PREPARATION OF 20*R* AND 20*S* ACETYLAMINO-30-NORLUPANE DERIVATIVES*

Václav KŘEČEK[a], Miloš BUDĚŠÍNSKÝ[b] and Alois VYSTRČIL[a]

[a] *Department of Chemistry, Charles University, 128 40 Prague 2*
[b] *Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, 166 10 Prague 6*

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A series of epimeric pairs of 20*R* and 20*S* acetylamino derivatives *VIII*—*XI* have been prepared by reduction and subsequent acetylation of the oximes *I*, *III*, *IV*, and *VI*. Their absolute configuration at C-20 (20*R* and 20*S* for the series *a* and *b*, respectively) has been suggested on the basis of their physical and spectral properties. The correctness of this assignment was confirmed by the synthesis of the acetylamino derivatives *Xa* and *Xb* from the acids *XIIa* and *XIIb*, respectively, with known configuration at C-20.

In our previous communication[1] we described the synthesis and properties of oximes of 30-norlupan-20-one and of their derivatives having various substituents at the 3 and 28 positions. The present paper deals with their reduction. The oximes *I*, *III*, *IV*, and *VI* used for the reductions were mixtures of the *E* and *Z* isomers in the ratio identical with that obtained from the oximation of the respective ketone[1]. Beside the oximes, in one case of the reduction we started also from the oxime acetate *II*, which gave approximately the same results like the parent oxime *I*. The reduction was accomplished by catalytic hydrogenation (Pt according to Adams) or by chemical reduction with sodium in 1-propanol or 1-pentanol. Attempts at reduction with hydrides failed: the reduction either did not take place ($NaBH_4$) or gave complex mixtures of products ($LiAlH_4$). The catalytic hydrogenations of oximes *IV* and *VI* were not quantitative: beside the amides *X* and *XI* we isolated also the starting oximes in the form of the acetates *V* and *VII*. Because of the high polarity and, hence, difficult separation of the 20-epimers, the amines produced by reduction were not isolated and were immediately acetylated to the acetylamino derivatives *VIII*—*XI*. Their 20*R* and 20*S* epimers can easily be separated by chromatography.

Earlier it was found[2] that during TLC of C-20 epimeric 30-nor-20-lupanol derivatives the 20*R* epimers are less adsorbed than the 20*S* epimers. Similar behaviour was found also with the C-20 epimers of 29-substituted lupane derivatives[3]. From these

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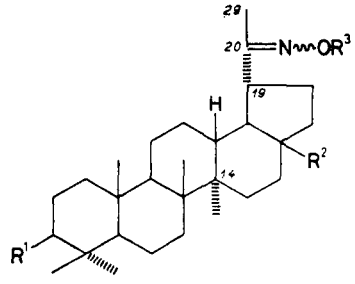
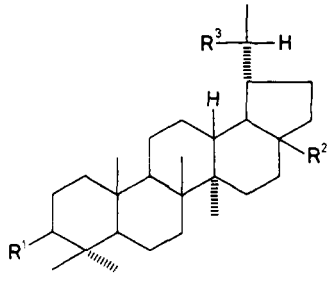
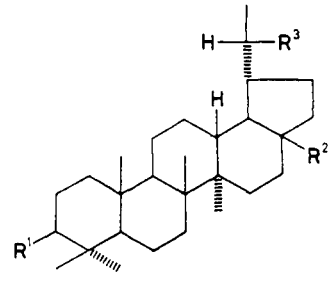
findings and the below-given facts we suggest the configurations 20*R* and 20*S* for the less adsorbed derivatives *VIIIa*–*XIa* and the more adsorbed derivatives *VIIIb* to *XIb*, respectively.



