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IRIDOIDS—II

LAMIOSIDE FROM *LAMIUM AMPLESSICAULE**

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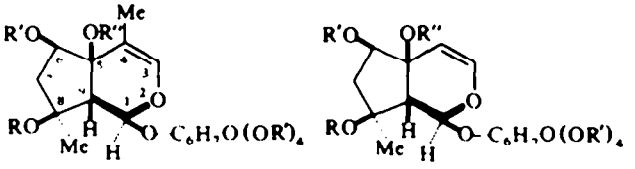
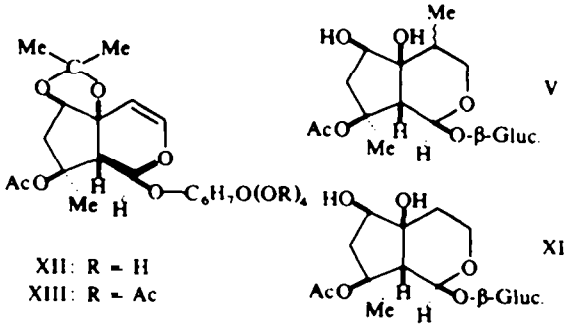
Abstract—Isolation of two new iridoid glucosides, Lamioside and Lamiol, from *Lamium amplessicaule* (Labiatae) is described. Their structure and configuration have been elucidated.

CHROMATOGRAPHIC examination[2] of an ethanolic extract of *Lamium amplessicaule* (Labiatae) revealed the presence of at least 5 compounds, with probable iridoid[1] skeleton. These compounds were separated by repeated chromatography on various adsorbents and the results on two of these compounds (with R_f 0·46 and 0·30 respectively, see Experimental) are now reported.

The less polar compound I is a hygroscopic amorphous powder, $[\alpha]_D^{16}$ −125°, with molecular formula $C_{18}H_{28}O_{11}$. Like other natural occurring iridoids, I is converted, by acid hydrolysis into *glucose* (1 mole) and insoluble black products, due to decomposition of the aglycone.



II ..... R = R' = R'' = H IV
I R = Ac ..... R' = R'' = H III
VI R' = Ac ..... R = R'' = H VIII
VII R = R' = Ac ..... R'' = H IX
R = R' = R'' = Ac X



XII: R = H
XIII: R = Ac

* The investigations were supported by the "Consiglio Nazionale delle Ricerche".

[1] L. H. Briggs, B. F. Cain, P. W. Le Quesne and J. N. Shoolery, *Tetrahedron Letters* 70 (1963).
[2] R. Paris and M. Chaslot, *Ann. Pharm. Fr.* 13, 648 (1955).

