TRITERPENES. XXXI.* ABSOLUTE CONFIGURATION AT $C_{(20)}$ IN 30-NOR-20ξ-LUPANOL DERIVATIVES

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Received February 20th, 1073

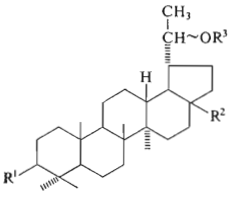
Two series of epimeric 30-nor-20ξ-lupanol derivatives differing by their adsorptivity on silica gel were internally correlated on the basis of the molecular rotation changes connected with the benzoylation of the $C_{(20)}$-hydroxy group, IR and PMR spectra. Without regard to the substitution of $C_{(19)}$ the hydroxy derivatives of the same elution order form configurationally homogeneous wholes. On the basis of the benzoate rule the more easily eluted epimeris (*a*) were assigned configuration 20*R*, while configuration 20*S* was assigned to the more strongly adsorbed epimers (*b*). The conformation of the side chain in both epimeric series are distinctly stabilised. The spectral properties (IR and PMR of hydroxy derivatives or 20-O-acyl derivatives, and CD acetates *IIab*, *XIab*) agree with the conformations close to 1*A*,*B* for the 20*R* series, or to 3*A*,*B* for the 20*S* series. At a given configuration on $C_{(20)}$ neither the substitution of the position $C_{(19)}$ by an oxygen bridge (epoxidic or lactone), nor the increase in steric interactions of the $C_{(20)}$—O ligand on acylation have a fundamental effect on conformation.

In previous communications of this series[1-3] we described several 30-nor-20ξ-lupanol derivatives prepared[2,3] mainly by reduction of 30-nor-20-lupanon derivatives with sodium boro-hydride in aqueous dioxan. The $C_{(20)}$-epimeric hydroxy derivatives formed (*IVab*, *Xab*, *XIIIab*, *XVIIIab*) could be separated by column chromatography on silica gel, and it was observed that in addition to different adsorptivity all more easily eluted epimers (*a*) and all more strongly adsorbed epimers (*b*) could be internally correlated by additional physical properties. In order to increase the number of the compared members we have completed now these series by 20ξ-hydroxy derivatives *Iab*, *IIIa*, *VIIab* the 30-norlupane skeleton of which is unmodified, and by two epimers *XVab* with a 28 → 19β-lactone ring. For the preparation of the pairs of hydroxy derivatives *IVab* and *VIIIab* the shortened procedure according to[1] was employed in this paper.

The relationships observed may be summarised as follows:

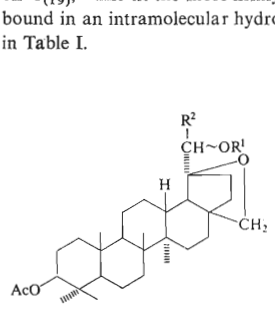
Stretching vibrations of the hydroxy group in tetrachloromethane. In hydroxy derivatives unsubstituted on $C_{(19)}$ (*Iab* *IIIa*, *IVab*, *VIIab*) all more easily eluted

* Part XXX: This Journal *38*, 3521 (1973).

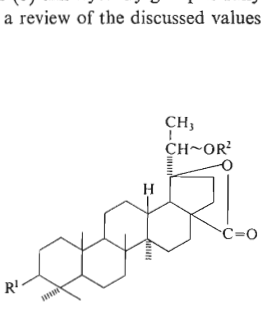


Iab; $R^1 = R^3 = H$, $R^2 = CH_3$
IIab; $R^1 = H$, $R^2 = CH_3$, $R^3 = Ac$
IIIa; $R^1 = AcO$, $R^2 = CH_3$, $R^3 = H$
IVab; $R^1 = AcO$, $R^2 = CH_2OAc$, $R^3 = H$
Vab; $R^1 = AcO$, $R^2 = CH_2OAc$, $R^3 = Ac$
VIab; $R^1 = AcO$, $R^2 = CH_2OAc$, $R^3 = Bz$
VIIab; $R^1 = AcO$, $R^2 = COOCH_3$, $R^3 = H$
VIIIab; $R^1 = AcO$, $R^2 = COOCH_3$, $R^3 = Ac$
IXab; $R^1 = AcO$, $R^2 = COOCH_3$, $R^3 = Bz$

epimers (*a*) have an asymmetric absorption band of the hydroxy group ($\alpha/\beta = 0{\cdot}63$ to $0{\cdot}66$), which was resolved by computer to two components. The main component shows a maximum at higher frequency ($3633{\cdot}7-3636{\cdot}0\ cm^{-1}$) than the minor component the frequency of which ($3622{\cdot}5-3625{\cdot}3\ cm^{-1}$) coincides with the symmetrical band of the stretching vibration of the hydroxy group of more firmly adsorbed epimers (*b*) ($3621{\cdot}9-3623{\cdot}8\ cm^{-1}$). As in the case of the more easily eluted epimers *IIIa*, *IVa* the multiplicity of the absorption band persists after deuteration ($\nu_{(OD)} = 2681\ cm^{-1}$, $\alpha/\beta = 0{\cdot}555$), it may be interpreted as an effect of the equilibrium of conformers. In 30-nor-20ξ-lupanol derivatives substituted by a 19β,28-epoxidic (*Xab*, *XIIIab*) or a 28 → 19β-lactonic (*XVab*, *XVIIIab*) substituent the more easily eluted epimers (*a*) show an equilibrium between the free 20-hydroxy group and that intramolecularly associated with the oxygen containing substituent on $C_{(19)}$, while in the more firmly adsorbed epimers (*b*) this hydroxy group is fully bound in an intramolecular hydrogen bond. This is a review of the discussed values in Table I.



Xab; $R^1 = H$, $R^2 = CH_3$
XIab; $R^1 = Ac$, $R^2 = CH_3$
XIIab; $R^1 = Bz$, $R^2 = CH_3$
XIIIab; $R^1 = H$, $R^2 = CH{=}CH{-}C_6H_5$
XIVab; $R^1 = Ac$, $R^2 = CH{=}CH{-}C_6H_5$



XVab; $R^1 = R^2 = H$
XVIab; $R^1 = H$, $R^2 = Ac$
XVIIab; $R^1 = H$, $R^2 = Bz$
XVIIIab; $R^1 = AcO$, $R^2 = H$
XIXab; $R^1 = AcO$, $R^2 = Bz$

The adsorptivity of 30-nor-20ξ-lupanol derivatives may be correlated with the chemical shifts of $C_{(20)}$ and $C_{(29)}$ protons in the PMR-spectra without regard to the substitution on $C_{(19)}$, as follows from Tables II and III. Generally it applies that in the series of more easily eluted (*a*) hydroxy derivatives, as well as their acetates and benzoates, the signals of $C_{(29)}$ protons are at a lower magnetic field, while the signals of $C_{(20)}$ protons are at higher magnetic fields than in the more firmly adsorbed (*b*) epimers.

