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INVESTIGATION ON THE CHEMISTRY OF BERBANS—VII[1]

SYNTHESIS OF 10,11-DIMETHOXY(DEPYRROLO)RAUNESCINE STEREOISOMERS

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Abstract—Acyloxy-ketone rearrangement, proceeding by the action of base, has been observed in the case of ketone **2**. By the reduction of ketones **2** and **3** with sodium boron hydride, new 10,11-dimethoxy(depyrrolo)raunescine stereoisomers (**5a–7a**) have been prepared. Previously known alcohols with alloberban skeleton (**12, 13**) have been similarly converted into tetracyclic raunescine stereoisomers (**8a, 9**) by the oxido-reductive method. The stereochemistry of these compounds has been investigated by physical (^{1}H NMR, IR) and by chemical methods.

Raunescine[2] isolated from the plant *Rauwolfia canescens*, has a sedative and blood pressure lowering action similar to that of reserpine. The structure of the substance has been elucidated by Huebner and Schlittler[3] but it has not yet been synthesized.

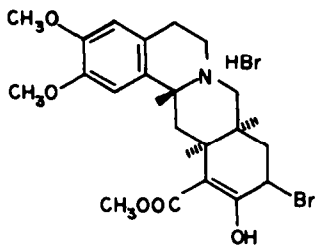
After the successful synthesis of 10-methoxy(depyrrolo)-reserpine[1] we set ourself the aim of synthesizing 10,11-dimethoxy(depyrrolo)raunescine and its stereoisomers utilizing the principle of linear approximation. This method permits the preparation of derivatives with different steric positions in the D-ring, the investigation of their physical and chemical properties and their pharmacological action.

A. *Preparation of ketones with* epi-allo*berban skeleton* (**2, 3a**) *and proof of their structure*

Following the method developed by us[6] when the bromo-ketoester[4,5] **1** in abs dimethyl formamide was treated with the potassium salt of 3,4,5-trimethoxy benzoic acid, the mixture of the tautomeric forms **2A–B** has been obtained in a good yield. On recrystallization of the substance obtained from methanol the **2A** keto-form separates from the solution at room temperature, so that the equilibrium can gradually be shifted in the direction of this form, after 1 h to about 50%, and after 2 h to about 80%.

The IR spectrum of the solid ketone **2A**, (1750, 1730, 1710 cm^{-1}) indicates a non-enolic structure and a strong Bohlmann band system,[7] (2800–2750 cm^{-1}) indicative of the *trans* junction of rings B/C, can be observed in the spectrum. The IR spectrum of **2B**, precipitated after methanolic recrystallization with water from the mother liquor (1730, 1660, 1620 cm^{-1}), indicates an enolized structure. The ^{1}H NMR spectra of the crystalline ketone **2A** and of the raw enolic form **2B** are identical.

The coupling constants of 15-H (Table 1) show the presence of equatorial 15-acyloxy group. From the structure of alcohols **5a** and **7a**, obtained by the reduction of ketone **2A**, conclusions can be drawn on the steric position of the 13-methoxy carbonyl group (see Section C).



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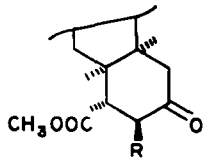
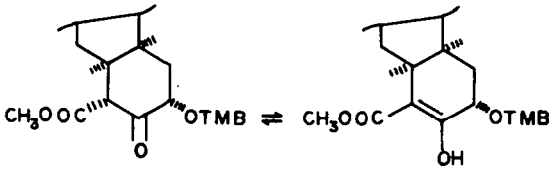
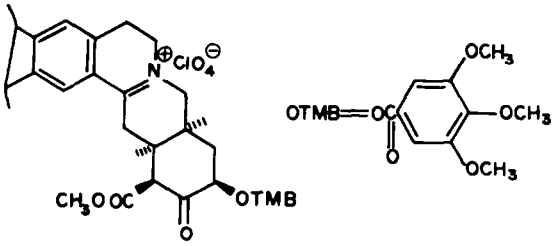


3 R
a OTMB
b H



2A **2B**



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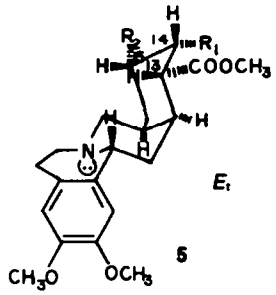
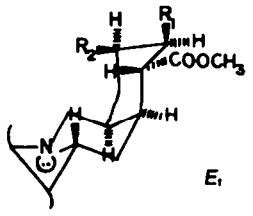


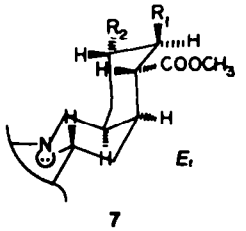
5

	R_1	R_2
a	OH	OTMB
b	OTMB	OH
c	OH	OH
d	$OCOCH_3$	OTMB



6

	R_1	R_2
a	OH	OTMB
b	OTMB	OH
c	OH	OH
d	OTMB	$OCOCH_3$
e	$OCOCH_3$	OTMB



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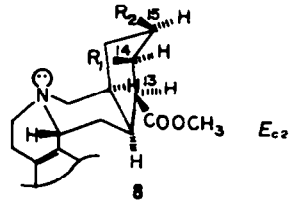
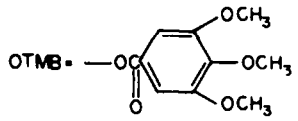
	R_1	R_2
a	OH	OTMB
b	OTMB	OH
c	OH	OH
d	Cl	OTMB
e	OCHO	OTMB



8

	R_1	R_2
a	OH	OTMB
b	$OCOCH_3$	OTMB



Williamson[8a] found in the exchange of the halogen atom of α-bromo ketone with a steroid skeleton for potassium acetate in hot acetone in the presence of tetramethyl ammonium acetate that the acyloxy and the keto functions may be exchanged. Other authors[8b-e] report on the acyloxy-ketone rearrangement of α-acetoxy ketones with the steroid skeleton, occurring on active aluminum oxide.

A similar reaction has been observed by us in the case of ketone **2A**. When compound **2A** was heated in dimethyl formamide in the presence of potassium 3,4,5-trimethoxy benzoate and diethyl amine to 100°C, the 3,4,5-trimethoxybenzoyl group migrated from 15-C to 14-C while a ketone function was formed at 15-C (**3a**).

Ketone **3a** is also obtained when bromo ketoester **1** is reacted in dimethyl formamide with potassium 3,4,5-trimethoxy benzoate in the presence of diethylamine. In contrast to ketone **2A**, compound **3a** does not give an enol reaction with Fe^{III} chloride. In the ^1H NMR spectrum of **3a** the 1-H signal appears at a value lower than δ 3.9 ppm and its IR spectrum contains a stronger Bohlmann band system. All this data proves the *epi-allo-trans* (E_t) conformation of the ring system. In the ^1H NMR spectrum of ketone **3a** the coupling constant of 14-H (Table 1) makes the diequatorial position of substituents 13 and 14 very similar.[10,11] The stereochemistry of ketone **3a** is also proved by the structure of alcohols **6b**, **7b** obtained from it by reduction (Section C).

For the verification of the position of the 3,4,5-trimethoxybenzoyloxy group in molecules **2A** and **3a**, the method of Bridgeman[12] has been used involving the reduction of ketone **2A** with activated zinc dust in hot acetic acid to give 7,8-dimethoxy-14-oxo-*epi-allo*berban-13-carboxilic acid methyl ester[4] of known structure. Ketone **3a** gave under similar conditions compound **3b**. The two isolated carbonyl bands appearing at 1710 and 1730 cm^{-1} in the IR spectrum of ketone **3b**, support the mass spectrum and the ^1H NMR spectrum of the substance and unequivocally prove the structure of the compound.

