Chemistry of mediterranean gorgonians. II. Pregna 4,20-dien-11α-ol-3-one acetate, a novel steroid from the gorgonian *Eunicella cavolini*

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Summary. The compound titled **1** has been isolated from the gorgonian *E. cavolini* and synthesized from 11α-acetoxy-progesterone (**3**).

Gorgonians (Alcyonaria) have proved to be a rich source of a great variety of interesting organic compounds, among which the prostaglandins are the most striking[2]. Very recently[3,4] unusual pregnane derivatives, characterized by the presence of a vinyl group in the 20,21 position, have been isolated from Alcyonaria.

We wish to report now the isolation of the steroid **1**, the latest addition to this group of pregnane derivatives, from the mediterranean gorgonian *Eunicella cavolini,* and its synthesis from 11α-acetoxy-progesterone (**3**). The acetone extracts of the animals were partitioned between diethyl ether and water. The ethereal extract, after repeated chromatography on silica gel, afforded **1** in 0.13% yield based on the dry weight of the animal. The compound **1** is an oil, $|\alpha|_D^{CHCl_3} = +30°$, whose molecular formula was established as $C_{23}H_{32}O_3$ by high resolution mass spectrometry.

The IR-spectrum displayed a conjugated ketone absorption (ν_{max} 1675 cm^{-1}) whose presence was confirmed by the UV-spectrum (λ_{max} 243 nm, ε 12,500). In addition, the IR-spectrum showed an ester function (1730 and 1250 cm^{-1}) and a terminal vinyl system (995 and 915 cm^{-1}).

The PMR-spectrum showed signals at δ 1.3 and 0.74 (tertiary methyls), 2.02 (acetyl methyl), an ABC system with signals at δ 5.77, 5.00 and 4.98 ($J_{AB}=2.5$ Hz; $J_{AC}=17$ Hz; $J_{BC}=10$ Hz) attributable to the vinyl group, a signal at δ 5.26 (m, 1 H) due to the C*H*OAc and a signal at δ 5.8 (bs, 1 H) for the olefinic proton of the conjugated ketone system.

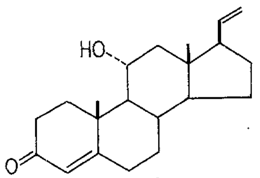
On treatment with KOH/MeOH, compound **1** yielded the alcohol **2**, m.p. 156–158 °C from $MeOH/H_2O$, $|\alpha|_D^{CHCl_3} = +59°$, m/e 314 ($M^+$, 55%) and 124 ($\Delta^4$-3one[5]; 100%), which in the PMR-spectrum showed a signal at δ 4.05 (m, 1 H) due to 11β proton with a shape characteristic for an 11α-OH substitution in a steroid skeleton[6].

Confirming evidence for the proposed structure came from the CMR-spectrum, which was compared, where relevant, with the spectrum of 11α-acetoxy-progesterone[7], and from synthesis which made the stereochemistry clear at C-17.

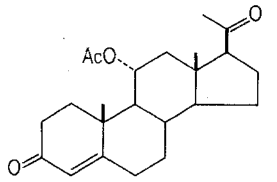
Compound **1** was synthesized as follow. Treatment[8] of 11α-acetoxy-progesterone (**3**) with boiling 2-methyl-2-ethyl-1,3-dioxolane in the presence of a catalytic amount of p-toluene sulfonic acid monohydrate yielded the bisethylenedioxy-derivative (**4**) (45%; m.p. 173–177 °C from MeOH; $|\alpha|_D^{CHCl_3} = -33.2°$; M^+/e 460) and a minor amount (18%) of the monoethylene dioxy-derivative (**5**) (m.p. 144–149 °C from MeOH; $|\alpha|_D^{CHCl_3} = +14°$; M^+/e 416; no UV-absorption above 220 nm) which were separated on silica gel column chromatography.

4 was further transformed to **5** by selective removal of the 20-ketal group with boron trifluoride at room temperature[9] (75%). **5** was treated with $NH_2OH \cdot HCl$ in 95% EtOH containing $CH_3COONa \cdot 3\,H_2O$ at 80 °C to give **6** in 80% yield (m.p. 177–180 °C from $EtOH/H_2O$; $|\alpha|_D^{CHCl_3} = -31.6°$; M^+/e 431); PMR δ 7.73 (1 H, bs, NO*H*), which was reduced to a mixture of the epimeric amines (**7**) with Na in boiling isoamyl alcohol in 50% yield (m.p. 205–215 °C from benzene/light petroleum; 2 closely related spots in TLC; M^+/e 375), hydrolysis of the acetyl group having taken place.

The amines (**7**) were methylated and quaternized with methyl iodide and anhydrous potassium carbonate in boiling absolute EtOH, and, after the filtration of the inorganic salts, the trimethylammonium iodide derivatives (**8**) were washed with $CHCl_3$ and subjected to the Hoffmann degradation[10] in boiling ethylene glycol with an aqueous solution of KOH to give **9** (35% yield from **7**; m.p. 178–180 °C from light petroleum; $|\alpha|_D^{CHCl_3} = -42°$; M^+/e 358). **9** on treatment with boiling acetone and a catalitic amount of p-toluene sulfonic acid for a few minutes, afforded in quantitative yield a compound identical in all respects with **2** which, in turn, on acetylation was transformed into the desired pregna-4,20-dien-11α-ol-3-one acetate (**1**).



