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REVISED ABSOLUTE CONFIGURATIONS OF NATURAL KHELLACTONE ESTERS (1)

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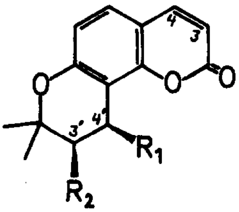
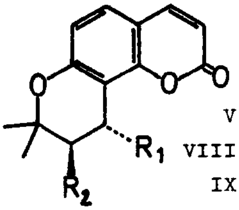
The vasodilatory constituents of Ammi visnaga L. visnadin(I), samidin(II), and dihydrosamidin(III) (2,3) are prominent examples of natural khellactone esters. Epimerization at the 4′-position during their alkaline hydrolysis gives rise to a mixture of the glycols (+)-cis-khellactone(IV) and (-)-trans-khellactone(V). Schroeder et al. (3) unambiguously established the relative configurations of the two glycols. They also assigned the configuration cis to the native esters(I), (II), and (III) mainly by spectral comparisons with synthetic material (see also ref.4). Furthermore, they suggested the absolute configuration 3′(S),4′(S) for (+)-cis-khellactone(IV) on the basis of optical comparisons. Recently Seshadri and Sood (5) (see also ref.6) on inadequate grounds suggested that lomatin(VI) and the khellactones (IV) and (V) possess the same absolute configuration at the 3′-position. From a comparison of UV-data, melting points, and directions of optical rotation they were misled (7) into assuming the identity of dihydrolomatin(VII) with a compound earlier prepared by Smith et al. (2) by hydrogenation of (-)-trans-ethylkhellactone(VIII). However, according to the description given by these authors, the compound referred to, is the 3,4-dihydroderivative of (VIII), not a hydrogenolysis product.

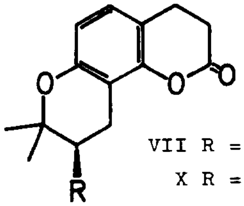
Now, hydrogenation (1 atm., 21°) of (-)-trans-diacetyl-khellactone(IX) m.p. 163-64° $[\alpha]_D^{20}$ -7.4 (c 1.1, $CHCl_3$) (3,4) with 10 % Pd-C as the catalyst and acetic acid/perchloric acid (0.006 N) as the solvent has afforded the hydrogenolysis product acetyldihydrolomatin(X) m.p.109.0-109.5° $[\alpha]_D^{20}$ -45.5 (c 1.2, MeOH). In the **absence** of perchloric acid only the 3,4-dihydroderivative of (IX) was formed. (X) was identical with a sample prepared by hydrogenation of acetyllomatin (XI) m.p.137.5-138.0° $[\alpha]_D^{18}$ -2.6 (c 5.0, $CHCl_3$) (ref.8 m.p.137-138°) $[\alpha]_D^{30}$ -6.79). (XI) was prepared from a sample of lomatin(VI), characterized earlier (9).



I R_1 = acetoxy-, R_2 = (R)-α-methylbutyryloxy-
II R_1 = acetoxy-, R_2 = senecioyloxy-
III R_1 = acetoxy-, R_2 = isovaleryloxy-
IV R_1 = R_2 = hydroxy-
VI R_1 = H-, R_2 = hydroxy-
XI R_1 = H-, R_2 = acetoxy-



V R_1 = R_2 = hydroxy-
VIII R_1 = ethoxy-, R_2 = hydroxy-
IX R_1 = R_2 = acetoxy-



VII R = hydroxy-
X R = acetoxy-

Hydrogenolysis of visnadin(I) (10) m.p.80-84° $[\alpha]_D^{20}$ +8.3 (c 1.0, EtOH 96 %) in a similar manner, followed by saponification and relactonisation afforded dihydrolomatin(VII) m.p.126.5-127.0° $[\alpha]_D^{20}$ -9.5 (c 1.0, EtOH 96 %) (ref.6 m.p.124-126) identical with a sample prepared by hydrogenation of lomatin(VI). Recently lomatin(VI) was shown (9) to possess the configuration 3'(R). Therefore, the evidence presented above indicates the configurations 3'(R),4'(R) for (+)-cis-khellactone(IV) and 3'(R),4'(S) for (-)-trans-khellactone(V). The majority of natural khellactone esters, including (I),(II), and (III), are derived from (+)-cis-khellactone(IV). Only two, (+)-anomalin and peuformosin (11) are derived from (-)-cis-khellactone and accordingly possess the configurations 3'(S),4'(S).

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