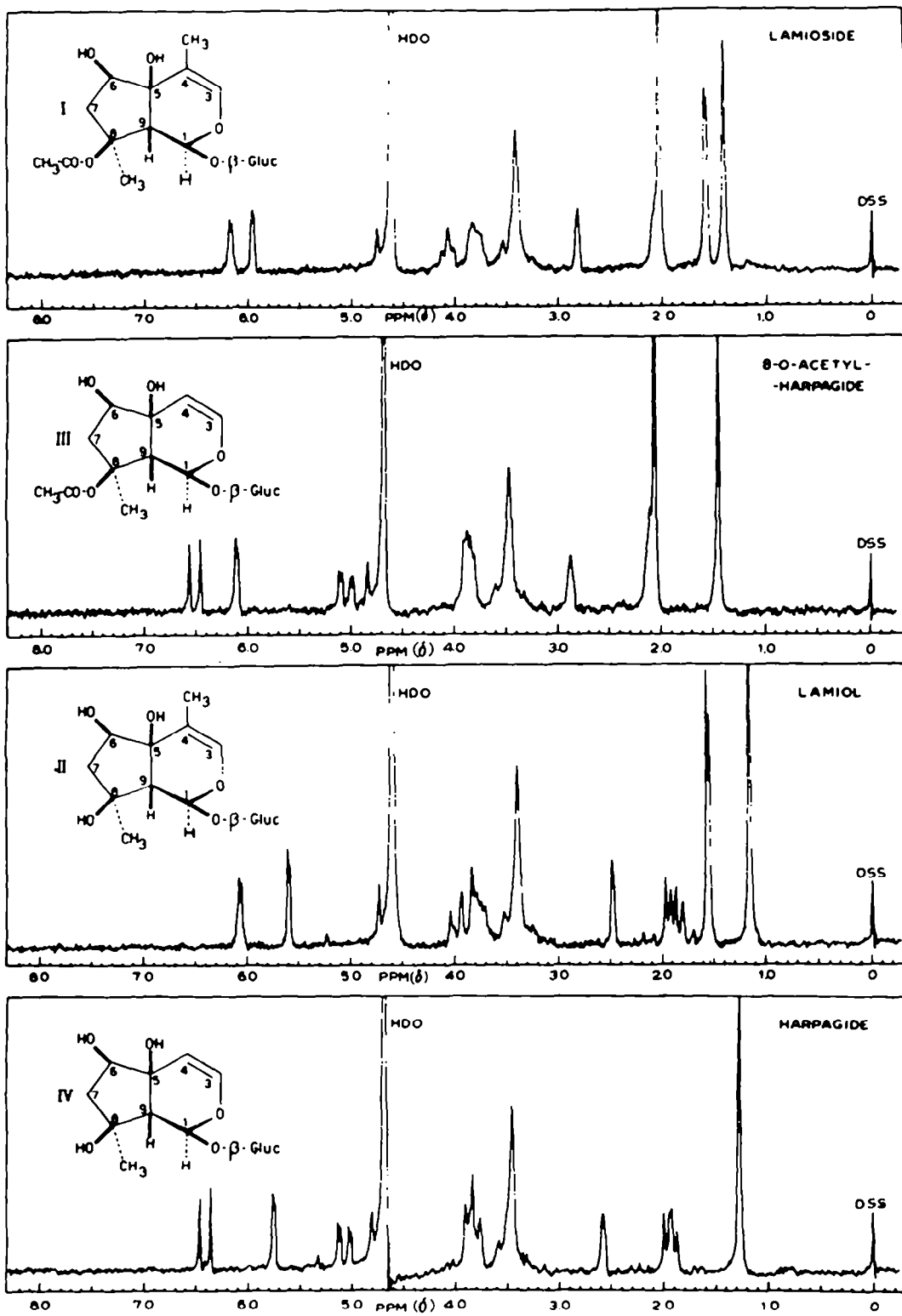


FIG. 1. NMR spectra in D_2O.

Compound I, named Lamioside, shows UV absorption at 208 mμ (log ε 3·6), due to the double bond of the enol-ether grouping. The presence of an O-acetyl group is shown by the peak in the NMR spectrum of I at 2·03 δ, which disappears in the spectrum of the new glucoside (II, obtained by alkaline hydrolysis of I.

Compound II, named Lamiol, is an amorphous powder and differs from lamioside by the loss of the acetyl group in accordance with its molecular formula $C_{16}H_{26}O_{10}$, $[\alpha]_D^{26}$ −153°. It proved identical with the component of *Lamium amplessicaule* having R_f 0·30. The NMR spectrum of lamioside confirmed an iridoid structure and indicated a close relationship with 8-O-acetylharpagide (III), isolated from *Melittis melissophyllum*.[3] The NMR spectra of I, II, III and of harpagide[4] (IV) are shown in Fig. 1 and relative assignments are reported in Table 1. It is evident that the signals of the protons on C_1, C_6, C_7, C_9 and of the Me group (C_{10}), attached to C_8, correspond one to the other for the two sets of compounds: I, III and II, IV. The differences between the NMR spectra of I and III are as follows and all support location of the second Me group of I, (C_{11}), at C_4:

(1) In the spectrum of III the signals of the two coupled vinylic protons —at C_3 and C_4—appear as doublets (J = 6·5 c/s) centered at δ 6·53 and 5·04, whereas in I we found only the signal at lower field (δ 6·17).

