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CHEMICAL COMPONENTS OF THE ROOTS OF *SELINUM VAGINATUM*—I

COUMARINS OF THE PETROLEUM ETHER EXTRACT

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Abstract—Five coumarins, angelicin, oroselol, lomatin, selinidin and vaginidin, have been isolated from the petroleum ether extract of the roots of *Selinum vaginatum*. The structure of the new coumarins selinidin and vaginidin have been established by spectral studies and chemical degradation to known compounds.

THE roots of *Selinum vaginatum* (Umbellifereae) form an aromatic drug and are commonly used in the fumigation of houses. It is generally an adulterant[1] of another drug *Nardostachys jatamansi* (Valerianaceae), whose roots are well known for their medicinal properties.[2] They resemble each other in their external appearance though they can be differentiated by close study and particularly by microscopic examination. Recently Shanbhag *et al.*[3] have reported the presence of the same coumarins in *N. jatamansi* as have been isolated from *S. vaginatum* but do not mention the presence of jatamansone (I) which is the characteristic component of *N. jatamansi*.[4] In view of the unusual features of their report, petroleum ether extracts of authentic samples of the roots of both plants have been examined and shown to differ markedly.[5] It is clear that *S. vaginatum* was mistaken for *N. jatamansi*. Consequently the name jatamansin is not justified and selinidin alone should be used.

The present work on *S. vaginatum* has led to the isolation in good yields of two new coumarins, selinidin and vaginidin and three known coumarins, angelicin, oroselol and lomatin. These are not artefacts, since the crude petroleum ether extract showed their presence on TLC.

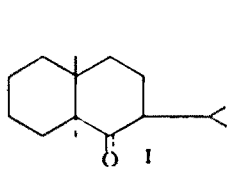
Selinidin. It is a highly crystalline compound, m.p. 97–98° and its homogeneity has been proved by TLC. It has the molecular formula $C_{19}H_{20}O_5$, based on analysis and mol. wt determination. It does not contain any alcoholic or phenolic OH, CO, MeO or acetoxy groups. Comparison of its spectral data with those of known coumarins[6] provided at the outset strong evidence for the presence of a 7-oxygenated

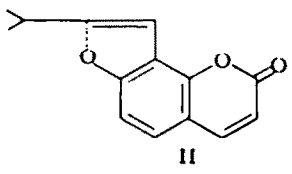
[1] P. N. Mehra and S. S. Jolly, *Planta Medica* **11**, 8 (1963).
[2] A. K. Nadkarni, *Indian Materia Medica* (3rd Edition) Vol. 1; p. 980 Popular Book Depot, Bombay (1954).
[3] S. N. Shanbhag, C. K. Mesta, M. L. Maheshwari, S. K. Paknikar and S. C. Bhattacharyya, *Tetrahedron* **20**, 2605 (1964); *Ibid.* **21**, 3591 (1965).
[4] T. R. Govindachari, B. R. Pai and S. Rajadurai, *Tetrahedron Letters* 5 (1959).
[5] T. R. Seshadri and M. S. Sood, *Phytochemistry* in press.
[6] F. Smith, N. Hosansky, W. G. Bywater and E. E. Van Tamelen, *J. Am. Chem. Soc.* **79**, 3534 (1957).

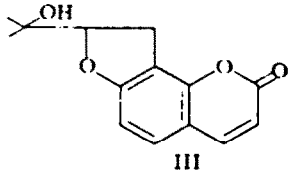
coumarin chromophore, an assignment also supported by chemical reactions. On catalytic hydrogenation, selinidin gave a tetrahydro derivative, $C_{19}H_{24}O_6$, m.p. 107–108°, which showed two strong absorption bands at 1775 and 1745 cm^{-1} in IR spectrum. The first can be assigned to a CO of the dihydro coumarin system[7] and the second to the CO of an aliphatic ester group. In the IR spectrum of selinidin itself there was only one CO frequency obviously due to the merging of the coumarin and unsaturated ester frequencies. This showed that there is a reduceable double bond in selinidin other than that of the coumarin. The mass spectrum of selinidin (Fig. 1) not only gave the mol. wt, but also the characteristic break down of the ester unit.

