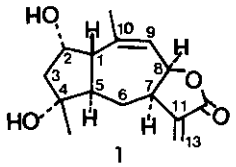
CD STUDY OF GUAIANOLIDE SESQUITERPENES HAVING 8-FUSED LACTONE: THE ABSOLUTE CONFIGURATION OF HELENIUM LACTONE AND PLENIRADIN

Fumio Hamada, Tomihisa Ohta, and Shigeo Nozoe*
Faculty of Pharmaceutical Sciences, Tohoku University,
Aobayama, Sendai 980, Japan

9,10-Saturated and unsaturated guaianolide sesquiterpenes having cis- and trans-8-fused α-methylene-γ-lactone were prepared and those CD's have been studied to complement the rule by Geissman et al.

The CD rule by Geissman et al.[1] has been applied to the determination of the chirality in the α-methylene-γ-lactone ring of sesquiterpene lactones.[2] In the case of pleniradin (1),[1,3,4] however, X-ray analysis proved the relative stereochemistry of the B/C ring fusion to be cis despite being assigned as trans by the Geissman's rule. We have recently found the similar inconsistency for helenium lactone (2)[5] isolated by Hikino et al. The B/C ring juncture, although the positive Cotton effect implied it as trans, has been assigned as cis with the observed nuclear Overhauser effect between 7- and 8-hydrogen signals in the ^{1}H-NMR spectrum of 9,10-epoxy helenium lactone (3).[6] Those discrepancies forced us studying CD's of cis- and trans-8-fused Δ^9-guaianolides.

We report here the result obtained by CD study of helenium lactone (2), 8-epi-helenium lactone (4) and their 9,10-dihydro derivatives (5 and 6). The absolute configuration of helenium lactone (2) was first established prior to the CD analysis by the transformation of it (2) to carolenalin (7)[7] as shown in the scheme. Configuration at C-4 of 2 was assigned as R with the fact that dehydration did not occur toward C-5 but toward C-3, indicating that 4-hydroxyl and 5-hydrogen are cis oriented. 9,10-Dihydro helenium lactone (5) was obtained by hydrogenation of 13-dimethylamino helenium lactone with diimide following by the removal of dimethylamine.



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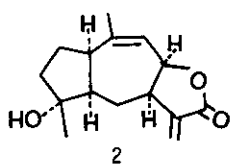

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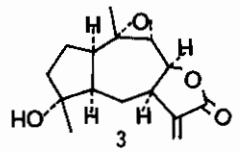

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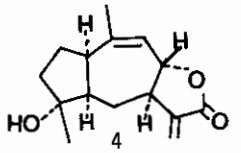
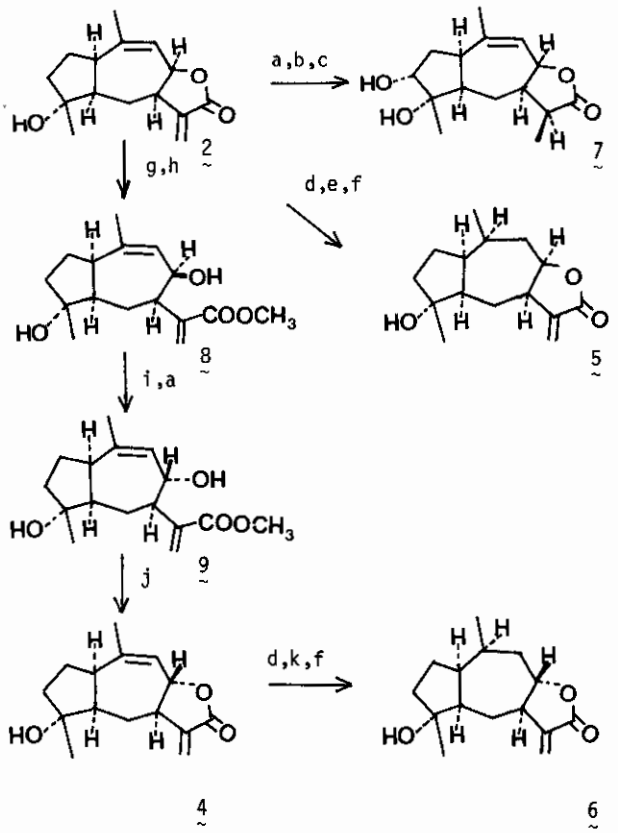


4

8-Epi-helenium lactone (4) was derived from helenium lactone (2) in 5 steps. Thus 2 was hydrolyzed with 5N KOH in aq.DMSO, the methyl ester (8) of the hydrolyzate was then oxidized with Jones' reagent and reduced with $NaBH_4$ to yield 8-epi carbinol 9. The reduction proceeded stereoselectively and no 8 was recovered. The carbinol (9) on subsequent treatment with p-TsOH afforded 8-epi-helenium lactone (4). The overall yield was 46.5%. 8-Epi-9,10-dihydro helenium lactone (6) was given through oxidative deamination following the catalytic hydrogenation of dimethylamino adduct of 4.



