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The Cyclization of Some *cis*-Alkenynoic Acids to α-Pyrones

II. Lactonization of Dec-2*cis*-ene-4,6,8-triynoic Acid, and 5-(5-Methyl-2-thienyl)-pent-2*cis*-en-4-ynoic Acid

KÅRE HAUGE

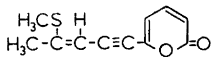
Institutt for organisk kjemi, Norges tekniske høgskole, Trondheim, Norway

In a previous note[1] the lactonization of dec-2*cis*-ene-4,6-diynoic acid (*cis*-lachnophyllum acid) (I), and of deca-2*cis*, 8*cis*-diene-4,6-diynoic acid (*cis*, *cis*-matricaria acid) (II) to the corresponding 6-substituted α-pyrones was described. The cyclization of two other *cis*-alkenynoic acids: dec-2*cis*-ene-4,6,8-triynoic acid (*cis*-dehydromatricaria ester) (III) and 5-(5-methyl-2-thienyl)-pent-2*cis*-en-4-ynoic acid (IV) to give the α-pyrones V and VI respectively, is now reported. The methyl esters of these acids are naturally occurring substances.[2,3]

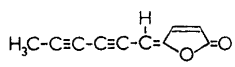
V

VI

The α-pyrone V has recently been synthesized by another method by Bohlmann *et al.*;[4] namely by cyclization of 1,1-dichlorodeca-1*trans*, 3*trans*-diene-6,8-diyn-5-one in a mixture of dioxane and 0.2 N HCl. Bohlmann also has reported the isolation of the naturally occurring acetylenic α-pyrone VII[5] and the synthesis of this by addition of methylmercaptan to V.[4]



VII



VIII

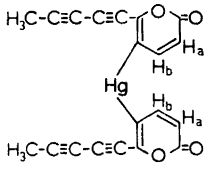
A sufficient quantity of *cis*-dehydromatricaria ester was obtained partly by isolation from *Artemisia vulgaris*[2] and partly by UV-isomerization of synthetic *trans*-dehydromatricaria ester.[6] Acid hydrolysis of the ester by the method given in the previous note[1] was then attempted. However, the acidic medium notwithstanding, the formed *cis*-dehydromatricaria acid showed a pronounced tendency toward formation of the corresponding butenolide VIII, and the yield of free *cis*-dehydromatricaria acid was small. No α-pyrone formation could be detected. Attempts were then made to combine the dehydromatricaria ester hydrolysis with Hg-catalysed ring closure to the C_5-carbon atom of the formed free acid. The best yield was obtained as follows: 100 mg *cis*-dehydromatricaria ester was dissolved in a mixture of 28 ml dioxane and 56 ml tetrahydrofuran, 30 ml sulfuric acid and 40 ml of water added together, and the mixture heated to reflux. After 9—10 min, a solution of 35 mg $HgSO_4$ in 25 ml 25 % H_2SO_4 was added slowly, addition time 45 min. The mixture was refluxed for another 15 min before work-up. After separation on an SiO_2-column, one main substance and smaller quantities of two others were isolated; all absorbed ultraviolet light.

The least polar of them was identified as the desired α-pyrone V. Initially this compound was contaminated by some of the butenolide VIII, but the pyrone was obtained pure after careful crystallization. Yield: 56 %, m.p. 108° (m.p. 110°, Bohlmann[4]). The UV, IR, NMR, and mass spectral data for the compound agree well with the data reported by Bohlmann.[4]

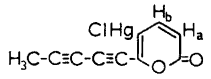
The most polar of the isolated compounds was identified as the Hg-containing bilactone derivative IX. Yield: 10 %. Solid, decomposes slowly on heating.

UV (in methanol): λ_{max} 341, 266.5, 252 mμ (ε=30 750, 15 240, and 12 340). IR (KBr-disc): α-pyrone: 1735, 1710 (split), 1580 (split), 1513 (split). $-C\equiv C-$: 2244 cm^{-1}. NMR (in hexadeutero-dimethylsulfoxide): H_a: d, τ=3.50, J=9.5 cps. H_b: d, τ=2.29, J=9.5 cps. CH_3-: s, τ=7.90. Mass spectrum: Parent peak (^{200}Hg-isotope): *m/e* 514. The relative abundances of the parent peak cluster and other peak clusters above *m/e* 200 showed that Hg is present.

In acid medium, IX is converted into V.



IX



X

The third isolated substance was the HgCl-substituted derivative X. Small quantities of X, apparently originating from some chlorine-containing impurities, were extracted from the reaction mixture together with V and IX, and further X was liberated from the aqueous layer after addition of NaCl. Combined yield: 6 %. Solid, decomposes gradually on heating. UV (in methanol): λ_{max}: 341, 264.5, 251 mμ (ε=15 600, 6510, 6430). IR (KBr-disc): α-pyrone: 1727, 1712, 1583, 1517 cm^{-1}. $-C\equiv C-$: 2240 cm^{-1}. NMR (in hexadeutero-dimethylsulfoxide): H_a: d, τ=3.54, J=9.4 cps. H_b: d, τ=2.42, J=9.4 cps. CH_3-: s, τ=7.87. Mass spectrum: Parent peak (^{35}Cl, ^{200}Hg-isotopes): *m/e* 392. The observed isoptopic abundances agree well with the theoretical abundances for $C_{10}H_5O_2HgCl$.

