The Homo-Isoflavones III. Isolation and Structure of Punctatin, 3,9-Dihydro-Punctatin, 4′-*O*-Methyl-3,9-Dihydro-Punctatin, 4′-Demethyl-Eucomin and 4′-Demethyl-5-*O*-Methyl-3,9-Dihydro-Eucomin

In earlier communications the isolation and structure of eucomin and eucomol from *Eucomis bicolor* Bak.[1] and of eucomnalin, 3,9-dihydro-eucomnalin and 4′-*O*-methyl-punctatin from *Eucomis autumnalis* Graeb.[2] were described. In this paper 5 additional new homo-isoflavones, isolated from the bulbs of *Eucomis punctata* L'Hérit. (Liliaceae) are reported.

Punctatin (**1**), $C_{17}H_{14}O_6$, orange coloured needles, mp 189–190°. The UV-spectrum (EtOH) exhibits a main broad absorption band at 368 nm (log $\varepsilon = 4.49$). Addition of $AlCl_3$ and anhydrous Na-acetate causes red shifts of 28 and 31 nm respectively, which are characteristic of hydroxyl groups in the 5 and 7 positions[3,4]. The NMR-spectrum at 100 MHz (d_6-DMSO) reveals the presence of one methoxyl group (singlet, $\delta = 3.64$ ppm), 3 hydroxyl groups (sharp singlet of the hydrogen bonded OH at 12.60 ppm and 2 broad bands between 10.60 and 9.80 ppm) and 5 aromatic protons. The C-6 proton occurs as a sharp singlet at 5.98 ppm and the other 4 form a perturbed AA′BB′ system centred at ca. 7.35 and 6.88 ppm ($J \sim 9$ Hz). The C-9 proton at 7.69 ppm is split into a triplet by coupling with the two C-2 protons which appear as a doublet at 5.40 ppm ($J \sim 2$ Hz). The mass spectrum shows peaks at m/e 314 (M^+, 100%), 299 ($M^+ - 15$, 35.5%), 183 (31.5%), 182 (25%), 167 (182-15, 100%), 133 (48%), 132 (25.5%) and 131 (28%), indicating a type D fragmentation[5a].

4′-*O*-Methyl-punctatin (**2**), $C_{18}H_{16}O_6$, has been previously described[2]. In addition, the *cis* isomer (amorphous yellow compound) was isolated and we believe this is not an artefact.

Treatment of **1** and **2** with dimethyl sulphate/K_2CO_3 in acetone led to the fully methylated derivative **3**, $C_{20}H_{20}O_6$, mp 147–148°. In the NMR-spectrum, the 4 methoxyl groups appearing at 3.95, 3.95, 3.86 and 3.80 ppm in $CDCl_3$ are shifted to 3.80, 3.57, 3.35 and 3.28 ppm in C_6D_6, which is consistent with a 5,7,8-oxygenation pattern of ring A[6,7].

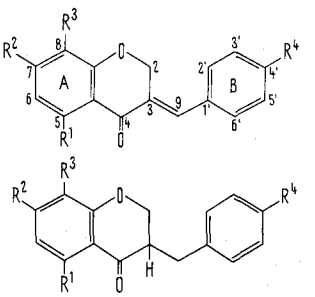
4′-Demethyl-eucomin (**4**), $C_{16}H_{12}O_5$, yellow coloured needles, mp 209–213°. The main absorption band of the UV-spectrum (364 nm, log $\varepsilon = 4.47$) undergoes red shifts of 32 and 18 nm on addition of $AlCl_3$ and Na-acetate, respectively, to the ethanolic solution. The NMR-spectrum is very similar to that of eucomin[1]. The mass spectrum shows peaks at m/e 284 (M^+, 100%), 153 (100%), 132 (35.5%), 131 (39.5%).

