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# REVISION OF THE CONFIGURATION OF AN ACETOLYSIS PRODUCT OF 3-O,N-DIACETYLTETRAHYDROJERVINE (1)

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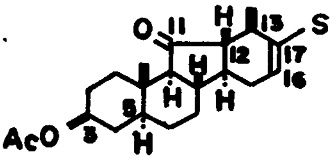
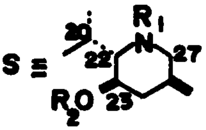
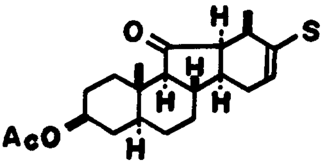
We present herewith evidence that the entitled compound is correctly represented by formula I rather than I' as previously advanced (2).



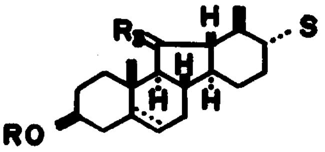
I $R_1=R_2=Ac$





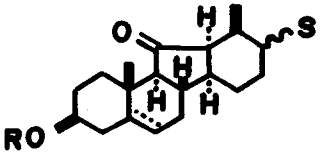
I' $R_1=R_2=Ac$

In the previous paper (3) we reported on the conversion of jervine (4) into a compound (IIa) formulated then as N-acetyl-22,27-imino-12α-jerv-5-ene-3β,23β-diol-11-one (IIa', 12αH) (5). The Wolff-Kishner reduction of IIa gave an 11-deoxo compound (III), which was further degraded to 20-oxime (IV). In a continuing study, the oxime was readily hydrolyzed to 20-ketone (V), m.p. 128-129°, (6) under mild conditions ($NaHSO_3$ and $H^+$) (7) and, after hydrogenation (Pt), gave a 5α,6-dihydro derivative (VI), m.p. 147-148°, in 70% yield from IV. Compound VI was oxidized with $C_6H_5CO_3H$ and then hydrolyzed ($OH^-$) to give etiojervane-3β,17α-diol (VII), m.p. 169-170°, in 15% yield (50% of VI recovered). This compound VII was also derived from the 5,6-dehydro compound (8) (VIII), m.p. 182.5-183.5°, by hydrogenation (Pt), which has been prepared ($NaBH_4$ and $NH_2NH_2$-KOH) from O-acetyletiojerv-5-en-3β-ol-11,17-dione (9) (IX), while compound VIII was converted into O-acetyletiojerv-4-en-17α-ol-3-one (X) by Oppenauer oxidation followed by acetylation. Since the configuration of X (12βH) has recently been confirmed (9b) and the transformation from III to VII involves no reactions affecting the respective configuration of $C_{12}$, the previous configurational assignment (α) (3) to 12-hydrogen of III, IV and V (also $C_{17}$ of III) must be revised to β.



II $\Delta^5$, $R=R_1=R_2=Ac$, $R_3=O$
IIa $\Delta^5$, $R=R_2=H$, $R_1=Ac$, $R_3=O$
III $\Delta^5$, $R=R_1=R_2=H$, $R_3=H_2$

XI 5αH, $R=R_1=R_2=Ac$, $R_3=O$
XIa 5αH, $R=R_2=H$, $R_1=Ac$, $R_3=O$
XII 5αH, $R=R_1=R_2=H$, $R_3=H_2$

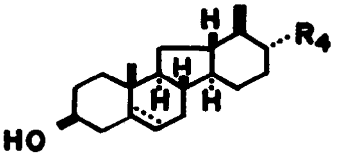


IIa' $\Delta^5$, 17αH, $R=R_2=H$, $R_1=Ac$

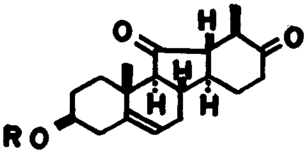
XI' 5αH, 17αH, $R=R_1=R_2=Ac$
XIa' 5αH, 17αH, $R=R_2=H$, $R_1=Ac$
XVIII 5αH, 17βH, $R=R_1=R_2=Ac$

On the other hand, an acetolysis product (I) of 3-O,N-diacetyltetrahydrojervine has recently been shown to possess α-hydrogen atoms at $C_{12}$ and $C_{13}$ as well as a double bond at $C_{16}$ and $C_{17}$ (2), which on hydrogenation formed the 16,17-dihydro derivative (XI). Both XI and its deacetyl derivative (XIa), identical with a compound (3) obtained by hydrogenation of IIa, have been formulated as XI' and XIa' (both 12αH) (2). In the present study we treated XIa under the Huang-Minlon conditions and obtained an 11-deoxo compound (XII), m.p. 207-208°, in a moderate yield, which was naturally identical with a hydrogenation product of III (12βH). These facts led us to have a doubt as to the assigned configurations of XI and, accordingly, of I, and it became desirable to correlate XI or IIa with a compound with known configuration through a series of reactions involving no epimerization at $C_{12}$.