The other acetylenic acid, *cis*-5-(5-methyl-2-thienyl)-pent-2-en-4-ynoic acid, was isolated as the methyl ester from *Artemisia vulgaris*.[3] The ester was first hydrolysed by refluxing in acid medium, in a mixture of 82 % dioxane, 5.5 % conc. H_2SO_4 and 12.5 % water. After 3 h reflux, a thin layer chromatogram of the reaction mixture showed that no significant amount of ester remained and a zone with polarity as expected for a corresponding lactone was observed. The hydrolysis was then stopped, and the reaction mixture worked up. Besides small quantities of unhydrolysed ester only one product was isolated. This was found to be the desired α-pyrone VI. Yield *ca.* 76 %, m.p. 75.2–76°. UV (in hexane): λ_{max} 360, 260 mμ (ε=15 700, 6060). IR (in CCl_4): α-pyrone carbonyl: 1731, α-pyrone ring and thiophene ring: 1623, 1547, 1528, 1471 cm^{-1}. NMR (in $CDCl_3$): H_a: dd, τ=3.89, J=9.5+0.8 cps. H_b: dd, τ=2.69, J=9.5+7.0 cps. H_c: dd, τ=3.66, J= 7.0+0.8 cps. H_d: d, τ=2.63, J=3.9 cps. H_e: dq, τ=3.26, J=3.9+1 cps. H_f: d, τ=7.49, J=1 cps. Mass spectrum: Parent peak (and base peak): *m/e* 192. Other prominent peaks M−28, M−29, M−56 and M−67.

Thus, this thiophene-containing *cis*-alkenynoic acid IV is easily converted to the corresponding α-pyrone under reaction conditions where none of the straight-chain *cis*-alkenynoic acids I–III show any tendency toward α-pyrone formation. Further, the *cis*-dehydromatricaria acid is readily lactonized to the butenolide VIII in spite of the strongly acidic medium. The different behaviour of these acids may have an explanation analogous to that proposed by Bohlmann in connection with the isolation of 6-(4-methylmercaptopent-3-en-1-ynyl)-α-pyrone (VII).[4,5] He suggests that the immediate precursor for this α-pyrone is 9-methylmercapto-deca-2*cis*, 8-diene-4,6-diynoic acid, and that the methylmercapto group has a decisive polarising influence on the C_4-C_5 triple bond and thereby on the course of the cyclization.

The α-pyrone derivatives V, VI, IX, and X have been submitted to trial for eventual cytotoxic properties. The Hg-containing derivatives IX and X showed only a limited degree of cytotoxicity in the KB-cell culture test system; the other lactones are still under trial. The cytotoxic tests were performed by National Cancer Institute, Bethesda, Md., USA.

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Bacterial Carotenoids
XXX.* 2-Isopentenyl-3,4-dehydrorhodopin — A C_{45}-Carotenoid

SISSEL NORGÅRD and SYNNØVE LIAAEN-JENSEN

Organic Chemistry Laboratories, Norway Institute of Technology, Trondheim, Norway

It has been postulated that bacterial C_{50}-carotenoids are synthesized *in vivo* by addition of two isopentenyl units to the 2,2′-positions of a traditional C_{40}-carotenoid skeleton.[1,2] The existence of C_{45}-carotenoids has consequently been expected.

The first C_{45}-carotenoid (*1*) has now been isolated from *Corynebacterium poinsettiae* (Starr and Pirone). *1* had m.p. 153°C, λ_{max} 458, 486 (ε=172 500), and 518 nm, % III/II=79 in acetone, corresponding to an aliphatic dodecaene chromophore, M=620 ($C_{45}H_{64}O$), ν_{max} (KBR) 1160 and 905 cm^{-1} (tertiary hydroxyl), gave no acetate on acetylation and a mono(trimethylsilyl) ether on silylation. PMR signals (τ-values) and diagnostically important fragments in the mass spectrum indicated below, support structure *1*, 2-isopentenyl-3,4-dehydrorhodopin, for the new carotenoid. Although the spectroscopic evidence does not rule out an alternative attachment of the C_3H_7O unit to position x, biosynthetic considerations strongly favour structure *1*.

Further details will be published.

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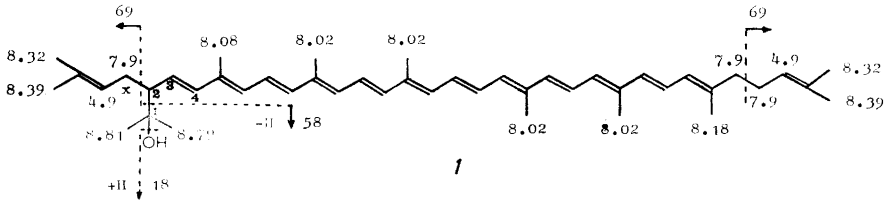

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