Since there were indications for the presence of unsaturated ester group, selinidin was subjected to the following reactions: (i) Ozonolysis gave acetaldehyde as a volatile fragment, its identity being established through its DNP; this observation indicated the presence of an ethylidene group. (ii) Hydrolysis with methanolic alkali gave equimolar quantities of tiglic acid and a hydroxy compound. The constitution of the hydroxy compound was determined as follows: It had the molecular formula $C_{14}H_{14}O_4$, m.p. 183–184°, and one free OH group which was not phenolic in nature. It gave a mono acetate, $C_{16}H_{16}O_5$, m.p. 136–137°. That hydrolysis had not brought about any change in the chromophore was shown by comparison of its UV spectrum with that of selinidin.

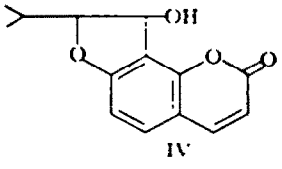
Important evidence was obtained by the dehydration of the hydroxycoumarin with acid, the product being identified as dihydro-oroselone (II) from its m.p., UV and IR spectral data and confirmed by comparison with an authentic sample. It could have arisen from the structures III to VI by dehydration, with or without rearrangement; mechanisms of these changes are well-known.[8]


I

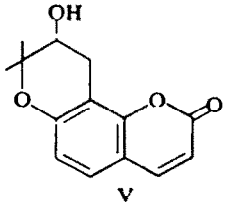

II



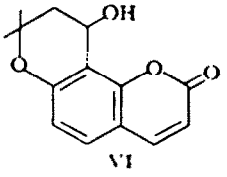
III



IV



V



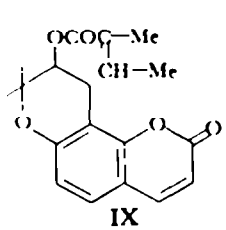
VI

Structures IV and VI could be ruled out because the hydroxycoumarin did not undergo hydrogenolysis and did not, therefore, have a benzylic alcoholic group. Structure III has already been assigned to columbianetin,[9] which is different from the present hydroxycoumarin in m.p., UV, IR and NMR data; thus only structure V

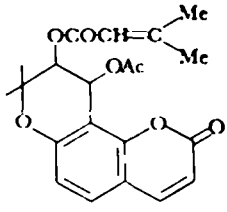
[7] J. Lecomte, *Handbuch der Physik* (Edited by S. Flugge) Vol. 22; p. 556. Springer, Berlin (1956).
[8] W. Bencze, J. Eisenbeiss and H. Schmid, *Helv. Chim. Acta* 39, 923 (1956).
[9] R. E. Willette and T. O. Soine, *J. Pharm. Sci.* 53, 275 (1964).

is left as possible. This was confirmed by catalytic hydrogenation of the hydroxy compound to give dihydro derivative VII, $C_{14}H_{16}O_4$, m.p. 124–126°, which agreed in m.p. and UV spectrum with the product of known constitution obtained from samidin (VIII), by hydrolysis followed by hydrogenolysis. This structure V (3'-hydroxy-3',4'-dihydroseselin) has been recently assigned to lomatin isolated from *Lomatinum nuttallium* by Soine *et al.*,[10] and comparison with lomatin has confirmed its identity. Hence selinidin could be tiglyl ester of lomatin.

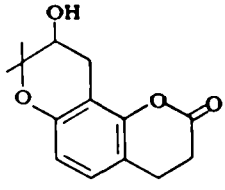
In the earlier note[11] we gave details of the NMR spectrum of the alcohol (lomatin) in support of its constitution, subsequently we have obtained the NMR spectrum of the ester, selinidin itself. Particular mention may be made of the signal due to the β-proton of the ester side chain, which is a multiplet centered at τ 4·02 (1H), characteristic of the β-proton of angelyl ester[12] and hence selinidin should be assigned the structure of angelate of lomatin (IX); the formation of tiglic acid on hydrolysis is due to easy isomerization during hot alkaline hydrolysis. Its mass spectrum (Fig. I) also gave support to this structure. It showed a molecular ion peak at *m/e* 328. Other major fragmentation peaks were obtained at *m/e* 228, 213 (base peak), 83 and 55. The peak at 228 corresponds to a loss of $C_5H_8O_2$ from molecular ion peak. The base peak at *m/e* 213 corresponds to a further loss of $—CH_3$ group. Another prominent peak at *m/e* 83 corresponds to an aliphatic side chain of C_5H_7O residue from which a further loss of CO unit gives the peak at *m/e* 55.



