

## The Mechanism of the Reduction of Ketones

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WHEN a cyclic ketone is reduced by a complex hydride, the main product is usually, but not always, the more stable epimer. It has recently been shown by Richer<sup>1</sup> that the facts can be accounted for by considering only the steric hindrance to approach of a hydride ion, since in a simple cyclohexanone, contrary to previous expectation, this is less when the hydride ion is to be attached in an axial position.

Reduction of cyclic ketones with alkali metals and alcohols, in liquid ammonia or not, normally, but not always, gives almost exclusively the more stable epimer. The situation has been extensively reviewed recently by Huffman and Charles,<sup>2</sup> who suggest a dual mechanism. According to this, steric control in the case of a simple cyclohexanone is due to hindrance of donation of a proton to a radical-anion intermediate. This theory cannot be correct, because it would lead to production of similar proportions of epimers to borohydride reduction, whereas dissolving metals typically give much higher yields of the stable epimer.

The first study of this problem was by Barton and Robinson,<sup>3</sup> who suggested that the intermediate was a dianion, which was able to equilibrate rapidly to the more stable epimer, and then on protonation gave the product.

It was tacitly assumed that the rate of protonation of both epimers of the anion would be the same, so that the product composition depended solely on the equilibrium composition of the mixture of epimeric anions. This assumption seems quite unjustified. If on the contrary it is assumed that one anion will be protonated more rapidly than the other, following the rules of steric hindrance suggested by Richer,<sup>1</sup> then this simple modification of Barton and Robinson's original hypothesis appears capable of accounting for all the known facts. In the case of a simple cyclohexanone, the epimeric anion with equatorial oxygen will be present in greater amount, and also protonated more rapidly;<sup>1</sup> thus giving the first explanation of the almost quantitative yield of the equatorial alcohol produced in this way. In more complex cases the two effects, of anion stability and rate of protonation, may oppose; and the result will then depend on their relative magnitude. It would appear that in the case of norcamphor<sup>2</sup> steric hindrance to protonation is the dominant factor; while in the reduction of an 11-oxo-steroid the great hindrance of the 11 $\beta$ -oxygen atom, and the consequent small amount of the corresponding epimeric anion at equilibrium, is dominant.

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<sup>1</sup> J. C. Richer, *J. Org. Chem.*, 1965, **30**, 324.

<sup>2</sup> J. W. Huffmann and J. T. Charles, *J. Amer. Chem. Soc.*, 1968, **90**, 6486.

<sup>3</sup> D. H. R. Barton and C. H. Robinson, *J. Chem. Soc.*, 1954, 3045.