(2) This signal is an imperfectly resolved quartet with a small J = 1·3 c/s.

(3) A similar small coupling constant is shown by the signal of the second Me group of I, which appears as a doublet at δ 1·58, a rather low field, justified by location of the Me on a double bond. The J = 1·3 c/s corresponds to a cisoid allylic coupling between the protons of this Me[5] and the proton at C_3.

Structure I is sufficiently supported by spectroscopic evidence. In this structure the *O-acetyl group* has been located at C_8, as in III, owing to the equal values of the shifts that the signals of the Me group at C_8 and of the neighbouring protons at C_1 and C_9 undergo by the loss of the acetyl group either in II or in IV[3] (Table 2). Furthermore, no other proton geminal with primary or secondary OH undergo shift through this transformation, confirming that the ester bond arises from a tertiary OH.

The *glucosyl group* must be attached to the hemiacetalic OH at C_1, either in accordance with the good stability of lamioside —whereas iridoid aglycones are unstable[6] — or by analogy of other glucosides of this class. Spectroscopic evidence of this location is given by the resonance of the anomeric proton at C_1 at a rather low field (δ 5·60 for II and δ 5·75 for IV), when compared with reported resonance of the same proton of aglycones (i.e. δ 5·45 for dihydroharpagide, δ 4·93 for its aglycone[4]).

Glucose is in the *β-configuration*, as shown by the signal of the anomeric proton at C_1' (δ 4·70, doublet J = 7 c/s).[7,8] Chemical and further spectroscopic evidence, supporting structure I, are given below.

[3] M. L. Scarpati, M. Guiso and L. Panizzi, *Tetrahedron Letters* 3439 (1965)

[4] H. Lichti and A. von Wartburg, *Helv. Chim. Acta* **49**, 1552 (1966); *Tetrahedron Letters* 835 (1964).

[5] Lamioside seems to be the first iridoid compound of vegetable origin, which retains the methyl C_{11}, whereas in the other iridoids, isolated until now from plants, this group has been oxidized to carboxyl, as in asperuloside, monotropein etc, or has been lost as in aucubin, catalposide etc

[6] I. H. Briggs, G. A. Nicholls, *J. Chem. Soc.* 3940 (1954).

[7] R. W. Lenz, *J. Polymer Science* **51**, 247 (1961)

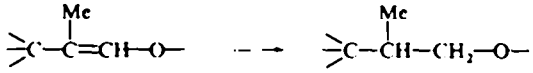
[8] This signal, partially covered by that of HDO in the NMR spectra of Fig. 1, is visible when NaI is added to D_2O solution, through the shift to higher fields of the HDO signal, induced by this salt [J. N. Shoolery, B. Alder, *J. Chem. Phys.* **23**, 805 (1955)].

TABLE 1.

	1H C_1	1H C_3	1H C_4	1H C_6	2H C_7	1H C_9	3H C_{10}	3H C_{11}
I	5·96	6·17	–	4·07	2·05	2·81	1·42	1·58
D_2O	d	q		m	m	s*	s	d
	J 0·8	*J* 1·3						*J* 1·3
II	5·60	6·08	–	~3·9	1·90	2·49	1·17	1·57
D_2O	d	q	-	m	m	s*	s	d
	J 0·8	*J* 1·3						*J* 1·3
III	6·11	6·53	5·04	~3·9	2·10	2·88	1·45	
D_2O	d	d	dd	m	m	s*	s	
	J 0·8	*J* 6·5	*J* 6·5·1·5					
IV	5·75	6·41	5·09	~3·9	1·93	2·58	1·27	-
D_2O	d	d	dd	m	m	s*	s	–
	J 0·8	*J* 6·5	*J* 6·5·1·5					
V	5·84			~4·0	2·27	2·53	1·54	0·83
D_2O	s			m	m	s	s	d
								J 7
XI	5·82				2·25	2·46	1·53	
D_2O	s				m	s	s	
VI	5·61	6·02	–	between δ 4·6 5·5	1·86	2·78	1·28	1·67
$CDCl_3$	d	q			m	s*	s	d
	J 1·2	*J* 1·3						*J* 1·3
VIII	5·63	6·25				2·74	1·28	-
$CDCl_3$	d	d				s*	s	
	J 1·2	*J* 6·1						
VII	6·04	6·04	–		under CH_3CO signals	3·02	1·45	1·66
$CDCl_3$	s*	s*	-			s*	s	d
								J 1·2
IX	6·04	6·32				3·00	1·46	
$CDCl_3$	d	d				s*	s	
	J 1·5	*J* 6·5						
XII	5·86	6·29				2·95	1·42	1·63
D_2O	s*	d				s*	s	d
		J 1·5						*J* 1·5
XIII	5·73	6·13	-		2·34	2·95	1·45	1·64
$CDCl_3$	s*	d			m	s*	s	d
		J 1·5						*J* 1·5