I, $R^1 = R^3 = H$; $R^2 = CH_3$
II, $R^1 = H$; $R^2 = CH_3$; $R^3 = Ac$
III, $R^1 = CH_3O$; $R^2 = CH_2OCH_3$; $R^3 = H$
IV, $R^1 = AcO$; $R^2 = CH_2OAc$; $R^3 = H$
V, $R^1 = AcO$; $R^2 = CH_2OAc$; $R^3 = Ac$
VI, $R^1 = AcO$; $R^2 = COOCH_3$; $R^3 = H$
VII, $R^1 = AcO$; $R^2 = COOCH_3$; $R^3 = Ac$



a, 20*R*



b, 20*S*

VIII, $R^1 = H$; $R^2 = CH_3$; $R^3 = NHAc$
IX, $R^1 = CH_3O$; $R^2 = CH_2OCH_3$; $R^3 = NHAc$
X, $R^1 = AcO$; $R^2 = CH_2OAc$; $R^3 = NHAc$
XI, $R^1 = AcO$; $R^2 = COOCH_3$; $R^3 = NHAc$
XII, $R^1 = AcO$; $R^2 = CH_2OAc$; $R^3 = COOH$
XIII, $R^1 = AcO$; $R^2 = CH_2OAc$; $R^3 = COCl$
XIV, $R^1 = AcO$; $R^2 = CH_2OAc$; $R^3 = CONH_2$
XV, $R^1 = AcO$; $R^2 = CH_2OAc$; $R^3 = NCO$

From Table I it can be seen that all the acetylamino derivatives *VIII*–*XI* retain the same sign and approximately also the same magnitude of differences of molar rotations between the epimers 20*R* and 20*S*. The sign and the order of magnitude

of these differences are identical with the differences of molar rotations found for the 20*R* and 20*S* 29-substituted lupane derivatives (refs[3,4]) and with the M_D differences of compounds *XIV* and *XV* with known configuration at C-20. The comparison with the 20*R* and 20*S* 30-nor-20-lupanol derivatives, however, does not lead to any univocal conclusion. With some of these derivatives the M_D difference between both epimers has a very low value or, as the case may be, the opposite sign (refs[2,4–7]). In another case[7] both the sign and magnitude remain equal to those in Table I.

The ^{1}H NMR spectra (Table II) exhibit a downfield shift ($\Delta\delta$ 0·03–0·04) of the CH_3-20 signal (i.e. H-29) between the 20*R* epimers *VIIIa–Xa* and the 20*S* epimers *VIIIb–Xb*. The 20*R* acetylamino derivatives *VIIIa* and *IXa* show a lower value of coupling constant between H-20 and H-19β ($J(20, 19) \neq 0 < 2$ Hz) than show the epimeric 20*S* acetylamino derivatives *VIIIb* and *IXb* ($J(20, 19) = 3{\cdot}5–4{\cdot}0$ Hz). Similar shifts of the CH_3-20 signal as well as lower values of $J(20, 19)$ of the 20*R* epimers were found between the 20*R* and 20*S* 30-nor-20-lupanol derivatives[2,4,7] as well as between the 20*R* and 20*S* lupane derivatives having oxygen functions at C-29 (refs[3,4]). Moreover, we observed that similar with that of CH_3-20 group but opposite (upfield) is the shift of the CH_3-14α group (i.e. H-27) between the 20*R* epimers *VIIIa–Xa* and 20*S* epimers *VIIIb–Xb* ($\Delta\delta$ 0·04–0·06). A similar shift of this signal in the same direction, however, was found only between the C-20 epimeric 30-norlupane derivatives having an acetoxy group at C-20 (ref.[7]). With other oxygen-containing substituents at C-20 this shift can be zero or even of opposite direction[4].

TABLE I

Differences of molecular rotations between 20*S* and 20*R* epimers of compounds *VIII–XI*, *XIV* and *XV*

Compound	M_D		ΔM_D[a]
	a, 20*R*	*b*, 20*S*	
VIII	−91	+50	+141
IX	−67	+57	+124
X	−80	+46	+126
XI	−117	+11	+128
XIV	−167	+28	+195
XV	−267	+28	+295

[a] $\Delta M_D = M_D(20S) - M_D(20R)$.