1 R = Ac
2 R = H



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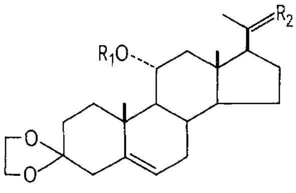
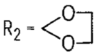
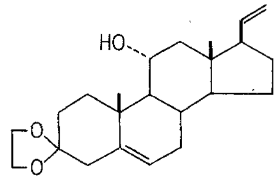


4 R_1 = Ac R_2 =



5 R_1 = Ac R_2 = O
6 R_1 = Ac R_2 = NOH
7 R_1 = H R_2 = H,NH_2
8 R_1 = H R_2 = $H,\overset{+}{N}(CH_3)_3\,\bar{I}$



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Reactions of sodium hypochlorite with some compounds having reactive methylene groups

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Summary Alkaline sodium hypochlorite solution oxidises a number of compounds having reactive methylene groups to the corresponding gem diols, but in some cases only decarboxylation occurs at room temperature.

During investigations into the use of sodium hypochlorite as a halogenating reagent in organic chemistry, the reaction between this compound and malonic acid was studied. In acidic solution, low yields of chloro- and dichloroacetic acids, and chloro- and dichloromalonic acids were obtained. In alkaline solution, the product, in 22% yield, was 2,2-dihydroxypropan-1,3-dioic acid, disodium salt (sodium mesoxalate). Previous syntheses of this compound had either been via diethyl 2-oxopropan-1,3-dioate[1]; or 2,2-dibromopropandioate[2].

It seems possible that the reaction producing the sodium mesoxalate is as follows:

$$\begin{tikzcd} \mathrm{CH_2(CO_2Na)_2} \arrow[r, "\mathrm{NaOCl}", "\mathrm{OH^-},\,25^\circ"'] & \mathrm{Cl_2C(CO_2Na)_2} \arrow[d, "25^\circ"', "\mathrm{OH^-}"] \\ & \mathrm{(HO)_2C(CO_2Na)_2} \end{tikzcd}$$

We were able to show by gas chromatography that small amounts of dichloromalonate were present in the reaction mixture. Also, synthesis of sodium dichloromalonate[2] and reaction of the latter with sodium hydroxide yielded sodium mesoxalate.

In an attempt to determine the scope of the reaction, we also carried out the following reactions:

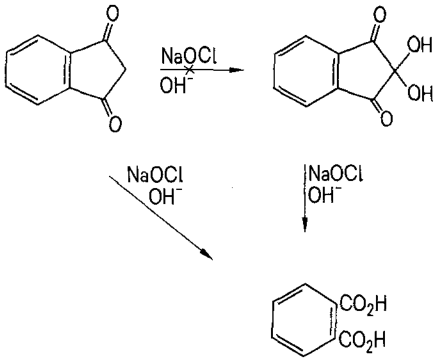
$$\mathrm{CH_3COCH_2COCH_3} \xrightarrow[\mathrm{OH^-},\,25^\circ]{\mathrm{OCl^-}} \mathrm{CH_3COC(OH)_2COCH_3}$$

$$\mathrm{HOOCCH_2COCH_2CO_2H} \xrightarrow[\mathrm{OH^-},\,25^\circ]{\mathrm{OCl^-}} \mathrm{CH_3COCH_3}$$

$$\mathrm{HOOCCOCH_2CO_2H} \xrightarrow[\mathrm{OH^-},\,25^\circ]{\mathrm{OCl^-}} \mathrm{CH_3COCO_2H}$$

3,3-dihydroxypentan-2,4-dione for reference purposes was synthesised by the method of Calvin and Wood[3].

We were hopeful that indan-1,3-dione could be converted to 2,2-dihydroxyindan-1,3-dione (ninhydrin) with alkaline hypochlorite. In the event we obtained an almost quantitative yield of phthalic acid. We found, however, that ninhydrin was also converted almost quantitatively to phthalic acid with alkaline hypochlorite:



All products have been characterized by comparison of melting points and spectra (UV, IR and NMR) with those obtained from authentic material.

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A possible biomimetic synthesis of fluoroacetic acid

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Summary. We propose that fluoroacetate may be formed in plants by fluorodecarboxylation of malonic acid.

Fluoroacetate and a number of related organofluorine compounds are biosynthesised in plants either naturally[1] or as the result of fluoride pollution[2]. Fluorination of organic molecules generally takes place under fairly drastic conditions in the laboratory, and the fluorinating agent is normally hydrogen fluoride or some other inorganic fluoride, or elemental fluorine[3]. Since these conditions are not likely to obtain in a living plant cell, the precise method by which fluorine is introduced into organofluorine compounds in plants has so far remained unknown. A number of specula-