3,9-Dihydro-punctatin (**6**), $C_{17}H_{16}O_6$, pale yellow crystals, mp 204–206°, $[\alpha]_D^{24} = -37°$ (dioxan), is the main homo-isoflavonoid component of *Eucomis punctata* L'Hérit. Addition of $AlCl_3$ and Na-acetate shifts the main absorption band of the UV-spectrum (293 nm, log $\varepsilon = 4.53$) to 315 (+22) and 331 (+38) nm respectively. The NMR-spectrum (60 MHz, d_6-DMSO) shows the presence of 1 methoxyl group (singlet, 3.62 ppm) and 3 hydroxyl groups (sharp singlet of the hydrogen bonded OH at 11.90 ppm and 2 broad bands at 10.56 and 9.18 ppm). The C-6 proton appears as a singlet at 5.94 ppm whilst the 4 aromatic protons of ring B form a perturbed AA′BB′ system centred at ca. 7.01 and 6.67 ppm ($J \sim 9$ Hz). Multiplets at 4.4–3.8 ppm, 3.1–2.8 ppm and 2.8–2.5 ppm are assigned to the protons at C-2 (2H), C-3 (1H) and C-9 (2H). The mass spectrum shows the molecular ion, m/e 316 (51.5%), the very stable hydroxy-tropylium ion, m/e 107 (100%), and further peaks at m/e 210 (37%) and 195 (210–15, 21.5%) indicating a type A_4 fragmentation[5b].

4′-*O*-Methyl-3,9-dihydro-punctatin (**7**), $C_{18}H_{18}O_6$, isolated as amorphous yellowish compound, contaminated with traces of **2**. In the UV-spectrum the main absorption band at 293 nm is shifted to 311 (+18) and 335 (+42) nm on treatment with $AlCl_3$ and Na-acetate respectively. The NMR data are similar to those of **6**, whereas the mass spectrum shows m/e 330 (13%) as molecular ion and the methoxy tropylium ion m/e 121 as base peak.

Treatment of **6** and **7** with dimethyl sulphate/K_2CO_3 in acetone gave the fully methylated derivative **8**, $C_{20}H_{22}O_6$, mp 99–100°, $[\alpha]_D^{24} = -2°$ ($CHCl_3$). In the NMR-spectrum 4 methoxyl groups appearing at 3.94, 3.92, 3.80, 3.80 ppm in $CDCl_3$ are shifted to 3.75, 3.48, 3.34, 3.34 ppm in C_6D_6 which is consistent with a 5,7,8-oxygenation pattern of ring A[6,7].

4′-Demethyl-5-*O*-methyl-3,9-dihydro-eucomin (**9**), $C_{17}H_{16}O_5$, colourless crystals, mp 196–197°, $[\alpha]_D^{24} = -38°$ (dioxan) exhibits an UV-absorption maximum at 285 nm (log $\varepsilon = 4.51$) which is not shifted with $AlCl_3$ but is shifted with Na-acetate (322 nm, +37). The NMR-spectrum (100 MHz, d_6-DMSO) shows the presence of 1 methoxyl group (singlet, 3.74 ppm), 2 hydroxyl groups (broad bands between 10.4 and 9.0 ppm), 6 aromatic protons (C-6 and C-8 protons: AB system, 6.07 and 5.92 ppm, $J \sim 2.5$ Hz; protons of ring B: AA′BB′ system, 7.01 and 6.68 ppm, $J \sim 9$ Hz) and 5 aliphatic protons as multiplets between 4.4–3.8 ppm (2H), 3.1–2.8 ppm (1H) and 2.8–2.5 ppm (2H). In the mass spectrum, the most



1 $R^1 = R^2 = R^4 = OH$; $R^3 = OCH_3$ Punctatin
2 $R^1 = R^2 = OH$; $R^3 = R^4 = OCH_3$ 4′-*O*-Methyl-punctatin
3 $R^1 = R^2 = R^3 = R^4 = OCH_3$
4 $R^1 = R^2 = R^4 = OH$; $R^3 = H$ 4′-Demethyl-eucomin
5 $R^1 = R^2 = R^4 = OCH_3$; $R^3 = H$
6 $R^1 = R^2 = R^4 = OH$; $R^3 = OCH_3$ 3,9-Dihydro-punctatin
7 $R^1 = R^2 = OH$; $R^3 = R^4 = OCH_3$ 4′-*O*-Methyl-3,9-dihydro-punctatin
8 $R^1 = R^2 = R^3 = R^4 = OCH_3$
9 $R^1 = OCH_3$; $R^2 = R^4 = OH$; $R^3 = H$ 4′-Demethyl-5-*O*-methyl-3,9-dihydro-eucomin
10 $R^1 = R^2 = R^4 = OCH_3$; $R^3 = H$