These three criteria (*i.e.* adsorptivity, IR and PMR) show that both series form homogeneous wholes configurationally. For the determination of absolute configuration on $C_{(20)}$ we made use of the change in molecular rotation after benzoylation

TABLE I

Stretching Vibrations of the Hydroxy Group in 30-Nor-20ξ-lupanol Derivatives (CCl_4)

Less polar epimer					More polar epimer				
Compound	c, M.10^{-3} (d, cm)	ν_{OH}, cm^{-1} [a]	$\Delta\nu_{1/2}$, cm^{-1}	E	Compound	c, M.10^{-3} (d, cm)	ν_{OH}, cm^{-1}	$\Delta\nu_{1/2}$, cm^{-1}	E
Ia	2·65 (4)	3633·7 3623·5	— —	— —	*Ib*	2·77 (4)	3623·9[b]	19·0	0·4900
IIIa	3·43 (4)	3634·8 3622·5	20·3 20·0	0·6640 0·2545	*IIIb*	—	—	—	—
IVa	2·88 (4)	3634·4 3623·4	17·0 25·0	0·4528 0·2092	*IVb*	3·88 (2)	3621·9[b]	20·0	0·4300
VIIa	1·82 (4)	3636·0 3625·3	16·5 23·5	0·5786 0·2618	*VIIb*	6·27 (2)	3622·0[b]	20·0	0·6610
Xa	9·45 (1)	3628·4 3622·8 3575·7	11·0 11·6 29·0	0·2450 0·2736 0·2502	*Xb*	1·25 (4) 5·00 (1)	3588·0[b,c]	28·0	0·4200
XVa	9·85 (1)	3626·5 3619·9 3599·3	14·0 15·0 20·0	0·6425 0·1059 0·2062	*XVb*	2·34 (1)	3607·0[a] 3597·0	13·5 13·5	0·7100 0·3410

[a] On separation with Elliot 503 computer using the programme of A. Vítek (Programme FA — 520), library of the programmes of the Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague 1969. [b] Read directly from the record. [c] Recorded with UR — 20 apparatus.

of the $C_{(20)}$-hydroxy group. From Table IV it is evident that regardless of the substitution at $C_{(19)}$ benzoylation of the more easily eluted (*a*) hydroxy derivatives shifts the molecular rotation strongly to the left, while in the case of the more firmly adsorbed epimers (*b*) strongly to the right. On the basis of the benzoate rule[5] it may be

TABLE II

Chemical Shifts of 20-H and 29-H in 30-Nor-20ξ-lupanol Derivatives with the Basic Skeleton Unsubstituted at $C_{(19)}$ (p.p.m., Hz; Varian HA 100)

Less polar epimers (20β,*R*)			More polar epimers (20α,*S*)		
Compound	29-H ($J_{29,20}$)	20-H ($J_{20,19}$)	Compound	29-H ($J_{29,20}$)	20-H ($J_{20,19}$)
Ia	1·115 d (6·3)	3·99 bq (≠ 0 < 1)	*Ib*	1·085 d (6·1)	4·11 dq (4·0)
IIIa	1·115 d (6·3)	3·98 bq (≠ 0 < 1)	—	—	—
IVa	1·125 d (6·3)	3·95 bq (≠ 0 < 1)	*IVb*	1·09 d (6·3)	4·08 dq (4·2)
Va	1·165 d (6·2)	5·09 bq (≠ 0 < 2)	*Vb*	1·138 d (6·2)	5·14 dq (4·0)
VIa	1·30 d (6·5)	5·36 bq (≠ 0 < 1)	*VIb*	1·285 d (6·5)	5·425 dq (4·2)
VIIa	1·136 d (6·2)	3·895 bq (≠ 0 < 1)	*VIIb*	1·077 d (6·2)	4·033 dq (4·0)
VIIIa	1·172 d (6·3)	5·05 bq (≠ 0 < 2)	*VIIIb*	1·10 d (6·2)	5·09 dq (4·0)
IXa	1·303 d (6·3)	5·33 bq (≠ 0 < 2)	*IXb*	1·261 d (6·3)	5·40 dq (4·2)

TABLE III

Chemical Shifts of 20-H and 29-H in 30-Nor-20ξ-lupanol Derivatives with an Oxygen Containing Substituent at $C_{(19)}$ (p.p.m., Hz; Varian HA 100)

Less polar epimers (20β,*R*)			More polar epimers (20α,*S*)		
Compound	29-H ($J_{29,20}$)	20-H ($J_{20,29}$)	Compound	29-H ($J_{29,20}$)	20-H ($J_{20,29}$)
Xa	1·21 d (6·2)	4·075 bq (6·2)	*Xb*	1·15 d (6·1)	4·285 bq (6·1)
XIa	1·235 d (6·3)	5·04 bq (6·3)	*XIb*	1·227 d (6·2)	5·32 q (6·2)
XIIa	1·344 d (6·4)	5·29 q (6·4)	*XIIb*	—	—
XIIIa	6·316 dd (6·0)	4·58 d (6·0)	*XIIIb*	6·185 dd (4·5)	4·72 bd (4·5)
XIVa	6·13 dd (6·5)	5·58 d (6·5)	*XIVb*	6·14 dd (5·0)	5·90 bd (5·0)
XVa	1·325 d (6·3)	4·19 bq (6·3)	*XVb*	1·218 d (6·5)	4·29 bq (6·5)
XVIa	1·351 d (6·3)	5·075 q (6·3)	*XVIb*	1·271 d (6·45)	5·39 q (6·45)
XVIIIa	1·31 d (6·1)	4·21 bq (6·1)	*XVIIIb*	1·22 d (6·5)	4·31 bq (6·5)
XIXa	1·47 d (6·0)	5·42 q (6·0)	*XIXb*	1·41 d (6·2)	5·62 q (6·2)

