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STRUCTURE AND STEREOCHEMISTRY OF MEXICANIN F, A NOVEL DIMERIC NOR-SESQUITERPENE LACTONE FROM *Helenium mexicanum*

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Abstract. The structure and stereochemistry of mexicanin F, a novel dimeric nor-sesquiterpene lactone isolated from *Helenium mexicanum*, have been stablished from spectral and single-crystal X-ray analyses.

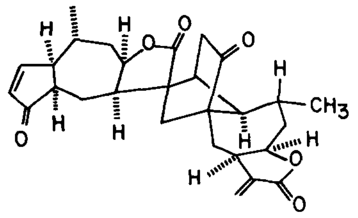
Several years ago, one of us reported the physical constants of the mexicanins A, B,..., H which, in addition to helenalin, are constituents of *Helenium mexicanum* H.B.K.[1,2] The structure and stereochemistry of the mexicanins A,[3] C,[4] D,[3] E,[5,6] H,[7] and I,[8] were subsequently established by chemical, spectral and crystallographic methods. We now report the structure and stereochemistry of mexicanin F, established from spectral and single-crystal X-ray analysis of an original sample still extant from the earlier work.[2]

Mexicanin F[1] (1) m.p. 311-315 °C, $[\alpha]_D^{25}$ = 102 (c 0.40, EtOH) is a dimeric nor-sesquiterpene lactone as indicated by its molecular formula $C_{28}H_{32}O_6$ (elemental analysis, MS and ^{13}C NMR).

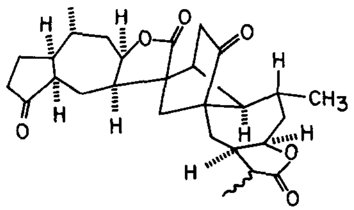
The dimeric structure of mexicanin F is consistent with the presence of two methyl doublets in the ^1H NMR spectrum,[9] the low extinction coefficient of the UV spectrum[1] as well as the signals observed in the ^{13}C NMR spectrum (four carbonyls, two double bonds, two secondary carbons bearing oxygen, two methyls, six methylenes, eight methines and two fully substituted carbons, table 1). Furthermore, the similar profile displayed in the 1765-1590 cm^{-1} region[9] of the combined IR spectra of mexicanin E[1] (3) and tetrahydromexicanin E[7] (4), suggested the presence in mexicanin F of four carbonyl groups as those found in 3 and 4.

Catalytic hydrogenation of 1 (Pd/C, AcOEt) gave tetrahydromexican F (2, 85% yield) m.p. 303-305 °C, $C_{28}H_{36}O_6$ (m/e 468), whose spectral data (IR, ^1H and ^{13}C NMR)[10] indicate the absence of carbon-carbon double bonds and the presence of four carbonyls. This is in agreement with the heptacyclic nature of 1 and 2 (six rings arising from two sesquiterpene lactone units and the additional one from a cycloaddition reaction).

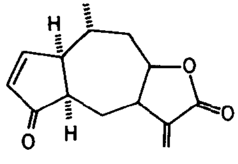
The co-occurrence of mexicanin F and the nor-pseudoguaianolide mexicanin E (3) in *Helenium mexicanum* coupled with the foregoing evidence suggested that 1 is one of the eight possible diastereomeric adducts which arise from a regio- and stereo-differentiated Diels-Alder reaction which involved the 11,13-double bond of mexicanin E (3) and the kinetic enol form of the cyclopentenone ring of the same nor-pseudoguaianolide. In order to distinguish from these diastereomeric possibilities a single X-ray analysis was carried out.[11] Crystals of 1 are monoclinic, space group $P2_1$, with a = 7.6263(3), b = 11.7955(3), c = 14.1300(6) Å, β = 100.79(3). Z = 2 and D_{calc}= 1.2338 g cm^{-3}. The intensity data were measured on a Nicolet R3m diffractometer (monochromated CuK_α radiation, ω-scan). A total of 1885 independent reflections were measured for $2\theta < 45$, of which 1540 were considered observed with $I > 2.0\ \sigma\ (I)$. The structure was solved by direct methods[12] and was refined by blocked cascade matrix least square methods. In the final refinement, anisotropic thermal parameters were used for the non hydrogen atoms and fixed isotropic temperature factor U=0.06 A^2 for the hydrogen atoms. These were included in the structure factor calculations. The final discrepancies indices are R = 0.0449 and R_ω = 0.0478 for the 1540 observed reflections. The final difference map has no peaks greater than ± (0.1761) $eÅ^{-3}$. Figure 1 is a computer generated perspective drawing of the final X-ray model. The ring B of mexicanin F is a half chair while the saturated lactone is somewhat puckered due to the presence of the bicyclo [2,2,1] (rings D and E) and the ring F is a distorted twist boat.



