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THE ACTION OF PHOSPHORUS PENTACHLORIDE AND THIONYL CHLORIDE ON SANTONIN

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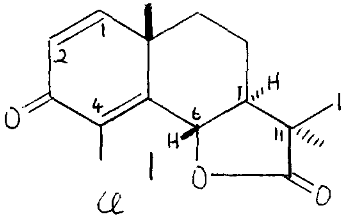
Some eighty years ago, it was reported[1] that santonin (1) reacts with phosphorus pentachloride in chloroform to afford a trichloride, $C_{15}H_{15}O_2Cl_3$. Our interest in the action of phosphorus trichloride in acetic acid on santonin[2] prompted us to reinvestigate this reaction. We have found that two products are formed, a monochloride $C_{15}H_{15}O_2Cl$ (2) and a trichloride, $C_{15}H_{15}O_2Cl_3$ (3). Stoichiometrical studies show that the monochloride is a precursor of the trichloride.

The monochloride shows spectral properties similar to those of 3 O-acetylsantonene (4).[2,3] In particular, the ultraviolet spectrum is characteristic of the conjugated tetraenolide, and its n.m.r. spectrum indicates the presence of an angular methyl group, two methyl groups attached to double bonds, and two olefinic protons on adjacent carbon atoms.



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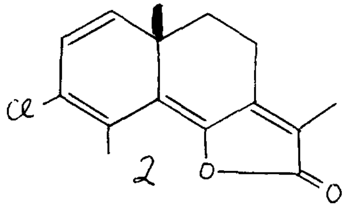

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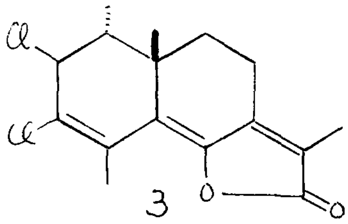

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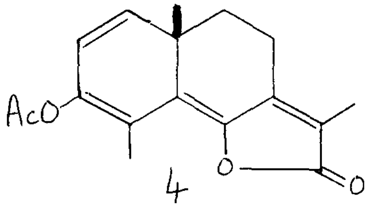

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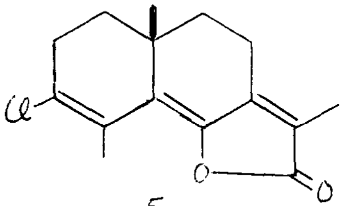
The trichloride has an ultraviolet spectrum characteristic of the trienolide chromophore as exists in the chlorotrienolide (5)[2], or acetoxytrienolide (6)[3] and the n.m.r. spectrum shows three methyl groups, at similar positions to those in (5), and (6). Compared with the n.m.r. of the chlorotetrene (2), the olefinic protons have disappeared and have been replaced by a multiplet at τ 5.0 and doublet at 5.59, characteristic of hydrogen adjacent to chlorine in the 1-[2] and 2-positions. The coupling constant (J 2 Hz) indicates a dihedral angle of ca. 60° between hydrogens.

We believe that the 1- and 2- chlorine atoms are trans diaxial. Dehalogenation using iodide in acetone[4] (slow), or preferably in dimethyl formamide, causes elimination to give the chlorotetraenolide (2). This elimination would be expected if the two chlorines are trans diaxial.



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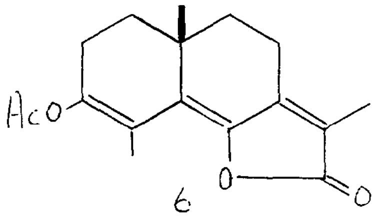

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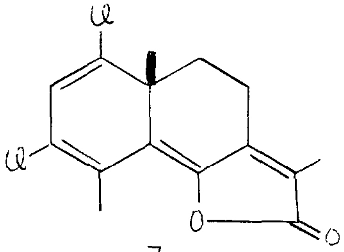

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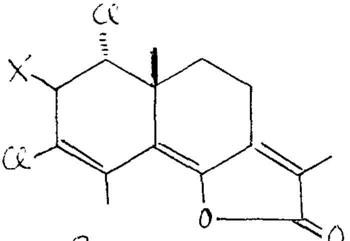
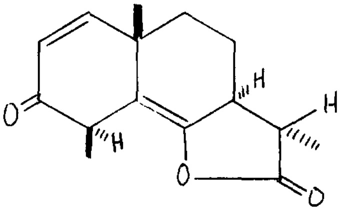


8a, X = OH
b X = OAc

The trichloride does not lose hydrogen chloride easily eg. with pyridine, but with triethylamine in pyridine at 95° (slow), or diazabicyclooctane or 1,5-diazobicyclo-[4,3,0]non-5-ene[5] in toluene at room temperature, dehydrochlorination occurs to afford the 1,3-dichlorotetraene (7). This reaction presumably proceeds by a <u>syn</u> E_2 mechanism. Both the trichlorotriene (3) and monochlorotetraene (2) on hydrogenation over palladium afford among other products the chlorotriene (5).

The trichloride (3) is also formed by the action of thionyl chloride on santonin, together with traces of the hydroxydichloride (8a), whose structure follows from its n.m.r. spectrum. The same hydroxydichloride is formed by the action of silver nitrate in aqueous acetone on the trichloride (3). Acetylation of (8a) gives the acetate (8b), which can also be obtained from the trichloride (3) by the action of silver acetate in acetic acid. The trichloride (3) can be obtained from the hydroxy compound by the action of phosphorus pentachloride, thionyl chloride, phosphoryl chloride-pyridine or carbon tetrachloride-triphenyl phosphine.[6]

N.o.e. measurements have been used to deduce the stereochemistry and structure of (3), (7) and (8a). Irradiation of the 10-methyl group in (3) or (8a) causes an enhancement in the size of the 1-proton signal (16.0% amd 9.5% respectively) but the 2-proton signal remains unchanged. This indicates that the 1-hydrogen is β-oriented, and the 2-hydrogen α-oriented. Irradiation of the 10-methyl group in (7) causes no enhancement of the vinyl proton signal, indicating that this proton is in the 2- rather than the 1-position.



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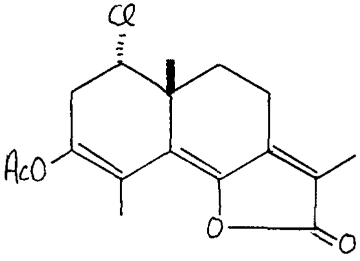

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The formation of both (2) and (3) from santonin using phosphorus pentachloride involves a change in oxidation state. In the treatment of pyrosantonin (9) with phosphorus trichloride in acetic acid,[2] oxidation does occur in the formation of the 1α-chloro-1,2-dihydro santonene 3-acetate (10), though we were unable to determine the stage at which this occurred . In the present case, phosphorus^{V} could be reduced to phosphorus^{III}, thus causing the change of oxidation state. Certainly this must be true of the step at which (2) is converted to (3).

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