The structure of ketone **2A** has also been proved by boiling 7,8-dimethoxy-15-(3',4',5'-trimethoxybenzoyloxy)-14-oxo-*allo*berban-13-carboxilic acid methyl ester[6] of known structure, in glacial acetic acid with Hg^{II} acetate, and subsequently converting it into the immonium salt **4** by treatment with perchloric acid. The immonium salt **4**, on reduction with zinc/hydrochloric acid in acetone gave, in addition to the initial ketone of *allo*berban skeleton, a substance having from every aspect, the same properties as ketone **2** of *epi-allo*berban skeleton.[13a-c] The substituent at position 15 of the ketone with *allo*berban skeleton[6] is in the β-equatorial position, and in ketone **2** of *epi-allo*berban skeleton, obtained from it by oxido-reduction, this substituent is in the α-equatorial position, thus, during the reaction 15-C is simultaneously epimerized. The conversion of the axial 15-acyloxy group into the thermodynamically more stable isomer of equatorial position has already been observed.[6]

During the development of the enolic form, the 13-

Table 1. Data of ^{1}H-NMR[a], configuration and conformation of compounds 2A, 3a, 5a–d, 6a–e, 7a–d, 8a–b, 9, 10 and 16

Compound	14-H[a] $J_{13,14}$[b] $J_{14,15}$[b]	15-H[a] $J_{15,16ax}$[b] $J_{15,16eky}$[b]	1-H[a] $J_{1,11ax}$[b] $J_{1,11eky}$[b]	14-substituent	15-substituent	Aromatic ring	Ring system	13-$COOCH_3$
2A[d]		5.58 (11;8)			α-eq	eq	E_t	α-eq
3a	5.72 12			β-eq		eq	E_t	α-eq
5a	4.74 (2;2.5)	5.34 (12;5)		α-ax	α-eq	eq	E_t	α-eq
5b	5.96 (2.5;2.5)	3.75 (11;4)		α-ax	α-eq	eq	E_t	α-eq
5c	4.52 (2.5;2.5)	3.82 (12;4)		α-ax	α-eq	eq	E_t	α-eq
5d[c]	5.85 (2.5;2.5)	5.35 (11;4)		α-ax	α-eq	eq	E_t	α-eq
6a	4.25 (11;3)	5.79 (3;3)		β-eq	β-ax	eq	E_t	α-eq
6b	5.60 (11;2.5)	4.63 (3;3)		β-eq	β-ax	eq	E_t	α-eq
6c	3.95 (11;3)	4.02 (3;3)		β-eq	β-ax	eq	E_t	α-eq
6d	5.69 (11.5;3)	5.96 (3;3)		β-eq	β-ax	eq	E_t	α-eq
6e	5.60 (11.5;3)	6.07 (3;3)		β-eq	β-ax	eq	E_t	α-eq
7a	4.32 (10;9.5)	5.45 (11.5;4.5)		β-eq	α-eq	eq	E_t	α-eq
7b	5.71 (9.5;10)	4.10 (12;4)		β-eq	α-eq	eq	E_t	α-eq
7c	4.0 (covered)	4.04 (covered)		β-eq	α-eq	eq	E_t	α-eq
7d[d]	4.52 (11;11)	5.57 (11;5)		β-eq	α-eq	eq	E_t	α-eq
8a	483 (2.5;3.5)	5.10 (11;4)	4.16 (3;3)	β-ax	β-eq	ax	E_{c2}	β-eq
8b	6.06 (2.5;3.5)	4.95 (12;4.5)	4.21 (3;3)	β-ax	β-eq	ax	E_{c2}	β-eq
9	4.73 (2.5;4)	5.88 (3;3)	4.14 (3;3)	β-ax	α-ax	ax	E_{c2}	β-eq
10	3.77 (5.5;3)	5.72 (3;2.5)		α-eq	α-ax	eq	A_t	α-ax
16	4.83 (2.5;4)	5.75 (3;3)		β-ax	α-ax	eq	A_t	α-ax

a/ Solvent C_6D_6 + DMSO
a/ Chemical shifts δ ppm ($\delta_{TMS} = 0$)
b/ Coupling constants Hz
c/ 60 MHz
d/ Solvent C_6D_6

methoxycarbonyl group adjacent to the oxo group moves without any difficulty into the most stable α-equatorial steric position.

B. *Reduction of ketones* **2** *and* **3a** *accompanied by acyl migration*

By reduction of ketone **2A**, carried out in methanol suspension, alcohol **5a** is obtained as the main product (70%) in addition to epimer **7a** (16%) and structural isomer **5b** (10%). These could be isolated partly by crystallization and partly by thin-layer chromatography.

Reduced of **3a** at 0°C in methanol, yielded primarily, as expected,[14] two isomeric alcohols **6b** and **7b** which were in equilibrium with two further alcohols **6a** and **7a**. Starting from any of the pure alcohols, this equilibrium (**5a**⇌**5b**, **6a**⇌**6b**, **7a**⇌**7b**) is established again in the presence of catalytic quantities of acid or base. To determine the structural relationship between the pairs of isomeric alcohols, compounds **5a + b**, **6a + b** and **7a + b** were deacylated by boiling in methanol containing hydrochloric acid and from the compounds **5a, b** the dialcohol **5c** was obtained, from alcohols **6a, b** the dialcohol **6c**, and from the pair of compounds **7a, b** the dialcohol **7c**. All this proves that substances which yield identical dialcohols differ only with respect to the position of the 3,4,5-trimethoxybenzoyloxy group.

Since in the reduction of ketone **2**, **5a** is formed as a primary product, it is to be assumed that this alcohol contains the 3,4,5-trimethoxybenzoyl group in the same position (C-15) as the initial ketone while **5b**, formed from it by acyl migration, contains the group on the neighbouring carbon atom (C-14).

In ketone **3a** the 3,4,5-trimethoxybenzoyloxy group is in position 14, thus, alcohols formed primarily from it (**6b, 7b**) contain the 3,4,5-trimethoxybenzoyloxy group similarly in position 14 while the compounds formed by acyl migration (**6a, 7a**) contain the group in position 15.

C. *Investigation of the stereochemistry of alcohols* **5a, b, 6a, b** *and* **7a, b**

The stereochemistry of the alcohols formed by the reduction of ketone **2** and **3a** and of their derivatives has been verified by IR and ^{1}H NMR spectroscopy and by chemical methods. Spectral data of **5a, b, 6a, b, 7a, b** alcohols of their *O*-acetyl derivatives, and of the diols (**5c, 6c, 7c**) obtained by the deacylation of the alcohols, indicate E_t conformation. The coupling constant 14-H in alcohol **5a** and of its acylated derivative **5d** (Table 1) indicate an axial substituent at C-14.

The coupling constants J_{HCOH} yield further information on the steric position of the OH groups.[15a,b] It is well known that these depend on the preferential orientation of rotation of the OH-group, reflecting on the other hand the steric interactions of the OH group and the neighbouring groups. In vicinal di- and tri-substituted six-membered ring systems, equatorial OH groups generally reveal a larger (6–7 Hz) and axial OH groups systematically a smaller (3–4 Hz) J_{HCOH} coupling constant. (Relevant data are contained in the experimental part.) The 15-H coupling constants of **5a** and **5d** indicate equatorial position of the 15-(3,4,5-trimethoxybenzoyloxy) group.

The steric position of 13-H can be generally deduced from the coupling constants $J_{12,13}$ and $J_{13,14}$ of 13-H. If the signal of 13-H is overlapped by other resonances, the $J_{13,14}$ value of 14-H gives information on its steric position. It follows from the coupling constants of the 13-H ($J_{12a,13a}$ 13 Hz), 14-H and 15-H of alcohol **5b**, obtained by acyl migration from alcohol **5a** (Table 1), that the substituents have 13α-equatorial, 14α-equatorial and 15α-equatorial position.

This stereochemistry of the compounds is also supported by their chemical behaviour. It has been shown in our earlier investigations that Vilsmeier's reaction is suitable for the elucidation of the steric position of 13-methoxycarbonyl and of the 14-OH group.[1] Alcohol **5a** gave with Vilsmeier's reagent ($SOCl_2$/DMF) the unsaturated ester **14** in good yield. The formation of compound **14** proceeds smoothly only if the 14-α OH group and 13-H are in *trans*-diaxial position, i.e. if substituent 13-H occupies steric position 13α. Vilsmeier's reaction permits also the replacement of the hydroxyl group by a chlorine atom which proceeds according to an S_{N2} mechanism. This reaction gave by inversion a byproduct—the chloro compound **7d**. In the ^{1}H NMR spectrum of **7d**, the coupling constants of 14-H and 15-H (Table 1) indicate in a compound of E_t conformation triequatorial 13α-, 14β- and 15α substituents. The formation of these compounds similarly supports the structure established above for the alcohol **5a**.

The steric structure of alcohols, formed in the reduction of compound **3a**, containing a ketone group in position 15, has been elucidated by ^{1}H NMR spectroscopy.

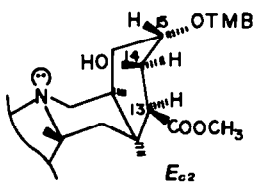
The coupling constants of 14-H and 15-H of alcohols **6a–e** (Table 1) also indicate the presence of equatorial 13α-, equatorial 14β- and axial 15β-substituents.

The coupling constants of 14-H and 15-H of the other stereoisomeric alcohols **7a** and **7b** (Table 1), indicate equatorial 13-, 14- and 15-substituents. In view of the E_t conformation of the compounds, this means that the said substituents are respectively α, β and α configuration. This orientation of the substituents on ring D of compounds **7a–c** is fully supported by the fact that no water elimination could be produced from compound **7a** under the condition of Vilsmeier's reaction.

