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# STRUCTURES OF TWO CHOLESTEROL OXIDATION PRODUCTS BY 2D-NMR SPECTROSCOPY

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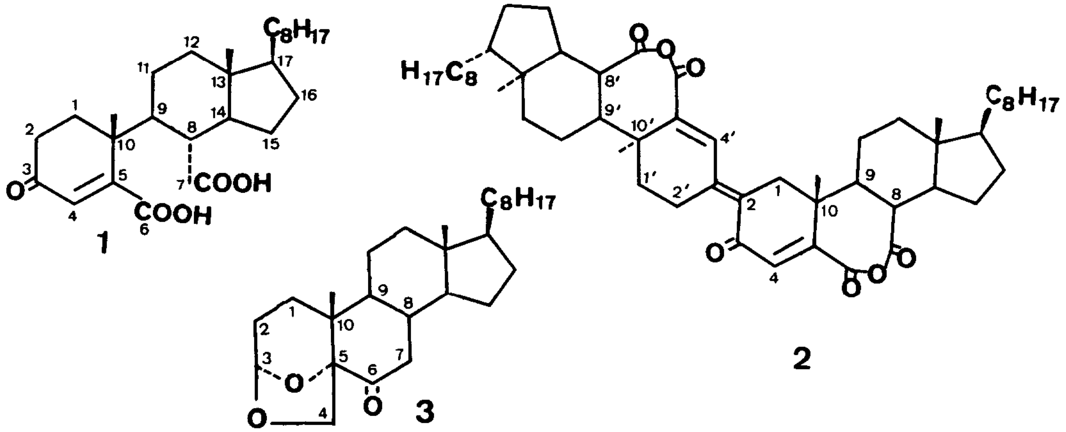
Summary
The structure of a dimeric steroid compound, isolated via basic treatment of Butenandt acid, is described. The previously known "ketone 104" is also fully analysed by means of 2D-nmr spectroscopy.

In the course of the chemical reduction of Butenandt acid 1 we have recently described the structures of new steroid derivatives (1, 2). As a continuing study we now report the structure of a dimeric steroid compound 2 and we confirm the structure of a substance first isolated by Fieser in 1953 (3) and referred initially as "ketone 104" 3 for lack of understanding of its nature.



1

2

3

In an attempt to obtain cleavage transformation of Butenandt acid 1 by hot concentrated (50% w/w) KOH aqueous solution followed by $Ac_2O$ treatment we isolated 2 (15% overall yield) as yellow crystals,m.p. 259-260°C.
The molecular formula was deduced from mass spectroscopy and elementary analysis.

The uv spectrum showed two maxima at 243 and 326 nm ( ε = 5490 and 7310) while ir spectrum indicated the presence of 3 carbonyl functions (1790 and 1760 cm$^{-1}$ : C=0 anhydride; 1650 cm$^{-1}$ : C=0 unsaturated) and conjugated double bonds (1620-1560 cm$^{-1}$).

The 100.6 MHz $^{13}$C spectrum (Table 1) of 2 provided further confirmation for 5 carbonyls and 3 double bonds. The relative shielding of the carbon at 188.6 ppm confirmed the presence of the conjugated ketone at position C3.

Table 1: 100.6 MHz $^{13}$C nmr data (CDCL$_3$, δTMS=0 ppm) for compounds 2 and 3

| | 2 | | 3 |
|---|---|---|---|
| C1 & C1' | 38.8 & 33.9 | C1 | 28.6 |
| C2 & C2' | 129.8 & 23.5 | C2 | 26.8 |
| C3 & C3' | 188.6 & 154.8 | C3 | 102.5 |
| C4 & C4' | 128.7 & 131.9 | C4 | 65.2 |
| C5 & C5' | 143.1 & 148.6 | C5 | 89.9 |
| C6 or C6' | 161.7 or 163.6 | C6 | 206.9 |
| C7 or C7' | 171.3 or 171.8 | C7 | 44.5 |
| C8 or C8' | 47.1 or 47.4 | C8 | 38.8 |
| C9 or C9' | 49.6 or 50.6 | C9 | 42.1 |
| C10 & C10' | 42.0 & 38.9 | C10 | 43.7 |
| C11 or C11' | 23.4 or 22.8 | C11 | 22.3 |
| C12 or C12' | 39.0 or 39.8 | C12 | 40.2 |
| C13 or C13' | 42.5 or 42.2 | C13 | 43.5 |
| C14 or C14' | 50.8 or 51.2 | C14 | 57.1 |
| C15 or C15' | 24.6 or 24.7 | C15 | 24.2 |
| C16 or C16' | 28.1 or 28.2 | C16 | 28.5 |
| C17 or C17' | 56.0 or 56.3 | C17 | 56.6 |
| C18 or C18' | 12.2 or 12.1 | C18 | 12.4 |
| C19 or C19' | 20.1 or 19.6 | C19 | 17.8 |

Assignements are supported by INEPT experiments; carbons C20 to C27 at usual frequencies within ± 0.1 ppm.

Due to its dimeric nature anhydride 2 exhibits a pseudo-symmetry which renders very difficult a detailed analysis of its proton nmr spectrum by standard methods, even at 400 MHz (table 2).

However 2D nmr spectroscopy (cosy 45) followed by a Wagner 2D sequence (4) showing long range correlations led us to propose structure 2 (i.e. 3-oxo-2(3')en-bis 6,7 seco-4-cholesten-6,7-dioic anhydride).

