acid (**12**)	−39.90°	+22.66°	+62.56°
Lupane-3β,29-diol (**13**)	−14.09°	−5.79°	+8.30°
3β-Hydroxylupan-29-oic acid (**14**)	−52.64°	+8.71°	+61.35°
3β-Acetoxy-30-norlupan-20-ol (**20**)	+4.29°	+0.46°	−3.83°
30-Norlupane-3β-20-diol (**21**)	−6.90°	−11.28°	−4.38°

Table 3. ^{13}C N.m.r. chemical shifts (δ) of lupane derivatives

	(24)*	(21a)	(21b)	(7)	(11a)	(11b)	(10a)	(10b)	(12a)	(12b)
C-1	38.7	38.7	38.8	38.5	38.4	38.5	38.4	38.4	38.4	38.5
C-2	27.4	27.5[a]	27.5[a]	23.8	23.7	23.8	23.7	23.7	23.7	23.8
C-3	78.8	79.0	79.0	81.0	81.0	81.1	80.9	81.0	81.0	81.0
C-4	38.8	38.9	38.9	37.9	37.9	37.9	37.9	37.9	37.9	37.9
C-5	55.2	55.3	55.4	55.5	55.4	55.4	55.4	55.4	55.3	55.4
C-6	18.3	18.4	18.4	18.2	18.3	18.2	18.2	18.2	18.2	18.2
C-7	34.4	34.4	34.4	34.3	34.3	34.4	34.3	34.3	34.3	34.4
C-8	40.8	40.9	41.0	40.9	41.0	41.0	40.9	40.9	40.9	40.9
C-9	50.1	50.1	50.2	50.3	50.0	50.1	49.9	50.0	49.9	50.0
C-10	37.1	37.2	37.3	37.2	37.1	37.1	37.1	37.1	37.1	37.1
C-11	20.9	20.9	21.0	21.1	21.0	20.9	20.9	20.8	20.9	20.9
C-12	26.8	27.2[a]	27.4[a]	26.9[a]	27.2[a]	27.0	27.6[a]	26.6[a]	27.0[a]	26.4[a]
C-13	37.8	37.7	37.5	37.3	38.1	37.9	37.9	37.9	37.9	37.9
C-14	43.0	43.0	43.0	43.0	43.1	43.1	43.1	43.1	43.1	43.1
C-15	27.4	27.3[a]	27.3[a]	27.2	27.3[a]	27.4	27.3	27.3	27.4	27.4
C-16	35.5	35.3	35.4	35.5	35.5	35.5	35.3	35.4	35.4	35.5
C-17	43.1	43.3	43.4	43.5	43.1	42.9	43.0	42.9	43.1	43.1
C-18	47.5	46.0	48.9	46.5[b]	47.5	47.3	49.0	47.3	48.7	47.3
C-19	44.6	47.0	45.9	49.5[b]	43.7	39.3	42.8	37.5	43.5	40.2
C-20	29.3	68.8	69.8	60.3	38.0	38.0	49.0	49.7	41.9	41.0
C-21	21.9	21.4	22.0	26.0[a]	23.1	22.0	25.2[a]	23.7[a]	23.8[a]	23.8[a]
C-22	40.4	40.2	40.4	39.8	40.2	40.6	40.0	40.5	39.7	40.5
C-23	28.0	28.1	28.1	28.0	28.0	28.0	28.0	28.0	28.0	28.0
C-24	15.4	15.4	15.4	16.5	16.5	16.6	16.6	16.6	16.6	16.6
C-25	16.0	16.0[b]	16.0[b]	16.0[c]	16.0[b]	16.0[b]	16.1[b]	16.1[b]	16.2[b]	16.2[b]
C-26	16.0	16.1[b]	16.1[b]	16.2[c]	16.1[b]	16.1[b]	16.0[b]	16.0[b]	16.0[b]	16.0[b]
C-27	14.4	14.5	14.4	14.4	14.5	14.4	14.4	14.4	14.4	14.4
C-28	18.0	18.2	18.0	18.0	18.1	18.1	18.0	17.7	17.8	18.0
C-29	15.1	23.1	17.2	57.5	64.5	68.5	207.0	205.0	[d]	[d]
C-30	23.0	—	—	18.2	17.7	10.3	14.5	7.4	17.2	9.6
$OCOCH_3$				21.3	21.3	21.3	21.3	21.3	21.3	21.3
$OCOCH_3$				171.0	171.0	171.0	171.0	171.0	171.0	171.0

