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127. A Photo-initiated *Wagner-Meerwein* Rearrangement

Preliminary communication

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(14. IV. 76)

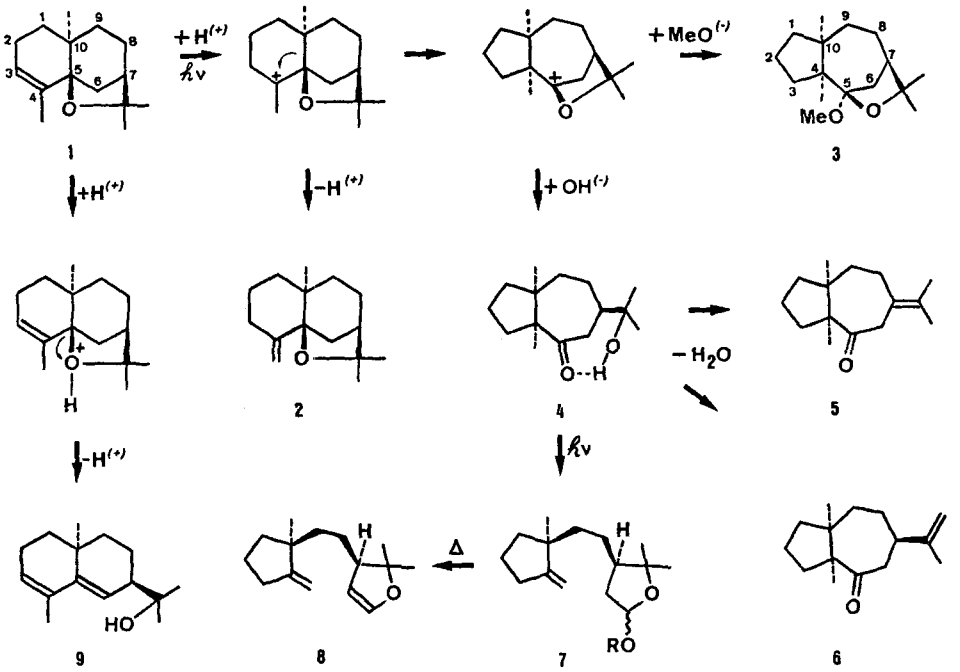
Summary. Irradiation of the octalin-derived sesquiterpene oxide α-agarofuran in methanol leads to rearrangement to the perhydroazulene system, in addition to simple double-bond migration to β-agarofuran. This rearrangement apparently proceeds through a carbonium-ion-like intermediate, whereas conventional generation of a carbocation leads only to opening of the oxide ring without rearrangement.

α-Agarofuran (**1**) is converted into the exocyclic alkene β-agarofuran (**2**) in moderate yield by irradiation in isopropyl alcohol with xylene as sensitizer [1]. Using methanol instead of isopropyl alcohol we isolated in addition, the acetal **3** and the related hydroxy-keton **4**. The structure of the latter was established as follows. All four methyl groups were attached to quaternary carbon atoms (NMR.), and the presence of a hydrogen-bridged hydroxy-keton system was shown by bands in the IR. spectrum[1]) at 3610 (free OH), 3470 (bonded OH), and 1680 cm^{-1} (bonded C=O). The position of the isopropyl group with respect to the carbonyl group was provided by a fortuitous dehydration that occurred on one occasion when compound **4** was injected onto an OV-17 gas chromatography column that had become acid with long use. Of the two substances recovered from the column, one (**5**) had a ^{1}H-NMR. spectrum[2]) showing the presence of only two quaternary methyl groups (0.96 and 1.09 ppm), two methyl groups on a double bond (1.71 ppm), and a methylene group between two double bonds (*AB* system, 3.08 and 3.45 ppm, $J = 15$ Hz). The other dehydration product (**6**) had the same two quaternary methyl groups (1.04 and 1.16 ppm) and an isopropenyl group (1.76 and 4.77 ppm). The acetal **3** had a ^{1}H-NMR. spectrum with five methyl groups (1.13, 1.16, 1.24, 1.36, and 3.30 ppm) and a single

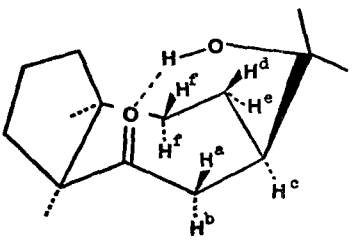
[1]) IR. spectra are measured in $CHCl_3$ solution.
[2]) ^{1}H-NMR. spectra are measured in $CDCl_3$ solution on a *Bruker* HX-90 instrument.

proton (2.32 ppm) coupled with two others (J = 5 and 12 Hz), which was assigned to the 6β proton, appearing at low field because of the influence of the nearby oxygen atoms.