Alcohol **7a** is the same as the alcohol formed in small quantities by the reduction of ketone **2**. This substance will be formed from ketone **2** if the attack of the boron hydride anion occurs from the generally prefered convex α-side.[1] However, in the case of compound **2**, this side is strongly shielded by the α-substituents of high space requirement in positions 13 and 15. If the boron hydride anion attacks from the concave β-side, then alcohol **5a**, isolated as the main product, will be formed.

D. *Conversion of the alcohols of established alloberban skeleton,* **11a, b, 10, 12, 13,** *to analogues of* epi-allo*berban skeleton,* **6a, b, 5a, 8a, 9**

We wished to establish a correlation between the alloberban skeleton alcohols **11a** and **11b** of known structure[1] and the compounds **6a** and **b** with *epi-allo*berban skeleton. When boiling alcohols **11a** and **b** with Hg^{II} acetate in glacial acetic acid, subsequent treatment with perchloric acid yielded the immonium salts **15b** and **c**. On reducing the latter in acetone medium with zinc/hydrochloric acid in the presence of catalytic quantities of Hg^{II} chloride and Fe^{III} chloride, alcohol **6a** can be isolated from compound **11a** and alcohol **6b** from **11b** (along with the starting substances **11a** and **b**). It should also be mentioned that the reaction mixture always contains the pair of alcohols obtained by acyl migration, **6a**⇌**6b**. The fact that alcohol **5a** could be prepared by the above methods from alcohol **10** with



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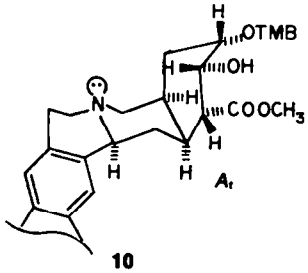

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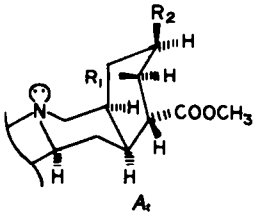
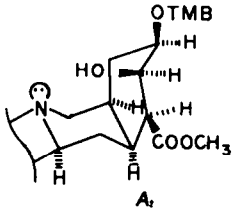


11

	R_1	R_2
a	OH	OTMB
b	OTMB	OH



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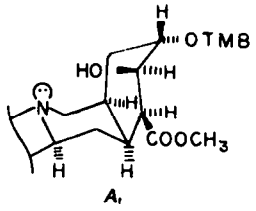

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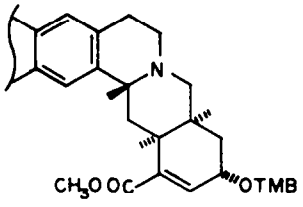

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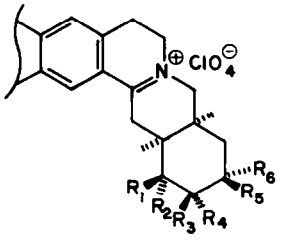
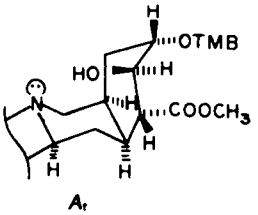


15

	R_1	R_2	R_3	R_4	R_5	R_6
a	H	$COOCH_3$	H	OH	H	OTMB
b	H	$COOCH_3$	OH	H	OTMB	H
c	H	$COOCH_3$	OTMB	H	OH	H
d	$COOCH_3$	H	OH	H	OTMB	H
e	$COOCH_3$	H	OH	H	H	OTMB
f	H	$COOCH_3$	OH	H	H	OTMB



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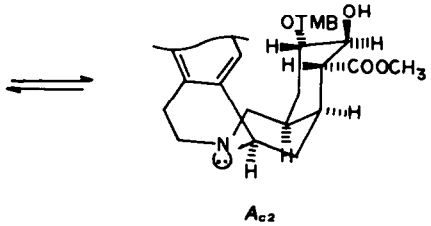

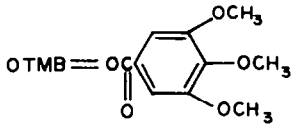

alloberban skeleton, supports the structure of compound **5a**.

With the aim to make the series of 9,10-dimethoxy(depyrrolo)raunescine stereoizomers more complete, hydroxy compounds **12** and **13** of known structure with *allo*berban skeleton[1] have been oxidized with Hg^{II} acetate into compounds **15d** and **15e**. On reducing the product with zinc/hydrochloric acid, alcohols **8a** and **9** with *epi-allo*berban skeleton were obtained in addition to the initial substances.

Chemical shift of 1-H in alcohol **8a** and in its *O*-acetyl derivative **8b** and the fact that in the IR spectrum of these compounds, recorded in chloroform, only weak Bohlmann bands appear, indicate that these compounds exist only in *epi-allo-cis* (E_{c2}) conformation.[16] On the basis of the 14- and 15-H δ values of these compounds (**8a, b**) and the coupling constants measured (Table 1) they contain 13β-equatorial, 14β-axial and 15β-equatorial substituents.

In the spectrum of the hydroxyl compound **9**, the 1-H signal indicates the presence of *epi-allo-cis* conformation. The IR spectra of the compound both in the solid state and in solution, exhibited extremely weak Bohlmann bands. The coupling constants of 14-H and 15-H (Table 1) proved equatorial 13β-, axial 14β- and axial 15α-substituents.

The re-conversion of compounds **5a** and **7a** with *epi-allo*berban skeleton into compounds with *allo*berban skeleton revealed interesting stereochemical properties of these compounds. If the hydroxy compound **7a** of E_t conformation is oxidized with Pb^{IV} acetate, and the immonium salt **15f** which is obtained, is reduced with sodium boron hydride,[10] hydroxyl compound **16** with *allo*berban skeleton is formed. In the ^{1}H NMR spectrum of **16** the band characteristic of B/C *trans* ring junction appears below δ 3.9 ppm, strong Bohlmann bands are revealed in the IR spectrum indicating that the ring system is of *allo trans* (A_t) conformation. The coupling constants of 14-H and 15-H (Table 1) indicate triaxial 13α-, 14β- and 15α-substituents.

Based on data in the literature,[10c,12] it was expected that the large substituents of ring D, since they attempt to attain equatorial position, force the ring system which has in principle a flexible conformation, to take up the less stable *allo cis* (A_{c2}) conformation where the aromatic ring prefers the axial position. In this case, the substituents of ring D would be in the tri-equatorial position. Actually this does not happen since the A_t conformation of the ring system, proving very stable, is maintained and ring D contains all three substituents in axial position.

We described in our earlier communication[1] that in the case of hydroxy compound **10** [which has also been prepared by the oxidation of **5a** (**15a**) and subsequent reduction] the established conformational equilibrium ($A_t \rightleftharpoons A_{c2}$) can be shifted under the conditions of Vilsmeier-dehydratation in the A_{c2} direction. In the ^{1}H NMR spectrum of product **10**, taken in C_6D_6–DMSO solvent, the 1-H signal can not be observed, and coupling constants of 14-H and 15-H (Table 1) indicate the compound **10** contains 13α-axial, 14β-equatorial and 15α-axial substituents. This is supported also by the ^{13}C-NMR spectrum of the compound. All this proves that compounds with alloberban skeleton whether present in the solid state or in solution are mainly in the A_t conformation, even if the substituents on ring D are in the axial position.

According to data in the literature[10b,c] compounds with berban skeleton and *cis* C/D ring junction, containing 1-2 double bonds, yield on reduction with sodium boron hydride exclusively compounds with alloberban skeleton. In the two cases discussed above, in the reduction leading to alcohols **10** and **16** in contrast to data in the literature, compounds with *epi-allo*berban skeleton (**5a, 7a**) are also always formed; the *allo* : *epi-allo* ratio being about 1 : 1.

The possible explanation of this finding is that besides the compounds with *allo*berban skeleton of A_t conformation, containing triaxial or axial, equatorial, axial substituents (**16, 10**), the energetically more favourable compounds with *epi-allo*berban skeleton of E_t configuration, containing triequatorial or equatorial, axial, equatorial substituents (**7a, 5a**) are also formed. This assumption seems to be supported by the fact that in the case when alcohol **6a** has been oxidized with Pb^{IV} acetate, then reduced with sodium boron hydride, no substance with *epi-allo*berban skeleton has been formed but only substances with *allo*berban skeleton (**11a** and **11b**).

The ^{13}C NMR analysis of the new compounds discussed above has also been performed. These results will form the subject of a later publication.