* Wenkert *et al.*[9] [a–c] Signals within a column may be interchanged. [d] Not recorded.

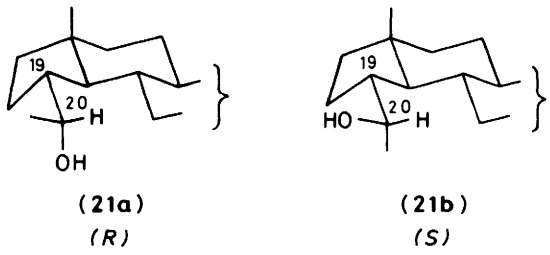


Figure 1.

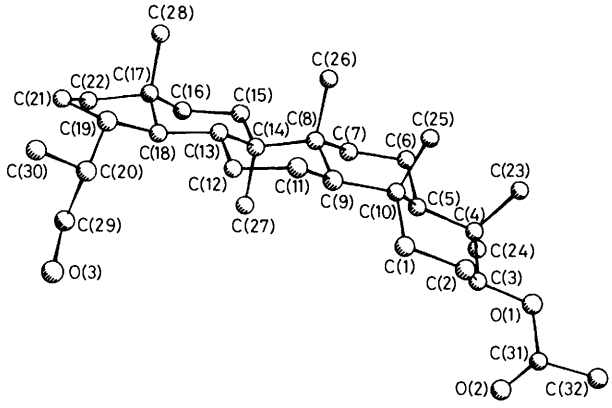


Figure 2.

We have found that the C-29 substituted (20*RS*)-aldehydes (**10a**) and (**10b**), acids (**12a**) and (**12b**), and alcohols (**11a**) and (**11b**) can be similarly distinguished. In each case the C-30 signals of the respective (20*R*)-epimers (Table 3) occurred at a shift value *ca.* 7 p.p.m. greater than is the case for the corresponding (20*S*)-epimers. This is in accord with the view that in the (20*R*)-epimers the C-20 methyl group is equatorially inclined with respect to the pentacyclic ring system.[9] The ^{13}C n.m.r. assignments in Table 3 follow directly from those reported by Wenkert *et al.*[9] for related compounds. In addition to C-30, only C-18, C-19, C-20, C-29, and to a lesser extent C-21, were sensitive to C-29 substitution and the absolute configuration at C-20. By far the most diagnostic of these shifts was that of the C-30 carbon.

The absolute configuration at C-20 of the C-29 substituted lupanes was also inferred from ^1H n.m.r. data (Table 1), since in the (20*R*)-epimers the 17β-methyl group signal occurred at higher field (δ 0.73—0.75) than the corresponding (20*S*-epimer (δ 0.77—0.79). The 20-methyl doublets similarly distinguished the (20*R*)- and (20*S*)-epimers.[2] In this case it was the (20*S*)-epimer doublet which appeared at higher field. The noracetoxy alcohols (**20a**) and (**20b**) could be distinguished by the same pairs of signals and while the 20-methyl signals of the nordiols (**21a**) and (**21b**) followed the usual pattern, the 17β-methyl signals could not be separated from the 4β-methyl signals. Both appeared under an envelope centred at δ 0.78 for each of the (20*R*)- and (20*S*)-epimers. Whilst the 17β-methyl signal of the epoxide (**7**) occurred at δ 0.74 this was not considered to be indicative of the absolute configuration at C-20 since it is probable that the more bulky epoxide functionality would be equatorially disposed in each of the epimeric epoxides.

