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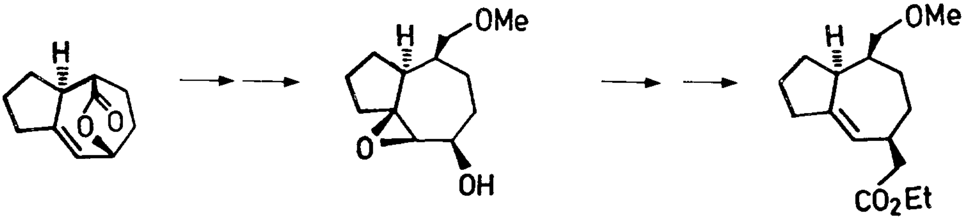
AN INTERMEDIATE FOR THE TOTAL SYNTHESIS OF GUAIANOLIDES; A CORRECTION

Peter Metz, Hans-J. Schäfer*
Organisch-Chemisches Institut der Universität, Orléansring 23,
D-4400 Münster, Germany

Gerald Henkel, Bernt Krebs
Anorganisch-Chemisches Institut der Universität, Corrensstr. 36,
D-4400 Münster, Germany

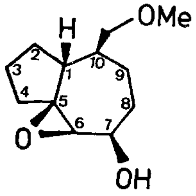
SUMMARY. The X-ray analyses of epoxy alcohol 2 and the immediate precursor of lactone 1 demand a revision of published hydroazulenic structures regarding their relative configuration at C-1.

Recently two of us[1] reported a stereospecific synthesis of ester 3 from the known lactone 1[2] :



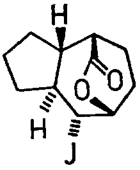
1 2 3

We now determined the structure of the intermediate epoxy alcohol 2 (m.p. 92 - 93° C, n-hexane) by X-ray diffraction[3a]. Entirely unexpected, this analysis revealed a relative configuration at C-1[4] that was opposite to the one shown in structure 2 (see stereodiagram of 2'):

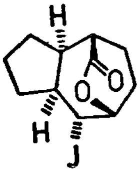


2' instead of 2

Since an epimerization at C-1 during the conversion 1 ⟶ 2' was not possible[1], the reported structure of crystalline iodolactone 4 (m.p. 121 - 122° C, ethanol) - the immediate precursor of oily 1[2] - was examined by X-ray diffraction[3b]. Already here, the relative configuration at C-1 is opposite to the postulated one (see stereodiagram of 4'):

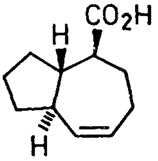


4' instead of

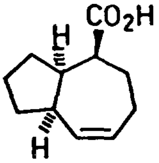


4

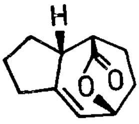
As a consequence, the configuration at C-1 in all hydroazulenic structure described in ref. 2 must be inverted, e.g.:



5' instead of



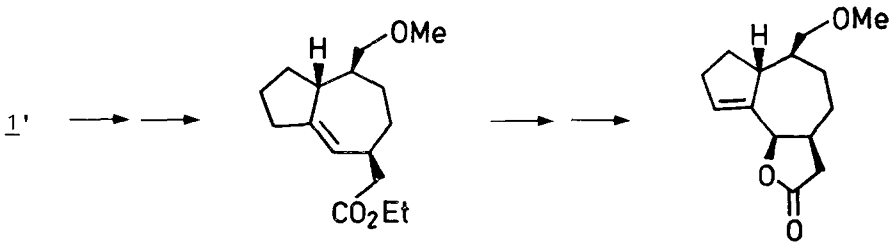
5



1' instead of 1

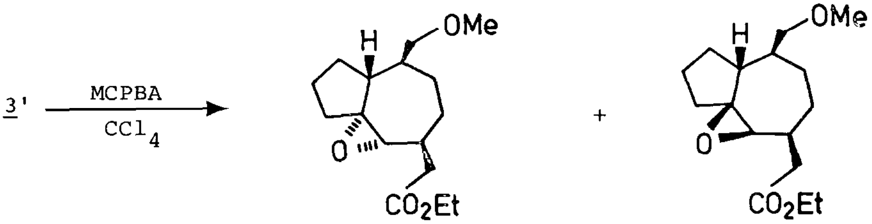
Moreover, the experimental prove of the cis-fusion in acid 5 reported[5] must be incorrect, possibly due to an insufficient glc-resolution.