2 7 8 5 9 4 6

a) $NaBH_4$, b) $POCl_3$, c) OsO_4, d) Me_2NH, e) N_2H_2, f) MCPBA , g) OH^-, h) CH_2N_2,
i) Jones' reagent, j) p-TsOH, k) H_2/PtO_2

Contrary to that helenium lactone (2) whose chirality of B/C cis-(7R, 8S)-juncture is now obvious shows positive Cotton effect at 248 nm in its CD, 9,10-dihydro helenium lactone (5) exhibits the opposite sign at 251 nm, negative as expected from the rule by Geissman et al. Interestingly, both 8-epi-helenium lactone (4) and its dihydro derivative (6) show the same positive sign of Cotton effect which are consistent with those for reported guaianolides whose lactone ring is C-8 trans-fused (7R).

Table 1. CD Data of C-8 Fused Guaianolides

Compds No.	Cotton effect [θ] (nm)	B/C ring fusion
1	+5700 (250)[4]	cis (7R)
2	+5630 (248)	cis (7R)
3	-720 (246)	cis (7R)
5	-4710 (251)	cis (7R)
4	+4900 (255)	trans (7R)
6	+4660 (255)	trans (7R)

Dreiding models for the cis-8-fused lactones suggests little changes of torsion angles on the γ-lactone ring between the pairs of 9,10-unsaturated and saturated congeners (2 vs. 5, 4 vs. 6). This indicates that the introduction of double bond at C-9,10 may not change the helix of enone system on the α-methylene-γ-lactone ring. Therefore the reversed sign of the Cotton effect for cis-8-fused lactones in Δ^9-guaianolides may not be attributed to the change of the enone helix but to the 9,10-double bond nearly surrounding the α,β-unsaturated lactone chromophore, and it may be worth noting that the rule by Geissman et al. must be carefully applied to lactones when a functional group which may influence a Cotton effect is located by.

Since pleniradin (1) shows positive Cotton effect as the case of helenium lactone (2), the chirality in its lactone moiety must be the same (7R, 8S) as that of 2. Hence the absolute configuration of pleniradin is confirmed as shown in the structure 1 which was assumed with the result given by Waddell and Geissman[3] and from a biogenetic point of view.[4,8]

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References and Notes

1. W. Stöcklin, T. G. Waddell, and T. A. Geissman, Tetrahedron, 26, 2397 (1970).
2. W. Herz, S. V. Bhat, H. Crawford, H. Wagner, G. Maurer, and L. Farkas, Phytochem., 11, 371 (1972); W. Vichnewski and B. Gilbert, Phytochem., 11, 2563 (1972); M. A. Irwin and T. A. Geissman, Phytochem., 12, 863 (1973); A. Corbella, P. Gariboldi, and G. Jommi, Phytochem., 13, 459 (1974); K. H. Lee, T. Ibuka, M. Kozuka, A. T. McPhail, and K. D. Onan, Tetrahedron Lett.,2287 (1974); T. Osawa, D. Taylor, A. Suzuki, and S. Tamura, Tetrahedron Lett., 1169 (1977); W. Vichnewski, F. W. L. Machado, J. A. Rabi, R. Murai, and W. Herz, J. Org. Chem., 42, 3910 (1977).
3. T. G. Waddell and T. A. Geissman, Tetrahedron Lett., 515 (1969); A. Yoshitake and T. A. Geissman, Phytochem., 8, 1735 (1969); T. G. Waddell and T. A. Geissman, Phytochem., 8, 2371 (1969).
4. W. Herz, R. Murai, and J. F. Blount, J. Org. Chem., 44, 1873 (1979).
5. H. Hikino, D. Kuwano, and T. Takemoto, Chem. Pharm. Bull., 16, 1601 (1968).
6. unpublished data.
7. A. T. McPhail, P. A. Luhan, K. H. Lee, H. Furukawa, R. Meck, and C. Piantandosi, Tetrahedron Lett., 4087 (1973).
8. Herz et al. did not give an assurance because of that exceptions of Horeau's rule are known as they pointed: e.g. R. W. Doskotch and F. S. El-Feraly, J. Org. Chem., 35, 1928 (1970).

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