EXPERIMENTAL

IR spectra were recorded in KBr with Spectromom 2000 spectrophotometer. The ^{1}H NMR spectra were obtained using a Varian XL-100-15 Fourier transform instrument, chemical shifts are reported as ppm (δ) downfield from TMS. Mass spectra (MS) were recorded with an AEI MS 902 instrument (70 eV, ion source temp. 150°C, direct insertion). The source of the reaction was checked by qualitative TLC for which DC-Alufolien Kieselgel 60 F 254 (Benzene : MeOH 14 : 3) and alumina PF_{254} (CH_2Cl_2 : MeOH 20 : 0.5) indicative absorbents were used. For the quantitative separation Kieselgel $PF_{254-366}$, layer 1.5 mm (Benzene : MeOH 14 : 3 with CH_2Cl_2) [System A]; alumina PF_{254} Type E, layer 1.0 mm (CH_2Cl_2 : MeOH 20 : 0.5 eluating with CH_2Cl_2) [System B]; or alumina PF_{254} Type E, layer 1.0 mm (CH_2Cl_2 : MeOH 20 : 0.2 eluating with CH_2Cl_2) [System C]; indicative absorbents were used. The reactions were carried out under argon; M.ps were uncorrected.

7,8 - Dimethoxy - 14 - oxo - 15 - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13 - carboxylic acid methylester **2**

A mixture of bromo-keto ester **1** HBr (1.00 g, 1.87 mmoles) and potassium-3,4,5-trimethoxy benzoate (1.20 g, 4.75 mmoles) in abs DMF (10 ml) was stirred at 100°C for 1 h. The reaction mixture was poured into ice water (15 ml) and alkalized (pH 8) with 5% $NaHCO_3$. The precipitate was filtered off (1.00 g) and an addition crude product (0.06 g) was obtained by etheral extraction of the mother liquor. Crude product **2B** 1.06 g, (97%). IR (KBr): 2800–2750 (Bohlmann's absorption), 1730 ($OCOC_6H_2(OCH_3)_3$), 1660 (conjugated $COOCH_3$), 1620 cm^{-1} (C=C). Recrystallization from MeOH gave **2A**. The precipitated **2A** was after 1 h 0.50 g (46%), after 24 h 0.85 g (78%) m.p. 210–212°C. $C_{31}H_{37}NO_{10}$ (583.6) Calc.: C, 63.79; H, 6.39; N, 2.40. Found: C, 63.70; H, 6.40; N, 2.51%. IR (KBr): 2800–2750 (Bohlmann's absorption), 1750, 1730, 1710 cm^{-1} [$COOCH_3$, C=O, $OCOC_6H_2(OCH_3)_3$]. ^{1}H NMR (C_6D_6): 3.41, 3.48, 3.80, 3.51 (18 H, s, OCH_3, $COOCH_3$) 5.58 (1 H, dd, J_{ae} = 11 Hz, J_{ae} = 8 Hz, 15-H), 6.51 6.66 (2 H, s, 6-H, 9–H), 7.63 (2 H, s, 2'-H, 6'-H) MS *m/e* (%): 583(9, M^+), 582(12), 568(3), 552(1), 525(10), 524(24), 510(4), 388(6), 372(12), 371(20), 370(12), 356(9), 330(20), 328(8), 314(25), 313(50), 312(25), 232(45), 226(10), 212(100), 205(65), 197(50), 195(40), 191(30), 190(25).

7,8 - Dimethoxy - 15 - oxo - 14β - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester **3a**

A. A mixture of ketone **2A** (50 mg, 0.097 mmoles), diethylamine (2 drops) and potassium-3,4,5-trimethoxy benzoate (50 mg,

0.2 mmoles) in abs DMF (1 ml) was stirred at 100°C for 1 h. The cold reaction mixture was poured into ice water (5 ml) and extracted with ether. The solvent was evaporated, the residue after recrystallization (MeOH) gave **3a** 30 mg, (60%), m.p. 197–201°C.

B. A mixture of bromo-keto ester **1** (0.5 g, 0.94 mmoles) potassium-3,4,5-trimethoxy benzoate (0.50 g, 2.00 mmoles) and diethylamine (10 drops) in abs DMF (8 ml) was stirred at 100°C for 1 h. The cold reaction mixture was poured into ice water (50 ml), extracted with ether. The solvent was evaporated and the residue after recrystallization (MeOH) gave **3a** 0.31 g, (56.6%), m.p. 197–201°C. $C_{31}H_{37}NO_{10}$ (583.6). Calc.: C, 63.79; H, 6.39; N, 2.40. Found: C, 63.81; H, 6.39; N, 2.54%. IR (KBr): 2800–2750 (Bohlmann's absorption), 1750–1730 cm^{-1} [$COOCH_3$, C=O, $OCOC_6H_2(OCH_3)_3$]. ^1H NMR ($CDCl_3$ + DMSO): 3.78, 3.79, 3.83, 3.88 (18 H, s, OCH_3, $COOCH_3$), 5.72 (1 H, d, J_{aa} = 12 Hz, 14-H), 6.56, 6.65 (2 H, s, 6-H, 9-H), 7.26 (2 H, s, 2'-H, 6'-H). MS *m/e* (%): 583(M^+, 40), 582(45), 568(12), 552(3), 525(1), 524(3), 388(25), 372(55), 371(70), 370(30), 356(20), 330(1), 328(5), 313(15), 312(50), 232(20), 226(4), 212(45), 205(100), 197(30), 195(75), 191(40), 190(35).

7,8 - Dimethoxy - 14 - oxo - epialloberban - 13 - carboxylic acid methylester[4]

Ketone **2A** (0.20 g, 0.34 mmoles) was refluxed in acetic acid (10 ml) with Zn powder (1.00 g) for 2 h. The cold solution was filtered, evaporated *in vacuo*, the residue was dissolved in water (5 ml), made alkaline (pH 9) with 20% NH_4OH and extracted with CH_2Cl_2. After drying ($MgSO_4$) the solvent was evaporated and the residue crystallized in MeOH. Yield: 30 mg (23.6%), m.p. 137–138°C.

7,8 - Dimethoxy - 15 - oxo - epialloberban - 13 - carboxylic acid methylester **3b**

With the reduction method described above, ketone **3a** (0.12 g, 0.21 mmoles) gave ketone **3b** (50 mg, 65%), m.p. 160–161°C (methanol). $C_{21}H_{27}NO_5$ (373.3) Calc.: C, 67.54; H, 7.29; N, 3.75. Found: C, 67.55; H, 7.35; N, 3.88%. IR (KBr): 2800–2750 (Bohlmann's absorption), 1735, 1715 cm^{-1} ($COOCH_3$, C=O). ^1H NMR ($CDCl_3$): 3.79, 3.86 (9 H, s, $COOCH_3$, OCH_3), 6.54, 6.58 (2 H, s, 6-H, 9-H). MS *m/e* (%): 373 (M^+, 75), 372(100), 358(20), 342(8), 330(2), 314(15), 286(3), 273(1), 272(1), 258(17), 244(4), 242(3), 232(40), 205(50), 191(25), 190(20), 177(3), 176(6).

14α - Hydroxy - 7,8 - dimethoxy - 15α - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester **5a**, *14β - hydroxy - 7,8 - dimethoxy - 15α - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester* **7a**, *and 15α - hydroxy - 7,8 - dimethoxy - 14α - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester* **5b**

Ketone **2A** (1.00 g, 1.72 mmoles) was stirred in abs MeOH (35 ml) at 0°C and $NaBH_4$ (0.30 g, 6.55 mmoles) was added to the reaction mixture in portions. After 0.5 h stirring the precipitate was filtered off (**5a**, 0.65 g, 64.7%). The mother liquor was neutralized with acetic acid, the solvent was evaporated *in vacuo*, the residue treated with 2.5% $NaHCO_3$ and extracted with CH_2Cl_2. After drying ($MgSO_4$) the solvent was evaporated and the residue separated by system A: R_f **5a**, **7a** > R_f **5b**, and then the upper layer by system B: R_f **7a** > R_f **5a**.

5a 0.70 g (69.8%), m.p. 201–203°C (methanol). $C_{31}H_{39}NO_{10}$ (585.6) Calc. C, 63.57; H, 6.71; N, 2.39. Found: C, 63.55; H, 6.72; N, 2.39%. IR (KBr): 3520 (OH), 2800–2750 (Bohlmann's absorption), 1720, 1695 cm^{-1} [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$]. ^1H NMR (C_6D_6 + DMSO): 7.73 (2 H, s, 2'-H, 6'-H), 6.77, 6.52 (2 H, s, 6-H, 9-H), 5.31 (1 H, d, $J_{14,OH}$ = 4 Hz, OH), 5.34 (1 H, m, J_{aa} = 12 Hz, J_{ae} = 5 Hz, 15-H), 4.74 (1 H, m, J_{ae} = 2 Hz, J_{ee} = 2.5 Hz, 14-H), 3.82, 3.62, 3.58, 3.52 (18 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 585(M^+, 50), 584(65), 570(20), 568(4), 554(6), 553(5), 552(7), 526(5), 390(20), 373(90), 372(80), 358(30), 356(20), 342(15), 340(7), 314(40), 232(45), 212(70), 205(100), 197(40), 195(60), 191(70), 190(40).