Long range contour plot correlations (crosspeaks) between H2' and H4'; H2' and H1; H4' and H1 were supported by the analysis of the corresponding matrix rows while the "E" double bond isomerism of the two subunits was readily established by the 1D NOE experiments.(A large NOE effect is measured between H1 and H4').This stereochemistry explains the rather important high field shielding observed for carbon C2', due to 1-3 diaxal interaction with the ketone in position C3.

Ketone 104, isolated by Fieser in 1953, was identified as (3,5)(3,4)dioxa-3,4-secocholestane-6-one 3 in 1959 after a long and detailed chemical analysis (3,5).

Oxidation of cholesterol by sodium dichromate followed by the usual purification work, led to this expected compound (m.p. 124°C). 2D-nmr data (Fifure 1)

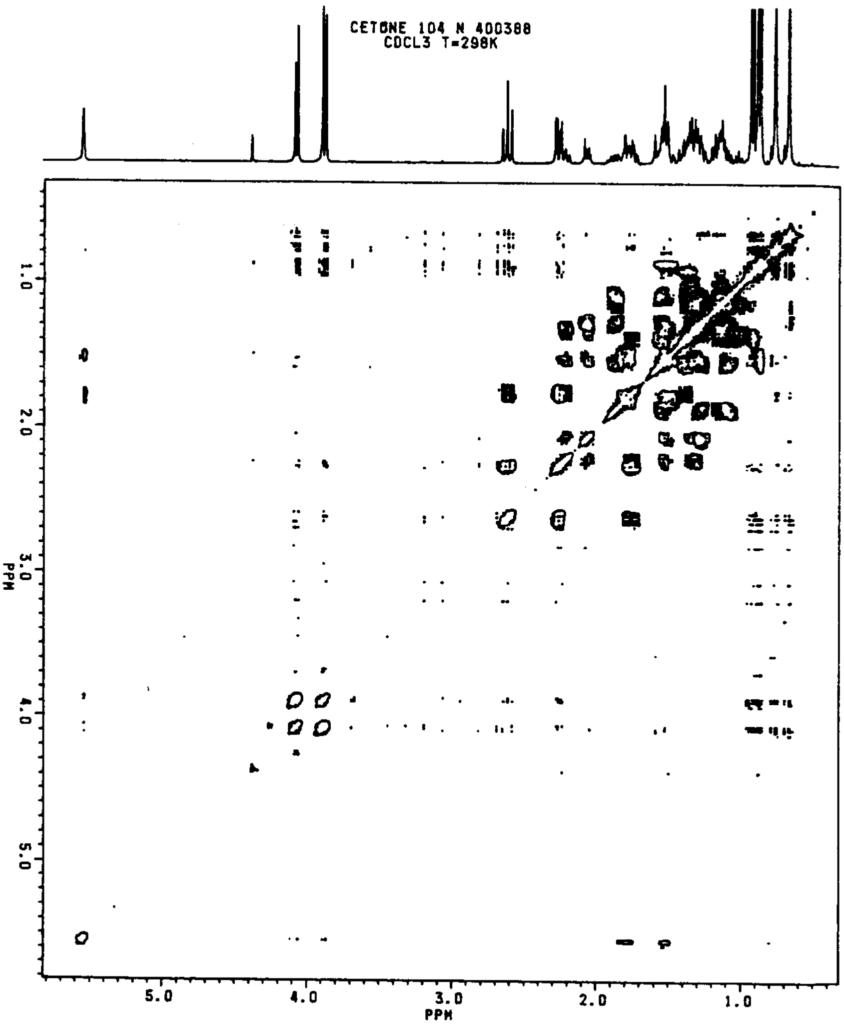


Figure 1. Ketone 104 : 2D-nmr spectrum (cosy 45)

and inspection of $^{13}$C nmr spectrum provided confirmation of the published structure (ketal carbon at position C3; methylene at C4 and tertiary alcohol at C5) while the previously reported stereochemistry was confirmed by strong NOE effects between H4 and 19-methyl.

Nmr spectral data are summarized in tables 1 and 2.

Table 2: Partial 400 MHz $^{1}$H nmr data (CDCL$_3$, $\delta$TMS=0) for substances 2 and 3

| 2 | | 3 | |
|---|---|---|---|
| H1 | : 3.2 & 2.5 (d);J1-1=15 Hz | H1 & H2 | : 1.8 & 1.5 (m) |
| H1' | : 2.0 (ddd);J1'-1'=14 Hz; | H3 | : 5.55 (broad s) |
| | : J1'-2'=4 & 4 Hz | H4 | : 4.1 & 3.9 (d);J=8.5 Hz |
| H2' | : 3.7 & 2.45 (ddd); | H7 | : 2.6 & 2.25 (dd) |
| | : J2'-2'=19 Hz;J2'-3'=3 & 3Hz | | : J7-7=12 Hz;J7-8=12 & 4Hz |
| H4 | : 6.2 (s) | H9 | : 2.2 (ddd);J9-8=12 Hz; |
| H4' | : 6.85 (s) | | : J9-11=12 & 4 Hz |
| H8 & H8' | : 2.70 & 2.65 (dd); | H12 | : 2.05 (ddd);J12-12=12 Hz |
| | : J=11 & 11 Hz | | : J12-11=4 & 4 Hz |
| H12 & H12' | : 2.18 & 2.08 (ddd); | H18 | : 0.70 (s) |
| | : J=14, 3 & 3 Hz | H19 | : 0.80 (s) |
| H18 & H18' | : 0.70 & 0.65 (s) | | : |
| H19 & H19' | : 1.4 & 1.3 (s) | | : |
| Wagner long range correlations between H2′ and H4′; H2′ and H1 ;H4′ and H1 .Strong NOE effects between H1 and H4′ | | Strong NOE effects between H4 and 19-methyl . | |

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