On the Mechanism of Homobenzylic Hydroxyl and Acetoxyl Hydrogenolyses

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HYDROGENOLYSES of benzylic hydroxyl groups catalysed by Raney nickel occur readily under moderate conditions and proceed stereospecifically with high degrees of retention of configuration.[1] Bonner and co-workers have recorded[2] equally easy Raney nickel-catalysed hydrogenolyses of homobenzylic hydroxyl groups. They observed[2] for primary homobenzylic carbinols of the type

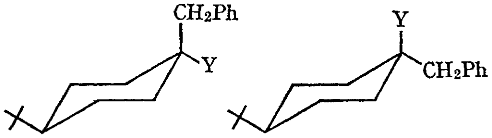
$$\mathrm{PhR^1R^2C \overset{a}{—} CH_2 \overset{b}{—} OH}$$

that hydrogenolyses of bonds a and b were competitive when R^1 and/or R^2 = H, but that the hydrogenolysis of the former proceeded exclusively when $R^1 = R^2$ = alkyl (*i.e.*, no benzylic C–H bond is present). They noted that dihomobenzylic hydroxyl groups and purely aliphatic ones were not hydrogenolysed under conditions which affected the homobenzylic hydrogenolyses.

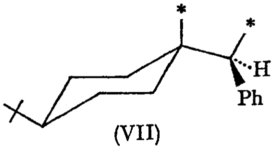
This suggests that a benzylic C–H bond may be a structural prerequisite for these hydrogenolyses, cleavage of this bond being mechanistically correlated with the cleavage of the C–OH bond. This means that these hydrogenolyses could formally proceed by way of a β-elimination of benzylic hydrogen and homobenzylic hydroxyl.

To examine this possibility, the Raney nickel-catalysed hydroxyl and acetoxyl hydrogenolyses of (I)—(IV) were undertaken.† If these hydrogenolyses proceed *via* β-elimination, the initial intermediate species could conceivably be di-adsorbed alkenes (VII) and (VIII) arising from (II) [(IV)] and (I) [(III)], respectively, or desorbed alkene (IX) arising from (I)—(IV). If intermediates (VII) and (VIII) are involved, stereospecific (retention of configuration) hydrogenolyses are expected, the stereospecificity being determined by subsequent surface chemistry.[3] Should intermediate (IX) be involved, stereoconvergent hydrogenolyses would result, the stereochemistry being that for the hydrogenation of (IX). Only this latter event would clearly indicate a β-elimination mechanism.

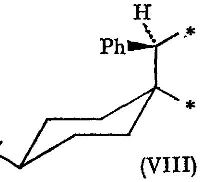
For Raney nickel-catalysed benzylic hydroxyl and acetoxyl hydrogenolyses in stereoisomeric *cis*- and *trans*-4-t-butyl-1-phenyl-1-Y-cyclohexanes, the hydroxyl and acetoxyl groups hydrogenolyse stereospecifically with nearly complete retention and inversion of configuration, respectively.[4] This suggests that these hydrogenolyses occur by fundamentally different surface processes. Whether a similar difference is observed for the hydrogenolyses of homobenzylic hydroxyl and acetoxyl groups needs to be determined.



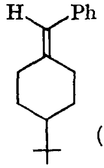
(I) Y=OH (II)
(III) Y=OAc (IV)
(V) Y=H (VI)



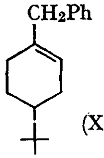
(VII)



(VIII)



(IX)



(X)

Using reaction times which lead to negligible product equilibration[1b] [(V) ⇄ (VI)], (I) and (II) hydrogenolyse *stereoconvergently* at 25° to give a mixture of 80% of (V) and 20% of (VI). The thermodynamic equilibrium (palladium-catalysed) composition at 169° is 8·4% (V) and 91·6% (VI). Hydrogenolyses of (III) and (IV) at 78° led to 61% (after 8% reaction) and 85% (after 6% reaction) of (V), respectively. Product equilibration[1b] is competing significantly with the hydrogenolysis of

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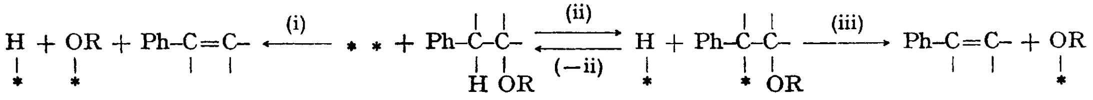
† The reaction between benzyl Grignard and 4-t-butylcyclohexanone gave a mixture of (I) and (II) which were characterised by relative retention times upon adsorption chromatography and by n.m.r. spectral correlations. Both (III) and (IV) derived directly from (I) and (II) upon acetylation.

(III), the substrate of lowest reactivity,‡ and the 61% of (V) cited above may be low by as much as 10%. Therefore, it appears that the principal hydrogenolysis process proceeds *stereoconvergently* for (III) and (IV) giving about 75 ± 10% of (V). Under comparable conditions no hydroxyl or acetoxyl hydrogenolyses were observed for the cyclohexylmethyl (phenyl-reduced) derivatives of (I)—(IV).