NMR spectra assignments. Coupling constants (*J*) are expressed in c/s. s = singlet, d = doublet, dd = double doublet, q = quartet, m = multiplet. The asterisk marks unshapen signals.

Lamioside is slowly converted, by H_2 and Pd/C reduction at room pressure and temperature, into a dihydroderivative V as an amorphous powder, $C_{18}H_{30}O_{11}$. In the NMR spectrum of V the peak at δ 6·17 of I, due to vinylic proton at C_3, disappears. At the same time the signal at δ 1·58 is shifted to δ 0·83 and is converted into a doublet spacing 7 c/s.[9] Furthermore, the value of the integral between δ 3·2 and δ 4·2 shows an increase of two protons in the NMR spectrum of V, when compared with that of I in the same field. All these changes demonstrate a transformation:



The existence of one secondary and two tertiary OH in the aglycone residue of lamiol is demonstrated by acetylation of II and I. Acetylation of II yields a mixture

TABLE 2.

$\Delta\delta$*	HC_1	HC_9	$3HC_{10}$
I II	0·36	0·32	0·25
III IV	0·36	0·30	0·18
VII VI	0·43	0·24	0·17
IX VIII	0·41	0·26	0·18

* Differences between δ in NMR spectra

of penta-O-acetyl-lamiol (VI), as main product, m.p. 168-170°, $[\alpha]_D^{27}$ −119°, and hexa-O-acetyl-lamiol (VII), m.p. 205-207°, $[\alpha]_D^{31}$ −116°.

Acetylation of I gives only VII. This compound is not converted into hepta-O-acetyl-lamiol, even by acetylation under forcing conditions.

The NMR spectrum of VI shows signals corresponding to two OH. In comparison with the spectrum of II, shifts to lower field are observed for two protons geminal with primary OH (at C_6'),and five protons geminal with secondary OH (four of the glucosyl group and one of the aglycone residue). The NMR spectrum of VII shows the signal corresponding to one OH. The OH, esterified in the transformation VI → VII, must be that at C_8, as shown by the shifts of the signals of the protons at C_1, C_9 and C_{10}, similar to those observed for the transformation II → I (Table 2). At the same time, no signal of proton geminal with OH is shifted, showing that the ester bond arises from a tertiary OH.

Acetylation of harpagide, made for comparative purposes, affords as main product the penta-O-acetyl-harpagide (VIII) m.p. 174 176°, $[\alpha]_D^{27}$ −118°, in addition to other acetyl derivatives. Acetylation of III affords a mixture of hexa-O-acetyl-harpagide (IX),[4] as main product, and hepta-O-acetyl-harpagide (X).[4] The mixture is converted into X under forcing conditions.

[9] The sharpness of this doublet may suggest that the reduction has been stereo-selective. Hence the $-CH_3$ (C_{11}) ought to be in an α-configuration, the more probable attack being at the convex side of the molecule.

The NMR spectra of VIII and IX are similar to those of VI and VII respectively (Table 1).