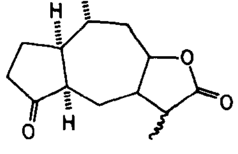
1 mexicanin F



2 tetrahydro mexicanin F



3 mexicanin E



4 tetrahydro mexicanin E

TABLE 1

^{13}C NMR Shifts of Mexicanin F (1) and Tetrahydromexicanin F (2).[13]

(+, *, †, § : Assignments may be interchanged)

	1	2		1	2
C-1	50.26 d	49.03 d	C-1'	47.85 d	48.72 d
C-2	166.32 d	20.27 t	C-2'	43.27 d	44.31 d
C-3	132.98 d	37.04 t	C-3'	38.88 t	38.81 t
C-4	211.03 s	221.46 s	C-4'	213.32 s	213.58 s
C-5	57.89 d	57.73 d	C-5'	59.01 s	59.03 s
C-6	28.41 t*	27.42 t^{+}	C-6'	26.04 t*	24.36 t^{+}
C-7	37.61 d	38.53 d	C-7'	54.33 d	51.19 d
C-8	78.43 d*	78.78 d*	C-8'	76.03 d*	77.25 d*
C-9	36.68 t	37.19 t	C-9'	36.32 t	36.70 t
C-10	26.29 d†	28.54 d†	C-10'	26.04 d†	26.56 d†
C-11	56.22 s	55.58 s	C-11'	139.18 s	38.81 d
C-12	178.06 s	178.19 s	C-12'	169.29 s	178.03 s
C-13	34.23 t	34.50 t	C-13'	123.34 t	10.56 q
C-14	21.37 q§	21.27 q§	C-14'	21.14 q§	21.23 q§

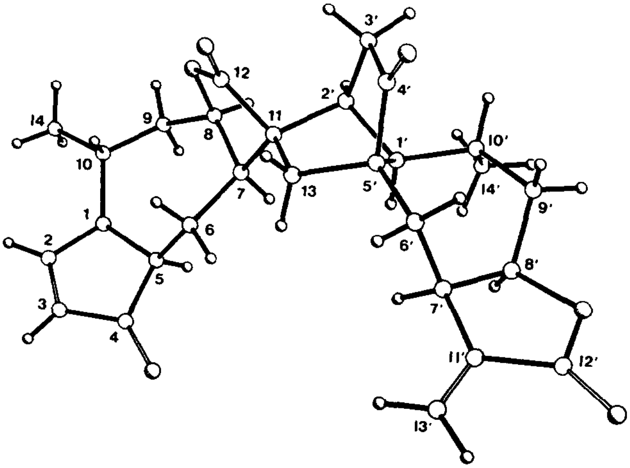


Figure 1
Computer-generated perspective drawing of Mexicanin F (1).

Mexicanin F is one of the rather rare adducts of a nor-pseudoguaianolide found in nature. Handelin[14] and microlenin[15] are the only similar substances isolated up to date.

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9. For *1*: IR ($CHCl_3$): 3005, 2962, 2935, 1765, 1705, 1660, 1590, 1475, 1450, 1380, 1350, 1338, 1290, 1185, 1170, 1150, 1120 and 1020 cm^{-1}; MS: M^+ at m/e = 464 for $C_{28}H_{32}O_6$; ^1H NMR (80 MHz, $CDCl_3$): δ 7.76 (1H, *dd*, *J* = 6, 2 Hz, H-2), 6.34 (1H, *d*, *J* = 3.5, H-13'a), 6.25 (1H, *dd*, *J* = 6, 3 Hz, H-3), 5.66 (1H, *d*, *J* = 3 Hz, H-13'b), 4.82 (2H, *m*, $W_{h/2}$ = 9 Hz, H-7'), 1.20 (3H, *d*, *J* = 7 Hz, H-14 or H-14'), 1.12 (3H, *d*, *J* = 7 Hz, H-14 or H-14'); ^{13}C NMR (20 MHz, $CDCl_3$): See Table 1.
10. For *2*: IR ($CHCl_3$): 2960, 2922, 2885, 1765, 1740, 1460, 1455, 1420, 1355, 1290, 1180, 1150, 1120, 1060, 970 cm^{-1}; MS: M^+ at m/e = 468 for $C_{28}H_{36}O_6$; ^1H NMR (80 MHz, $CDCl_3$): δ 4.75 (2H, *m*, $W_{h/2}$ = 12 Hz, H-8 and H-8'), 1.15 (3H, *d*, *J* = 7 Hz, H-14 or H-14'), 1.05 (3H, *d*, *J* = 7 Hz, H-14 or H-14'); ^{13}C NMR (20 MHz, $CDCl_3$): See Table 1.
11. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre.
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