Presence of the partial structure $COCH_2CHCH_2CH_2$ in the hydroxy-ketone **4** was confirmed by the ^{1}H-NMR. spectrum in the presence of the shift reagent, Eu(fod)$_3$ (see Fig.). Exact values for all coupling constants could not be measured, but J_{ab} and J_{de} were clearly *ca.* 13 Hz, J_{ac} was 6 Hz, and J_{bc} 5 Hz. Double irradiation showed couplings between H_{df} and H_{ef}, and the less shifted (by Eu(fod)$_3$) methylene



signals of the other ring were unaffected by irradiation of protons a to f. Models show that only a *cis* ring junction permits easy formation of a hydrogen bond.



Proton	Shift (ppm)/0.1 equiv. Eu(fod)$_3$
H^a	1.3
H^b, H^c, H^d	0.9
H^e	0.6
H^f	0.3
gem-Me_2	0.7

The hydroxy-ketone **4** is converted by further irradiation to another acetal (**7**, R = Me). Both this acetal, and the corresponding one (**7**, R = i-C_3H_7) obtained in isopropyl alcohol were identified spectrally, and by the fact that pyrolysis (occurring readily when R = i-C_3H_7) leads to the dihydrofuran **8** with the following

^{1}H-NMR. spectrum: 3 methyl groups (1.01, 1.23, 1.32 ppm), 3 protons next to double bonds (2.2–2.6 ppm), a methylene group (4.67 and 4.86 ppm, almost unchanged from the acetal **7**) overlapping part of the vinyl ether system (4.88 and 6.20 ppm, $J = 3$ Hz). The isomerisation **4** to **7** involves a known photochemical α-cleavage of the bond between the carbonyl group and the angular carbon atom, followed by transfer of a methyl hydrogen atom to the acyl group in the diradical intermediate.

Formation of 'carbonium-ion-like' intermediates by sensitized irradiation is known [2], and methyl migration under these conditions has been described [3], added potassium carbonate lowering the rate. In our case adding potassium carbonate only improved the yield of the acetal **3**, but, in any case, the intermediate is not the same as that obtained by standard techniques of proton addition. Thus treatment of α-agarofuran (**1**) in ether with *Dowex* 50 resin leads exclusively to opening of the oxide ring with formation of the dienalcohol **9** described by *Deslongchamps* [4].

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128. Stereospezifität der neuroleptischen Wirkung und Chiralität von (+)-3-{2-[4-(8-Fluor-2-methyl-10,11-dihydrodibenzo[*b,f*]thiepin-10-yl)-1-piperazinyl]-äthyl}-2-oxazolidinon (16)

4. Mitteilung über tricyclische Antidepressiva und Neuroleptica [1]

von **Werner Aschwanden, Emilio Kyburz** und **Peter Schönholzer**[1])

Chemische und Physikalische Forschungsabteilungen der F. Hoffmann-La Roche & Co. AG Basel.

Diese Arbeit ist Herrn Prof. *V. Prelog* zu seinem 70. Geburtstag gewidmet.

(19. III. 76)

Stereospecifity of the neuroleptic activity and chirality of (+)-3-{2-[4-(8-fluoro-2-methyl-10, 11-dihydrodibenzo[*b, f*]thiepin-10-yl)-1-piperazinyl]ethyl}-2-oxazolidinone (16). – *Summary.* The synthesis and stereospecific neuroleptic action in animals of the (+)-enantiomer of 3-{2-[4-(8-fluoro-2-methyl-10,11-dihydrodibenzo [*b,f*]thiepin-10-yl)-1-piperazinyl]ethyl}-2-oxazolidinone (**16**) are briefly described. The (10 S)-configuration of this compound was determined by X-ray diffraction.

Eine kürzlich erschienene Arbeit [2] über die stereospezifische Wirksamkeit und die absolute Konfiguration des (+)-Enantiomeren des Antipsychoticums Clorotepin **1**[2]) veranlasst uns zu dieser Mitteilung. Auf der Suche nach antipsychotisch wirksamen

[1]) Mitbearbeitet von Herrn *W. Gassner*.

[2]) Als Clotepin®-Spofa in der CSSR für die Therapie von Psychosen eingeführt. Von *Protiva et al.* [3] synthetisiert.