IX



VIII



VII

Vaginidin. The second new coumarin has been recently isolated from the neutral fraction of the petroleum ether extract by elaborate column chromatography. It is a highly crystalline compound, m.p. 133–134°, has the molecular formula $C_{19}H_{22}O_6$, and has been named "*Vaginidin*". It gave IR absorption bands at 3410 (—OH group), 1740 and 1622 (conjugated δ-lactone), 1492, 1260, 1150 and 840 cm^{-1} (tetra substituted benzene), and UV absorption bands at 246, 258 and 323 mμ (log ε 3·52 3·49 and 4·18 respectively). The spectral data and colour reactions suggested that vaginidin has the same basic chromosphere as selinidin and is probably also an ester.

Based on the above arguments vaginidin was subjected to hydrolysis under acidic as well as basic conditions. In both cases it yielded 1 mole of angelicin (X) and isovaleric acid. The easy formation of angelicin may be explained by the structures XI to XIV for vaginidin. Structures XI and XII can undergo ring contraction during hydrolysis to the diol XV, while XIII and XIV will give rise to the same diol without rearrangement. Compound XV will further undergo retro-aldol cleavage

[10] T. O. Soine and F. H. Jawad, *J. Pharm. Sci.* 53, 990 (1964).
[11] T. R. Seshadri, M. S. Sood, K. L. Handa and Vishwapaul, *Tetrahedron Letters* 3367 (1964).
[12] R. R. Fraser, *Canad. J. Chem.* 38, 549 (1960).

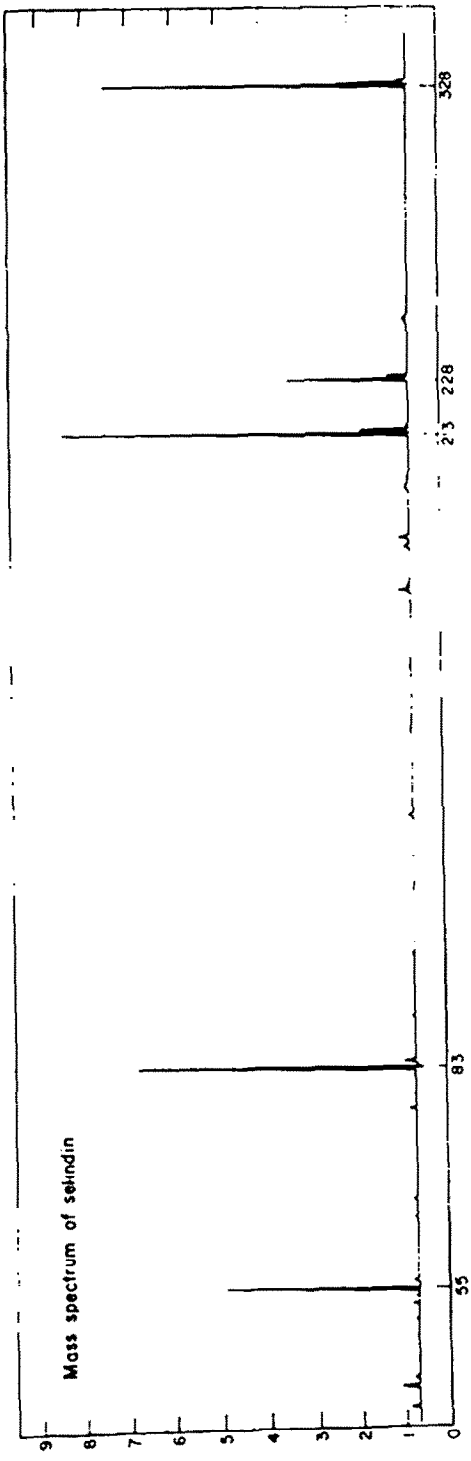
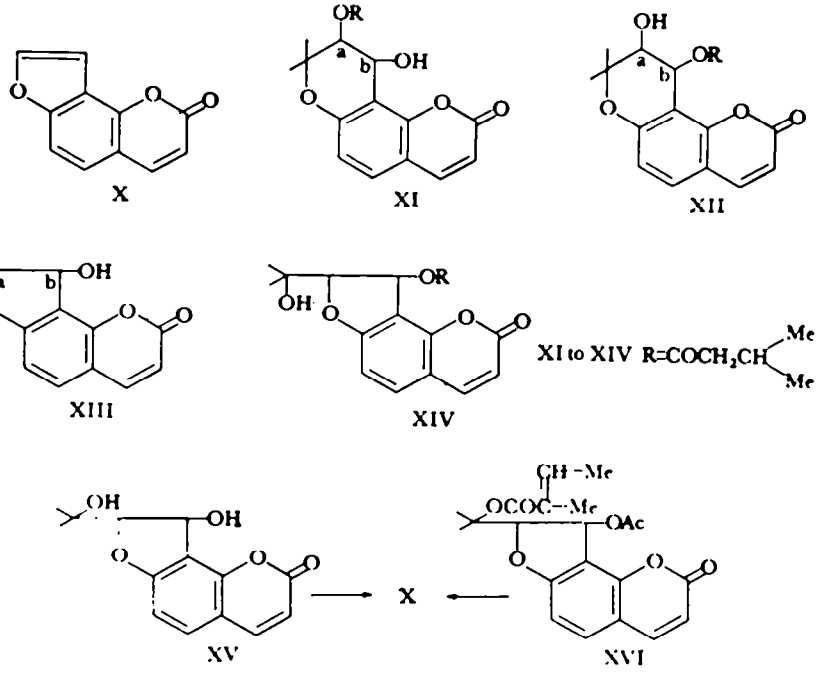
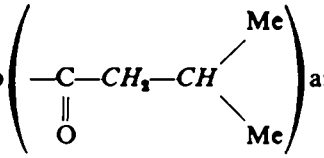


