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STRUCTURES OF TWO MAJOR PRODUCTS IN HYPOIODITE REACTION OF 3α- AND 3β-HYDROXY-Δ^5-STEROIDS. A CORRECTION. [1]

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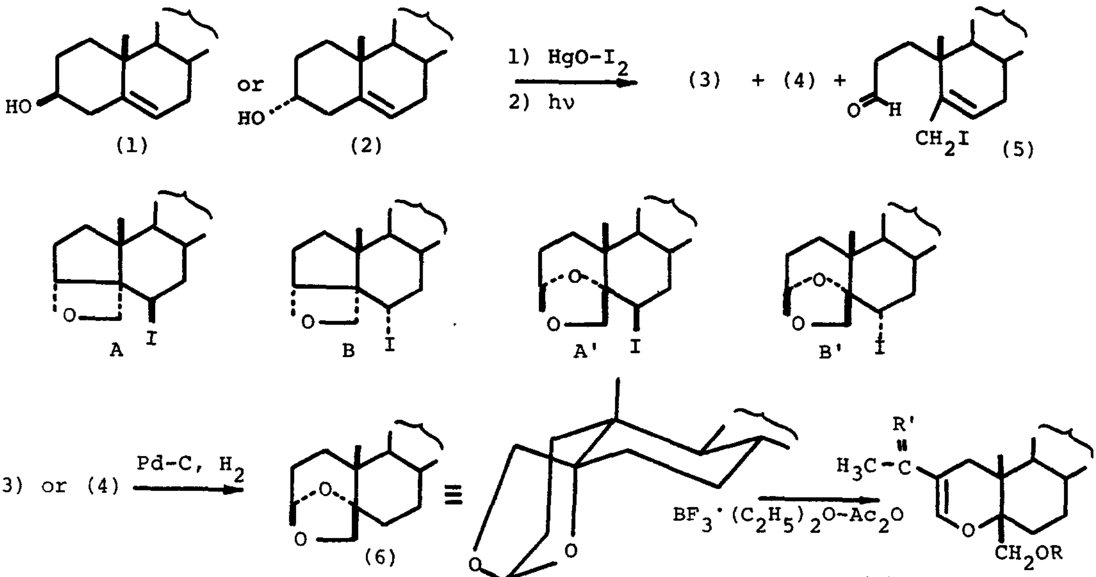
In our recent paper [2] it was reported that the photoinduced hypoiodite reaction of cholesterol (1) or epicholesterol (2) with HgO and I_2 in benzene under an argon atmosphere afforded two iodine-containing products (3) and (4) and 4-iodo-3,4-seco-cholest-5-en-3 al (5). Oxidomethylene-3α,5α-A-nor-cholestane structures (A) and (B) were proposed for these iodine-containing products on the basis of the ^1H n.m.r. and the spin-decoupling experiments of these compounds and the D-incorporated compounds as well as consideration of probable mechanistic pathways of their formation. In this paper we wish to report that the proposed structures for these two compounds are not correct and these compounds should be formulated as (A') and (B').

The inadequacy of the assigned formulae was immediately exposed when we inspected ^{13}C n.m.r. spectra ($CDCl_3$, 22.64 MHz, ppm from TMS) of the two products (3) and (4) [3]. The spectrum of (3) exhibited 25 signals including three signals at 103.4 ppm, 83.8 ppm and 73.3 ppm in the downfield region. By the aid of off-resonance decoupling, these signals were assignable to an acetal type carbon bearing one hydrogen atom ($HC{<}^{O-}_{O-}$), a quaternary carbon bearing one oxygen atom (H_2C-O-) and to a carbon bearing two hydrogens and an oxygen (H_2C-O-) respectively. The ^{13}C n.m.r. spectrum of (4) was very similar to that of the product (3), exhibiting 26 signals. The three signals, ascribable to the oxygen-bearing carbons as in the case of the product (3), were present at 101.7 ppm, 85.2 ppm, and 73.8 ppm respectively. The oxetane structures we initially proposed apparently could not accommodate these ^{13}C n.m.r. data.



(7) R=Ac, R'=O
(8) R=H, R'=O
(9) R=Ac, R'=NOH

Scheme 1

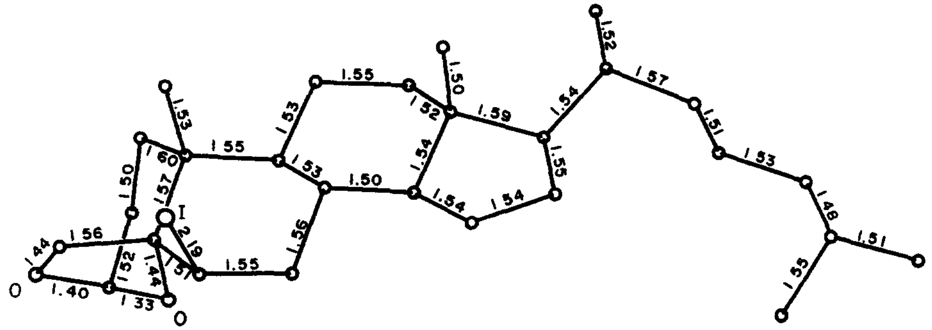
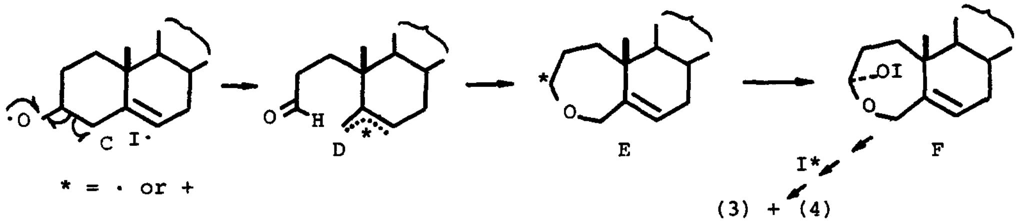