TABLE IV

Changes of Molecular Rotations Connected with Benzoylation of the ($C_{(20)}$-hydroxy Group

Less polar epimer (20β,*R*)			More polar epimer (20α,*S*)		
Compound	M_D,°	ΔM_D,°	Compound	M_D,°	ΔM_D,°
IVa	− 55	−431	*IVb*	− 59	+300
VIa	−486		*VIb*	+241	
VIIa	− 68	−522	*VIIb*	− 41	+265
IXa	−590		*IXb*	+224	
Xa	+193	−211	*Xb*	+200	+190
XIIa	− 18		*XIIb*	+390	
XVa	+169	−212	*XVb*	+170	+332
XVIIa	− 43		*XVIIb*	+502	
XVIIIa	+205	−215	*XVIIIb*	+203	+314
XIXa	− 10		*XIXb*	+517	

TABLE V

Changes of Chemical Shifts of 20-H on Acylation

Configuration 20β(*R*)			Configuration 20α(*S*)		
Compound	p.p.m.	Δp.p.m.	Compound	p.p.m.	Δp.p.m.
IVa	3·95	+1·14	*IVb*	4·08	+1·06
Va	5·09		*Vb*	5·14	
VIIa	3·895		*VIIb*	4·033	
VIIIa	5·05	+1·155	*VIIIb*	5·093	+1·06
Xa	4·075	+0·965	*Xb*	4·285	+1·035
XIa	5·04		*XIb*	5·32	
XVa	4·19	+0·85	*XVb*	4·29	+1·10
XVIa	5·075		*XVIb*	5·39	
IVa	3·95	+1·41	*IVb*	4·08	+1·34
VIa	5·36		*VIb*	5·42	
VIIa	3·895	+1·44	*VIIb*	4·033	+1·37
IXa	5·335		*IXb*	5·40	
Xa	4·075	+1·215	—	—	
XIIa	5·29		—	—	
XVIIIa	4·22	+1·20	*XVIIIb*	4·31	+1·31
XIXa	5·42		*XIXb*	5·62	

inferred from this that all more easily eluted epimers (*a*) have at $C_{(20)}$ configuration β, *i.e.* 20*R*, and all more firmly adsorbed epimers (*b*) have configuration α, *i.e.* 20*S*.

This, however, means that the relative chemical shifts of $C_{(20)}$ protons are in the corresponding 20*R* and 20*S* epimers opposite from those established[6] in epimeric 17α-pregnan-20ξ-ols (4·08 p.p.m. for 20β-hydroxy derivatives and 3·80 p.p.m. for 20α-hydroxy derivatives). However, the coupling constants $J_{20,17}$ or $J_{20,19}$ in corresponding series of 17α-pregnan-20ξ-ol or 30-nor-20ξ-lupanol derivatives *Iab*, *IIIab* to *IXab* are analogous and differentiate characteristically both configurational series, 20α or 20β.

From the above it is evident that in both epimeric series certain conformations of the side chain are favorised to an appreciable extent. For these conformers those forms are most probable in which *1*. the sterically most demanded space, adjacent

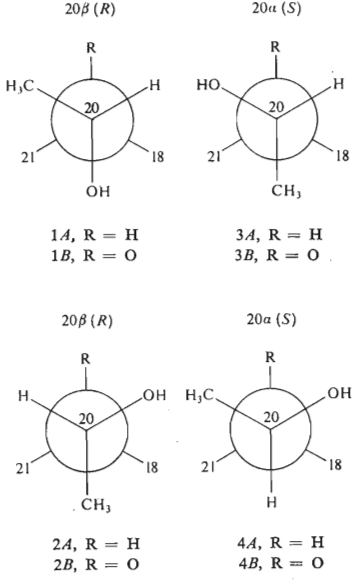


FIG. 1

Newman's Projections of the Conformations 1*A*,*B*—4*A*,*B*

to $C_{(12)}$, is occupied by a small ligand, and *2.* the $C_{(20)}$-methyl group displays the lowest interaction with its surroundings. These conformations are represented in Fig. 1 in an idealised form. Direct information on these relationships can be obtained with 30-nor-20ξ-lupanol derivatives unsubstituted on $C_{(19)}$, from coupling constants $J_{20,19}$, and with 30-nor-20ξ-lupanol derivatives substituted by an oxygen containing function in 19β, from their intramolecular hydrogen bridges.

Coupling constants $J_{20,19}$ do not change in either basic series, 20α and 20β, on different substitutions at $C_{(20)}$ (OH, $OCOCH_3$, $OCOC_6H_5$); therefore the frequencies of the conformers involved in these derivatives may be considered as identical. If the configuration is 20β (*Ia*–*IXa*), then the coupling of 20αH and 19βH is so small ($J_{20,19} \neq 0 < 1$) that it manifests itself only by the broadening of the 20αH quartet. Although this constants can represent the mean time of several conformers[7], we consider the participation of the conformers with $J_{20,19} < 1$ as unsubstantial, then the dominant conformer is characterised by the dihedral angle of 20αH and 19βH in the 80–90° (derived from the conformation 2*A* according to Fig. 1) or 260–270° range (close to conformation 1*A* according to Fig. 1); an inspection of model shows clearly that in both possibilities conformer 1*A* is preferred. This conformation is also in accordance with the transitional state preferred during dehydration, as was already described in the preceding paper[8].

The coupling constant $J_{20,19} = 4{\cdot}0$ Hz in 20α-epimers *Ib*, *IVb*–*IXc* corresponds according to the modified Karplus equation[9–11] to dihedral angles 44°, 131°, 224° and 312°. According to the models the first two values may be excluded, the remaining two values approximate to the conformers 3*A* and 4*A* represented in Fig. 1 the coupling constants of which should according to steroidal analogies[9–11] have the values 2·0 (3*A*) or 9·0 (4*A*) Hz. From the observed coupling constant, 4·0 Hz it follows that 20α-epimers *Ib*, *IVb*–*IXb* are under the given conditions in an equilibrium in which the conformer 3*A* prevails (approx. 70%).