The differences in behaviour during acetylation, between either I and III or II and IV, confirm that the last tertiary OH ought to be at C_5, where it is more hindered in I than in III, owing to the presence of the Me group at C_4.

The existence in I of two free OH on contiguous carbon atoms has been confirmed by periodic acid oxidation of V. Dihydrolamioside (V) and dihydro-8-O-acetyl-harpagide (XI), prepared from III for comparative purposes, consume three molecules of periodic acid, two of which are due to the glucosyl grouping and one to the aglycone residue.

Periodic acid oxidation of I does not give significant results, because consumption of reagent goes beyond forecast, as it has already been observed for III.[3] Behaviour of III was attributed to the ease of hydrolysis of the β-keto-enol-ether, formed by attack at C_5-C_6, with subsequent hydrolysis of the glucosyl group. This suggestion is confirmed by the stability to hydrolysis, shown by the saturated keto-ethers, yielded by periodic acid oxidation of V and XI (see Table 3).

Hence, the described behaviour of I and V to periodic acid oxidation is in favour of the location of the glycol function contiguous to the double bond, i.e. at C_5-C_6[10] as in III and IX.

TABLE 3.

Time in min	Moles $NaIO_4$ Moles of substrate V	XI
15	2·67	2·77
30	3·01	3·07
45	3·08	3·07
60	3·08	3·10

In lamiol the two OH on C_5 and C_6 have the *cis*-configuration as indicated by the reaction of lamioside with acetone in the presence of $SnCl_2$.[4] An amorphous mono-O-isopropylidene derivative XII, whose NMR spectrum shows the peaks of isopropylidene grouping at δ 1·42 and δ 1·51 (3H), was isolated. Compound yields, by acetylation under mild conditions, a tetra-acetyl derivative XIII, m.p. 194–195°. The NMR spectrum of XIII shows four acetyl peaks and the shift to lower field of two protons geminal with primary OH (at C_6) and of three protons geminal with secondary OH. The absence of free OH and the introduction of four acetyl groups demonstrate that the isopropylidene residue is part of the aglycone unit.[11]

[10] The remaining possible arrangements on C_6 C_7 or C_5 C_9 would be in evident contrast with reported results of the acetylation reactions. Furthermore the existence in I of three protons (HC_9, $2HC_7$) of hydrocarbonic nature, shown by the NMR spectrum, is only possible if the two free OH of I are on C_5 and C_6.

[11] As it is reported in: *Advances in Carbohydrate Chemistry* Vol. 20, p. 254. Academic Press, New York and London (1965), glucopyranosides do not give with acetone isopropylidene acetals, under the usual conditions.

Lamiol II must have the configu ation assigned to harpagide (IV),[4] by comparison of rotatory power values[12] (Table 4) and NMR spectra of these compounds and of their acetyl derivatives. (Table 1).

TABLE 4.

Lamiol series			Harpagide series		
	M_D*	ΔM_D		M_D*	ΔM_D
II	579	I II +55	IV	536	III IV +36
I	-524	VI II -121	III	-500	VIII IV -142
VI	-700	VII VI -32	VIII	-678	IX VIII 13
VII	-732		IX	-691	

* Optical rotations were measured in dioxan, $c \cong 12.10^{-3}$ mole/l.

The similar M_D values (Table 4) for the two series of compounds and expecially the similar changes of M_D (ΔM_D), caused by transformations of similar asymmetric centers, support the assignment of configuration. For instance, the ΔM_D values between I and II (+55°) and III and IV (+36°) show that acetylation of the OH at C_8 gives a positive contribution to the M_D of both I and III. Furthermore, the very similar shifts—caused by this transformation—of the protons attached to the asymmetric carbons C_1 and C_9, either in the NMR spectrum of I or III, show that the relative configurations of the points C_8, C_1 and C_9 must be the same in I and in III. (Table 2).

Acetylation of the glucosyl group and the OH at the asymmetric C_6, results in a ΔM_D value of −121° between VI and II and −142 between VIII and IV. Since the difference between the contribution of the β-glucosyl group and of the β-O-tetracetyl-glucosyl group is negligible,[13] the observed variations are due to the aglycone residue and are similar for both sets of compounds. Hence, the asymmetric center at C_6 must have the same configuration in I and III.