FIG. 1

followed by loss of water to yield angelicin (X). A known example of this type is provided by libanotin (XVI)[13] which also yields angelicin on hydrolysis.



Structures XII and XIV can be eliminated by consideration of the following chemical reaction. Vaginidin on catalytic hydrogenation yielded a colourless crystalline compound, $C_{19}H_{24}O_5$; m.p. 105–106°, which did not show any absorption in the OH region but showed two strong absorption bands at 1770 and 1740 cm^{-1} in IR spectrum. These can be assigned to the carbonyls of the dihydrocoumarin system and of the aliphatic ester group respectively. This indicated that besides the coumarin double band, vaginidin has lost one oxygen atom belonging to a free benzylic alcohol group.

The correct choice between structures XI and XIII was based on a comparison of the NMR spectrum of vaginidin with other known compounds. The NMR spectrum of vaginidin (Fig. II) shows two pairs of doublets one at τ 2·38 (1H) and 3·80 (1H), J = 9·5 c/s corresponding to protons at 4 and 3, and the second at τ 2·58 (1H) and 3·16 (1H), J = 8·5 c/s, can be assigned to the protons at 5 and 6 positions of the coumarin. The singlet at τ 7·25 (1H) was eliminated by exchange with D_2O and hence can be assigned to the proton of the OH group, which is also indicated in the IR spectrum of vaginidin. A singlet at τ 8·55 (6H) can be assigned to two Me groups of the tertiary C-atom and a doublet at τ 9·1 (6H), J = 7 c/s, is indicative of two Me groups attached to the secondary carbon of the isovaleryl group. Other protons of the isovaleryl group  are indicated by the signals

[13] A. P. Prokopenko, *Khim. Prisoden Socdin. Akad. Nauk* U2 *USSR*, 3 (1965); *Chem. Abstr.* 14638 (1965).

