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STEREOCHEMICAL CONTROL OF KETONE REDUCTIONS IN LIQUID AMMONIA

W. S. Murphy* and D. F. Sullivan,

Department of Chemistry, University College, Cork, Ireland.

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Ourisson and Rassat[1] noted stereochemical control during the reduction of ketones with active metals in liquid ammonia. Their results aroused considerable interest[2] since the method had hitherto been generally considered[3] to lead to a preponderance of the more stable epimer. Nevertheless, the mechanism of the reaction has not yet been resolved. Huffmann and Charles[4] suggested a dual mechanism: (a) in the case of unhindered ketones the anion radical is protonated in accordance with the rules outlined by Richer[5] and (b) hindered ketones form dianions which are protonated by the stereochemical pathway suggested by Barton and Robinson.[3] Taylor[6] considered that a single mechanism wherein the equilibrium position of equilibrating dianions coupled with the differing rates of protonation of these species accounted for the results satisfactorily. Coulombeau and Rassat[7] however conclude that the addition of the first or second electron is the critical step leading to anions which do not equilibrate. Their[8] recent results prompted us to report this facet of our investigations.

Our results in Table 1 confirm those of Rassat[1,7] and leave still unexplained[9] the results of Huffmann and Charles.[4]

TABLE 1

Reduction of d-Camphor in the absence of an added Proton Donor[10]

	Metal	% Yield of borneol + isoborneol	Isoborneol % a)	% Yield of Pinacol b)
1	Li	25	20	70
2	Na	75	40	20
3	K	95	58	0
4	Cs	95	78	0
5	Ca	95	27	0
6	Sr	99	30	0
7	Ba	95	29	0

a) These figures represent the ratio of isoborneol to borneol.

b) M.p. 114-115°,[11] M^+ 306 (Found C, 78.4; H, 11.0. $C_{20}H_{34}O_2$ requires C, 78.38; H, 11.18%). Oxidation with $Pb(OAc)_4$[12] gave 100% yield (v.p.c.) of camphor.

Table II outlines our results when reduction is undertaken in the presence of a metal cation and in the absence of an added proton donor.

TABLE II

Reduction of d-Camphor in the presence[a] of alkali salts[10]

	Metal	Salt	Ratio (metal) : (salt)	Isoborneol % b	% Yield of Pinacol
1	Li	LiBr	1 : 5	20 (20)[c]	75 (70)[c]
2	K	LiBr	1 : 5	24 (26)	60 (62)
3	Li	KBr	1 : 5	47 (51)	30 (17)
4	K	LiBr	1 : 1	34 (39)	40 (40)
5	Li	KBr	1 : 1	33 (39)	40 (40)
6	K	CsBr	1 : 1.5[d]	68 (70)	0 (0)

a) Metal added to solution of d-camphor and salt.

b) These figures represent the ratio of isoborneol to borneol.

c) Figures in brackets are those predicted by averaging the effects of the metal cations.

d) Ammonia saturated with CsBr. Ratio based on known[13] solubility of CsBr.

Comparison of the first entry in each Table indicates that a salt effect is inoperative. The results in Table II are almost exactly those predicted for the statistical ratio of metal cations. The results of Table II emphasise that contrary to earlier suggestions[8b] the carbonyl does not associate preferentially with the dissolving metal. Table II provides strong evidence for complete ionisation of metals before association with the carbonyl according to Scheme 1. Steps (1) and (2) follow from the results of Table II.

$$\begin{array}{lllll}
(1) & M + M_1\ Br & \rightarrow & M^+ + M_1{}^+ + e^- + Br^- \\
(2) & C = O + e^- & \rightleftarrows & \dot{C} - \bar{O} \\
(3) & \dot{C} - \bar{O} + M^+ + M_1{}^+ & \rightarrow & C - \bar{O}\ M^+ + \dot{C} - \bar{O}\ M_1{}^+
\end{array}$$

Scheme 1

Step (3) is considered irreversible since the results depend on the ratio of M^+ to $M_1{}^+$ not on the tendency of the metal cations to form intimate or solvent separated ion pairs.[14] To explain the effect of increasing atomic weight of the alkali metal on the exo/endo ratio Huffmann[4] invoked the reducing power of the metals. This suggestion complied with his concept of a dual mechanism. We consider that Scheme 1 invalidates this suggestion since the metal is completely ionised before it attacks the carbonyl group. Also the relative percentages of pinacol formed (Table 1) are in the reverse order to that expected on the basis of the reducing power of the metals. Association of the metal with the carbonyl is a two-step process (step 1 and 2 in Scheme 1). Therefore, addition of the first or second electron *per se* cannot be the crucial step as suggested[7] since the exo/endo ratio would then be independent of the nature of the metal cation. These results may also have some synthetic value since the use of a hazardous metal such as Cs for stereospecific reductions may be avoided by using an excess of a Cs salt in association with another metal. Full details of our results are in preparation.

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