Regarding the asymmetric carbon of lamiol at C_5, probably the cyclopentane and dihydropyrane rings have a *cis* junction in accordance with all the known iridoid compounds, and in particular harpagide.

Concerning the stereochemistry of C_1 we would like to add some deductions resulting from M_D values of lamiol, −579 ; harpagide, −536 ; dihydroharpagide,

[12] This comparison is possible because the only difference between structure II and IV concerns the symmetric C_4. The presence of the Me at C_4, in fact, cannot affect considerably the M_D values of lamiol and lamiol acetates

[13] M_D of β-methyl-glucoside −64°, M_D of β-methyl-O-tetraacetyl-glucoside −68 [O Halpern, H Schmidt, *Helv Chim Acta* **41**, 1133 (1958)]

$-392°$;[4] methyl dihydroharpagenines: α, $+187°$ and β, $-169°$.[4] As it has been deduced, for instance, for plumieride[13] and gentiopicroside[14] etc, an absolute β-configuration of C_1 can also be assigned to dihydroharpagide and therefore to harpagide.

If all the other asymmetric centers have similar configurations in II and IV, lamiol must also have an *absolute β-configuration* of C_1. Furthermore, the same axial orientation of the β-O-substituent of C_1 may be assigned to lamiol, considering the values of the coupling constant of the protons at C_1 and C_9.[4]

Research on the structure of the other iridoid components of *Lamium amplessicaule* is in progress.

EXPERIMENTAL

M.ps were taken on a Kofler block and are uncorrected. Merck silica gel was used for column chromatography (140–230 mesh), it was washed several times with hot water, acetone and afterwards dried *in vacuo* and activated at 120° for 8 hr. Woelm polyamide powder was used for chromatography, it was washed several times with water, acetone and dried *in vacuo* at 40–50°. Merck Kieselgel G was used in TLC. Chromatograms on paper (Schleicher & Schüll nr 2043 Mgl) were run in n-ButOH–AcOH–H_2O 63:10:27 and detected by spraying with a soln of vanillin (1 g) and conc HCl (3 ml) in MeOH (150 ml) and heating for 2–3 min at 100°. NMR spectra were determined on a Varian A-60. Sodium 2,2-dimethyl-2-silapentane-5-sulfonate was used as internal reference for D_2O solns and TMS for $CDCl_3$ solns. Chemical shifts are expressed in δ values downfield from the internal standard.

All described amorphous compounds, after chromatographic purification and before analytical determinations, were dissolved in water; the soln was filtered through Schleicher and Schüll "blauband" filter paper and dried *in vacuo* to constant wt (at 60°).

Isolation of iridoid fraction. Lamium amplessicaule (fresh plant; 20 Kg) was roughly chopped and extracted with EtOH (17 l. × 2) at room temp for 24 hr. The combined EtOH solns were evaporated *in vacuo* (1·5 l.) to an aqueous suspension which was extracted 4 times with AcOEt (2·5 l.) and further concentrated *in vacuo* to 1·3 l. A chromatogram on paper revealed 5 spots with R_f 0·60 (pink spot), 0·46 (pink lilac) *lamioside*, 0·40 (violet), 0·30 (pink lilac) *lamiol*, 0·25 (blue green).

The final water soln was filtered through 1·4 Kg of decolorizing charcoal (Erba) – suspended in water and stratified in a Gooch funnel (Ø 17 cm). Mono and disaccharides were removed by elution with water (12 l.), water–EtOH 9:1 (12 l.) and water–EtOH 7:3 (2·3 l.). At this point elution of iridoid compounds began (positive test with vanillin reagent). *Fraction* A. Compound with R_f 0·25 was eluted with *lamiol* (II) by water–EtOH 7:3 (3 l.) and 6:4 (4 l.). *Fraction B. Lamioside* (I), lamiol and compounds with R_f 0·40 and 0·25 were eluted all together by water–EtOH 6:4 (2 l.) and 4:6 (16 l.). Finally, EtOH eluted the compounds with R_f 0·60.