TABLE II

^{1}H NMR parameters of compounds *VIII*—*X*, for conditions see Experimental

Compound	Methyl protons							Other protons
	H-23	H-24	H-25	H-26	H-27	H-28	H-29[a]	
VIIIa	0·839	0·792	0·839	1·037	0·880	0·763	1·070	NAc: 1·97 s; H-20: 4·27 m, J(20, 29) = 6·5, J(20, NH) ≈ 9, J(20, 19) ≈ 2; NH: 5·23 bd, J(NH, 20) ≈ 9
VIIIb	0·842	0·800	0·842	1·028	0·922	0·756	1·030	NAc: 1·92 s; H-20: 4·26 m, J(20, 29) = 6·6, J(20, NH) ≈ 8, J(20, 19) ≈ 3·5—4; NH: 5·41 bd, J(NH, 20) ≈ 8
IXa	0·952	0·746	0·835	1·037	0·890	[b]	1·073	NAc: 1·985 s; H-3: 2·63 dd, J(3, 2) ≈ 11·5 and 4; OCH_3: 3·33 s, 3·36 s; H-28: 2·98 d and 3·47 d, J(28, 28) ≈ 9·5; H-20: 4·25 m, J(20, 29) ≈ 6·5, J(20, NH) = 9·7, J(20, 19) ± 0 ≦ 1·5; NH: 5·31 d, J(NH, 20) = 9·7
IXb	0·934	0·751	0·840	1·030	0·954	[b]	1·032	NAc: 1·925 s; H-3: 2·64 m; OCH_3: 3·325 s, 3·355 s; H-28: 2·99 d and 3·44 d, J(28, 28) = 9·5; H-20: 4·23 m, J(20, 29) = 6·6, J(20, NH) ≈ 8, J(20, 19) = 3·5—4; NH: 5·36 bd, J(NH, 20) ≈ 8
Xa	0·838	0·838	0·855	1·037	0·899	[b]	1·070	NAc: 1·995 s; OAc: 2·03 s, 2·055 s; H-28: 3·79 d and 4·25 d, J(28, 28) ≈ 11; H-20: 4·30; H-3: 4·48 m; NH: 5·26 d, J(NH, 20) = 9·6
Xb	0·845	0·845	0·860	1·039	0·941	[b]	1·041	NAc: 1·918 s; OAc: 2·037 s, 2·049 s; H-28: 3·82 d and 4·23 d, J(28, 28) ≈ 11; H-20: 4·25 m; H-3: 4·48 m; NH: 5·42 bd, J(NH, 20) ≈ 8

[a] Doublets with J(29, 20) = 6·5—6·6; [b] see other protons.

In contrast to the C-20 epimeric 30-nor-20-lupanol derivatives, it was impossible to differentiate between the two epimeric acetylamino derivatives *VIIIa*, *VIIIb* by means of the IR spectra. The valence vibrations of OH group of 30-nor-20-lupanol derivatives show different values[2] for the two epimers 20*R* and 20*S*, the difference being 10–14 cm^{-1}. The valence vibrations of NH groups of 20*R* amide *VIIIa* and 20*S* amide *VIIIb* measured in very dilute solutions in tetrachloromethane, however, show no distinct difference (the respective values are 3 447 and 3 449 cm^{-1}).

The preliminary assignment of the 20*R* and 20*S* configurations to the less and the more adsorbed epimers, respectively, was confirmed finally by the synthesis of both epimeric triacetates *Xa*, *Xb* from the acids *XIIa*, *XIIb* with known[3] configuration at C-20. The chloride *XIIIa* prepared earlier[3] from the 20*R* acid *XIIa* was amonolyzed to give the amide *XIVa* which was submitted to oxidative rearrangement by action of lead tetraacetate[8] to give the isocyanate *XVa*. Its hydrolysis and subsequent acetylation gave the 20*R* acetylamino derivative *Xa*. The same procedure was adopted to convert the chloride *XIIIb* (prepared according to ref.[3]) into the 20*S* acetylamino derivative *Xb*.