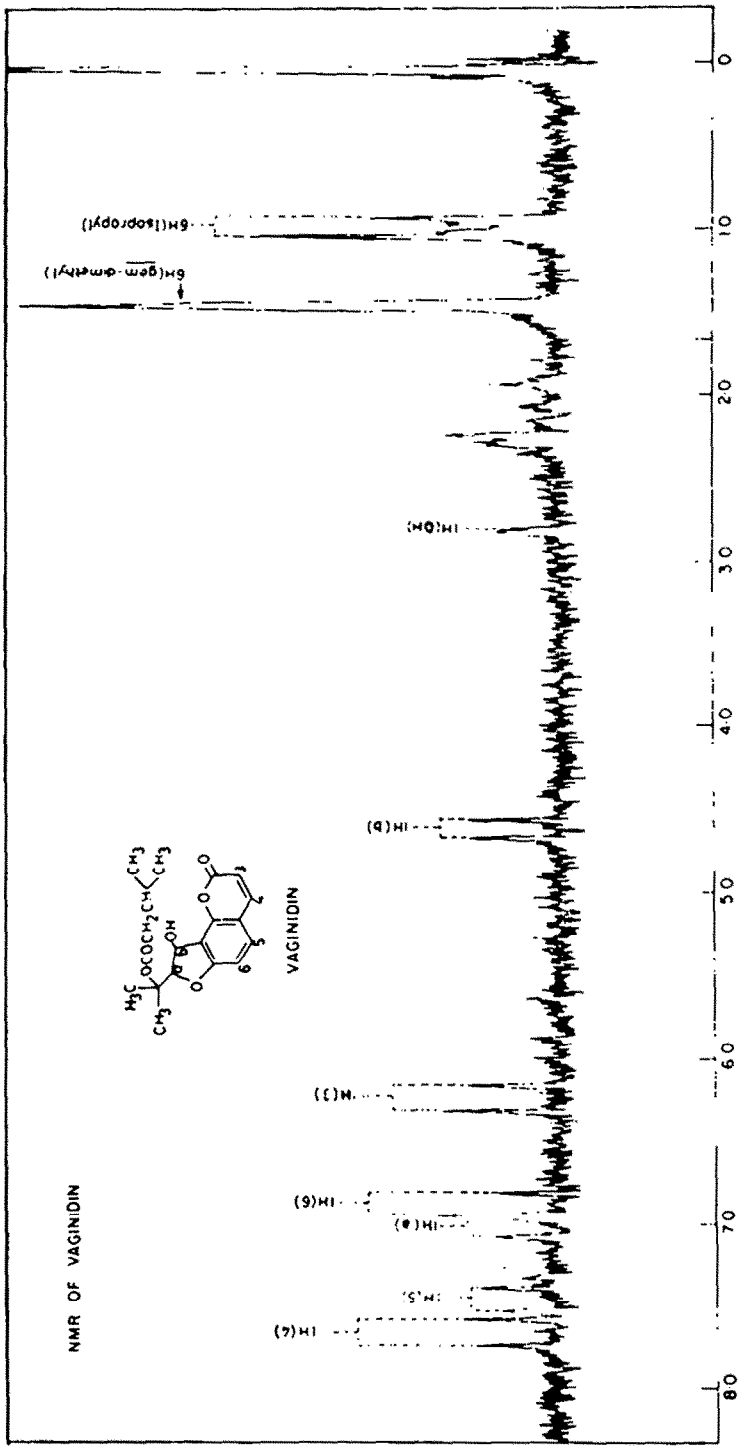
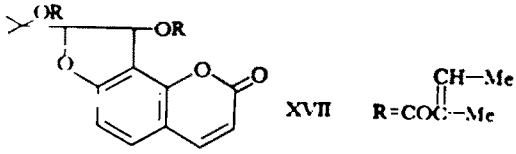


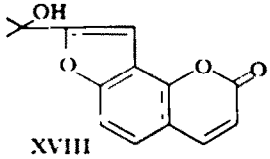
FIG. 2

at τ 7·80 (2H, doublet) and 8·1 (1H, multiplet). These features are common to both the formulae.

The doublets at τ 3·0 (1H) and 5·5 (1H), J = 7 c/s, lead to the correct choice of formula XIII for vaginidin. The former can be assigned to proton (a) and latter to proton (b); the signal for proton (a) is the same as found in the analogous compound archangelicin (XVII),[14] but the signal of proton (b) has undergone a shift of 0·8 τ to higher frequency region because this hydrogen is linked to the carbon atom bearing a secondary OH instead of an ester group,[15] causing interaction between the two hydrogen atoms of the HO—CH group. Hence vaginidin is 3′-hydroxy-2′,3′-dihydro-oroselol isovalerate (XIII).