Fraction A was evaporated but if the partially concentrated soln was acid, it was neutralized with $Ba(OH)_2$aq and evaporated. To the dry residue MeOH was added, the suspension was filtered and the soln evaporated to give 4·6 g of an amorphous product.

Fraction B was similarly treated to give 9·6 g of amorphous residue.

Lamioside (I). Fraction B (6·6 g) was chromatographed on silica gel (330 g). Elution with n-ButOH saturated with water gave in the first fractions lamioside and a compound with R_f 0·40 (4·26 g); afterwards a mixture of all the 4 compounds (0·5 g); and finally lamiol and a compound with R_f 0·25 were eluted together (0·5 g).

The first mixture (4·26 g) was further chromatographed on 210 g of polyamide. Elution with acetone gave in the first fractions *lamioside* (1·7 g); afterwards lamioside was eluted with the compound with R_f 0·40.

Since lamioside is an amorphous powder, its purification, for analytical purposes, was achieved by further chromatography on silica gel and elution with 7% EtOH–AcOEt; $[\alpha]_D^{27}$ $-133°$ (MeOH, *c* 0·5%); $[\alpha]_D^{27}$ $-125°$ (dioxan, *c* 0·5%). (Found: C, 51·29; H, 6·95. $C_{18}H_{28}O_{11}$ requires: C, 51·42, H, 6·71%.)

[14] L. Canonica, G. Jommi, P. Manitto, F. Pelizzoni and C. Scolastico, *Gazz. Chim. Ital.* **95**, 167 (1965).

Lamiol (II) *from* Lamium amplessicaule. Fraction A (from charcoal; 4·6 g) was chromatographed on silica gel as described for fraction B. Lamiol (0·34 g), was first eluted; afterwards a mixture of lamiol and a compound with R_f 0·25 and finally the compound with R_f 0·25.

Lamiol was further purified on silica gel (ratio compound: adsorbent, 1:100) by elution with 11% MeOH AcOEt.

Lamiol from lamioside. Lamioside (0·20 g) was treated with 3·5 ml sat $Ba(OH)_2$ at room temp for 12 hr. Excess $Ba(OH)_2$ was precipitated as $BaCO_3$ and the filtrate was evaporated *in vacuo* to dryness. The residue was purified on silica gel by elution with 11% MeOH–AcOEt.

The compound shows the same chromatographic behaviour of lamiol from the fresh plant, identical NMR spectrum; $[\alpha]_D$ −153° (dioxan); (Found: C, 50·66; H, 6·92. $C_{16}H_{26}O_{10}$ requires: C, 50·79; H, 6·93%.)

Dihydro-lamioside (V). Lamioside (200 mg), dissolved in EtOH–water 8:2 (9·6 ml), was added to 60 mg of 10% Pd-C, previously suspended in EtOH (3 ml) and saturated with H_2. About 1 mole of H_2 was absorbed during 8 hr and then the catalyst was removed by filtration and washed several times with EtOH. The combined washings were evaporated to give an amorphous residue, which on TLC (n-BuOH AcOH H_2O) showed that dihydro-lamioside was contaminated by small amounts of another compound with very similar R_f. The latter was removed by chromatography on polyamide and acetone. Its NMR spectrum showed peaks corresponding to an ethoxide, demonstrating that its formation was due to a reaction between I and EtOH (probable addition to the double bond).

Acetone eluted pure V (100 mg) in the next fractions (Found: C, 50·78; H, 7·52; $C_{18}H_{30}O_{11}$ requires: C, 51·18; H, 7·16%.)

8-O-*Acetyl-dihydro-harpagide* (XI). 8–O-acetyl-harpagide was treated as above to give pure XI rapidly (2 hr). It was chromatographed on silica gel and elution with 5% water–acetone gave XI as an amorphous powder. (Found: C, 49·91; H, 6·75. $C_{17}H_{28}O_{11}$ requires: C, 50·00; H, 6·91%.)