5b 0.095 g (9.5%), m.p. 212–214°C (methanol). $C_{31}H_{39}NO_{10}$ (585.6) Calc.: C, 63.57; H, 6.71; N, 2.39; Found: C, 63.63; H, 6.73; N, 3.47%. IR (KBr): 3400 (OH), 2800–2750 (Bohlmann's absorption), 1745, 1730 cm^{-1} [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$]. ^1H NMR (C_6D_6 + DMSO): 7.65 (2 H, s, 2'-H, 6'-H), 6.76, 6.52 (2 H, s, 6-H, 9-H), 5.96 (1 H, m, J_{aa} = 2.5 Hz, J_{ae} = 2.5 Hz, 14-H), 3.75 (1 H, m, J_{aa} = 11 Hz, J_{ae} = 4 Hz, 15-H), 4.46 (1 H, brs, OH), 3.16 (1 H, dd, J_{aa} = 13 Hz, 13-H), 3.84, 3.52, 3.50, 3.48 (18 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 585 (M^+, 70), 584(100), 570(18), 553(23), 552(28), 390(20), 374(45), 373(80), 372(50), 358(14), 356(10), 342(27), 340(14), 314(36), 232(27), 212(30), 205(57), 195(40), 191(53).

7a 0.16 g (15.9%), m.p. 178°C (methanol). $C_{31}H_{39}NO_{10}$ (585.6), Calc.: C, 63.57; H, 6.71; N, 2.39. Found: C, 63.61; H, 6.74; N, 2.42%. IR (KBr): 3550 (OH), 2800–2750 (Bohlmann's absorption), 1750–1730 cm^{-1} [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$]. ^1H NMR (C_6D_6 + DMSO): 7.66 (2 H, s, 2'-H, 6'-H), 6.62, 6.51 (2 H, s, 6-H, 9-H), 5.48 (1 H, brs, OH), 5.45 (1 H, m, J_{aa} = 11.5 Hz, J_{ae} = 4.5 Hz, 15-H), 4.32 (1 H, dd, J_{aa} = 10 Hz, J_{aa} = 9.5 Hz, 14-H), 3.82, 3.64, 3.60, 3.54 (18 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 585 (M^+, 45), 584(60), 570(19), 568(4), 554(6), 553(4), 552(6), 526(3), 390(18), 373(100), 372(40), 358(10), 356(13), 342(8), 314(28), 232(20), 212(30), 205(45), 197(12), 195(30), 191(30), 190(15).

15β - Hydroxy - 7,8 - dimethoxy - 14β - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester **6b**, *15α - hydroxy - 7,8 - dimethoxy - 14β - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester* **7b**, *and 14β - hydroxy - 7,8 - dimethoxy - 15β - (3',4',5' - trimethoxybenzoxyloxy) - epialloberban - 13α - carboxylic acid methylester* **6a**

Ketone **3a** (2.0 g, 3.4 mmoles) was stirred in abs MeOH (70 ml) at 0°C and $NaBH_4$ (0.8 g, 21.2 mmoles) was added to the reaction mixture. After 0.5 h stirring acetic acid (10 drops) was added and the solvent evaporated *in vacuo*. The residue was treated with 2.5% $NaHCO_3$, extracted with CH_2Cl_2. The CH_2Cl_2 was evaporated after drying ($MgSO_4$) and the residue separated by system A: R_f **6a** > R_f **6b**, **7b** and then the bottom layer by system C: R_f **7b** > R_f **6b**.

6b 0.73 g (36.7%), m.p. 170–171°C (methanol). $C_{31}H_{39}NO_{10}$ (585.6). Calc.: C, 63.57; H, 6.71; N, 2.39. Found: C, 63.71; H, 6.75; N, 2.45%. IR (KBr): 3485 (OH), 2830–2760 (Bohlmann's absorption), 1735–1700 cm^{-1} [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$]. ^1H NMR (C_6D_6 + DMSO): 7.65 (2 H, s, 2'-H, 6'-H), 6.80, 6.53 (2 H, s, 6-H, 9-H), 5.60 (1 H, dd, J_{aa} = 11 Hz, J_{ae} = 2.5 Hz, 14-H), 4.63 (1 H, m, J_{aa} = 3 Hz, J_{ae} = 3 Hz, 15-H), 4.3 (1 H, brs, OH), 3.80, 3.56, 3.53, 3.52, 3.51 (18 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 585 (M^+, 40), 584(60), 570(18), 568(3), 544(5), 553(2), 552(3), 526(2), 390(16), 373(100), 372(40), 358(8), 356(10), 342(5), 314(30), 232(18), 212(16), 205(40), 197(8), 195(30), 191(30), 190(10).

7b 0.355 g (17.8%) m.p. 150–152°C (methanol) $C_{31}H_{39}NO_{10}$ (585.6) Calc.: C, 63.57; H, 6.71; N, 2.39. Found: C, 63.57; H, 6.72; N, 2.44%. IR (KBr) 3545 (OH), 2820–2740 (Bohlmann's absorption), 1730–1695 cm^{-1} [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$]. ^1H NMR (C_6D_6 + DMSO): 7.60 (2H, s, 2'-H, 6'-H) 6.68, 6.49 (2H, s, 6-H, 9-H), 5.71 (1H, dd, J_{aa} = 9.5 Hz, J_{ae} = 10 Hz, 14-H), 4.10 (1H, m, J_{ae} = 12H, J_{ee} = 4 Hz, 15-H), 3.78, 3.55, 3.52, 3.51 (18H, s, OCH, $COOCH_3$). MS *m/e* (%): 585 (M^+, 70), 584(85), 570(33), 568(2), 544(4), 526(4), 390(12), 373(100), 372(40), 358(10), 356(15), 342(4), 314(14), 232(20), 212(25), 205(50), 197(10), 195(45), 191(40), 190(20).

6a 0.155 g (7.7%) m.p. 178.5–181°C (methanol) $C_{31}H_{39}NO_{10}$ (585.6). Calc.: C, 63.57; H, 6.71; N, 2.39. Found: C, 63.59; H, 6.73; N, 2.43%. IR (KBr): 3470 (OH), 2830–2770 (Bohlmann's absorption), 1725, 1700 cm^{-1} [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$]. ^1H NMR (C_6D_6 + DMSO): 7.67 (2 H, s, 2'-H, 6'-H), 6.83 (1 H, s, 9-H), 6.51 (1 H, s, 6-H), 5.79 (1 H, m, J_{ae} = 3 Hz, J_{ee} = 3 Hz, 15-H), 5.17 (1 H, d, $J_{14,OH}$ = 6.5 Hz, OH), 4.25 (1 H, dd, J_{aa} = 11 Hz, J_{ae} = 3 Hz, 14-H), 3.81, 3.62, 3.54, 3.49, 3.48 (18 H, s, OCH_3, $COOCH_3$). MS *m/e* (%): 585 (M^+, 80), 584(95), 570(30), 568(2), 554(6), 526(3), 390(30), 373(100), 372(40), 358(9), 356(14), 342(4), 314(13), 232(21), 212(22), 205(50), 197(10), 195(40), 191(40), 190(25).

Table 2. Data of hydrolysis and decarboxylation of compounds **5a–b, 6a–b, 7a–b**

Starting material	Reaction product	Yield mg	Yield %	Melting point °C
5a	5c	37.6	56.5	223–223.5
5b	5c	32.3	48.6	223–223.5
6a	6c	35.2	53.0	207
6b	6c	40.0	60.1	207
7a	7c	28.6	43.0	226–227.5
7b	7c	38.0	57.1	226–227.5

14α, 15α - Dihydroxy - 7,8 - dimethoxy - epialloberban - 13α carboxylic acid methylester **5c**, *14β, 15β - dihydroxy - 7,8 - dimethoxy - epialloberban - 13α - carboxylic acid methylester* **6c**, *and 14β, 15α - dihydroxy - 7,8 - dimethoxy - epialloberban - 13α - carboxylic acid methylester* **7c**

Alcohol **5a–b, 6a–b** or **7a–b** (0.1 g, 0.17 mmoles) was refluxed in 15% HCl/MeOH (5 ml) for 4 h. The solvent was evaporated *in vacuo*, the residue dissolved in water (5 ml), extracted with ether (3 × 10 ml) and made alkaline (pH 9) with 10% NaOH then extracted with CH_2Cl_2. After drying ($MgSO_4$) the organic layer was evaporated and the residue crystallized in MeOH. Data of experiments are summarized in Table 2.