XVII



XVIII

In addition to selinidin and vaginidin we have also isolated from the pet. ether extract angelicin, oroselol (XVIII) and the free hydroxy compound, lomatin. Their identity has been confirmed by direct comparison with authentic samples.

EXPERIMENTAL

All m.ps are uncorrected. Rotations unless otherwise stated were taken in dioxan soln. Deactivated alumina, was used in chromatography. Pet. ether refers to the fraction b.p. 60–80°. The IR spectra were recorded in a nujol suspension on a Perkin–Elmer Model No. 137 infracord spectrophotometer and the UV spectra were measured in MeOH soln on Perkin–Elmer spectrophotometer Model No. 4000-A.

Extraction. Powdered roots of *Selinum vaginatum* (obtained from Jammu; 1·2 kg) were extracted with pet. ether (5 l.) in a soxhelet, and the extract concentrated under reduced press. Selinidin separated out partly on freezing the extract at 0° for several days. Complete separation of the 5 coumarins angelicin, selinidin, vaginidin, oroselol and lomatin, as indicated on TLC plate (Silica Gel G.) was effected by chemical fractionation and elaborate column chromatography of the residual extract on deactivated (AcOH) alumina as follows: After the separation of selinidin from the pet. ether extract, the residue was extracted successively with $NaHCO_3$aq and Na_2CO_3aq and NaOHaq. $NaHCO_3$aq and Na_2CO_3aq extracts did not give any crystalline compound while NaOHaq extract gave a yellow solid (designated as compound-A) on acidification.

Compound A (*Angelicin*): It melted at 136–137°; had IR bands at: 1740, 1655, 1620, 835 and 750 cm^{-1}; UV spectrum: λ_{max} 251 and 301 mμ (log ε 4·39 and 4·0 respectively); NMR in DMSO: a pair of doublets at τ 1·90 (1H) and 3·65 (1H), J = 9 c/s (due to protons at 4 and 3 respectively); another pair of doublets at τ 1·95 (1H) and 2·85 (1H), J = 2 c/s (due to protons 5′ and 4′ respectively) and singlet at τ 2·48 (2H), due to protons at 5 and 6); it did not depress the m.p. of an authentic sample of angelicin. (Found: C, 71·4; H, 3·2. Calc. for $C_{11}H_6O_3$: C, 71·0; H, 3·3%.)

The neutral fraction (10 g) of the pet. ether extract was chromatographed on a deactivated alumina column (300 g). The column was first eluted with pet. ether, which on concentration yielded a colourless crystalline substance marked compound B. The column was then eluted with pet. ether–benzene (3:1) when compound C was obtained. Pet. ether–benzene (1:1) eluted compounds D and E.

Compound B (*selinidin*). It had m.p. 97–98°, $[\alpha]_D^{25}$ +20·3 (*c*, 1·474); IR bands at: 1724, 1613, 1242, 1117 and 846 cm^{-1}; UV spectrum: λ_{max} 256 and 325 mμ (log ε 3·52 and 4·17 respectively).

[14] B. Eichstedt Nielsen and John Lemmich, *Acta. Chem. Scand.* **18**, 932 (1964).

[15] L. M. Jackman, *Application of NMR spectroscopy in Organic Chemistry* p. 55. Pergamon Press, New York, N.Y. (1959).

NMR spectrum in $CDCl_3$: doublets at τ 2·32 (1H), J = 9 c/s (due to one proton at 4); τ 2·70 (1H) J = 8 c/s (due to one proton at 5); τ 3·20 (1H), J = 8 c/s (due to one proton at 6); τ 3·73 (1H), J = 9 c/s (due to one proton at 3); a multiplet centered at τ 4·02 (1H) due to olefinic proton of angelyl residue. A triplet at τ 4·75 (1H) due to one proton at 3'; a multiplet centered at τ 6·82 (2H) due to two benzylic protons at 4'; a multiplet centered at τ 8·1 (6H) due to two Me groups of angelyl residue; a strong singlet at τ 8·58 (6H) due to *gem*-dimethyl group at 2'. (Found: C, 69·5; H, 6·0. Calc. for $C_{15}H_{20}O_4$: C, 69·5; H, 6·0%.)