With respect to our own communication[1] the stereochemistry of all compounds described has to be corrected regarding the relative configuration at C-1:



3' 6

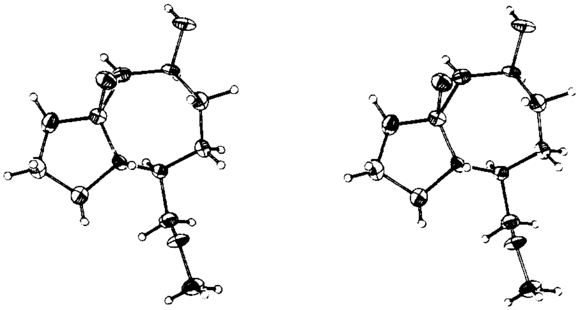
Furthermore, according to a qualitative conformational analysis[6], the α-epoxy strucutre 7a must now be assigned to the major epoxide obtained from 3'



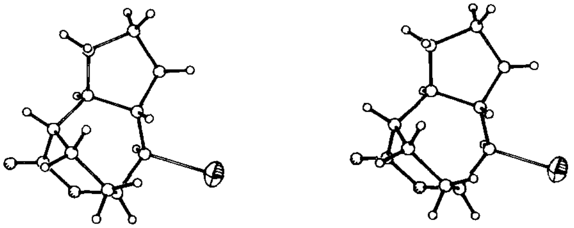
7a 7b

(1.7 : 1)

Since most of the naturally occuring guaianolides display a trans-relationship between 1-H and the C-7 side chain, the synthetic value of 3' as an intermediate for the total synthesis of guaianolides is considerably reduced.



Stereodiagram of epoxy alcohol 2' (arbitrarily chosen antipode).



Stereodiagram of iodolactone 4' (arbitrarily chosen antipode).

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References and Notes

1) P. Metz, H.J. Schäfer, Tetrahedron Lett. 1982, 4067.

2) a) J.B. Hendrickson, R.K. Boeckman, Jr., J. Am. Chem. Soc. 93, 1307 (1971); b) we thank Prof. Dr. R.K. Boeckman, Jr., University of Rochester, Rochester, New York, for sending us a detailed description of the synthesis of this lactone, as well as IR- and NMR-spectral data of this lactone and its precursors.

3) Intensity data were collected with a Syntex $P2_1$ diffractometer (MoKα radiation, graphite monochromator, scintillation counter, 2θ - θ - scan); all calculations were performed on a computer Eclipse S/200 (Data General), using programs of the Syntex EXTL and SHELXTL systems. Complete data are available on request, see: Tetrahedron Lett. 1978, 3081.
   a) 2' crystallizes orthorhombic in the space group $P2_12_12_1$ with $a = 15.183(3)$ Å, $b = 15.796(3)$ Å, $c = 4.717(2)$ Å, and 4 molecules in the unit cell; the structure was solved by direct methods and refined to $R_1 = 0.039$ and $R_2 = 0.033$ respectively.
   b) 4' crystallizes triclinic in the space group $P\bar{1}$ with $a = 7.938(3)$ Å, $b = 7.968(3)$ Å, $c = 9.519(3)$ Å, $\alpha = 98.87(3)°$, $\beta = 99.04(3)°$, $\gamma = 107.28(3)°$, and 2 molecules in the unit cell; the structure was solved by heavy atom methods and refined to $R_1 = 0.033$ and $R_2 = 0.038$ respectively.

4) Guaianolide numbering.

5) R. Srinivasan, V.Y. Merritt, G. Subrahmanyam, Tetrahedron Lett. 1974, 2715.

6) See Ref. 1; we are indebted to Dr. P.J. De Clercq, Rijksuniversiteit Gent, België, for informing us about an extension of his method; b) see also: C. Ehret, G. Ourisson, Tetrahedron 25, 1785 (1969).

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