EXPERIMENTAL

The melting points were determined with a Kofler apparatus and were not corrected. The optical activities were measured in chloroform using an automatic polarimeter ETL-NPL (Bendix Ericsson) with the accuracy of ±2°. The IR spectra were measured in chloroform (if not otherwise stated) using a UR-20 or a Unicam SP-700 apparatus; the wavenumbers are given in cm^{-1}. The ^1H NMR spectra were measured with a Varian HA-100 apparatus (100 MHz) in deuteriochloroform; the chemical shifts are related to tetramethylsilane and given in ppm (δ-scale); the coupling constants (J) were obtained by the first-order analysis and are given in Hz. The chromatography was performed on neutral alumina (activity II according to Brockmann) or silica gel according to Pitra. The samples for analyses were dried under reduced pressure over phosphorus pentoxide at 100°C for 10 h. The identity of samples was verified by TLC, mixed melting point, optical rotation, and IR spectra.

The acetylations were carried out in the following way: Acetanhydride (10 parts by wt.) was added to a solution of the sample (1 part by wt.) in pyridine (20 parts by wt.), and the reaction mixture was left to stand at room temperature 2 days, whereafter it was diluted with water, and the product was extracted with ether. The extract was washed with dilute hydrochloric acid (1 : 4) and with a 5% sodium carbonate solution. After drying with anhydrous sodium sulfate, the ether was distilled off.

Reduction of Oxime *I*

a) A solution of 500 mg (1·17 mmol) oxime *I* in 100 ml acetic acid was treated with 50 mg platinum dioxide (according to Adams), and the reaction mixture was shaken under hydrogen 8 h, whereafter the catalyst was removed by filtration, and the solution was evaporated until dry. The evaporation residue was submitted to acetylation to give a raw product which was purified by column chromatography (50 g silica gel, eluens petroleum ether–ether 1 : 1, 810 ml). Yield 390 mg (73%) amide *VIIIa*, m.p. 252–253°C (ether–petroleum ether), $[\alpha]_D$ −20°. (*c* 0·59). IR spectrum: 3 455, 3 350, 1 665, 1 517 (NHAc); as a $2{\cdot}23 \cdot 10^{-3}$M solution in tetrachloro-

methane: 3 447, $\varepsilon^a = 84$, $\Delta\nu_{1/2} = 13\ cm^{-1}$ (NH). For $C_{31}H_{53}NO$ (455·7) calculated: 81·69% C, 11·72% H, 3·07% N; found: 81·85% C, 11·70% H, 3·10% N. Further elution with a mixture of petroleum ether and ether (1 : 2, 540 ml) gave 78 mg (15%) amide *VIIIb*, m.p. 297°C (chloroform–methanol), $[\alpha]_D$ +11° (*c* 0·46). IR spectrum: 3 455, 3 340, 1 660, 1 517 (NHAc); 2·11 . 10^{-3}M solution in tetrachloromethane: 3 449, $\varepsilon^a = 94$, $\Delta\nu_{1/2} = 13\ cm^{-1}$ (NH). For $C_{31}H_{53}NO$ (455·7) calculated: 81·69% C, 11·72% H, 3·07% N; found: 81·57% C, 11·77% H, 2·99% N.

b) A solution of 500 mg (1·17 mmol) oxime *I* in 130 ml 1-propanol was heated to boiling, and 5 g sodium was added thereto portionwise during 8 h. After dissolution of the sodium, the reaction mixture was diluted with water, the product was extracted with ether, the ethereal solution was washed with water and dried with sodium sulfate. The evaporation residue was acetylated to give a raw product which was purified by column chromatography (50 g silica gel, eluens petroleum ether–ether 1 : 1, 690 ml). Yield 208 mg (39%) amide *VIIIa*, m.p. 252·5 to 253·5°C (chloroform–methanol), $[\alpha]_D$ −20° (*c* 0·62). Further elution with a mixture of petroleum ether and ether (1 : 2, 600 ml) gave 265 mg (50%) amide *VIIIb*, m.p. 297–297·5°C (chloroform–methanol), $[\alpha]_D$ +12° (*c* 0·60).

The corresponding products from the procedures *a*) and *b*) were identical.