Tetrahydroselinidin. Selinidin (1 g) dissolved in AcOEt (20 ml) was stirred in H_2 with prereduced Pd–C catalyst (1 g) for 24 hr. The equivalent of 2 moles of H_2 was absorbed in 4 hr, after which there was no further absorption. The catalyst was filtered off and the solvent removed under reduced press to furnish a residue, which on crystallization from pet. ether, afforded tetrahydroselinidin as colourless needles (800 mg), m.p. 107–108°; IR bands at: 1775, 1745, 1137, 833 and 760 cm^{-1}; λ_{max} 280 mμ (log ε 3·47). (Found: C, 68·6; H, 7·6; $C_{15}H_{24}O_5$ requires: C, 68·7; H, 7·2%.)

Hydrolysis of selinidin. Selinidin (4 g) in EtOH (10 ml) was treated 1N MeOH in KOH (50 ml) and the soln allowed to stand at room temp overnight. The mixture was diluted with water, concentrated under reduced press to remove the solvent, acidified with dil. H_2SO_4aq and extracted with ether (4 times). The combined ether extract was washed well with $NaHCO_3$aq to separate the acidic portion.

Acidic portion (tiglic acid). The $NaHCO_3$ extract of the ethereal soln was acidified with H_2SO_4aq and extracted thoroughly with ether. The ether extract was dried (Na_2SO_4) and the solvent removed to give an oily residue, which sublimed during distillation under reduced press. It agreed in m.p., (mixed m.p., undepressed), UV and IR spectra with tiglic acid, yield, 1 g.

Isolation of hydroxy compound (lomatin). The ethereal extract containing the neutral product of hydrolysis of selinidin was washed with water, dried (Na_2SO_4) and the ether removed to furnish a solid residue, which crystallized from benzene as colourless needles (3 g) m.p. 183–184°; $[\alpha]_D^{26}$ +17·2 (*c*, 0·815); IR bands at: 3500, 1700, 1281, 1075 and 830 cm^{-1}; λ_{max} 247, 257 and 329 mμ (log ε 3·63, 3·52 and 4·19); NMR spectrum in DMSO; a pair of doublets at τ 2·09 (1H) and 3·78 (1H), J = 9·5 c/s (due to protons 4 and 3 respectively); another pair of doublets at τ 2·52 (1H) and 3·28 (1H), J = 8·5 c/s (due to protons at 5 and 6 respectively); multiplets centered at τ 6·2 (1H), due to proton at 3' and τ 7·15 (2H), due to benzylic protons at 4'; a singlet at τ 6·48 (1H), due to the proton of the OH at 4' and two singlets at τ 8·6 (3H) and 8·70 (3H) due to *gem*-dimethyl group at 2'. It has been found identical in all properties with lomatin. (Found: C, 68·3; H, 5·6. $C_{14}H_{16}O_4$ requires: C, 68·3; H, 5·7%.)

Acetate of lomatin. Lomatin (0·25 g) was treated with Ac_2O (30 ml) and pyridine (10 ml) and kept at room temp over night. The product when worked up crystallized from pet. ether as colourless needles (0·30 g), m.p. 136–137°. (Found: C, 66·3; H, 5·6. $C_{16}H_{18}O_5$ requires: C, 66·7; H, 5·6%.)

Ozonolysis of selinidin. Selinidin (1 g) was dissolved in AcOEt (20 ml) and ozonized O_2 passed for 1 hr at 0°. The ozonide was decomposed by catalytic hydrogenation using prereduced Pd–C (500 mg) as catalyst. After the absorption of H_2 ceased the reaction mixture was filtered and the solvent removed from the filtrate under reduced press. The residue was mixed with water and steam distilled.

The volatile product was converted into 2,4-dinitrophenylhydrazone m.p. 147–148°; mixed m.p. with that of acetaldehyde undepressed. The non-volatile product left after steam distillation was extracted with ether. The ether extract was dried, concentrated and the residue on chromatography on deactivated (AcOH) alumina, furnished a crystalline compound, m.p. 183–184°, identical with lomatin.

Dehydration of lomatin. Lomatin (0·5 g) was refluxed with glacial AcOH–conc. HCl (1:1) on a water bath. It was worked up as described by Soine *et al.*[16] when dihydrooroselone was obtained as colourless needles m.p. 139–140°. It agreed in m.p. (mixed m.p. undepressed), UV and IR spectra with the authentic specimen of dihydro-oroselone.