5c $C_{21}H_{29}NO_6$ (391.45). Calc.: C, 64.43; H, 7.47; N, 3.58. Found C, 64.59; H, 7.49; N, 3.70%. IR (KBr): 3500, 3450 (OH), 2800–2750 (Bohlmann's absorption), 1720 cm^{-1} ($COOCH_3$). ^1H NMR (C_5D_5N + DMSO): 6.80, 6.52 (2 H, s, 6-H, 9-H), 4.52 (1 H, dd, J_{ac} = 2.5 Hz, J_{ae} = 2.5 Hz, 14-H), 4.42 (1H, brs, 14-O), 3.82 (1 H, m, J_{aa} = 12 Hz, J_{ae} = 4 Hz, 15-H), 3.59, 3.51, 3.50 (9 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 391 (M^+, 75), 390(100), 376(25), 374(25), 360(9), 359(14), 358(19), 344(2), 342(6), 332(11), 314(4), 290(2), 288(2), 260(6), 258(6), 256(2), 246(5), 245(6), 244(6), 242(5), 232(17), 230(8), 205(36), 191(51), 176(13).

6c $C_{21}H_{29}NO_6$ (391.45). Calc.: C, 64.93; H, 7.47; N, 3.58. Found: C, 64.51; H, 7.50; N, 3.61%. IR (KBr): 3500, 3400 (OH), 2800–2750 (Bohlmann's absorption), 1735 cm^{-1} ($COOCH_3$). ^1H NMR (C_5D_5N + DMSO): 6.70, 6.50 (2 H, s, 6-H, 9-H), 4.50, 4.13 (2 H, brs, OH), 4.02 (1 H, m, J_{aa} = 3 Hz, J_{ae} = 3 Hz, 15-H), 3.95 (1 H, dd, J_{aa} = 11 Hz, J_{ae} = 3 Hz, 14-H), 3.65, 3.59, 3.54 (9 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 391 (M^+, 68), 390(100), 376(20), 374(5), 360(4), 358(1), 342(2), 332(4), 314(1), 290(2), 288(2), 260(7), 258(5), 256(4), 246(5), 245(5), 244(5), 242(6), 232(17), 230(9), 205(39), 191(43), 176(12).

7c $C_{21}H_{29}NO_6$ (391.45). Calc.: C, 64.43; H, 7.41; N, 3.58. Found: C, 64.43; H, 7.42; N, 3.66%. IR (KBr): 3500, 3350 (OH), 2800–2750 (Bohlmann's absorption), 1722 cm^{-1} ($COOCH_3$). ^1H NMR (C_5D_5N + DMSO): 6.71, 6.56 (2 H, s, 6-H, 9-H), 4.04 (1 H, m, covered, 15-H), 4.0 (1 H, m, covered, 14-H), 3.68, 3.60, 3.57 (9 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 391 (M^+, 78), 390(100), 376(30), 374(31), 360(5), 358(5), 342(4), 332(6), 314(5), 290(3), 288(2), 260(7), 258(5), 256(4), 246(5), 245(5), 244(5), 242(6), 232(17), 230(9), 205(39), 191(43), 176(12).

7,8 - Dimethoxy - 15α - (3',4',5' - trimethoxybenzoyloxy) - 13,14 - didehydro - epialloberban - 13 - carboxylic acid methylester **14** *and 14β - chloro - 7,8 - dimethoxy - 15α - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester* **7d**

A mixture of alcohol **5a** (0.1 g, 0.17 mmoles) and abs DMF (1.2 ml) was stirred at 0°C and $SOCl_2$ (0.2 g, 1.68 mmoles) was added to the solution. After 24 h standing at room temp. the reaction mixture was diluted with ice water (5 ml), made alkaline (pH 9) with 10% NaOH and extracted with CH_2Cl_2. The solvent was evaporated, the residue separated by system A: R_f **7d** > R_f **14**.

14 0.045 g (46.7%), m.p. 151–156°C (methanol) $C_{31}H_{27}NO_9$ (567.5). Calc.: C, 65.60; H, 4.79; N, 2.47. Found: C, 65.71; H, 4.85; N, 2.39%. IR (KBr): 2800–2750 (Bohlmann's absorption), 1735–1705 [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$], 1610 cm^{-1} (C=C). ^1H NMR (C_5D_5N): 7.48 (2 H, s, 2'-H, 6'-H), 7.05 (1 H, dd, J = 4 Hz, J = 2 Hz, 14-H), 7.01, 6.48 (2 H, s, 6-H, 9-H), 5.84 (1 H, m, J_{aa} = 7 Hz, J_{ae} = 5 Hz, 15-H), 3.80, 3.77, 3.54, 3.42 (18 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 567 (M^+, 53), 566(29), 552(13), 526(3), 508(1), 373(21), 372(100), 370(5), 357(14), 356(65), 355(20), 340(2), 232(12), 230(8), 218(6), 212(16), 206(12), 205(65), 197(5), 195(13), 192(4), 191(9), 190(13), 177(5), 176(6), 105(6).

7d 0.027 g (26.4%), m.p. 200–201°C (methanol). $C_{31}H_{30}NO_9Cl$ (604.08). Calc.: C, 61.63; H, 6.34; N, 2.32. Found: C, 61.55; H, 6.31; N, 2.30%. IR (KBr): 2800–2750 (Bohlmann's absorption), 1740, 1720 cm^{-1} [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$]. ^1H NMR (C_5D_5N): 7.61 (2 H, s, 2'-H, 6'-H), 6.68, 6.48 (2H, s, 6-H, 9-H), 5.57 (1 H, m, J_{aa} = 11 Hz, J_{ae} = 5 Hz, 15-H), 4.52 (1 H, dd, J_{aa} = 11 Hz, J_{aa} = 11 Hz, 14-H), 3.80, 3.52, 3.44, 3.38 (18 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 603 (M^+, 78), 602(44), 568(100), 508(2), 392(7), 372(14), 356(32), 301(6), 232(9), 212(8), 205(23), 195(28), 191(13), 190(10), 176(6).

7,8 - Dimethoxy - 15 - (3',4',5' - trimethoxybenzoyloxy) - 13 - methoxy - carbonyl - 14 - oxo - $\Delta^{1,2}$ - berbenium perchlorate **4**, *7,8 - dimethoxy - 14α - hydroxy - 15α - (3',4',5' - trimethoxybenzoyloxy) - 13α - methoxycarbonyl - $\Delta^{1,2}$ - berbenium perchlorate* **15a**, *7,8 - dimethoxy - 14β - hydroxy - 15β - (3',4',5' - trimethoxybenzoyloxy) - 13α - methoxycarbonyl - $\Delta^{1,2}$ - berbenium perchlorate* **15b**, *7,8 - dimethoxy - 15β - hydroxy - 14β - (3',4',5' - trimethoxybenzoyloxy) - 13α - methoxycarbonyl - $\Delta^{1,2}$ - berbenium perchlorate* **15c**, *7,8 - dimethoxy - 14β - hydroxy - 15β - (3',4',5' - trimethoxybenzoyloxy) - 13β - methoxycarbonyl - $\Delta^{1,2}$ - berbenium perchlorate* **15d**, *7,8 - dimethoxy - 14β - hydroxy - 15α - (3',4',5' - trimethoxybenzoyloxy) - 13β - methoxycarbonyl - $\Delta^{1,2}$ - berbenium perchlorate* **15e**, *and 7,8 - dimethoxy - 14β - hydroxy - 15α - (3',4',5' - trimethoxybenzoyloxy) - 13α - methoxycarbonyl - $\Delta^{1,2}$ - berbenium perchlorate* **15f**

A. 7,8 - Dimethoxy - 14 - oxo - 15 - (3,4,5 - trimethoxybenzoyloxy) - alloberban - 13 - carboxylic acid methylester[4] *or compounds* **10**, **11a–b**, **12**, **13** *(1.0 mmole) were stirred with Hg $(OOCCH_3)_2$ (1.5 mmoles) in acetic acid (5 ml) at 100°C for 2 h. From the hot reaction mixture the precipitate was filtered off, the solvent was evaporated in vacuo* and the residue dissolved in MeOH (3 ml); 70% $HClO_4$ (2 drops) was added to the solution, the precipitated crystals were filtered off and washed with ether.