Periodic acid oxidation of V *and* XI. The oxidation of V and XI was carried out with 0·1 M $NaIO_4$ (40 ml of reagent diluted to 50 ml with the water soln of the substrate) at room temp. Samples (10 ml) were used for titrations, the results of which are reported in Table 3.

When lamioside was submitted to similar oxidation, it consumed, after 2 hr, more than 5 moles of $NaIO_4$.

Penta-acetyl-lamiol (VI) *and hexa-acetyl-lamiol* (VII). To lamiol (90 mg) in 0·36 ml anhyd pyridine was added 0·72 ml Ac_2O. The soln was allowed to stand at room temp for 5 hr, whereupon it was evaporated under reduced press and to the resulting residue $CHCl_3$ was added. The $CHCl_3$ soln was washed with dil H_2SO_4 aq, water and dried (Na_2SO_4). The solvent was evaporated. The residue was a mixture of two compounds, the main product was VI. It was chromatographed on 8 g of silica gel. Elution with 80% ether–20% AcOEt gave VII (30 mg) and afterwards VI (100 mg).

Compd VI was crystallized from abs EtOH as needles, m.p. 168–170°, $[\alpha]_D$ −119° (dioxan). (Found: C, 52·93; H, 6·42. $C_{26}H_{36}O_{15}$ requires: C, 53·09; H, 6·17%.)

Compd VII was crystallized from EtOH as needles, m.p. 205–207°, $[\alpha]_D$ −116° (dioxan). (Found: C, 53·12; H, 6·04. $C_{28}H_{38}O_{16}$ requires: C, 53·33; H, 6·03%.)

Hexa-acetate (VII) *from lamioside.* Lamioside (180 mg) was treated as above to give VII (330 mg). If the reaction was carried out for 7 hr at 76° (CCl_4 bath), VII was converted into an amorphous compound which had the molecular formula of the expected hepta-acetyl-lamiol, but as it was not reconverted into lamiol by alkaline hydrolysis, as occurs for VI and VII, the structure of this compound is being investigated.

Penta-acetylharpagide (VIII). Harpagide (115 mg) was treated as for II to give a product (230 mg) which yielded a mixture of VIII and small amounts of other acetates with higher R_f values, as it resulted on TLC.

It was chromatographed on silica gel (12 g). Elution with 80% ether–20% AcOEt removed the other compounds and gave in the last fractions pure VIII, (160 mg).

Compd VIII was crystallized from dry EtOH as needles, m.p. 174–176°, $[\alpha]_D$ −118° (dioxan). (Found: C, 52·39; H, 6·14. $C_{25}H_{34}O_{15}$ requires C, 52·26; H, 5·97%.)

Hexa-acetylharpagide (IX) *and hepta-acetylharpagide* (X) *from* III. Compd III was treated as for II to give IX and very small amounts of X.[4] If the reaction was carried out at 70° for 7 hr the main product was X.

5,6-O-*Isopropylidenelamioside* (XII) *and tetra-acetate* XIII. To lamioside (140 mg) in 1 ml of dry acetone was added 1·7 ml of an acetone soln of $SnCl_2$ (500 mg in 3 ml). The soln was allowed to stand at room temp for 1 hr and 10 min and then it was treated with sat $NaHCO_3$ aq and diluted with water. The mixture was filtered through 1 g of decolorizing charcoal. Soluble salts were removed by water elution and XII was eluted with MeOH. The alcohol was evaporated under reduced press to give 122 mg of amorphous

material which was chromatographed on silica gel. Elution with n-ButOH, saturated with water, gave 80 mg of XII, pure by chromatoplate (n-ButOH H_2O).

Acetylation of XII, carried out as described for II, gave pure XIII.

Compd XIII was crystallized from dry EtOH as needles, m.p. 194–195°. (Found: C, 55·68; H, 6·53. $C_{29}H_{40}O_{15}$ requires: C, 55·41; H, 6·42%.)

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