Catalytic hydrogenation of lomatin. Lomatin (0·5 g) was dissolved in dry AcOEt (25 ml) and the catalyst (Pd/C; 0·5 g) was added to the soln. The reaction mixture was stirred in H_2 atm for 24 hr. After the absorption of H_2 ceased, the reaction mixture was filtered. The filtrate on concentration yielded dihydrolomatin, which crystallized as shining needles from AcOEt–pet. ether, m.p. 124–126°. (Found: C, 67·4; H, 6·7. Calc. for $C_{14}H_{16}O_4$: C, 67·7; H, 6·5%.) UV spectrum λ_{max} 285 mμ (log ε 2·6).

Compound C (vaginidin). It was crystallized from aq.MeOH m.p. 133–134°; IR bands at 3410,

2950, 1740, 1622, 1580, 1492, 1425, 1407, 1370, 1345, 1282, 1260, 1180, 1150, 1115, 1085, 1035, 1025, 1000, 968, 935, 840 and 772 cm^{-1}; UV and NMR spectral data (described earlier). (Found: C, 66·1; H, 6·3. $C_{19}H_{22}O_6$ requires: C, 65·9; H, 6·3%.)

Hydrolysis of vaginidin. Vaginidin (1·0 g) in MeOH (5 ml) was treated with 0·5N methanolic KOH (10 ml) and the soln was allowed to stand at room temp for 24 hr. The mixture was diluted with water, concentrated under reduced press to remove the solvent, acidified with dil. H_2SO_4aq and extracted with ether (3 times). The combined extract was extracted fully with $NaHCO_3$aq to separate the acidic portion.

Acidic portion (*isovaleric acid*). The $NaHCO_3$ extract of the ethereal soln was acidified with dil. H_2SO_4aq and extracted thoroughly, with ether. The ether extract was dried and the solvent removed to give an oily residue with a very characteristic unpleasant smell. It distilled at 170–172°. It was proved identical with isovaleric acid by paper chromatography and co-chromatography with authentic sample.

Neutral fraction. The ethereal extract containing the neutral fraction of hydrolysis of vaginidin was washed with water, dried (Na_2SO_4) and the ether removed to furnish a solid residue, which crystallized from MeOH as colourless needles, m.p. 136–137°; identical with angelicin in chemical reactions and spectral data, yield, 0·5 g.

Catalytic hydrogenation of vaginidin. Vaginidin (0·1 g) was dissolved in dry AcOEt (25 ml) and the catalyst (Pd/C; 0·1 g) was added to the soln. The reaction mixture was stirred in the atm of H_2 for 24 hr. After the absorption of H_2 ceased, the reaction mixture was filtered. The filtrate on concentration yielded a colourless solid, which crystallized as shining needles (0·07 g), m.p. 105–106°. IR bands at: 1770, 1740, 1450, 823 and 770 cm^{-1}. (Found: C, 68·9; H, 7·2. $C_{19}H_{24}O_6$ requires: C, 68·8; H, 7·3%.)

Compound D (*oroselol*). It crystallized from benzene–pet. ether mixture, m.p. 147–148°; IR bands at: 3500, 1724, 1634, 840 and 770 cm^{-1}; λ_{max} 252 and 301 mμ (log ε 4·40 and 4·02 respectively). (Found: C, 68·9; H, 4·9. Calc. for $C_{14}H_{12}O_4$: C, 68·6; H, 5·0%.) It agreed in m.p. (mixed m.p. undepressed) UV and IR spectral data with those of oroselol.

Dehydration of oroselol. Oroselol (50 mg) was heated on a water bath for 0·5 hr with AcOH–conc. HCl (1:1). The mixture was diluted and the white ppt formed was washed well with water, dried and crystallized from MeOH to give white needles of oroselone, m.p. 174–176°. The dehydrated product agreed in m.p. mixed m.p. (undepressed). UV and IR spectra with the authentic sample of oroselone.

Compound E (*lomatin*). It had m.p. 183–184° mixed m.p. undepressed on admixture with an authentic sample of hydroxy compound obtained from hydrolysis of selinidin and with lomatin. The IR, UV and NMR spectra are also identical.

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