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SINGLE ELECTRON TRANSFER IN $LiAlH_4$ REDUCTION OF A STEROIDAL VINYL IODIDE

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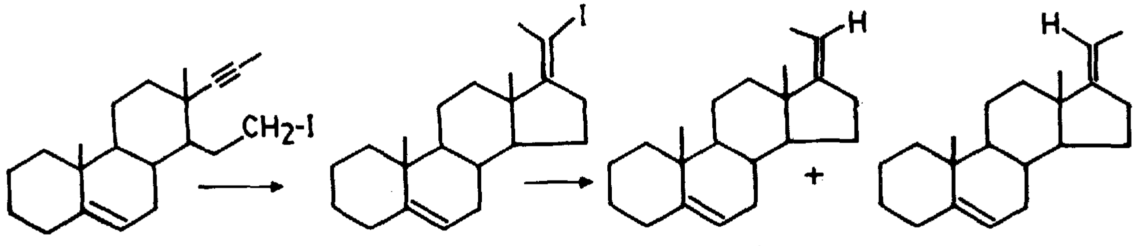
Abstract: Reduction of E-20-iodopregna-5,17(20)-diene with $LiAlH_4$ in three different ethereal solvents gave a mixture of E and Z pregna-5,17(20)-dienes. The E:Z ratio was 69:31. Bu_3SnH gave an E:Z ratio of 60:40. The observed stereochemistry points to a single electron transfer mechanism (SET).

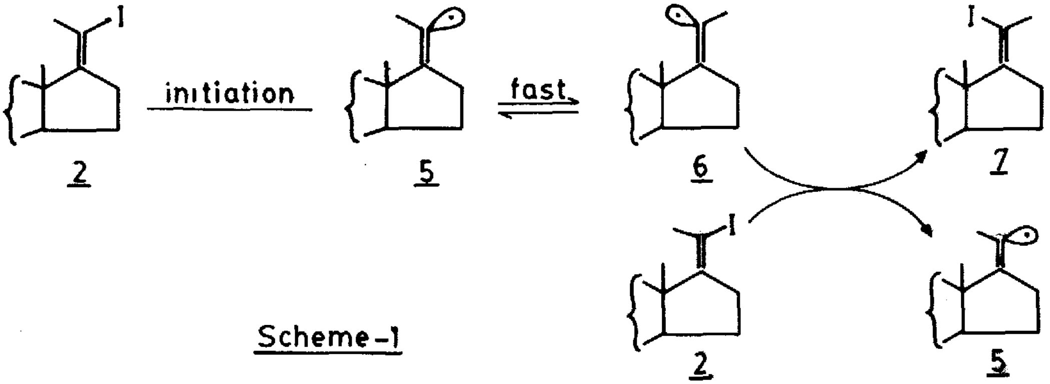
It is well known that $LiAlH_4$ reduces aryl[1] as well as alkyl iodides[2]. But reduction of vinyl iodides using this reagent have not been reported. We took up such a study using E-20-iodopregna-5,17(20)-diene 2 in view of the utility of suitably substituted vinyl halides in "detecting" radical intermediates[3]. A mixture of E and Z isomers of the corresponding hydrocarbons is expected to be produced in reductions proceeding via single electron transfer (SET). Rapid formation of a vinyl carbanion intermediate with retention of configuration should, on the other hand, give Z-pregna-5,17(20)-diene 3 as the sole product[4].

The required vinyl iodide 2[5] was the only iodo compound produced when the secosteroid 1[6] was treated with Bu_3SnH[7]. Treatment of 2 with $LiAlH_4$ dissolved in ether[8], THF or monoglyme gave 69±1% of E-pregna-5,17(20)-diene 4[9]. The only other product was the Z isomer 3 formed in 31±1% yield. The result rules out a hydride attack at halogen but is in agreement with a SET mechanism.

It was considered desirable to confirm that the vinyl radicals produced from 2 do indeed give a mixture of 3 and 4. Since both E and Z 2-bromo-2-butene give 65:35 ratio of E:Z 2-butene on treatment with Bu_3SnH at room temperature[10], we treated 2 with this reagent. As expected it gave a mixture of 4 and 3. The ratio of 4:3 (i.e. E:Z) was 60:40. The reaction was initiated by AIBN. Chain propagation consists of delivery of an hydrogen atom by Bu_3SnH to the vinyl radical. But for production of a mixture of 3 and 4 the rate of this step has to be less than the rate of isomerisation of the initially produced radical.



1 2 3 4



Scheme-1

Interconversion between 5 and 6 is expected to be very fast[11]. The ratio of products 3:4 will then be determined by the relative energies of the transition states for hydrogen atom abstraction by 5 and 6 respectively[12]. The "effective" bulk of the donor must be nearly the same for both Bu_3SnH and $LiAlH_4$ as the E:Z ratio is close. In reduction with the latter the initiation is ascribed to SET from $LiAlH_4$. But it is not clear whether the resulting $LiAlH_4^{+\bullet}$ is the hydrogen atom donor. The other candidates are AlH_4^- and the ethereal solvents.

Before the SET mechanism can be accepted it is necessary to establish that the iodine atom transfer as suggested in Scheme 1, does not take place. This has been confirmed. In the reaction of 1 with Bu_3SnH, 3 and 4 are formed along with 2 but the intermediate vinyl radical 6 fails to accept iodine atom to give 7.

The present finding of total SET in a $LiAlH_4$ reduction is expected to help in resolving the controversy surrounding $LiAlH_4$ reduction of alkyl iodides[13,14].

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3. G.D.Sargent and M.W.Browne, J.Amer.Chem.Soc., 89, 2788 (1967).
4. A high energy barrier exceeding 25kcals./gm.mol is given for interconversion of vinyl carbanions by J.F.Williams Jr.and A.Streitweiser Jr.ibid.,97,2634 (1975)
5. The stereochemistry of this compound follows from the observed homoallylic coupling (t,J=1 Hz) of the C-21 methyl at δ2.57 with the C-16 methylene.
6. This compound was prepared and characterised by J.N.Kolhe, Ph.D.thesis, Bombay University. 1981. Its use as a mechanistic probe will be published shortly.
7. Compound 1(280mg)refluxed in benzene(3ml)with AIBN(23mg)and Bu_3SnH(230mg) for 3 hr. gave equal amounts of iodide 2 and the hydrocarbons 3 plus 4. See ref.6.
8. To $LiAlH_4$(1.5 mmol)dissolved in ether(5ml)was added 2 (0.5 mmol) in ether(1ml) and stirred under nitrogen for 30 min. at room temperature.
9. The stereochemistry is based on ^{1}H NMR.The chemical shifts of C-18 methyls in the corresponding 16α-ols were reported by S.K.Pradhan,S.R.Kadam,J.N.Kolhe,T.V. Radhakrishnan,S.V.Sohani and V.B.Thaker, J.Org.Chem., 46, 2622 (1981).
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