Deductions concerning the conformation of 30-nor-20ξ-lupanol derivatives substituted on $C_{(19)}$ by an oxygen containing residue (*Xab*–*XIXab*) should be limited to an evaluation based on the extent of the measurements of the intramolecular hydrogen bridges carried out. From Table I it is evident that the 20*R* configuration is not advantageous for a synclinal conformation of the 20-hydroxy group with respect to the 19β oxygenated substituent, as shown in Fig. 1, 2*B*. Therefore in the equilibrium state of the conformers 19β,28-epoxide *Xa* and 28 → 19β-lactone *XVa* only a minor part contains an intramolecular hydrogen bond, while the major part remains in the conformation with a non-associated hydroxy group, *i.e.* in the conformation close to 1*B*. Its energy preference is therefore higher than the energy gain of the intramolecular hydrogen bond. In contrast to this the 20*S* epimers in both considered conformers 3*B* or 4*B* may form intramolecular hydrogen bonds. In agreement with this (Table I) both the epoxy derivative *Xb* and the lactone *XVb* display only an intramolecularly associated hydroxyl the absorption band of which

is in the case of the epoxide *Xb* symmetrical, but in the case of the lactone *XVb* it shows a mild deformation; the separation of this band afforded two independent bands, close to each other by their frequency, but differing in intensity.

These qualitative inferences show that at a given configuration on $C_{(20)}$ substantial differences between the preferred conformers do not exist, irrelevant of whether the position $C_{(19)}$ is unsubstituted or substituted by an oxygen bridge. Also, it is evident from the models that by the connection of the position $C_{(28)}$ and $C_{(19)}$ by an epoxide (*Xab–XIVab*) or lactone (*XVab–XIXab*) bridge the $C_{(18)}\alpha$-envelope conformation of the ring E is stabilised, which "elevates" the side chain and changes its interaction with the closest deployed skeletel positions; evidently, these changes

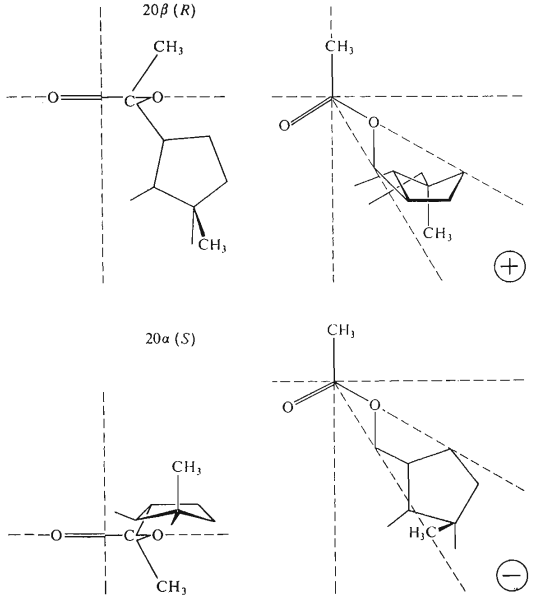


FIG. 2
Sector Diagrams of Acetates *IIa,b*

are not decisive for the preference of other conformations. Further we consider that the conformations 1*A*,*B* or 3*A*,*B* are not affected by the increase in steric interactions of the oxygenated substituent at $C_{(20)}$ on acylation either: according to the changes of the chemical shift of $C_{(20)}$—H (Table V) it is evident that in the 20α series these changes are almost constant, for the given 20-O-acyl derivatives, whether the position $C_{(19)}$ is unsubstituted (*IVb*, *VIIb*) or substituted (*Xb*, *XVb*). In the 20β series, however, the change in the chemical shift of 20α-H of 19β-substituted derivatives (*Xa*, *XVa*) is substantially smaller than in the unsubstituted derivatives (*IVa*, *VIIa*). Therefore, in 20β-hydroxy derivatives substituted in $C_{(19)}$ acylation must bring about the twisting of the ester bond $C_{(20)}$—O (in agreement with the model of con-

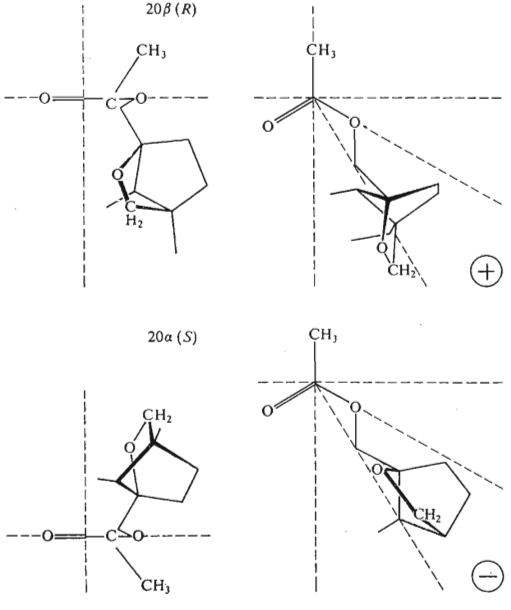


FIG. 3
Sector Diagrams of Acetates *XIa*,*p*

former 1*B* according to Fig. 1), because the steric hindrance of $C_{(12)}$ does not permit a synperiplanar arrangement of the acetate carbonyl and $C_{(20\alpha)}$—H when the conformation of the $C_{(19)}-C_{(20)}$ bond is unchanged.