Reduction of Oxime *III*

a) The catalytic reduction of oxime *III* (210 mg, 0·43 mmol) with hydrogen on platinum was carried out in the same way as that of oxime *I* sub *a*). After acetylation, the product was separated by column chromatography (20 g silica gel, eluens petroleum ether–ether 1 : 1, 600 ml) to give 130 mg (59%) amide *IXa*, m.p. 268–269°C (ether–petroleum ether), $[\alpha]_D$ −14° (*c* 0·54), identical with the product of the procedure *b*) below. Further elution with 420 ml ether gave 39 mg (18%) amide *IXb*, m.p. 252–254°C (ether–petroleum ether), $[\alpha]_D$ +12° (*c* 0·54), identical with the product of the procedure *b*) below.

b) Oxime *III* (300 mg, 0·62 mmol) was reduced with sodium in 1-pentanol in the same way as oxime *I* in the case *b*). After acetylation, the raw product was submitted to column chromatography (30 g silica gel, eluens petroleum ether–ether 1 : 1, 370 ml) to give 200 mg (63%) amide *IXa*, m.p. 266–267°C (ether), $[\alpha]_D$ −13° (*c* 0·55). IR spectrum: 3 453, 1 672, 1 521 (NHAc); 2 824, 1 099 (OCH_3). For $C_{33}H_{57}NO_3$ (515·8) calculated: 76·84% C, 11·14% H, 2·72% N; found: 76·60% C, 11·07% H, 2·54% N. Elution with 160 ml ether gave 85 mg (27%) amide *IXb*, m.p. 252–254°C (ether), $[\alpha]_D$ +11° (*c* 0·54). IR spectrum: 3 455, 1 665, 1 521 (NHAc); 2 825, 1 105 (OCH_3). For $C_{33}H_{57}NO_3$ (515·8) calculated: 76·84% C, 11·14% H, 2·72% N; found: 76·89% C, 11·25% H, 2·88% N.

Reduction of Oxime *IV*

a) The catalytic hydrogenation of 100 mg (0·18 mmol) oxime *IV* on platinum was carried out in the same way as that of oxime *I* in the case *a*). After acetylation, the raw product was separated by column chromatography (7 g silica gel, eluens benzene–ether 1 : 1, 30 ml) to give 49 mg (45%) oxime acetate *V*, m.p. 220–222°C (ether–petroleum ether), $[\alpha]_D$ +36° (*c* 0·55), identical with the substance prepared earlier[1]. Elution with 15 ml of the same mixture and 15 ml ether gave 33 mg (31%) amide *Xa*, m.p. 316–318°C (benzene–ethanol), $[\alpha]_D$ −14° (*c* 0·70). Further elution with 60 ml ether gave 14 mg (13%) amorphous amide *Xb* with $[\alpha]_D$ +6° (*c* 0·45).

b) The reduction of 500 mg (0·92 mmol) oxime *IV* with sodium in 1-pentanol was carried out in the same way as that of oxime *I* in the case *b*). Acetylation and recrystallization of the raw product from ether gave 133 mg (25%) amide *Xa*, m.p. 318–320°C, $[\alpha]_D$ −14° (*c* 0·58), identical

with the product prepared ad *a*). The mother liquors were separated by column chromatography (25 g silica gel). The elution with ether gave 280 mg unidentified compounds, 51 mg (10%) amide *Xa* and 31 mg (6%) amorphous amide *Xb* with $[\alpha]_D$ +6° (*c* 0·45), identical with the product prepared ad *a*).

Reduction of Oxime *VI*

a) The catalytic hydrogenation of 200 mg (0·38 mmol) oxime *VI* on platinum was carried out at the same conditions as that of oxime *I* sub *a*) above. The product obtained was acetylated and separated by column chromatography (20 g silica gel). Elution with 30 ml ether gave 80 mg (37%) oxime acetate *VII*, m.p. 133–135°C (ether–petroleum ether), $[\alpha]_D$ +21° (*c* 0·60) identical with the substance prepared earlier[1]. Subsequent elution with 200 ml ether gave 72 mg (34%) amide *XIa*, m.p. 331·5°C (chloroform–methanol), $[\alpha]_D$ −21° (*c* 0·62). IR spectrum: 1 731, 1 440, 1 152, 1 033 ($COOCH_3$); 1 731, 1 263, 1 033 (OAc); 3 460, 3 410, 1 680, 1 522 (NHAc). For $C_{34}H_{55}NO_5$ (557·8) calculated: 73·21% C, 9·94% H, 2·51% N; found: 73·22% C, 10·04% H, 2·27% N. Further elution with 120 ml ether gave 16 mg (8%) amide *XIb*, m.p. 156–159°C (ether), $[\alpha]_D$ +2° (*c* 0·52).

