

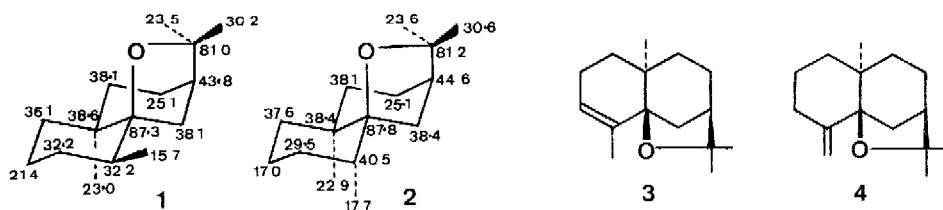
THE STEREOCHEMISTRY OF THE DIHYDROAGAROFURANS

Alan F. Thomas¹ and Michel Ozainne

Research Laboratory, Firmenich SA, 1211 Geneva 8, Switzerland

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The structures of dihydro- α -agarofuran (= isodihydroagarofuran, 1) and dihydro- β -agarofuran (2) have recently been questioned, and the structures shown were interconverted^{1, 2}, notwithstanding an unambiguous synthesis of isodihydroagarofuran (1)³. In this note we emphasize that the earlier structures, based on those of the agarofurans 3 and 4⁴ are undoubtedly correct, and we provide an explanation for the error of Paknikar et al.

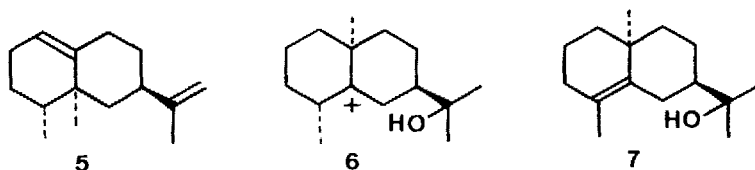


Catalytic hydrogenation of α -agarofuran (3) reportedly yields isodihydroagarofuran (1), hydrogenation of β -agarofuran (4) yielding the dihydroagarofuran (2) isolated from *Aquilaria agallocha*⁵. We have repeated these hydrogenations and find no catalyst-solvent system that reduced the double bond of α -agarofuran (3) without considerable hydrogenolysis of the tetrahydrofuran ring, reported to occur on 'prolonged hydrogenation'⁵, but which we believe is a matter of catalyst rather than time. Delongchamps achieved only a 55% yield of isodihydroagarofuran by hydrogenation of 3 - significantly lower than the original claim⁵. The isodihydroagarofuran we obtained using platinum oxide in acetic acid or ethanol⁵ was relatively pure, with less than 10% of the other isomer (2). Rhodium on charcoal was less satisfactory, yielding a 7 : 3 mixture of 1 and 2⁶. β -Agarofuran (4) is reduced more readily, but the dihydroagarofuran (2) obtained was contaminated with up to 37% of 1 using platinum, and 43% with rhodium. Because we were unable to separate preparatively sufficient amounts of dihydroagarofuran (2)⁶ for ¹³C NMR spectral examination, we used the material we had found to occur in galbanum resin (*Ferula* spp)⁷.

The ¹³C NMR spectra of the two dihydroagarofurans (1 and 2) are in accord with the

structures disputed by Paknikar et al.^{1, 2}. In particular, the shift to lower field of the C-4 signal on going from 1 to 2 is normal, although its magnitude suggests some further subtle change in the conformation⁸. The PMR spectra⁹ are also consistent with an equatorial methyl group for 1 0.88, d, J = 6.5 Hz, and an axial methyl group for 2 1.02, d, J = 8 Hz. Additional deshielding is also shown by the methyl group at C-10 (1.00 for 1, and 1.08 for 2) in going from an equatorial to an axial group at C-4.

The reason why it was suggested that the configuration of 1 and 2 should be inter-converted was based on formation of 1 from valencene (5) microbiologically. One of the intermediates was postulated to be the carbocation 6. This carbocation clearly does not maintain stereochemistry at C-4, but deprotonates (to 7) before undergoing cyclization to the thermodynamically more stable dihydroagarofuran configuration.



References

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3. A. Asselin, M. Mongrain, and P. Deslongchamps, *Can. J. Chem.*, **46**, 2817 (1968).
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6. The two isomers of dihydroagarofuran are very difficult to separate gas chromatographically. The only conditions we found that gave a shoulder using a packed column were Apiezon M 10% on Chromosorb W, 60-80 mesh, acid-washed, 3m x 4 mm i. d., at 200°. A capillary column of HB 5100 UCON 53m x 0.31 mm showed two distinct peaks, and the proportions were measured in this way.
7. The isolation of dihydroagarofuran (2) from galbanum resin has not been previously reported. It was accomplished by a combination of distillation, column chromatography on silica gel, and gas chromatography, and resulted in the isolation of dihydroagarofuran, identical in all respects with the major product from the hydrogenation of β -agarofuran⁵, accompanied by only trace amounts (ca 5%) of isodihydroagarofuran (1).
8. We are grateful to Dr. G. Lukacs, Institut de chimie des substances naturelles, Gif-sur-Yvette, France, for discussions about the ¹³C NMR spectra.
9. PMR spectra measured in CDCl₃ on a Bruker HX-90, for which we thank Mr. W. Thommen. Chemical shifts are given in ppm with tetramethylsilane 0.00 ppm.