Table 4. Final positional parameters for (20R)-3β-acetoxylupan-29-ol

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
C(1)	0.109 9(5)	0.611 1(4)	0.068(1)	C(18)	−0.232 0(5)	0.629 8(4)	0.536(1)
C(2)	0.198 3(5)	0.610 6(4)	−0.005(1)	C(19)	−0.319 1(5)	0.613 0(4)	0.462(1)
C(3)	0.257 7(5)	0.646 0(4)	0.098(1)	C(20)	−0.344 4(5)	0.644 4(4)	0.306(1)
C(4)	0.266 4(4)	0.621 0(3)	0.269(1)	C(21)	−0.380 6(7)	0.625 2(5)	0.605(1)
C(5)	0.176 1(5)	0.617 6(4)	0.339 3(9)	C(22)	−0.327 8(6)	0.646 8(5)	0.743(1)
C(6)	0.171 0(5)	0.596 4(4)	0.515(1)	C(23)	0.314 2(5)	0.560 1(3)	0.273(1)
C(7)	0.087 2(5)	0.615 7(4)	0.592(1)	C(24)	0.317 4(5)	0.666 2(4)	0.370(1)
C(8)	0.008 5(5)	0.592 5(3)	0.501 8(9)	C(25)	0.119 4(5)	0.514 3(4)	0.227(1)
C(9)	0.019 9(5)	0.601 7(3)	0.317 2(9)	C(26)	0.000 1(5)	0.523 7(4)	0.542(1)
C(10)	0.106 7(5)	0.584 3(3)	0.240(1)	C(27)	−0.062 7(5)	0.696 8(3)	0.519(1)
C(11)	−0.057 6(5)	0.577 8(4)	0.226(1)	C(28)	−0.246 4(6)	0.550 5(5)	0.759(2)
C(12)	−0.140 5(5)	0.605 8(3)	0.284 8(9)	C(29)	−0.354 2(7)	0.713 0(5)	0.322(2)
C(13)	−0.150 2(5)	0.602 1(3)	0.469 1(9)	C(30)	−0.424 7(8)	0.616 5(5)	0.238(2)
C(14)	−0.071 9(5)	0.627 9(3)	0.557 8(9)	O(1)	0.341 4(3)	0.646 9(3)	0.026 1(7)
C(15)	−0.083 5(6)	0.623 7(4)	0.742(1)	C(31)	0.359 9(6)	0.690 9(6)	−0.081(1)
C(16)	−0.168 8(6)	0.647 2(4)	0.806(1)	O(2)	0.309 4(5)	0.729 2(4)	−0.116(1)
C(17)	−0.241 2(6)	0.618 0(4)	0.715(1)	C(32)	0.447 2(6)	0.686 6(7)	−0.141(2)
O(3)	−0.367 3(6)	0.741 9(4)	0.171 0(1)				

The space group was uniquely determined as $P2_12_12_1$, $a = 15.895(6)$, $b = 22.14(1)$, $c = 8.298(3)$ Å, $U = 2\,920.5$ Å^3, $D_m = 1.13$, $D_c = 1.11$ g cm^{-3}, $Z = 4$.

Although the foregoing correlations, have rigorously established the (20*RS*)-configurations, we considered it desirable that the absolute configuration of one of the C-29 substituted compounds prepared in this study should be unequivocally established by an *X*-ray crystallographic determination. Suitable crystals of the acetoxy alcohol (**11a**) were obtained, and the (20*R*)-configuration was confirmed. In accord with expectations, the preferred conformation, at least in the solid state, was found to be that in which the C-20 hydroxymethylene and methyl groups were oriented axially and equatorially respectively with respect to the pentacyclic skeleton (Figure 2). The final positional co-ordinates of the heavy atoms appear in Table 4.

Tables of bond lengths, bond angles, thermal parameters, calculated hydrogen atom positional co-ordinates, appear in the Supplementary Publication [SUP. No. 56278 (7 pp.)].* The calculated and observed structure factors are available on request from the Editorial office.