b) The reduction of 300 mg (0·57 mmol) oxime *VI* with sodium in 1-propanol was carried in the same way as that of oxime *I* in the case *b*). After acetylation, the product was separated by column chromatography (40 g silica gel). Elution with 200 ml ether gave 100 mg (32%) amide *XIa*, m.p. 329–330°C, $[\alpha]_D$ −20° (*c* 0·50), identical with the product obtained ad *a*). The subsequent elution with 100 ml ether gave 41 mg unidentifled mixture, then elution with another 200 ml ether gave 121 mg (38%) amide *XIb* identical with the product prepared sub *a*). M.p. 158–160°C (ether–petroleum ether), $[\alpha]_D$ +2° (*c* 0·65). IR spectrum: 1 732, 1 443, 1 163, 1 037 ($COOCH_3$); 1 732, 1 263, 1 037, (OAc); 3 465, 3 410, 1 675, 1 525 (NHAc). For $C_{34}H_{55}NO_5$ (557·8) calculated: 73·21% C, 9·94% H, 2·51% N; found: 73·51% C, 10·10% H, 2·67% N.

Reduction of Oxime Acetate *II*

a) The catalytic reduction of 200 mg (0·43 mmol) oxime acetate *II* was carried out like that of oxime *I* in the case *a*). The chromatographic separation of the raw acetylated product was carried out on a column of 20 g silica gel with 360 ml mixture of petroleum ether and ether 1 : 1 and gave 121 mg (62%) amide *VIIIa*, m.p. 253–254°C (ether–hexane), $[\alpha]_D$ −19° (*c* 0·76), identical with the product prepared by the reduction of oxime *I*. Further elution with 150 ml mixture petroleum ether–ether 1 : 1 gave 38 mg (20%) amide *VIIIb*, m.p. 295–296·5°C (ether–hexane), $[\alpha]_D$ +11° (*c* 0·56), identical with the product obtained by reduction of oxime *I*.

b) The reduction of 200 mg (0·43 mmol) oxime acetate *II* with sodium in 1-propanol was the same as that of oxime *I* in the case *b*). After the acetylation, the product was separated by column chromatography (20 g silica gel). Elution with 260 ml mixture of petroleum ether and ether 1 : 1 gave 77 mg (40%) amide *VIIIa*, m.p. 252–253°C (ether–hexane), $[\alpha]_D$ −20° (*c* 0·55), identical with the product prepared by the reduction of oxime *I*. Subsequent elution with 150 ml mixture of petroleum ether and ether 1 : 2 gave 86 mg (44%) amide *VIIIb*, m.p. 295–297°C (chloroform–methanol), $[\alpha]_D$ +11° (*c* 0·59), identical with the product prepared by the reduction of oxime *I*.

(20*R*)-3β,28-Diacetoxylupan-29-amide (*XIVa*)

The chloride[3] *XIIIa* (900 mg, 1·56 mmol) was dissolved in excess benzene saturated with gaseous ammonia (100 ml) and left to stand at room temperature 3 days. After another saturation with

ammonia and 1 day standing, the solution was washed with water and dried with anhydrous sodium sulfate. Filtration of the evaporation residue through a silica gel layer in ether gave 830 mg (95%) amide *XIVa*, m.p. 239–241°C (ether–petroleum ether), $[\alpha]_D$ −30° (*c* 0·63). IR spectrum: 3 535, 3 415, 1 680, 1 586 ($CONH_2$); 1 725, 1 257, 1 030 (OAc). For $C_{34}H_{55}NO_5$ (557·8) calculated: 73·21% C, 9·94% H, 2·51% N; found: 73·40% C, 9·61% H, 2·82% N.

