Kinetic Isotope Effects in the Reduction of 2- and 3-Alkyl-substituted-indanone-(tricarbonyl)chromium Complexes by $NaBH_4$ and $NaBD_4$. Evidence for Displacement of the Transition State Depending on the Substrate

By BERTRAND CARO and GÉRARD JAOUEN*

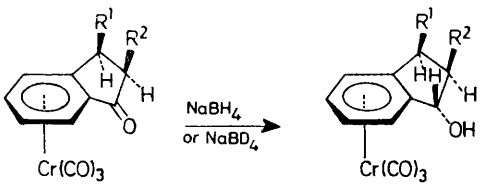
(*Laboratoire de Chimie des Organométalliques, E.R.A.* 477, *Université de Rennes*, 35031 *Rennes-Cedex, France*)

Summary The kinetic, primary, H–D isotope effects, measured when 2- and 3- alkyl-substituted-indanone-(tricarbonyl)chromium complexes are reduced with $NaBH_4$ and $NaBD_4$, exhibit significant variations of k_H/k_D values depending on the degree of steric hindrance around the ketone groups; this suggests that displacements of the transition states are involved in this type of reaction.

THE nature of the transition state in the reduction of ketones by metal hydrides has already attracted a great deal of attention,[1] but the situation is still unresolved. Using complex prochiral cyclic ketones as models some controversial theories have been developed. The origin of the stereoselectivity has been explained, *inter alia*, in terms of steric strain, torsional effects, conformational changes, and, recently, orbital factors.[2] Nevertheless, in all the main theories, the transition state is generally thought to be highly reactant-like irrespective of the reagent and substrate used.[3] Some evidence against this postulate has been reported, but it is rare.[4]

Most of the discussion is based on observations of the stereochemical course of reactions and has neglected the kinetic data, which are at least as important as the stereo-

chemical data. Using a kinetic approach, Lamaty *et al.*[4a] proposed that, in nucleophilic additions to carbonyl compounds, the transition state can be either reactant-like (*e.g.* with RMgX, NH_2OH) or product-like (*e.g.* with $NaBH_4$, HCN) or somewhere in between depending upon the nature of the incoming nucleophile. We extend these views and provide evidence that even for the same nucleophile (BH_4^-) the transition state is not always in the same position on the reaction co-ordinate. The magnitude of the kinetic primary deuterium isotope effect has been proposed as a criterion for the structure of the transition state from theoretical considerations.[5,6] On the basis of these derivations it is currently presumed that a fully symmetrical transition state will give the maximum kinetic isotope effect,[7] whereas asymmetric transition states (which are either more product-like or more reactant-like) will tend to exhibit smaller values of k_H/k_D. Rigid stereochemical models can be found, such as alkyl substituted-indanone-(tricarbonyl)chromium complexes, which exhibit dramatic variations in their k_H/k_D values. The most obvious interpretation of these results implies a considerable displacement of the transition state from a product-like structure towards one resembling the reactant with increasing steric hindrance around the ketone group.



(1)

2- and 3-Alkyl substituted-indanone(tricarbonyl)chromium complexes appear to be unique stereochemical models in that stereospecific *exo* nucleophilic attack occurs on the alicyclic ring irrespective of the bulkiness of the alkyl substituent.[8] The *endo* complexed indanols are always obtained in pure form and the effects of small variations in steric hindrance around the ketone group may be easily monitored. The Table shows the rate constants measured for the reduction of the indanonechromium complexes (**1a**—**g**) by $NaBH_4$ and $NaBD_4$ in propan-2-ol at 22 °C.

The rate constants were determined spectrophotometrically at 428 nm using an adaptation of Bayer and Smith's method.[9] The overall reproducibility of the measurements was *ca.* 2%.

The k_H/k_D value for the unsubstituted indanone complex (**1a**; $R^1 = R^2 = H$) is less than unity; with increasing bulk of the 3-*exo*-substituent it at first increases (**1b**; R^1 = Me) and then decreases to approaching unity (**1d**; $R^1 = Pr^i$). Similar, though less marked, trends are observed for the 2-*exo*-substituted compounds (**1e**—**g**).

TABLE. Rate constants for reduction of the indanonechromium complex (**1**) by $NaBH_4$ and $NaBD_4$ in propan-2-ol at 22 °C

Compound (1)			k_H /mol^{-1} min^{-1}	k_D /mol^{-1} min^{-1}	k_H/k_D
a;	H	H	3·48	5·15	0·67
b;	Me	H	4·24	1·72	2·46
c;	Et	H	3·00	1·50	2·00
d;	Pr^i	H	0·80	0·62	1·29
e;	H	Me	4·08	4·65	0·88
f;	H	Et	3·84	3·10	1·24
g;	H	Pr^i	0·76	0·80	0·95
(**2**), [$(CO)_3$CrPhCOMe]			6·00	7·92	0·75

Isotope effects previously reported in this reaction generally have a k_H/k_D value of *ca.* 0·7.[10] The measured value for acetophenone(tricarbonyl)chromium (**2**; k_H/k_D = 0·75) is very close to that of the free ligand (k_H/k_D = 0·70).[11] Therefore, complexation by the $Cr(CO)_3$ unit does not alter noticeably the nature of the reduction. The same conclusion may be reached from the calculated Hammett constant of the reaction, $\rho + 2·9$[12] for compound (**2**), compared with $\rho + 3·06$ for acetophenone.[13]

Theoretical predictions on isotope effects[6,14] are consistent with our experimental data implying that the degree of hydrogen transfer varies markedly with substituents. The occurrence of such a displacement of the transition state in an homogeneous series, which extends the range of variable parameters involved in this reaction, complicates the interpretation of the stereochemical results. Theories based upon simple models and definitively fixed transition state may thus suffer from excessive simplification.[15] This is not surprising since the difference in energies of the diastereoisomeric excited species is only in the region of 1—2 kcal mol^{-1}. Competing factors with opposite effects should be examined to account for stereoselective control of reaction products in the reduction of cyclic ketones.

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