In order to check this assumption further we investigated the Cotton effect of the pairs of epimeric acetates *IIab* and *XIab*. According to their circular dichroism (cyclohexane, 20°C) the 20β-epimers *IIa* and *XIa* have a positive Cotton effect (λ_{max} 215·5 nm, $\Delta\varepsilon = +0{\cdot}65$, or λ_{max} 215 nm, $\Delta\varepsilon = +0{\cdot}38$, resp.), while the 20α-epimers *IIb* and *XIb* under the same conditions differ both in the sign of the Cotton effect and in the intensity of the dichroic absorption (λ_{max} 217 nm, $\Delta\varepsilon = +0{\cdot}12$, or λ_{max} 216 nm, $\Delta\varepsilon = -1{\cdot}36$, resp.). At their given configuration at $C_{(20)}$ the sign of the Cotton effect ascertained corresponds to the sector diagrams[12,13] according to Fig. 2 for compounds *IIab* with a basic skeleton, or, according to Fig. 3 for the derivatives *XIab* with an epoxide cycle. When this is expressed in Newman projection, conformations 1*A*,*B* or 3*A*,*B*, resp. are again obtained. This means that the lower intensity of the dichroic absorption in the 20β-acetate *XIa* is a consequence of the decreased population of the form in which the ester group is synperiplanar with 20α-H; in the 20α-acetate *XIb* the more distinct Cotton effect is due to the protruding of the $C_{(19)}$—O into the negative sector. The skeletal residue (in *IIb*) is near the nodal plane and the dichroic absorption is minimal.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are uncorrected. Optical rotations were measured in chloroform on a polarimeter ETL-NPL (Bendix-Ericsson) with an objective indication and a ±2° accuracy. The infrared spectra were measured in chloroform using a UR-20 spectrophotometer, the frequencies of the stretching vibrations of the hydroxy group were determined with a Unicam SP-700 apparatus in tetrachloromethane. The PMR were taken on a Varian HA 100 (100 MHz) apparatus in deuteriochloroform with tetramethylsilane as internal standard. Circular dichroism was recorded with a Roussel-Jouan 185 dichrograph in cyclohexane. For acetylations acetic anhydride in pyridine (1 : 2) was used at room temperature. The benzoates were obtained on reaction with benzoyl chloride in pyridine (1 : 5), at 20°C, for 24 hours. The reaction mixtures after acylations were worked up in the following manner: Excess reagent was decomposed with water and the products were extracted with ether. For the washing of the ethereal extract 5% $NaHCO_3$ solution was employed, followed by dilute (1 : 5) hydrochloric acid. The extract was dried over sodium sulfate. After evaporation of the solvent the samples were either crystallised directly from chloroform–methanol or chloroform–n-heptane, or the residue was transferred into benzene and filtered through a column of silica gel before crystallisation. Chromatographic separations were carried out on a column of neutral silica gel according to Pitra (sorted by sedimentation, dried at 120°C, particle size 30—60 μ, Service Laboratory, Czechoslovak Academy of Sciences, Lysolaje near Prague). Purity of the samples was controlled by thin-layer chromatography on silica gel according to Stahl (Spolana, Neratovice). Samples for analysis and spectral measurements were dried over phosphorus pentoxide at 100°C and 0·1 Torr for 8—12 hours.

30-Nor-20ξ-lupanols (*Iab*)

On reduction of 30-nor-20-lupanone (120 mg) using a procedure according to[2] and repeated chromatography the following derivatives were prepared: (20*R*)-isomer *Ia* (60 mg) of m.p. 162–164°C, $[\alpha]_D$ −10° (*c* 0·60). PMR spectrum: 0·765 (CH_3), 0·80 (CH_3), 0·845 (2 × CH_3), 0·955 (CH_3), 1·045 (CH_3), 1·115 d, $J_{29,20}$ = 6·3 Hz ($C_{(20)}$—CH_3), 3·99 bq, $J_{20,29}$ = 6·3, $J_{20,19} \neq 0 < 1$ Hz (20-H) p.p.m.. *Ia* gave acetate *IIa* (23·6 mg) of p.m. 166–168°C and $[\alpha]_D$ −15° (*c* 0·534). Jones and Meakins[14] give for hydroxy derivative m.p. 160°C, for the acetate m.p. 166–167°C, $[\alpha]_D$ −22°. IR spectrum of *IIa*: 1732, 1268 (CH_3COO) cm^{-1}; CD (cyclohexane, *c* 0·08, λ_{max} in nm ($\Delta\varepsilon$): 215·5 (+0·65). For $C_{31}H_{52}O_2$ (456·7) calculated: 81·52% C, 11·48% H; found: 81·35% C, 11·38% H.

(20 *S*)-isomer *Ib* (20 mg) amorphous. PMR spectrum: 0·71 (CH_3), 0·785 (CH_3), 0·845 (2 × × CH_3), 0·91 (CH_3), 1·045 (CH_3), 1·085 d, $J_{29,20}$ = 6·1 Hz ($C_{(20)}$—CH_3), 4·11 dq, $J_{20,29}$ = = 6·1, $J_{20,19}$ = 4·0 Hz (20-H) p.p.m.. For acetate *IIb* (8·7 mg) the following data were found: m.p. 182–185°C, $[\alpha]_D$ 0° to +3° (*c* 0·33). IR spectrum: 1725, 1265 (CH_3COO) cm^{-1}. CD (cyclohexane, *c* 0·075, λ_{max} in nm ($\Delta\varepsilon$): 217 (+0·122).

3β-Acetoxy-30-nor-(20*R*)-lupanol (*IIIa*)

The preparation (90 mg) of m.p. 293–294°C was obtained by chromatography of the reaction mixture (320 mg) according to[2]. IR spectrum: 3635 (OH), 1728, 1258 (CH_3COO) cm^{-1}. PMR spectrum: 0·76 (CH_3), 0·845 (2 × CH_3), 0·865 (CH_3), 0·925 (CH_3), 1·045 (CH_3), 1·115 d, $J_{29,20}$ = 6·3 Hz ($C_{(20)}$—CH_3), 2·02 s (CH_3COO), 3·98 bq, $J_{20,29}$ = 6·3, $J_{20,19} \neq 0 < 1$ (20-H), 4·49 m (3 αH) p.p.m.

3β,28-Diacetoxy-30-nor-20ξ-lupanols (*IVab*)

Using the procedure according to[1] the prepared hydroxy derivatives had the following constants:

The more easily eluted (20*R*)-epimer *IVa* had m.p. 232–234°C, $[\alpha]_D$ −10° (*c* 0·68) (lit.[1] m.p. 229–231·5°C, $[\alpha]_D$ −11°). PMR spectrum: 0·87 bs (3 × CH_3), 0·975 (CH_3), 1·05 (CH_3), 1·125 d, $J_{29,20}$ = 6,3 Hz ($C_{(20)}$—CH_3), 2·03 s and 2·05 s (2x CH_2COO), 3·79 d + 4·25 d, J = 11 Hz (28-H_2), 3·955 bq, $J_{20,29}$ = 6·3, $J_{20,19} \neq 0 < 1$ Hz (20-H) p.p.m. For $C_{33}H_{54}O_5$ (530,7) calculated: 74,67% C, 10,26% H; found: 74,50% C, 10,40% H. 20-O-*Acetylderivative* Va of m.p. 190–193°C, $[\alpha]_D$ −19° (*c* 0,51). PMR spectrum: 0·841 bs (3x CH_3), 0·872 (CH_3), 1·037 (CH_3), 1·165 d, $J_{29,20}$ = 6,2 Hz ($C_{(20)}$—CH_3), 2·025 s, 2·04 s, 2·05 s (3x CH_3COO), 3·77 d + 4·23 d, J = 11 Hz, 4·48 m (3α H), 5·09 bq, $J_{20,29}$ = 6,2, $J_{20,19} \neq 0 < 2$ Hz (20-H) p.p.m. For $C_{35}H_{56}O_6$ (572,8) calculated: 73·38% C, 9·85% H; found: 73,33% C, 9·62% H. 20-O-*Benzoyl derivative* VIa $[\alpha]_D$ −77° (*c* 0,65). IR spectrum: 1725, 1280–1255 (CH_3COO and C_6H_5COO), 1025, 978 (CH_3COO), 1610, 1590, 1115 (C_6H_5COO), cm^{-1}. PMR spectrum: 0·765 (CH_3), 0·825 (2x CH_3), 0·855 (CH_3), 1·035 (CH_3), 1·30 d, $J_{29,20}$ = 6,5 Hz ($C_{(20)}$—CH_3), 2·02 s and 2·06 s (2x CH_3COO), 2·25 m (19β H), 3·815 d + 4·265 d, J = 11 Hz (28-H_2), 4·46 m (3α H), 5·36 bq, $J_{20,29}$ = 6·3, $J_{20,19} \neq 0 < 1$ Hz (20-H), 7·35– 7·65 m (3 H), 7·95 – 8,12 m (2 H) (C_6H_5) p.p.m. *VIa* would not crystallise.

The less easily eluted (20*S*)-epimer *IVb* had m.p. 253·5–256° C, $[\alpha]_D$ −11° (*c* 0·54) (lit.[1] m.p. 252–254°C, $[\alpha]_D$ −11°). PMR spectrum: 0·835 – 0·855 (2x CH_3), 0·865 (CH_3), 0·925 (CH_3), 1·05 (CH_3), 1·09 d, $J_{29,20}$ = 6,3 Hz ($C_{(20)}$—CH_3), 2·03 s, 2·05 s (2x CH_3COO), 3·79 d + 4·29 d, J = 11 Hz (28-H_2), 4·085 dq, $J_{20,29}$ = 6·4, $J_{20,19}$ = 4·2 Hz (20-H) p.p.m. For $C_{33}H_{54}O_5$ (530·7) calculated: 74·67% C, 10·26% H; found: 74·57% C, 10·27% H. 20-O-*Acetyl derivative Vb*,

m.p. 186—188°C, $[\alpha]_D$ +6·6° (*c* 0·30). PMR spectrum: 0·844 (2x CH_3), 0·86 (CH_3), 0·925 (CH_3), 1·037 (CH_3), 1·138 d, $J_{29,20}$ = 6,2 Hz ($C_{(20)}$—CH_3), 1·975 s, 2·025 s, 2·04 s (3x CH_3COO), 3·795 d +4·235 bd, J = 11 Hz (28-H_2), 4·48 m (3α H), 5·14 dq, $J_{20,29}$ = 6·2, $J_{20,19}$ = 4·0 Hz (20-H) p.p.m.. For $C_{35}H_{56}O_6$ (572·8) calculated: 73·38% C, 9·85% H; found: 73·22% C, 9·76% H. 20-O-*Benzoyl derivative* VIb: m.p. 210—213°C, $[\alpha]_D$ +38° (*c* 0·63). IR spectrum: 1725, 1255, 1025 (CH_3COO), 1725, 1610, 1590, 1282, 1120 (C_6H_5COO) cm^{-1}. PMR spectrum: 0·85 (2x CH_3), 0·87 (CH_3), 0·96 (CH_3), 1·05 (CH_3), 1·285 d, $J_{29,20}$ = 6,6 Hz, ($C_{(20)}$—CH_3), 2·03 s (2x CH_3COO), ~2·30 m (19β H), 3·815 d + 4·265 d, J = 11 Hz (28-H_2), 4·50 m (3α H), 5·425 d, $J_{20,29}$ = 6·4, $J_{20,19}$ = 4·2 Hz (20-H), 7·30 — 7·60 m (3 H) and 7·93 — 8·06 m (2 H) (C_6H_5) p.p.m. For $C_{40}H_{58}O_6$ (634·8) calculated. 75·67% C, 9·21% H; found: 75·58% C, 9·34% H.

Methyl Esters of 3β-Acetoxy-30-nor-20ξ-hydroxylupan-28-oic Acid (*VIIab*)

