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Stereochemistry of 4,5-Dihydroxy-α-santonin and Structure of a New Santonin Oxidation Product

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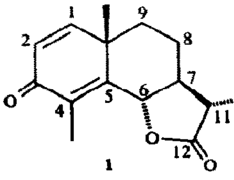
Abstract: The diol, mp 220 °C, obtained by $KMnO_4$ oxidation of α-santonin is shown by an nOe study to be 4β,5β- rather than 4α,5α-dihydroxy-α-santonin. On further oxidation with $Pb(OAc)_4$, it unexpectedly gives a new ketolactone, mp 268 °C, which is also obtained as a $KMnO_4$ oxidation product of α-santonin.

A diol, mp 261 °C, obtained by Angeli and Mannino[1] from potassium permanganate oxidation of α-santonin (1), was first assigned a 1,2-dihydroxy structure 2.[2] Hendrickson and Bogard[3] later suggested that this product might instead be 4α,5α-dihydroxy-α-santonin (3), from attack on the more electron-rich 4,5 double bond from the less-hindered α-face. Both by microbial and $KMnO_4$ oxidation of 1,[4] we obtained a 4,5-diol, mp 220 °C, which we presumed to be the 4α,5α-diol 3 as proposed by Hendrickson and Bogard.[3] In this letter, we report NMR evidence that the diol melting at 220 °C is actually 4β,5β-dihydroxy-α-santonin (4) and that a further product, mp 268 °C, obtained by oxidizing 1 with $KMnO_4$[5] or 4 with $Pb(OAc)_4$[6], is ketodilactone 5.

Hendrickson and Bogard's[3] structure 6 for α-santonin chlorohydrin was revised by Takayanagi, Ogura and McMurry[7] to **7a** after an X-ray study on methoxy derivative **7b**. In view of this result, we investigated the stereochemistry of dihydroxy-α-santonin using nOe methods. Irradiation of the C-4 methyl group at δ1.54 gave a 17% enhancement of the absorption of H-7 at δ2.31, which is only possible if both hydroxyl groups are β (see **4a**).[8] Thus 4,5-dihydroxy-α-santonin, mp 220 °C, is the 4β,5β stereoisomer 4. This revision of stereochemistry, expected by analogy with the chlorohydrin findings,[7] presumably indicates that for these reagents, the hindrance of the α-face of the 4,5-double bond by the 9-methylene and 6-oxygen outweighs the hindrance of the β-face by the 10-methyl group.

The oxidation product of mp 268 °C was expected to be **8** based on its formation by $Pb(OAc)_4$ oxidation of 4 and its mass spectrum (mol formula $C_{15}H_{18}O_5$, base peak at M-43).[9] However, its NMR parameters, especially the ^{13}C spectrum, clearly establish structure **5**.[10] Formation of **5** probably occurs via the usual cyclic intermediate **9** (M = Mn or Pb), perhaps via cleavage to intermediate **10** (see arrows on structures **9** and **10**).



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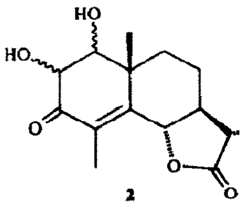

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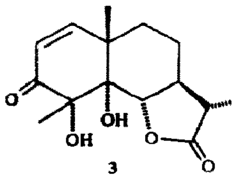

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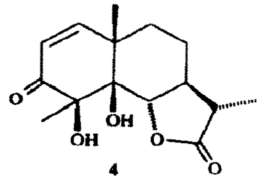

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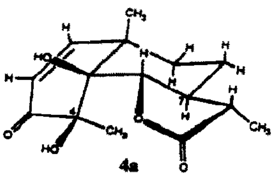
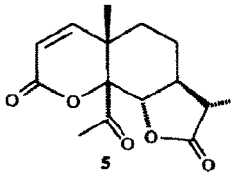


4a



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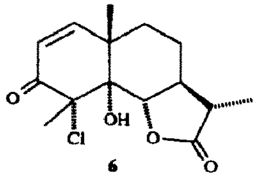

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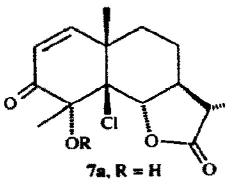
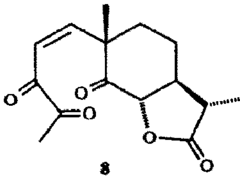
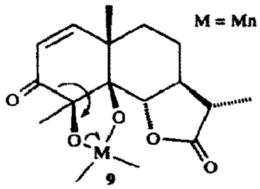


7a, R = H
7b, R = Me



8

M = Mn or Pb



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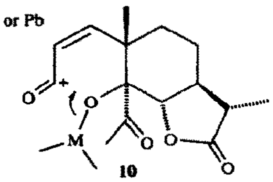

10

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References and Notes

1. Angeli, A.; Mannino, L. Memorie R. Accad. Lincei **1907**, 6, 385 (Chem. Abs. **1908**, 2953).
2. Simonsen, J.; Barton, D. H. R. The Terpenes, Univ. Press, Cambridge, 3, pp 260-261, 1952.
3. Hendrickson, J. B.; Bogard, T. L. J. Chem. Soc. **1962**, 1678.
4. Naik, U. P.; Mavinkurve, S.; Naik, U. S.; Paknikar, S. K. Ind. J. Chem. **1988**, 27b, 381.
5. The $KMnO_4$ oxidation of **1** to **5** was done like that of anisoxide (Barton, D. H. R.; Bhati, A.; de Mayo, P.; Morrison, G. A. J. Chem. Soc. **1958**, 4393).
6. After stirring a mixture of **4** (0.2 g), $Pb(OAc)_4$ (0.7 g) and AcOH (1 mL) for 30 min at 65 °C, workup and crystallization from ether:benzene (1:1) gave **5** in almost quantitative yield.
7. Takayanagi, H.; Ogura, H.; McMurry, T. B. H. Bull. Chem. Soc. Jpn. **1981**, 54, 1259.
8. Additional ^{1}H NMR parameters of **4** from 500 MHz spectra: 1.66qd(12.2,4.1Hz; H-8β), 1.82dt(14.2,3.5; H-9β), 1.91td(13.6,4.4; H-9α), 2.02dq(13.1,3.5; H-8α).
9. Naik, U. S., Studies in Natural Products (Ph.D. thesis), University of Bombay 1987.
10. NMR parameters of **5**: ^{1}H δ1.22d(6.8Hz; 11-Me), 1.31s(10-Me), 1.63qd(13.3,4.5; H-8β), 1.68ddd(13.1,4.5,1.5; H-9β), 1.95qd(12.1,3.9; H-7), 1.97m(H-8α), 2.30s(4-Me), 2.36dq(13.4,6.8; H-11), 2.77td(13.1,4.4; H-9α), 4.38d(11.1; H-6), 5.85d(9.6; H-2), 6.92d(9.6; H-1); ^{13}C C-1 through C-12, then 4-, 10- and 11-Me's δ158.5, 118.7, 162.0, 208.3, 90.1, 78.6, 45.6, 22.1, 31.4, 41.6, 41.0, 177.0, 31.9, 23.1, 12.3.

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