Experimental

Experimental procedures are as described in Part 6.[10] Ether refers to diethyl ether, LAH refers to lithium aluminium hydride.

3β-*Acetoxy*-20,29-*epoxylupane* (**7**).—This compound was prepared by the method of Hui *et al.*[4] and had m.p. 237—239 °C (from ether); $[\alpha]_D^{20}$ + 21.0° (*c* 6.9) (lit.,[4] m.p. 238—240 °C; $[\alpha]_D^{20}$ + 24.9°); $\nu_{max.}(CCl_4)$ 1 730, 1 238 (OAc), and 880 cm^{-1} (epoxy); δ 2.01 (3 H, s, OAc), H_A 2.63, H_B 2.59 (2 H, AB, J_{AB} 5.3 Hz, O–C–CH$_2$), and 4.47 (1 H, q, C*H*OAc) (Found: C, 79.4; H, 11.1. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%).

Boron Trifluoride–Diethyl Ether Rearrangement of 3β-*Acetoxy*-20,29-*epoxylupane* (**7**).—The epoxide (**7**) (376 mg) in ether (50 ml) was treated with BF_3–Et_2O (0.4 ml) and stirred at room temperature for 2 h. The product was worked-up in the usual way to give (20RS)-3β-*acetoxylupan*-29-*al* (**10a**) and (**10b**) (350 mg), m.p. 176—180 °C; δ 9.60 (s, CHO) and 9.85 (d, *J* 2 Hz, CHO) (3:2) (Found: C, 79.1; H, 10.9. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%). This epimeric mixture was recovered unchanged after passage in hexane–ether (1:6) through Merck, neutral, grade 2—3 alumina and after solution in deuteriochloroform–trifluoracetic acid (20:1) for 24 h.

(20R)- *and* (20S)-3β-*Acetoxylupan*-29-*ols* (**11a**) *and* (**11b**).—A solution of the mixture of epimeric aldehydes (**10a**) and (**10b**) (120 mg) in ethanol (20 ml) was stirred with an excess of $NaBH_4$ for 45 min. at room temperature. Work-up in the usual way gave (20*RS*)-3β-acetoxylupan-29-ol (**11a**) and (**11b**) (115 mg). This product in chloroform (4 ml) was applied to three preparative silica gel plates. Multiple (×4) p.l.c. with benzene–ether (93:7) gave at higher R_F value, the (20*S*)-epimer (**11b**) (60 mg) and at lower R_F value, the (20*R*)-epimer (**11a**) (40 mg). (20S)-3β-*Acetoxylupan*-29-*ol* (**11b**) had m.p. 229—230 °C (from methanol); $[\alpha]_D^{20}$ + 2.58° (*c* 6.0); $\nu_{max.}(CCl_4)$ 3 640 (OH), 1 730, and 1 238 cm^{-1} (OAc); δ 2.01 (3 H, s, OAc), 3.40 (2 H, A_2X, d, *J* 6.9 Hz, CH_2OH), and 4.47 (1 H, q, C*H*OAc) (Found: C, 78.8; H, 11.2. $C_{32}H_{54}O_3$ requires C, 79.0; H, 11.2%). (20R)-3β-*Acetoxylupan*-29-*ol* (**11a**) had m.p. 282—283 °C (from acetone); $[\alpha]_D^{20}$ − 6.00° (*c* 2.28); $\nu_{max.}(CCl_4)$ 3 637 (OH), 1 730, and 1 238 cm^{-1} (OAc); δ 2.01 (3 H, s, OAc), H_A 3.78, H_B 3.41 (2 H, ABX, J_{AX} 4 Hz, J_{BX} 9 Hz, J_{AB} 11 Hz, CH_2OH), and 4.47 (1 H, q, C*H*OAc) (Found: C, 79.2; H, 11.6. $C_{32}H_{54}O_3$ requires C, 79.0; H, 11.2%).