On reaction of methyl ester of acetylbetulinic acid (3 g) according to[1] a mixture of epimeric noralcohols *VIIab* was obtained which was further separated by repeated chromatography on alumina and silica gel. From the faster moving fractions on triple crystallisation from n-heptane 152 mg of (20*R*)-hydroxy derivative *VIIa* were obtained, m.p. 268—270°C, $[\alpha]_D$ −13° (*c* 0·60). IR spectrum: 3618 (OH), 1725, 1260, 1030 (CH_3COO), 1725, 1438, 1190, 1170, 1160, 1139 ($COOCH_3$) cm^{-1}. PMR spectrum: 0·842 bs (3x CH_3), 0·914 (CH_3), 0·965 (CH_3), 1·136 d, $J_{29,20}$ = 6·2 Hz ($C_{(20)}$—CH_3), 2·025 (CH_3COO), 3·65 ($COOCH_3$), 3·895 bq, $J_{20,29}$ = 6·2, $J_{20,19} \neq 0 < 1$ (20-H), 4·48 m (3α H) p.p.m. For $C_{32}H_{52}O_5$ (516·7) calculated: 74·37% C 10·14% H, found: 74·21% C. 9·92% H. Noralcohol *VIIa* gave 20-O-*acetyl derivative VIIIa* of m.p. 216—219°C $[\alpha]_D$ −24° (*c* 0,38). PMR spectrum: 0·836 bs (3x CH_3), 0·862 (CH_3), 0·892 (CH_3), 1·172 d, $J_{29,20}$ = 6,3 Hz ($C_{(20)}$—CH_3), 2·025 s (2x CH_3COO), 3·65 s ($COOCH_3$), 4·48 m (3α H), 5·05 bq, $J_{20,29}$ = 6·3, $J_{20,19} \neq 0 < 2$ Hz (20-H) p.p.m. For $C_{34}H_{54}O_6$ (558·8) calculated: 73·08% C, 9·74% H; found: 73·26% C, 9·88% H. 20-O-*Benzoyl derivative* IXa (amorphous) $[\alpha]_D$ −94° (*c* 0·61). PMR spectrum: 0·765 (CH_3), 0·82 (2x CH_3), 0·845 (CH_3), 0·893 (CH_3), 1·303 d, $J_{29,20}$ = 6·3 Hz ($C_{(20)}$—CH_3), 2·02 s (CH_3COO), 3·67 s ($COOCH_3$), 4·45 m (3α H), 5·335 bq, $J_{20,29}$ = 6·3, $J_{20,19} \neq 0 < 2$ Hz (20-H), 7·30 — 7·60 m (3 H) and 7·90 — 8·10 m (2 H) (C_6H_5) p.p.m. For $C_{39}H_{56}O_6$ (620·85) calculated: 75·44% C, 9·09% H; found: 75·63% C, 9·29% H. On sixfold crystallisation of the more firmly bound epimer *VIIb* from hexane 170 mg of analytical sample were obtained m.p. 184—185°C, $[\alpha]_D$ −8° (*c* 0·63). IR spectrum: 3610, (OH), 1720, 1257, 1030 (CH_3COO), 1720, 1435, 1191, 1169, 1158, 1138 ($COOCH_3$) cm^{-1}. PMR spectrum: 0·841 (2x CH_3), 0·858 (CH_3), 0·915 (2x CH_3), 1·077 d, $J_{29,20}$ = 6·2 Hz ($C_{(20)}$—CH_3), 2·02 s (CH_3COO), ~2·55 m (19β H), 3·65 s ($COOCH_3$), 4·033 dq, $J_{20,29}$ = 6,2, $J_{20,19}$ = 4·0 Hz (20-H), 4·48 m (2α H) p.p.m.. For $C_{32}H_{52}O_5$ (516·7) calculated: 74·37% C, 10·14% H; found: 73·81% C, 10·11% H. 20-O-Acetyl derivative *VIIIb*: m.p. 184—188°C, $[\alpha]_D$ −0·5° (0·76). PMR spectrum: 0·829 (2x CH_3), 0·842 (CH_3), 0·893 (CH_3), 0·906 (CH_3), 1·109 d, $J_{29,20}$ = 6·2 Hz ($C_{(20)}$—CH_3), 1·955 s, 2·01 s (2x CH_3COO), ~2·60 m (19β H), 3·63 s ($COOCH_3$), 4·47 m (3α H), 5·093 dq, J_{20^*29} = 6·2, $J_{20,19}$ = 4·0 Hz (20-H) p.p.m. For $C_{34}H_{54}O_6$ (558·8) calculated: 73·08% C, 9·74% H; found: 73·59% C, 9·97% H. 20-O-*Benzoyl derivative* IXb had m.p. 198—201°C, $[\alpha]_D$ +36° (*c* 0,73). PMR spectrum: 0·85 bs (3x CH_3), 0·91 (CH_3), 0·942 (CH_3), 1·261 d, $J_{29,20}$ = 6·2 Hz ($C_{(20)}$—CH_3), 2·03 s (CH_3COO), ~2·75 m (19β H), 3·64 ($COOCH_3$), 4·48 m (3α H), 5·40 dq, $J_{20,29}$ = 6·2, $J_{20,19}$ = 4·2 Hz (20-H), 7·35—7·55 m (3 H) and 7·90 — — 8·10 m (2 H) (C_6H_5) p.p.m. For $C_{39}H_{56}O_6$ (620·8) calculated: 75·44% C, 9·09% H; found: 75·39% C, 9·23% H.

3β,(20*R*)-Diacetoxy-19β,28-epoxy-30-norlupane (*XIa*)

Acetate *XIa*, described in the preceding communication[2], gave the following PMR spectrum: 0·84 (2x CH_3), 0·855 (CH_3), 0·91 (CH_3), 0·995 (CH_3), 1·235 d, $J_{29,20}$ = 6·3 Hz ($C_{(20)}$—CH_3), 2·015 s, 2·03 (2x CH_3COO), 3·32 d + 3·96 bd, J = 7 Hz (28-H_2), 4·49 m (3α H), 5·04 q, $J_{20,29}$ = = 6·3 Hz (20-H) p.p.m. CD (cyclohexane, *c* 0·08, λ_{max} in nm (Δε)): 215 (+0·382).

3β,(20*S*)-Diacetoxy-19β,28-epoxy-30-norlupane (*XIb*)

The analytical sample of the acetate *XIb* had m.p. 271—272°C, $[\alpha]_D$ +40° (*c* 0·855). PMR spectrum: 0·845 (2x CH_3), 0·876 (CH_3), 0·909 (CH_3), 1·009 (CH_3), 1·227 d, $J_{29,20}$ = 6·2 Hz ($C_{(20}$— —CH_3), 2·03 s (2x CH_3COO), 3·34 + 3·98 d, J = 7 Hz (28-H_2), 4·48 m (3α H), 5·32 q, J = 6·2 Hz (20-H) p.p.m. CD (cyclohexane, *c* 0·08, λ_{max} in nm (Δε)): 216 (—1·363).

3β-Acetoxy-(20*R*)-benzoyloxy-19β,28-epoxy-30-norlupane (*XIIa*)

For benzoate[2] *XIIa* the following PMR spectrum was measured: 0·808 (2x CH_3), 0·831 (CH_3), 0·861 (CH_3), 0·991 (CH_3), 1·344 d, $J_{29,20}$ = 6·4 Hz ($C_{(20)}$—CH_3), 2·00 s (CH_3COO), 3·34 d + + 3·97 bd, J = 7 Hz (28-H_2), 4·41 m (3α H), 5·29 q, $J_{20,29}$ = 6·4 Hz (20-H), 7·35 — 7·58 m (3 H) and 7·90 — 8·05 m (2 H) (C_6H_5) p.p.m. For $C_{38}H_{54}O_5$ (590·8) calculated: 77·25% C, 9·21% H; found: 77·41% C, 9·38% H.