1 P. BÖHLER and CH. TAMM, Tetrahedron Letters *1967*, 3479.
2 W. T. L. SIDWELL and CH. TAMM, Tetrahedron Letters *1970*, in press.
3 T. A. GEISSMAN, *The Chemistry of Flavonoid Compounds* (Pergamon Press, Oxford, London, New York, Paris 1962), p. 107.
4 L. JURD and R. M. HOROWITZ, J. org. Chem. *22*, 1618 (1957); R. M. HOROWITZ and L. JURD, *26*, 2446 (1961). – L. JURD, Phytochemistry *8*, 445 (1969).
5 K. BIEMANN, *Mass Spectrometry* (McGraw-Hill Book Co. Inc., New York, San Francisco, Toronto, London 1962) a) p. 102; b) p. 84.
6 R. G. WILSON, J. H. BOWIE, D. H. WILLIAMS, Tetrahedron *24*, 1407 (1968).
7 A. PELTER and P. I. AMENECHI, J. chem. Soc. (C), *1969*, 887.

significant peaks are at m/e 300 (M^+, 75%), 193 (50%), 167 (100%), 166 (57%) and 107 (41.5%).

The compounds **3** (mp 147–148°) and **5** (mp 141–144°) were synthesized by condensing the corresponding chroman-4-ones with *p*-methoxy-benzaldehyde in dry HCl and acetic acid. Catalytic hydrogenation of **3** and **5** with Raney-Ni in ethanol led to racemic **8** (mp 99–100°) and racemic **10** (amorphous) respectively. The IR- and NMR-spectra of the synthetic materials **8** and **10** were identical with those of the permethylated derivatives of the natural products **6**, **7** and of **9** respectively.

With the compounds described in this paper 10 members of the new family of the homo-isoflavones are now known. They differ from each other not only by variations in the oxygenation and methylation patterns of the aromatic rings but also by varying states of oxidation at C-3 and C-9. The biogenetic implications of these findings are being investigated[8,9].

Zusammenfassung. Aus den Zwiebeln von *Eucomis punctata* L'Hérit. (Liliaceae) wurden 5 neue Homoisoflavone isoliert und ihre Struktur aufgeklärt.

R. E. Finckh and Ch. Tamm

Institut für Organische Chemie der Universität Basel, CH-4056 Basel (Switzerland), 23 January 1970.

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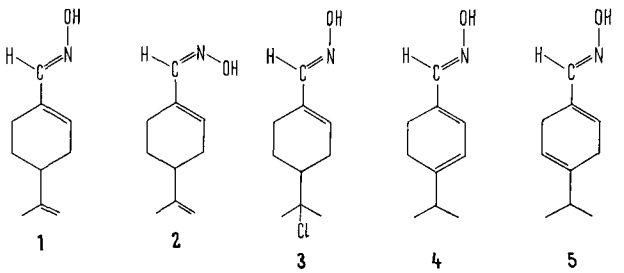
[9] We are indebted to Dr. W. Vetter, F. Hoffmann-La Roche & Co. A.G., Basel, for the mass spectra.

Perillartine and Some Derivatives: Clarification of Structures

The sweetening agent perillartine is the α-*syn*-oxime **1** of perillaldehyde, and should be recognized as the *syn* isomer, though it is commonly called '*α-anti*' in commerce and in review literature. The designation '*α-anti*' is inconsistent in terms of modern nomenclature and derives from the work of Furukawa and Tomizawa[1], published at a time when the true structure of α-oximes[2] as *syn* isomers and of β-oximes[2] as *anti* isomers was just becoming clear. Earlier, the reverse correlation was accepted, and the resultant confusion and error in names has persisted in the case of perillartine. Sometimes the correct (*syn*) structure is given[3] despite the name *α-anti*, but sometimes[4] in consequence the wrong (*anti*) structure **2** is drawn. The true *syn* structure of perillartine is now nicely confirmed by the elegant NMR technique[5] which states that for aldoximes in dimethylsulfoxide-d_6 solution, the difference $^{\delta}$NOH–$^{\delta}$CH=N is $\simeq$ 3 ppm for *syn* isomers and $\simeq$ 4 ppm for *anti* isomers. For perillartine, this difference is 3.02 ppm.