(20R)-3β-*Acetoxylupan*-29-*al* (**10a**).—The bulk Collins reagent was prepared as follows.[2] Anhydrous chromium trioxide (337 mg) and anhydrous magnesium sulphate (300 mg) were suspended in dichloromethane (16 ml) and stirred under a positive nitrogen pressure in a Schlenk tube. Pyridine (0.54 ml) in dichloromethane (4 ml) was then added through a serum cap with ice-cooling and stirring was continued for 1 h while a deep burgundy red colour developed. An aliquot (1.6 ml) of the oxidising solution was transferred under nitrogen to a stirred ice-cold solution of (20*R*)-3β-acetoxylupan-29-ol (**11a**) (40 mg), in dichloromethane (1.5 ml). After 30 min at 0 °C and a further 30 min at room temperature the mixture was decomposed with aqueous sodium carbonate and the product extracted into ether. Work-up in the usual way gave (20R)-3β-*acetoxylupan*-29-*al* (**10a**) (35 mg), m.p. 198—201 °C (sublimed sample); $[\alpha]_D^{20}$ − 24.12° (*c* 2.4); $\nu_{max.}(CCl_4)$ 2 820, 2 710, 1 730(CHO), 1 730, and 1 238 cm^{-1} (OAc); δ 2.01 (3 H, s, OAc), 4.47 (1 H, q,

* For details of the Supplementary publications scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1985, Issue 1.

C*H*OAc), and 9.85 (1 H, d, *J* 2 Hz, CHO) (Found: C, 79.3; H, 11.0. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%).

(20S)-3β-*Acetoxylupan*-29-*al* (**10b**).—Oxidation of the (20*S*)-alcohol (**11b**) (33 mg) was carried out in the same manner as for alcohol (**11a**). (20S)-3β-*Acetoxylupan*-29-*al* (**10b**) (27 mg) had m.p. 194—197 °C (sublimed sample); $[\alpha]_D^{20}$ + 22.0° (*c* 1.7); $\nu_{max.}$(CCl_4) 2 810, 2 700, 1 730 (CHO), 1 730, and 1 238 cm^{-1} (OAc); δ 2.01 (3 H, s, OAc), 4.47 (1 H, q, C*H*OAc), and 9.60 (1 H, s, CHO) (Found: C, 79.0; H, 10.7. $C_{32}H_{52}O_3$ requires C, 79.3; H, 10.8%).

(20R)-3β-*Acetoxylupan*-29-*oic Acid* (**12a**).—Jones reagent was added dropwise to (20*R*)-3β-acetoxylupan-20-ol (33 mg) in acetone (10 ml) until an orange colour persisted. Work-up followed by p.l.c. on silica gel with ether–hexane (6:4) gave (20R)-3β-*acetoxylupan*-29-*oic acid* (**12a**) (30 mg), m.p. 273—276 °C (from acetone); $[\alpha]_D^{20}$ −39.90° (*c* 7.28); $\nu_{max.}$(CCl_4) 3 530, 1 700 (COOH), 1 730, and 1 237 cm^{-1} (OAc); δ 2.01 (3 H, s, OAc) and 4.47 (1 H, q, C*H*OAc) (Found: C, 77.0; H, 10.7. $C_{32}H_{52}O_4$ requires C, 76.8; H, 10.5%).

(20S)-3β-*Acetoxylupan*-29-*oic Acid* (**12b**).—Oxidation of (20*S*)-3β-acetoxylupan-29-ol (**11b**) (63 mg) as described for the (20*R*)-epimer (**11a**) gave (20S)-3β-*acetoxylupan*-29-*oic acid* (**12b**) (53 mg), m.p. 287—290 °C (from acetone); $[\alpha]_D^{20}$ + 22.66° (*c* 8.72); $\nu_{max.}$(CCl_4), 3 538, 1 700 (CO_2H), 1 730, and 1 238 cm^{-1} (OAc); δ 2.01 (3 H, s, OAc), 4.47 (1 H, q, C*H*OAc) (Found: C, 77.0; H, 10.6. $C_{32}H_{52}O_4$ requires C, 76.8; H, 10.5%).