Fig. 1 The molecular framework and the bond distances (Å) of compound (3). The e.s.d.'s are about 0.02-0.04 Å.



Scheme 2

Although no parent peaks were observed in the routine electron impact mass spectra of the products (3) and (4), an iodine-free compound (6) [2] obtained by hydrogenolysis of (3) and (4) exhibited the molecular ion peak at m/e 402. This was in accord with the molecular formula of $C_{27}H_{46}O_2$ and this, in turn, confirmed the molecular formula of (3) and (4) to be $C_{27}H_{45}O_2I$. These new results together with analysis of the n.m.r. spectra which we have already described [2] were perfectly reconciled with the structures (A') and (B') for the products (3) and (4) with exception of the stereochemistry of the A ring. Treatment of the iodine-free compound (6) in benzene with BF_3- etherate and acetic anhydride at room temperature afforded a diacetyl compound (7), m.p. 71~73°C, which upon hydrolysis afforded a product (8), m.p. 72~74°C, and an oxime derivative (9), m.p. 144~145.5°C. The following spectral and analytical data could be adequately interpreted in terms of dihydropyran structures for these compounds. The formation of a dihydropyran (7) can reasonably be interpreted on the basis of the structure (6).

Compound (7), Mass. M^+, 486, I.r. 1740 cm^{-1} (OAc), 1652 cm^{-1} and 1622 cm^{-1} (COC=CH-). U.V. λ_{max}^{EtOH} 257 nm (ε; 15,500) ($CH_3CO-\underset{R}{C}=CH-OR$). N.m.r. (100 MHz, $CDCl_3$, TMS) τ2.48, S, (C-3-H), τ5.82, d, J=12.0 Hz and τ5.91, d, J=12.0 Hz, (C_5-CH_2OAc) [4], τ7.80, S, (C-$COCH_3$), τ7.94, S, (O-$COCH_3$), τ8.96, S, (19-H), τ9.35, S, (18-H).

Compound (8), Mass. M^+, 444, I.r. 1608 cm^{-1} (COC=CH-), 3400 cm^{-1} (OH). U.v. λ_{max}^{EtOH} 254 nm (ε; 10,900). N.m.r. τ2.31, S, (C-3-H), τ6.55, d, J=12.0 Hz and τ6.31, d, J=12.0 Hz. (C_5-CH_2OH) [4], τ7.82, S, (C-$COCH_3$), τ9.03, S, (19-H), τ9.37, S, (18-H).

The configuration of the oxygen bridge between C_3 and C_5 in (3), hence in (4), which cannot readily be distinguished by chemical and spectroscopic methods, was determined by X-ray crystallographic analysis of (3).

The crystal of (3) is monoclinic, with two molecules in a unit cell with the dimensions of a = 17.698(5), b = 7.018(3), c = 10.265(4) Å, and β = 92.11(3)°; the space group is $P2_1$. Intensities of 2210 unique reflections with 2θ values up to 140° were collected on an automatic four-circle diffractometer with Cu Kα radiation monochromatized with a LiF crystal. Although the sample used was not small enough (about 0.3 × 0.3 × 0.1 mm), no correction was applied for the absorption effect. The positions of all the non-hydrogen atoms were elucidated by using the Patterson-function and heavy-atom methods, and were refined by the block-diagonal-matrix least-squares method with anisotropic temperature factors. The final R value was 9.8%. The molecular framework of (3) thus obtained is shown in Fig. 1. In conclusion the structures (3) and (4) are completely elucidated as shown in A' and B'.

On the basis of the present results, the structure of a minor product (the product 12, R=H cited in a previous paper [5]) obtained in the hypoiodite reaction of N-acetyljervine, for which an oxetane structure, N-acetyl-11-oxo-oxidomethylene-3α,5α-A-nor-(22S,23R,25S)-jerva-5,12(13)-diene, was assigned, should also be revised to encompass the acetal structure shown in ring A in accord with (4).

We have already proposed the intervention of a common intermediate such as E to account for the formation of several compounds with oxepane rings in the present reaction [2,5]. The formation of the acetals (3) and (4) also seems to be rationalized by assuming the intermediacy of this species.

The transformation of this species into the products (3) and (4) may probably be a complex process and might involve hypothetical species such as ^{-}OI, $^{\cdot}OI$ or I_2O [6]. One of the probable transient species from E would be F, formed by an attack of the above species from the less-hindered side in E, as shown in Scheme 2.

REFERENCES AND NOTES

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3) ^{13}C n.m.r. spectra described in this paper were taken with a Brucker SXP pulsed FT NMR spectrometer.
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