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THE MECHANISM OF THE REDUCTION OF α,β-UNSATURATED (STEROID) KETONES WITH DIBORANE

Ian Midgley and Carl Djerassi

Department of Chemistry, Stanford University, Stanford, California 94305, U.S.A.
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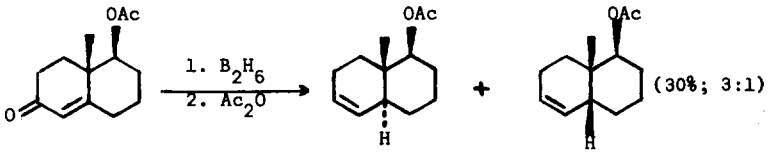
Caglioti and coworkers have shown that certain α,β-unsaturated ketones react with excess diborane, and after hydrolysis of the organoborane intermediate with acetic anhydride, good yields of an alkene are obtained.[1,2] The reaction undoubtedly follows the course depicted in the Scheme:

Scheme

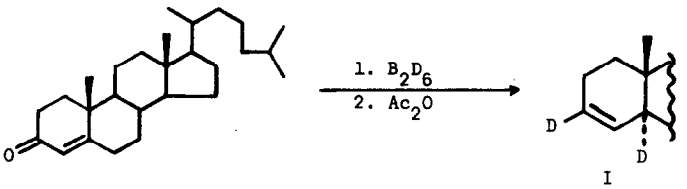
$$RC(=O)CH=CHR' \xrightarrow{"BH_3"} RCH(OBH_2)CH=CHR' \xrightarrow{"BH_3"} RCH(OBH_2)CH(BH_2)CH_2R' \xrightarrow{Ac_2O} RCH=CHCH_2R'$$

In the steroid series, for instance, the Δ^4-3-keto chromophore is efficiently and stereospecifically converted into a 5α-Δ^3-olefin, but the only available example of this reaction involving a bicyclic enone indicates that the yield is reduced, and the stereospecificity lost in smaller molecules[3]:



If the intervening organoborane is exposed to alkaline hydrogen peroxide, rather than acetic anhydride, the product (in the steroid series at least) is a trans-diequatorial-1,2-diol,[4] which is otherwise rather difficult to prepare. Apart from this, however, little attempt has been made to extend the scope or investigate the mechanism of this synthetically useful reaction.

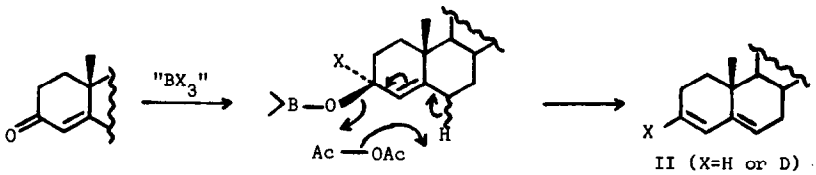
In accord with the above Scheme, we have found that treatment of Δ^4-cholesten-3-one with excess perdeuteriodiborane affords 3,5-d_2-5α-cholest-3-ene (I) with an isotopic purity of 92%:



I

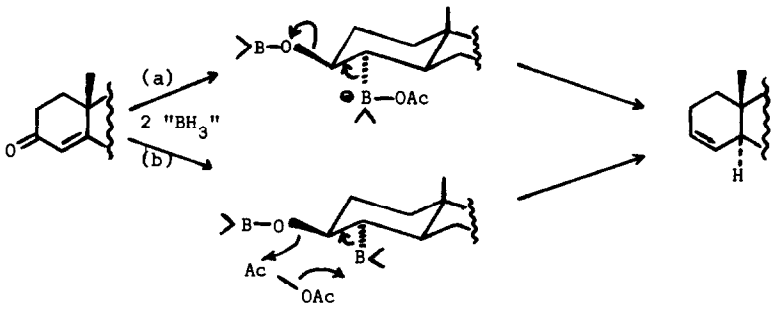
The position of the vinylic deuterium atom was deduced from the n.m.r. spectrum of I - the only signal in the olefinic resonance region (δ 5.26; 1H, d, J=1.5 Hz) corresponding to H-4. (The C-3 and C-4 protons in the unlabelled compound resonate sufficiently far apart at 100 MHz [δ 5.56 (d of d, J=10 and 2.8 Hz) and 5.26 (d of d, J=10 and 1.7 Hz) respectively] for them to be distinguished easily).

When cholestenone was treated with only <u>one</u> mole of diborane, and the product hydrolyzed as above, the only compound isolated in 70% yield was cholesta-3,5-diene (II, X=H). Upon repeating the reaction with B_2D_6, the product (II, X=D) incorporated only one deuterium atom, and this was shown by n.m.r. spectroscopy to be located at C-3. Our rationalization of this new reaction involves an eight-membered cyclic transition state in the hydrolysis stage, following addition of BH_3 to the carbonyl group:

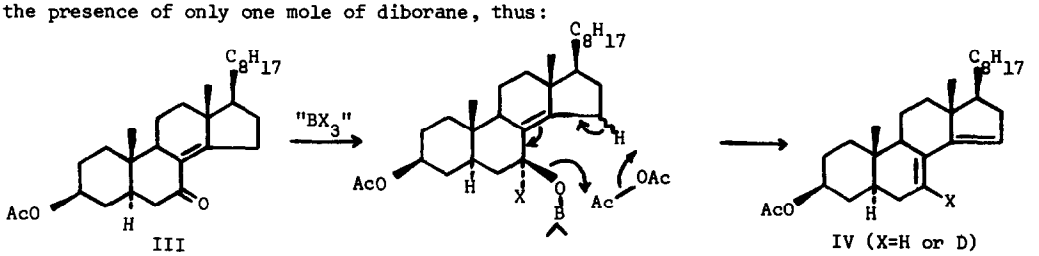


II (X=H or D)

If this representation is valid, then it appears reasonable to invoke the existence of a six-membered cyclic transition state (b) in the reaction with excess diborane, rather than the ionic intermediate (a) postulated previously[5]:



Sondheimer et al.[6] have found that 5α-cholest-8(14)-ene is inert to hydroboration, just as it is to catalytic hydrogenation. However, when conjugated to a 7-keto group, this double bond is readily reduced.[7,8] Therefore we decided to investigate the effect of diborane on the $\Delta^{8(14)}$-7-keto chromophore (as in III[9]). The only product with excess B_2H_6/Ac_2O was the $\Delta^{7,14}$-diene (IV, X=H), and with B_2D_6, the labelled analogue possessed a single deuterium atom which was shown by n.m.r. spectroscopy to be attached to C-7. Hence we infer that the $\Delta^{8(14)}$-double bond is still too hindered to react with the reagent, and the compound (III) behaves just as unhindered enones do in the presence of only one mole of diborane, thus:



III IV (X=H or D)

Future studies in these laboratories will be directed toward the extension of the scope of this reaction to endiones and cross- and linear-conjugated dienones.

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