1 **2** **3** **4** **5**

It was claimed[1] that the β-isomer of perillartine (called 'β-syn', but predictably the *anti* isomer **2**) was formed conventionally through the HCl salt of **1** and was tasteless – unlike **1**, said to be 2000 times sweeter than sugar. This result has been cited[6] (with some confusion in names) as an example of striking difference in taste properties of geometrically isomeric oximes. However, reinvestigation has now shown that the compound obtained on attempted isomerization of perillartine **1** is not **2**, but rather the *tert*-chloride **3**, formed by Markovnikov addition of the elements of HCl to the isopropenyl group.

When D,L-perillartine **1** in methanol solution was treated with hydrogen chloride, addition of ether precipitated the hydrochloride[7] of **3**, mp 127–129°, $C_{10}H_{17}Cl_2NO$, with one ionic Cl. Treatment of an aqueous slurry of the salt with sodium carbonate, or with 1 *M* sodium hydroxide, generated 4-(2-chloro-2-propyl)-1-cyclohexene-1-carboxaldehyde *syn*-oxime **3**, mp 133–134°, $C_{10}H_{16}ClNO$, no ionic Cl (mp 129° was reported[1] for the product called the β-isomer). Alternatively, upon solution of perillartine in concentrated hydrochloric acid, dilution with water precipitated **3**. The structure was confirmed in the NMR-spectrum ($CDCl_3$ solutions) by the absence of the isopropenyl signals of perillartine (i.e., narrow doublets at δ 4.75 and 1.74 for $=CH_2$ and $CH_3C=$, respectively, J = 1.0 Hz) and by the appearance of a 6-proton singlet at δ 1.53 (CH_3–CCl–CH_3). Identical signals in both **1** and **3** were observed for the olefinic ring proton (δ 5.95–6.15) and for the oxime CH=N (singlet, δ 7.71). It was clear that no isomerization of the oxime group had occurred, and the difference $^{\delta}$OH–$^{\delta}$CH for **3** in dimethylsulfoxide-d_6 of 2.99 ppm confirmed that **3** was a *syn*-oxime.

In a further attempt to form the *anti*-oxime **2**, perillartine **1** was treated with BF_3 by the procedure of Hauser and Hoffenberg[8]. A pure isomer, mp 54–57°, was obtained after 1–2 days, but was shown to be the

[1] S. Furukawa and Z. Tomizawa, J. Chem. Ind. Tokyo *23*, 342 (1920); Chem. Abstr. *14*, 2839 (1920).

[2] The α-, β- differentiation of isomeric oximes was based on a comparison of chemical properties; cf. N. V. Sidgwick, I. T. Millar and H. D. Springall, *The Organic Chemistry of Nitrogen*, 3rd edn. (Oxford, London 1966), p. 322.

[3] *The Merck Index*, 7th edn. (Merck and Co., Rahway, New Jersey), p. 786.

[4] Beilstein, *Handbuch der Organischem Chemie* (Springer-Verlag, Berlin, Heidelberg 1968), vol. 7, 3rd suppl., p. 566.

[5] G. G. Kleinspehn, J. A. Jung and S. A. Studniarz, J. org. Chem. *32*, 460 (1967).

[6] L. N. Ferguson and E. R. Lawrence, J. chem. Educ. *35*, 436 (1958). – K. Kulka, J. Agr. Food Chem. *15*, 48 (1967).

[7] Treatment of an ether solution of **1** with HCl gave only partial conversion to a hydrochloride, co-precipitated with **1**; by this means Furukawa and Tomizawa reported a hydrochloride, mp 114°, which upon basification gave the oxime of mp 129° (resumably **3**).

[8] C. R. Hauser and D. S. Hoffenberg, J. org. Chem. *20*, 1491 (1955).