These stereoconvergent hydrogenolyses mainly pass through a common intermediate. Desorbed alkene, (IX), is most likely this intermediate as its hydrogenation under the hydrogenolysis conditions gives 80% of (V) and 20% of (VI). Similarly, hydrogenation of (X) gives a mixture of 55% of (V) and 45% of (VI). These hydrogenolyses apparently proceed through the desorbed alkene arising from β-elimination of a benzylic hydrogen and the homobenzylic group, Y.

Considering the reaction mechanism formulated below, desorbed alkene may form by step (i) and/or by equilibration [(ii) + (−ii)] followed by step (iii).

Competitive hydrogenolyses of a mixture of benzylic-dideuterio-(I) and -(II) led after 0·5 hr. reaction time to 63% and 60% of isotopic exchange in (I) (50% reacted) and (II) (15% reacted), respectively. Similarly, competitive hydrogenolysis of a mixture of benzylic-dideuterio-(III) and -(IV) led after 13 hr. to 42% of isotopic exchange in both (III) (13% reacted) and (IV) (44% reacted). Although the relative hydrogenolysis rates k_1/k_2 = 4·3 and k_3/k_4 = 0·23,‡ the percentages exchanged in the epimers are equal. These results are most easily but not uniquely interpreted as indicating that the isotopic exchange rates are nearly the same for the epimers and that the exchange and elimination processes are occurring independently *via* steps [(ii) + (−ii)] and (i), respectively. If in fact the isotopic exchange rates for the epimers are nearly the same, the process [(ii) + (−ii)] + (iii) would have led to a substantially smaller extent of isotopic exchange in the more reactive substrates [(I) and (IV)] than in the less reactive ones [(II) and (III) respectively].



$$\underset{*}{\overset{}{\mathrm{H}}} + \underset{*}{\mathrm{OR}} + \mathrm{Ph{-}}\underset{|}{\mathrm{C}}{=}\underset{|}{\mathrm{C}}{-} \xleftarrow{\text{(i)}} *\ * + \mathrm{Ph{-}}\overset{|}{\underset{\mathrm{H}}{\mathrm{C}}}{-}\overset{|}{\underset{\mathrm{OR}}{\mathrm{C}}}{-} \underset{(-\text{ii})}{\overset{\text{(ii)}}{\rightleftharpoons}} \underset{*}{\mathrm{H}} + \mathrm{Ph{-}}\overset{|}{\underset{*}{\mathrm{C}}}{-}\overset{|}{\underset{\mathrm{OR}}{\mathrm{C}}}{-} \xrightarrow{\text{(iii)}} \mathrm{Ph{-}}\underset{|}{\mathrm{C}}{=}\underset{|}{\mathrm{C}}{-} + \underset{*}{\mathrm{OR}}$$

Finally, 10% palladium-on-charcoal is found to catalyse the hydrogenolyses of the hydroxyl and acetoxyl groups in (I)—(IV). With this catalyst in acetic acid at 25°, (I)—(IV) hydrogenolyse *stereoconvergently* under three atm. of hydrogen giving 34 ± 2% of (V) and 66 ± 2% of (VI). These hydrogenolyses proceed slowly as evidenced by their progressing less than 15% after 4 hr. Again, these reactions appear to pass through a common intermediate. As hydrogenation of a thermodynamic equilibrium (at 25°) mixture of 11·6% of (IX) and 88·4% of (X) leads to 29% of (V) and 71% of (VI) under the hydrogenolysis conditions,§ it is probable that these hydrogenolyses proceed to give desorbed (IX) and (X) in thermodynamically controlled β-elimination surface processes.[5]

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‡ Substrate pairs (I) and (II), (III) and (IV), and (II) and (IV) were hydrogenolysed competitively in ethanol over Ni(R, W-2) at 25°. The results from eleven experiments covering varying percentages reaction give first-order kinetics in terms of substrate. The relative hydrogenolysis rates for (I), (II), (III), and (IV) are 11, 2·5, 1·0, and 4·3, respectively.

§ Hydrogenation of (IX) and (X) over 10% Pd–C gives 72 and 23% of (V), respectively.

[1] (a) S. Mitsui and Y. Kundo, *Chem. and Ind.*, 1965, **381**, and references cited therein; (b) E. W. Garbisch, jun., *J. Org. Chem.*, 1962, **27**, 3363.

[2] J. A. Zderic, W. A. Bonner, and T. W. Greenlee, *J. Amer. Chem. Soc.*, 1957, **79**, 1696; T. W. Greenlee and W. A. Bonner, *ibid.*, 1959, **81**, 4303.

[3] S. Siegel, *Adv. Catalysis*, 1966, **16**, 123.

[4] E. W. Garbisch, jun., L. Schreader, and J. J. Frankel, *J. Amer. Chem. Soc.*, in the press.

[5] D. A. Denton, F. J. McQuillin, and P. L. Simpson, *J. Chem. Soc.*, 1964, 5535 have discussed β-eliminations of the type $\mathrm{Br{-}}\overset{|}{\underset{|}{\mathrm{C}}}{-}\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{{-}OCOR} \rightarrow \overset{|}{\underset{|}{\mathrm{C}}}{=}\overset{|}{\underset{|}{\mathrm{C}}}$ that occur upon palladium-on-charcoal-catalysed hydrogenolyses of certain bromo-lactones.