(20R)-*Lupane*-3β,29-*diol* (**13a**).—(20*R*)-3β-Acetoxylupan-29-oic acid (**12a**) (39 mg) in anhydrous ether (20 ml) was stirred with an excess of LAH for 5 h. Work-up followed by p.l.c. on silica gel with ether as eluant gave at higher R_F value, (20*R*)-3β-hydroxylupan-29-oic acid (**14a**) (15 mg) and at lower R_F value, (20R)-*lupane*-3β,29-*diol* (**13a**) (13 mg). (20*R*)-Lupane-3β,29-diol (**13a**) had m.p. 235 °C (sublimed sample); $[\alpha]_D^{20}$ − 14.09° (*c* 1.22); $\nu_{max.}$(CCl_4) 3 640 cm^{-1} (OH); δ 3.17 (1 H, m, C*H*OH), and H_A 3.78, H_B 3.41 (2 H, ABX, J_{AX} 4 Hz, J_{BX} 9 Hz, J_{AB} 11 Hz, CH_2OH) (Found: C, 80.7; H, 11.8. $C_{30}H_{52}O_2$ requires C, 81.0; H, 11.8%).

(20S)-*Lupane*-3β,29-*diol* (**13b**).—(20*S*)-3β-*Acetoxylupan*-29-oic acid (**12b**) (30 mg) in anhydrous ether (20 ml) was stirred with an excess of LAH for 12 h. Work-up in the usual way gave (20S)-*lupane*-3β,29-*diol* (**13b**) (24 mg), m.p. 257—259 °C (sublimed sample); $[\alpha]_D^{20}$ −5.79° (*c* 0.95); $\nu_{max.}$(CCl_4) 3 638 cm^{-1} (OH); δ 3.17 (1 H, m, C*H*OH) and 3.40 (2 H, A_2X, d, *J* 6.9 Hz, CH_2OH) (Found: C, 80.7; H, 11.9. $C_{30}H_{52}O_2$ requires C, 81.0; H, 11.8%).

(20R)-3β-*Hydroxylupan*-29-*oic Acid* (**14a**).—A solution of (20R)-3β-acetoxylupan-29-oic acid (**12a**) (40 mg) in 10% ethanolic potassium hydroxide (15 ml) was stirred for 2 h. The usual work-up gave (20R)-3β-*hydroxylupan*-29-*oic acid* (**14a**) (35 mg), m.p. 275—277 °C (from methanol); $[\alpha]_D^{20}$ −52.64° (*c* 2.65); $\nu_{max.}$(film) 3 350 (OH) and 1 700 cm^{-1} (CO_2H); δ 3.17 (1 H, m, C*H*OH) (Found: C, 78.8; H, 11.5. $C_{30}H_{50}O_4$ requires C, 78.5; H, 11.0%).

(20S)-3β-*Hydroxylupan*-20-*oic Acid* (**14b**).—Hydrolysis of (20*S*)-3β-acetoxylupan-29-oic acid (**12b**) (48 mg) as described for the (20*R*)-epimer (**12a**) gave (20S)-3β-*hydroxylupan*-29-*oic acid* (**14b**) (45 mg), m.p. 292—293 °C (from acetone); $[\alpha]_D^{20}$ + 8.71° (*c* 0.245); $\nu_{max.}$(film) 3 460 (OH) and 1 700 cm^{-1} (CO_2H); δ 3.17 (1 H, m, C*H*OH) (Found: C, 78.2; H, 10.9. $C_{30}H_{50}O_4$ requires C, 78.5; H, 11.0%).