B. Alcohol **5a**, **6a** or **9a** (1.0 mmole) was stirred with $Pb(OOCCH_3)_4$ (1.5 mmoles) in acetic acid (5 ml) at room temperature for 24 h. The mixture was poured in water (10 ml) and made alkaline (pH 9) with 25% NH_4OH then extracted with CH_2Cl_2. After evaporating the residue was dissolved in MeOH (3 ml) and 70% $HClO_4$ (2 drops) was added to the solution. The precipitated crystals were filtered off and washed with ether. Data of experiments are summarized in Table 3.

Table 3. Data of oxidation of compounds 7,8-dimethoxy-14-oxo-15-(3,4,5-trimethoxy-benzoyloxy)-alloberban-13-carboxylic acid methylester, **5a**, **6a**, **7a**, **10**, **11a–b**, **12** and **13**

Method	Starting material	Reaction product	Yield %	Mp. °C	OH	$COOCH_3$, C=O $OCOC_6H_2(OCH_3)_3$	IR (KBr) cm^{-1} C=N	Aromatic	Perchlorate
A.	[a]	4	94	168–72		1730	1650,1675	1610,1595	1110–1090
A.	10	15a	65	165–69	3400	1720	1640,1570	1606,1590	1110–1090
B.	5a	15a	60						
A.	11a	15b	76	187–89	3400	1720	1640,1565	1605,1690	1110–1090
B.	6a	15b	75						
A.	11b	15c	64	168–74	3300–3500	1720	1640,1560	1600,1590	1110–1090
A.	12	15d	90	170–75	3300–3500	1705 1715	1640,1570	1590,1605	1110–1090
A.	13	15a	74	260–62	3400	1735 1705	1640,1565	1597,1595	1110–1090
B.	7a	15f	80	201–09	3400	1730 1705	1640,1565	1600,1590	1110–1090

[a] 7,8-Dimethoxy-14-oxo-15-(3,4,5-trimethoxybenzoyloxy)-alloberban-13-carboxylic acid methylester

Reduction of **4**, **15a–f** *berbenium perchlorates*, 14β - *hydroxy* - 7,8 - *dimethoxy* - 15β - (3',4',5' - *trimethoxybenzoyloxy*) - *epiallober-ban* - 13β - *carboxylic acid methylester* **5a**, 14β - *hydroxy* - 7,8 - *dimethoxy* - 15α - (3',4',5' - *trimethoxybenzoyloxy*) - *epiallober-ban* - 13β - *carboxylic acid methylester* **9**, 14α - *hydroxy* - 7,8 - *dimethoxy* - 15α - (3',4',5' - *trimethoxybenzoyloxy*) - *alloberban* - 13α - *carboxylic acid methylester* **10**, *and* 14β - *hydroxy* - 7,8 - *dimethoxy* - 15α - (3',4',5' - *trimethoxybenzoyloxy*) - *alloberban* - 13α - *carboxylic acid methylester* **16**

A. A mixture of berbenium perchlorate **4** or **15a–e** (1.0 mmole), acetone (3 ml) water (4 ml), 10% HCl (0.7 ml), $HgCl_2$ (10 mg), $FeCl_3$ (10 mg) and Zn powder (0.30 g) was stirred at room temp. for 3 h. The residue was treated with water (2 ml) and made alkaline (pH 8) with 5% Na_2CO_3 then extracted with CH_2Cl_2. After drying ($MgSO_4$) the solvent was evaporated and the residue separated by system A: R_f 7,8 - dimethoxy - 15(3,4,5 - trimethoxybenzoyloxy) - 14 - oxo - alloberban - 13 - carboxylic acid methylester, **10**, **11a–b**, **12**, **13** > R_f **2**, **5a**, **6a–b**, **8a**, **9**. Data of experiments are summarized in Table 4.

B. A mixture of berbenium perchlorate **15a–b** or **15f** (1.0 mmole) abs MeOH (10 ml) was stirred at 0°C and $NaBH_4$ (5.0 mmoles) was added to the mixture by portions. After 0.5 h stirring, the solvent was acidified (pH 6) with acetic acid, evaporated *in vacuo* and the residue was treated with 2.5% Na_2CO_3 then extracted with CH_2Cl_2. After drying ($MgSO_4$) the solvent was evaporated and the crude product separated by system A: R_f **5a**, **11b**, **7a** < R_f **10**, **11a**, **16**. Data of experiments are shown in Table 5.

Table 4. Reduction of berbenium perchlorates **4**, **15a–e** with Zn/HCl

Starting material	Reaction product	Yield		Yield
4	2	29 %	[a]	20 %
15a	5a	21 %	10	22 %
15c	6a	10 %	11a	5 %
	6b	26 %	11b	16 %
15b	6a	22 %	11a	17 %
	6b	3 %	11b	20 %
15d	8a	28 %	12	34 %
15e	9	36 %	13	40 %

*See Table 3.

Table 5. Reduction of berbenium perchlorates **15a–b**, **15f** with $NaBH_4$/MeOH

Starting material	Reaction product (Yield)			
15a	5a	(25 %)	10	(27 %)
			11a	(18 %)
15b			11b	(25 %)
15f	7a	(27 %)	16	(24 %)

8a m.p. 202°C (methanol). $C_{31}H_{39}NO_{10}$(585.6). Calc.: C, 63.57; H, 6.71; N, 2.39. Found: C, 63.62; H, 6.73; N, 2.45%. IR (KBr): 3580(OH), 1735, 1720 [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$], 1615–1600 cm^{-1} (aromatic). ^1H NMR (C_6D_6 + DMSO): 7.77 (2 H, s, 2'-H, 6'-H), 7.20, 6.55 (2 H, s, 6-H, 9-H), 5.19 (1 H, d, J = 4 Hz, OH), 5.10 (1 H, m, J_{aa} = 11 H, J_{ae} = 4 Hz, 15-H), 4.83 (1 H, m, J_{ae} = 2.5 Hz, J_{ae} = 3.5 Hz, 14-H), 4.16 (1 H, m, J_{ee} = 3 Hz, J_{ee} = 3 Hz, 1-H), 3.86, 3.82, 3.60, 3.59, 3.54 (18 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 585 (M^+, 20), 584(50), 570(20), 568(2), 554(4), 553(3), 552(3), 526(2), 390(4), 373(100), 372(75), 358(61), 356(18), 342(10), 340(2), 314(10), 312(2), 232(20), 226(4), 212(60), 205(50), 197(24), 195(19), 191(30), 190(18).

9 m.p. 170°C (methanol). $C_{31}H_{39}NO_{10}$(585.6) Calc.: C, 63.57; H, 6.71; N, 2.39. Found: C, 63.57; H, 6.73; N, 2.44%. IR (KBr): 3400 (OH), 1725 [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$], 1600, 1585 cm^{-1} (aromatic). ^1H NMR (C_6D_6 + DMSO): 7.53 (2 H, s, 2'-H, 6'-H), 7.20, 6.57 (2 H, s, 6-H, 9-H), 5.88 (1 H, m, J_{aa} = 3 H, J_{ae} = 3 Hz, 15-H), 5.46 (1 H, d, J = 4 Hz, OH), 4.73 (1 H, m, J_{ea} = 2.5 Hz, J_{ee} = 4 Hz, 14-H), 4.14 (1 H, m, J_{ea} = 3 Hz, J_{ee} = 3 Hz, 1-H), 3.87, 3.80, 3.58, 3.52, 3.47 (18 H, s, OCH_3, $COOCH_3$). MS *m/e* (%): 585 (M^+, 50), 584(70), 570(20), 568(2), 554(6), 553(1), 552(1), 526(2), 390(10), 373(100), 372(80), 358(45), 356(13), 342(8), 340(2), 330(2), 328(2), 314(11), 312(2), 232(20), 226(4), 212(60), 205(50), 197(24), 195(19), 191(30), 190(18).

10[1] ^1H NMR (C_6D_6 + DMSO): 7.58 (2 H, s, 2'-H, 6'-H), 6.67, 6.51 (2 H, s, 6-H, 9-H), 5.72 (1 H, m, J_{aa} = 3 Hz, J_{ae} = 2.5 Hz, 15-H), 4.05 (1 H, brs. OH), 3.77 (1 H, dd, J_{aa} = 5.5 Hz, J_{ae} = 3 Hz, 14-H), 3.86, 3.70, 3.64, 3.53, 3.27 (18 H, s, $COOCH_3$, OCH_3).