(20*S*)-3β,28-Diacetoxylupan-29-amide (*XIVb*)

The preparation of amide *XIVb* from 700 mg (1·21 mmol) chloride[3] *XIIIb* was carried out analogously to that of the epimeric amide *XIVa*. Yield 654 mg (97%) amide *XIVb*, m.p. 226 to 227, 266–269°C (chloroform–methanol), $[\alpha]_D$ +5° (*c* 0·46). IR spectrum: 3 535, 3 415, 1 678, 1 586 ($CONH_2$); 1 722, 1 252, 1 029 (OAc). For $C_{34}H_{55}NO_5$ (577·8) calculated: 73·21% C, 9·94% H, 2·51% N; found: 73·18% C, 10·02% H, 2·70% N.

(20*R*)-3β,28-Diacetoxy-30-norlupane 20-Isocyanate (*XVa*)

A solution of 450 mg (0·81 mmol) amide *XIVa* in 30 ml benzene was treated with 900 mg (2·03 mmol) lead tetraacetate and the reaction mixture was refluxed 1·5 h. After filtration and addition of 2 ml glycerol, the benzene solution was washed with water and dried with anhydrous sodium sulfate. Yield 387 mg (86%) isocyanate *XVa*, m.p. 224–226°C (ether–petroleum ether), $[\alpha]_D$ −48° (*c* 0·49). IR spectrum (tetrachloromethane): 2 258 (NCO); 1 739, 1 244, 1 029 (OAc). For $C_{34}H_{53}NO_5$ (555·8) calculated: 73·47% C, 9·61% H, 2·52% N; found: 73·51% C, 9·90% H, 2·60% N.

(20*S*)-3β,28-Diacetoxy-30-norlupane 20-Isocyanate (*XVb*)

The isocyanate *XVb* was prepared from 490 mg (0·88 mmol) amide *XIVb* in the same way as was the epimeric isocyanate *XVa*. The raw evaporation residue was filtered through a silica gel layer in benzene. Yield 288 mg (59%) isocyanate *XVb*, m.p. 254–256°C (benzene–heptane), $[\alpha]_D$ +5° (*c* 0·63). IR spectrum (tetrachloromethane): 2 240 (NCO); 1 738, 1 243, 1 029 (OAc). For $C_{34}H_{53}$. $.NO_5$ (555·8) calculated: 73·47% C, 9·61% H, 2·52% N; found: 73·86% C, 9·81% H, 2·39% N.

(20*R*)-20-Acetylamino-30-norlupane-3β,28-diyl Diacetate (*Xa*)

A solution of 800 mg (1·44 mmol) isocyanate *XVa* in 50 ml dimethylformamide was treated with 2·5 ml conc. hydrochloric acid, and the mixture was refluxed 2 h. The solution was cooled, alkalized with aqueous solution of potassium hydroxide, diluted with water, and the separated solid was collected by suction and washed with water. After drying and subsequent acetylation, the product was dissolved in a mixture of benzene and ether (1 : 1) and filtered through a silica gel layer. Yield 703 mg (85%) amide *Xa*, m.p. 313–316°C (ethyl acetate), $[\alpha]_D$ −14° (*c* 0·66). IR spectrum: 3 450, 1 668, 1 516 (NHAc); 1 726, 1 252, 1 029 (OAc). For $C_{35}H_{57}NO_5$ (571·8) calculated: 73·51% C, 10·05% H, 2·45% N; found: 73·29% C, 10·06% H, 2·38% N.

(20*S*)-20-Acetylamino-30-norlupane-3β,28-diyl Diacetate (*Xb*)

The amide *Xb* was prepared from 200 mg (0·36 mmol) isocyanate *XVb* in the same way as was the epimeric amide *Xa*. Yield 194 mg (94%) amorphous amide *Xb*, $[\alpha]_D$ +8° (*c* 0·57). IR spectrum: 3 455, 1 664, 1 518 (NHAc); 1 725, 1 257, 1 033 (OAc). For $C_{35}H_{57}NO_5$ (571·8) calculated: 73·51% C, 10·05% H, 2·45% N; found: 73·20% C, 10·08% H, 2·27% N.

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