(20RS)-3β-*Acetoxylupan*-29-*al Dimethyl Acetal* (**18**).—The epoxide (**7**) (80 mg) in chloroform–methanol (1:1) (30 ml) and concentrated HCl (0.3 ml) was stirred at room temperature for 2 h by which time reaction was complete (t.l.c.). The solution was neutralized with saturated aqueous sodium hydrogen carbonate, extracted into ether, worked-up in the usual way, and purified by p.l.c. on silica gel with ether–hexane (7:13). (20RS)-3β-*Acetoxylupan*-29-*al dimethyl acetal* (**18**) (48 mg) had m.p. 215—221 °C (from methanol); $\nu_{max.}$(CCl_4) 1 730, 1 238 (OAc), 1 105, and 1 070 cm^{-1} (OMe); δ 2.01 (3 H, s, OAc), 3.27, 3.29 (OMe); 3.33 (OMe), 4.0 (d, *J* 8 Hz, C*H*OMe); 4.28 (d, *J* 6 Hz, C*H*OMe) (2:3), and 4.47 (1 H, q, C*H*OAc) (Found: C, 77.1; H, 11.4. $C_{34}H_{58}O_4$ requires C, 76.9; H, 11.0%).

Hydrolysis of (20RS)-3β-*Acetoxylupan*-29-*al Dimethyl Acetal* (**18**).—The acetal (**18**) (50 mg) was added to dioxane (25 ml) containing 2M-H_2SO_4 (8 ml) and stirred for 24 h. Work-up in the usual way gave (20*RS*)-3β-acetoxylupan-29-al (45 mg) identical in all respects (m.p., i.r., n.m.r.) with the product obtained by boron trifluoride–diethyl ether rearrangement of the epoxide (**7**).

An attempt to hydrolyse the acetal (**18**) with dioxane (20 ml) containing 2M-H_2SO_4 (2 ml) gave largely unchanged acetal (**18**).

Acid-induced Isomerization of 3β-*Acetoxylup*-20(29)-*en*-30-*ol* (**19**).—The alcohol (**19**) 14 mg) in chloroform (7 ml) was added to glacial acetic acid (5 ml) containing concentrated HCl (0.5 ml). After 18 h at room temperature and the usual work-up, the product had m.p. 175—180 °C and was identical in all respects (m.p., i.r., n.m.r.) with the (20*RS*)-3β-acetoxylupan-29-al (**10a**), (**10b**) obtained by boron trifluoride–diethyl ether rearrangement of epoxide (**7**).

(20R)- *and* (20S)-3β-*Acetoxy*-30-*norlupan*-20-*ol* (**20a**) *and* (**20b**).—3β-Acetoxy-30-norlupan-20-one (**22**) (110 mg) was stirred with an excess of sodium borohydride in ethanol (60 ml) for 6 h. Work-up in the usual way gave (20*RS*)-3β-acetoxy-30-norlupan-20-ol (**20a**), (**20b**) (99 mg). P.l.c. on silica gel with ether–hexane (3:2) gave at higher R_F value the (20*R*)-epimer (**20a**) (78 mg) and at lower R_F value the (20*S*)-epimer (**20b**) (15 mg). (20*R*)-3β-Acetoxy-30-norlupan-20-ol (**20a**) had m.p. 289—290 °C (sublimed sample) (lit.,[3] 293—294 °C; $[\alpha]_D^{20}$ +4.3° (*c* 3.05); $\nu_{max.}$(CCl_4) 3 630 (OH), 1 730 and 1 238 cm^{-1} (OAc); δ 2.02 (3 H, s, OAc), 3.98 (1 H, q, C*H*OH). 4.47 (1 H, q, C*H*OAc) (Found: C, 79.0; H, 11.2. Calc. for $C_{31}H_{52}O_3$: C, 78.8; H, 11.1%). (20S)-3β-*Acetoxy*-30-*norlupan*-20-*ol* (**20b**) had m.p. 248—252 °C (sublimed sample); $[\alpha]_D^{20}$ +0.46° (*c* 1.3); $\nu_{max.}$(CCl_4) 3 625 (OH), 1 730, and 1 238 cm^{-1} (OAc); δ 2.01 (3 H, s, OAc), 4.11 (1 H, m, C*H*OH), and 4.19 (1 H, q, C*H*OAc) (Found: C, 78.9; H, 11.5. $C_{31}H_{52}O_3$ requires C, 78.8; H, 11.1%).