16 m.p. 187–188°C (methanol). $C_{31}H_{39}NO_{10}$(585.6). Calc.: C, 63.57; H, 6.71; N, 2.39. Found: C, 63.61; H, 6.71; N, 2.36%. IR (KBr): 3450 (OH), 1740 [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$], 1620, 1600 cm^{-1} (aromatic). ^1H NMR (C_6D_6 + DMSO): 7.60 (2 H, s, 2'-H, 6'-H), 6.80, 6.52 (2 H, s, 6-H, 9-H), 5.75 (1 H, m, J_{ea} = 3 Hz,

Table 6. Acetylation of alcohols 5a, 6a–b, 8a

Starting material	Reaction product	Yield %	Mp. °C
5a	5d	90	205
6a	6e	79	228–31
6b	6d	65	189–90
8a	8b	40	198–200

J_{ac} = 3 Hz, 15-H), 5.60 (1 H, d, J=4 Hz, OH), 4.83 (1 H, m, J_{aa} = 2.5 Hz, J_{ae} = 4 Hz, 14-H), 3.82, 3.69, 3.59, 3.56, 3.26 (18 H, s, $COOCH_3$, OCH_3). MS *m/e* (%): 585 (M^+, 19), 584(55), 583(68), 568(24), 373(100), 205(37), 195(37), 191(32).

14α - Acetoxy - 7,8 - dimethoxy - 15α - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester **5d**, *14β - acetoxy - 7,8 - dimethoxy - 15β - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester* **6e**, *15β - acetoxy - 7,8 - dimethoxy - 14β - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13α - carboxylic acid methylester* **6d** *and 14β - acetoxy - 7,8 - dimethoxy - 15β - (3',4',5' - trimethoxybenzoyloxy) - epialloberban - 13β - carboxylic acid methylester* **8b**

A mixture of alcohol **5a** or **6a–b**, **8a** (1.0 g, 0.17 mmol), pyridine (1.0 ml) and acetic anhydride (1.0 ml) was allowed to stand for 2 days. The solvent was evaporated *in vacuo*, and the residue treated with 2.5% Na_2CO_3 (5.0 ml). The precipitate was filtered off and recrystallized from MeOH. Data of experiments are summarized in Table 6.

5d $C_{33}H_{41}NO_{11}$ (627.67). Calc.: C, 63.14; H, 6.58; N, 2.23. Found: C, 63.14; H, 6.59; N, 2.24%. IR (KBr): 2800-2750 (Bohlmann's absorption), 1750 – 1720 [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$, $OCOCH_3$], 1600 cm^{-1} (aromatic). ^1H NMR ($CDCl_3$): 7.29 (2 H, s, 2'-H, 6'-H), 6.64 (2 H, s, 6-H, 9-H), 5.85 (1 H, m, J_{aa} = 2.5 Hz, J_{ae} = 2.5 Hz, 14-H), 5.35 (1 H, m, J_{aa} = 11 Hz, J_{ae} = 4 Hz, 15-H), 3.93, 3.86, 3.76 (18 H, s, $COOCH_3$, OCH_3), 2.15 (3 H, s, $OCOCH_3$).

6e $C_{33}H_{41}NO_{11}$ (627.67). Calc.: C, 63.14; H, 6.58; N, 2.23. Found: C, 63.21; H, 6.62; N, 2.30%. IR (KBr): 2850–2750 (Bohlmann's absorption), 1755, 1730 [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$, $OCOCH_3$], 1600 cm^{-1} (aromatic). ^1H NMR (C_6D_6 + DMSO): 7.63 (2 H, s, 2'-H, 6'-H), 6.90, 6.67 (2 H, s, 6-H, 9-H), 6.07 (1 H, m, J_{ac} = 3 Hz, 15-H), 5.60 (1 H, dd, J_{aa} = 11.5 Hz, J_{ae} = 3 Hz, 14-H), 3.92, 3.72, 3.70, 3.66 (18 H, s, $COOCH_3$, OCH_3), 1.92 (3 H, s, $OCOCH_3$).

6d $C_{33}H_{41}NO_{11}$ (627.67). Calc.: C, 63.14; H, 6.58; N, 2.23. Found: C, 63.14; H, 6.59; N, 2.29%. IR (KBr): 2850–2800 (Bohlmann's absorption), 1740 [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$, $OCOCH_3$], 1650 cm^{-1} (aromatic). ^1H NMR (C_6D_6 + DMSO): 7.61 (2H, s, 2'-H, 6'-H), 6.92 (1 H, s, 9-H), 6.65 (1 H, s, 6-H), 5.96 (1 H, m, J_{ac} = J_{ec} = 3 Hz, 15-H), 5.69 (1 H, dd, J_{aa} = 11.5 Hz, J_{ae} = 3 Hz, 14-H), 3.91, 3.70, 3.64, 3.57 (18 H, s, $COOCH_3$, OCH_3), 1.88 (3 H, s, $OCOCH_3$).

8b $C_{33}H_{41}NO_{11}$ (627.67). Calc.: C, 63.14; H, 6.58; N, 2.23. Found: C, 63.14; H, 6.59; N, 2.29%. IR (KBr): 1750, 1725 [$COOCH_3$, $OCOC_6H_2(OCH_3)_3$, $OCOCH_3$], 1605 cm^{-1} (aromatic). ^1H NMR (C_6D_6) 7.52 (2 H, s, 2'-H, 6'-H), 7.06, 6.53 (2 H, s, 6-H, 9-H), 6.06 (1 H, m, J_{aa} = 2.5 Hz, J_{ae} = 3.5 Hz, 14-H), 4.95 (1 H, m, J_{aa} = 12 Hz, J_{ae} = 4.5 Hz, 15-H), 4.21 (1 H, m, J_{aa} = 3 Hz, J_{ae} = 3 Hz, 1-H), 3.85, 3.82, 3.58, 3.55, 3.39 (18 H, s, $COOCH_3$, OCH_3), 1.82 (3 H, s, $OCOCH_3$).

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REFERENCES

[1] L. Szabó, I. Tóth, L. Töke, J. Tamás and Cs. Szántay, *Liebigs Ann. Chem.* 642 (1977).
[2] N. Hosansky and E. Shmith, *J. Am. Pharm. Assoc.* **44**, 639 (1955).
[3] C. F. Huebner and E. Schlittler, *J. Am. Chem. Soc.* **79**, 250 (1957).
[4] L. Szabó, I. Tóth, K. Honty, L. Töke, J. Tamás and Cs. Szántay, *Chem. Ber.* **109**, 1724 (1976).
[5] L. Szabó, I. Tóth, L. Töke, P. Kolonits and Cs. Szántay, *Chem. Ber.* **109**, 3390 (1976).
[6] L. Szabó, I. Tóth, L. Töke and Cs. Szántay, *Liebigs Ann. Chem.* 634 (1977).
[7] F. Bohlmann, *Angew, Chem.* **69**, 541 (1957): *Chem. Ber.* **91**, 2157 (1958).
[8a] K. L. Williamson and W. J. Johnson, *J. Org. Chem.* **26**, 4563 (1961); [b] A. Leblance-Combier, B. Lacoume and J. Levisalles, *Bull. Soc. Chim. Fr.* 897 (1966); [c] H. B. Henbest, D. N. Jones and G. D. Slater, *J. Chem. Soc.* 4472 (1961); [d] L. F. Fieser and R. Stevenson, *J. Am. Chem. Soc.* **76**, 1728 (1954); [e] L. F. Fieser and M. A. Romero, *J. Am. Chem. Soc.* **75**, 4416 (1953).
[9] M. Uskokovic, H. Bruderer, C. von Planta, T. Williams and A. Brossi, *J. Am. Chem. Soc.* **86**, 3364 (1964).
[10] *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* (Edited by L. M. Jackman and S. Sternhell), Pergamon Press, Oxford, 1969.
[11] R. J. Abraham and G. Gatti, *J. Chem. Soc.* (B), 961 (1969).
[12] J. E. Bridgeman, C. E. Butchers, E. R. H. Jones, A. Kasal, G. D. Meakins and P. D. Woodgate, *J. Chem. Soc.* (C) 244 (1970).
[13a] R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey and R. W. Kierstead, *J. Am. Chem. Soc.* **78**, 2023, 2657 (1956); *Tetrahedron* **2**, 1 (1958); [b] J. O. Jilek, J. Pomikacek and M. Protiva; *Coll. Czech. Chem. Commun.* **26**, 1145 (1961); [c] I. Jirkovsky and M. Protiva, *Coll. Czech. Chem. Commun.* **28**, 2577 (1963)
[14] M. M. Robinson, W. C. Pierson, R. A. Lucas, I. Hsu and R. L. Dziemian, *J. Org. Chem.* **28**, 768 (1963).
[15a] J. L. Pierre, M. Vincens and M. Vidal, *Bull. Soc. Chim. Fr.* 1775 (1971); [b] B. Casu, M. Reggiani, G. G. Gallo and A. Vigeveni, *Tetrahedron* **22**, 3061 (1966).
[16] W. F. Trager, C. M. Lee and A. H. Beckett, *Tetrahedron* **23**, 365 (1967).