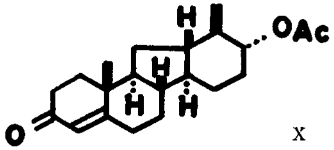
Reduction of IIa with $NaBH_4$ gave 11β-alcohol (XIIIa), m.p. 239-240°, which on partial acetylation (to XIII, m.p. 224.5-225.5°) followed by oxidation ($CrO_3$-Py) was reconverted into 3,23-diacetate (II), m.p. 211-212°, of IIa in 88% yield, indicating that no epimerization at $C_{12}$ took place during the reduction. The N-deacetyl derivative (XIIIb), m.p. 240-241°, obtained by hydrolysis ($OH^{-}$-$HOCH_2CH_2OH$) of XIIIa was degraded according to the procedure of Johnson et al. (10) to 20-oxime (XIV), m.p. 167-168°, which in turn was converted into 20-ketone (XV), m.p. 180-181°, in 69% yield from IIa. A 5,6-dihydro derivative (XVI), m.p. 173-174°, of XV was oxidized with $C_6H_5CO_3H$, hydrolyzed ($OH^{-}$) and then oxidized ($CrO_3$-Py) to give triketone (XVII), m.p. 173-175°, in 10% yield from XV (50% of XVI recovered). This ketone XVII was identified as etiojervane-3,11,17-trione (12βH), because XVII was readily derived from IXa (9a,b) with the established configuration (12βH, 13βMe) (9c) by hydrogenation (Pt) followed by oxidation ($CrO_3$-py). These findings not only lead to revision of configurations of XI and II, but also indicate that compound I in question should be represented by formula I (12βH, trans-fused C/D linkage). It follows that the hydrogen atoms at $C_{12}$ and $C_{13}$ of a 12-epimer (2) of I and those at $C_{12}$, $C_{13}$ and $C_{17}$ of two hydrogenation products, crystalline and amorphous (2), of the 12-epimer must be assigned as (α,α I'), (α,α,β XVIII) and (α,α,α XI'), respectively.



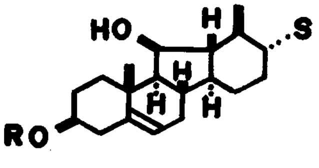
IV $\Delta^5$, $R_4$=C(=NOH)$CH_3$
V $\Delta^5$, $R_4$=Ac
VI 5αH, $R_4$=Ac
VII 5αH, $R_4$=OH
VIII $\Delta^5$, $R_4$=OH



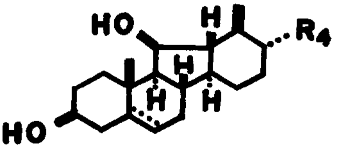
IX R=Ac
IXa R=H



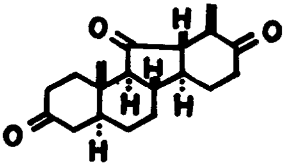
X



XIII $R=R_1=R_2$=Ac
XIIIa $R=R_2$=H, $R_1$=Ac
XIIIb $R=R_1=R_2$=H



XIV $\Delta^5$, $R_4$=C(=NOH)$CH_3$
XV $\Delta^5$, $R_4$=Ac
XVI 5αH, $R_4$=Ac



XVII

This assignment of C/D trans-configuration to I was supported by the ORD studies. All the 11-ketones examined showed ORD curves with negative Cotton effects. However, the amplitudes (in dioxane) for C/D trans-fused compounds (I -172°, II -183°, IIa -180°, XI -169° and XIa -174°) differed definitely from those for C/D cis-fused (I' -82°, XVIII -96°, XI' -84° and XIa' -80°). This difference is completely consistent with the revised configurations, when the octant rule is applied for these five-membered ring ketones (11).

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