(20R)- *and* (20S)-30-*Norlupane*-3β,20-*diol* (**21a**) *and* (**21b**).—A solution of 3β-hydroxy-30-norlupan-20-one (**23**) (80 mg) in anhydrous ether (20 ml) was heated under reflux with an excess of LAH for 5 h. Work-up in the usual way gave a mixture of products (70 mg) which after multiple (×3) p.l.c. with ether–hexane (2:1) gave at higher R_F value the (20*R*)-epimer (**21a**) (40 mg) and at lower R_F value the (20*S*)-epimer (**21b**) (15 mg) together with two other minor products which were not investigated. (20R)-30-*Norlupane*-3β,20-*diol* (**21a**) had m.p. 262—263 °C (sublimed sample); $[\alpha]_D^{20}$ −6.9° (*c* 1.11); $\nu_{max.}$(CCl_4) 3 630 cm^{-1} (OH); δ 3.17 (1 H, m, C*H*OH) and 3.98 (1 H, q, C*H*OH) (Found: C, 81.0; H, 11.8. $C_{29}H_{50}O_2$ requires C, 80.9; H, 11.7%). (20S)-30-*Norlupane*-3β,20-*diol* (**21b**) had m.p. 246—248 °C (sublimed sample); $[\alpha]_D^{20}$ −11.28° (*c* 0.9); $\nu_{max.}$(CCl_4) 3 628 cm^{-1} (OH); δ 3.18 (1 H, m, C*H*OH), 4.12 (1 H, m, C*H*OH) (Found: C, 81.0; H, 12.0. $C_{29}H_{50}O_2$ requires C, 80.9; H, 11.7%).

Crystal Data.—$C_{32}H_{54}O_3$, M = 486.4. Orthorhombic, a = 15.895(6), b = 22.14(1), c = 8.298(3) Å, U = 2 920.5 Å^3 (by least squares refinements on diffractometer angles for 25 automatically centred high angle reflections, λ = 0.7107 Å), space group $P2_12_12_1$ (No. 19), Z = 4, D_m = 1.13; D_c = 1.11 g cm^{-3}. Crystal dimensions 0.42 × 0.33 × 0.21 mm.

Data Collection and Processing.—Nicolet P3 diffractometer, θ-2θ mode, Mo-$K\alpha$ radiation; 1 659 reflections measured ($0 \leqslant \theta \leqslant 40°$, +h,k,l), 1 595 unique [merging R = 0.015], with 1 261 having $I \geqslant 3\sigma(I)$. Intensities were corrected for Lorentz polarization effects, but no absorption corrections were applied.

Structure Analysis and Refinement.—Direct methods using the programme package MULTAN[11] resulted in the elucidation of a structurally correct fragment (20 atoms) which was further refined using the difference Fourier procedures of the programme system SHELX.[12] The final cycles of full-matrix least squares refinements were performed with isotropic ring carbons, and the remaining heavy atoms anisotropic. Hydrogens in calculated positions; with C–H = 0.98 Å, were refined with separate overall thermal parameters for the methine, methylene, hydroxymethylene and methyl hydrogens. The hydroxy hydrogen (HO3) of the hydroxymethylene group was located directly in a final difference Fourier, and is clearly hydrogen bonded to the carbonyl oxygen of the C-3 acetoxy group [HO(3) ··· O(2)] = 1.97 Å. The weighting scheme $w = 1/[\sigma^2(F_o) + 0.0090 F_o^2]$ with $\sigma(F_o)$ from counting statistics gave satisfactory agreement analyses. Final R and R_w values were 0.064, 0.069.

Acknowledgements

We thank Dr M. Thomas for assistance with the measurement of ^{1}H n.m.r. spectra. Analyses were performed by the microanalytical laboratory of the Otago University Chemistry Department under the direction of Professor A. D. Campbell. One of us, (A. N. T. C.) thanks the University of Otago for a Senior Demonstratorship.

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Received 17th December 1984; *Paper* 4/2124