20ξ-Hydroxy-30-norlupan-28 → 19β-olides (*XVab*)

A mixture of hydroxy derivatives *XVab* (356 mg), obtained analogously as in [2,3], was separated chromatographically. The faster moving (20*R*)-epimer *XVa* (149·6 mg) was crystallised four times to give 103·5 mg of product of m.p. 315—318°C, $[\alpha]_D$ +38° (*c* 0·63). IR spectrum: 3625 (OH), 1778, 1185, 1140 (γ-lactone) cm^{-1}. PMR spectrum: 0·800 (CH_3), 0·848 (2x CH_3), 0·909 (CH_3), 0·954 (CH_3), 1·325 d, $J_{29,20}$ = 6·3 Hz ($C_{(20)}$—CH_3), 4·19 dq, $J_{20,29}$ = 6·3, $J_{20,OH}$ ≠ ≠ 0 Hz (20-H) p.p.m. For $C_{29}H_{46}O_3$ (442·7) calculated: 78·68% C, 10·47% H; found: 78·43% C, 10·35% H. *Acetate* XVIa: m.p. 260—262·5°C, $[\alpha]_D$ +30° (*c* 0·56). IR spectrum: 1782, 1185, 1140 (γ-lactone), 1745, 1255 (CH_3COO) cm^{-1}. PMR spectrum: 0·790 (CH_3), 0·826 (CH_3), 0·838 (CH_3), 0·884 (CH_3), 0·934 (CH_3), 1·351 d, $J_{29,20}$ = 6·3 Hz ($C_{(20)}$—CH_3), 2·02 s (CH_3COO), 5·075 q, $J_{20,29}$ = 6·3 Hz (20-H) p.p.m. For $C_{31}H_{48}O_4$ (484·7) calculated: 76·81% C, 9·98% H; found: 76·64% C, 9·61% H. *Benzoate* XVIIa had m.p. 266—268°C, $[\alpha]_D$ —8° (*c* 0·625). IR spectrum: 1784, 1182, 1140 (γ-lactone), 1728, 1610, 1590, 1278, 1120 (C_6H_5COO) cm^{-1}. For $C_{36}H_{50}O_4$ (546·8) calculated: 79·08% C, 9·22% H; found: 78·89% C, 9·06% H.

The less easily eluted (20*S*)-epimer *XVb* (184 mg) had m.p. 286—288°C, $[\alpha]_D$ +38° (*c* 0·73). IR spectrum: 3605 (OH), 1778, 1183, 1140 (γ-lactone) cm^{-1}. PMR spectrum: 0·794 (CH_3), 0·841 (2x CH_3), 0·884 (CH_3), 0·945 (CH_3), 1·218 d, $J_{29,20}$ = 6·5 Hz ($C_{(20)}$—CH_3), 4·29 bq, $J_{20,29}$ = 6·5 Hz (20-H) p.p.m. For $C_{29}H_{46}O_3$ (442·7) calculated: 78·68% C, 10·47% H; found: 78·44% C, 10·19% H. *Acetate* XVIb had b.z. 320—321°C, $[\alpha]_D$ +40° (*c* 0·55). IR spectrum: 1780, 1185, 1158, 1144 (γ-lactone), 1740, 1258 (CH_3COO) cm^{-1}. PMR spectrum: 0·795 (CH_3), 0·841 (2x CH_3), 0·883 (CH_3), 0·945 (CH_3), 1·271 d, $J_{29,20}$ = 6·45 Hz ($C_{(20}$—CH_3), 2·03 s (CH_3COO), 5·39 q, $J_{20,29}$ = 6·45 Hz (20-H) p.p.m. For $C_{31}H_{48}O_4$ (484·7) calculated: 76·81% C, 9·98% H; found: 76·68% C, 9·61% H. *Benzoate* XVIIb: m.p. 324—325°C, $[\alpha]_D$ +92° (*c* 0,48). IR spectrum: 1781, 1182, 1159, 1145 (γ-lactone), 1735, 1610, 1595, 1280, 1120 (C_6H_5COO) cm^{-1}. For $C_{36}H_{50}O_4$ (546·8) calculated: 79·08% C, 9·22% H; found: 79·10% C, 9·03% H.

3β-Acetoxy-(20*R*)-benzoyloxy-30-norlupan-28 → 19β-olide (*XIXa*)

M.p. 256–258°C, $[\alpha]_D$ −2° (*c* 0,46). IR spectrum: 1780, 1178, 1152, 1135 (γ-lactone), 1726, 1608, 1590, 1270 (C_6H_5COO), 1726, 1260, 1035 (CH_3COO) cm^{-1}. PMR spectrum: 0·817 (2x CH_3), 0·835 (2x CH_3), 0·940 (CH_3), 1·47 d, $J_{29,20}$ = 6·0 Hz ($C_{(20)}$—CH_3), 2·00 s (CH_3COO) 4·43 m (3α H), 5·42 q, $J_{20,29}$ = 6·0 Hz (20-H), ~7·30 — 7·60 m (3 H) and ~7·90 — 8·10 m (2 H) (C_6H_5) p.p.m. For $C_{38}H_{52}O_6$ (604·8) calculated: 75·46% C, 8·67% H; found: 75·44% C, 8·70% H.

3β-Acetoxy-(20*S*)-benzoyloxy-30-norlupan-28 → 19β-olide (*XIXb*)

M.p. 290–291°C, $[\alpha]_D$ +86° (*c* 0·69). IR spectrum: 1782, 1180, 1156, 1140 (γ-lactone), 1730, 1612, 1595, 1275 (C_6H_5COO), 1730, 1258, 1030 (CH_3COO) cm^{-1}. PMR spectrum: 0·833 bs (3x CH_3), 0·885 (CH_3), 0·934 (CH_3), 1·41 d, $J_{29,20}$ = 6·2 Hz ($C_{(20)}$—CH_3), 2·02 s (CH_3COO), 4·47 m (3α H), 5·62 q, $J_{20,29}$ = 6·2 Hz (20-H), 7·30 — 7·65 m (3 H) and 7·95 — 8·15 m (2 H) (C_6H_5) p.p.m. For $C_{38}H_{52}O_6$ (604·8) calculated: 75·46% C, 8·67% H; found: 75·98% C, 8·84% H.

For elemental analyses we thank Mrs H. Rusová, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague, and the staff of the Analytical Laboratory Department of Chemistry, Charles University, Prague. For the infrared spectra measurements our thanks due to Dr J. Pecka and Dr S. Hilgard of the same Department, for PMR spectra we thank Dr M. Buděšínský and for the CD spectra Dr I. Frič, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague.

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Translated by Ž. Procházka.