The Induced Kinetic Isotope Effect as a Tool for Mechanistic Discrimination

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Summary Conditions are described under which an isotope effect on the rate of formation of one reaction product can induce an apparent isotope effect on the label distribution in a second product; reaction of *trans*-2,3-diphenylmethylene[2-$^2H_1$]cyclopropane with $Fe_2(CO)_9$ serves to illustrate the utility of the method.

THE purpose of this communication is to point out the existence of an isotope effect criterion for distinguishing between subtly different classes of reaction mechanism.

Consider the generalized set of reactions (1)—(3).

$$\mathrm{I} \underset{k_1}{\overset{k_{-1}}{\rightleftharpoons}} \mathrm{A} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{I'} \qquad (1)$$

$$\mathrm{B} \xleftarrow{k_2} \mathrm{I} \xrightarrow{k_3} \mathrm{C} \qquad (2)$$

$$\mathrm{B'} \xleftarrow{k_2} \mathrm{I'} \xrightarrow{k_3/z} \mathrm{C'} \qquad (3)$$

The initial reactant in this scheme is defined to be A; I′, B′, and C′ differ from the corresponding species I, B, and C only by the location of an isotopic label (we will call pairs of species such as I and I′ label-isomers). The step I′ → C′ is subject to a normal (primary or secondary) isotope effect of magnitude *z*. If I and I′ are steady state intermediates then equation (4) will hold.

$$\frac{[\mathrm{B'}]}{[\mathrm{B}]} = \frac{k_{-1} + k_2 + k_3}{k_{-1} + k_2 + k_3/z} \qquad (4)$$

Thus the isotope effect on the step I′ → C′ induces an apparent isotope effect on the product ratio [B′]/[B], despite the fact that the steps I → B and I′ → B′ have rate constants of equal magnitude.

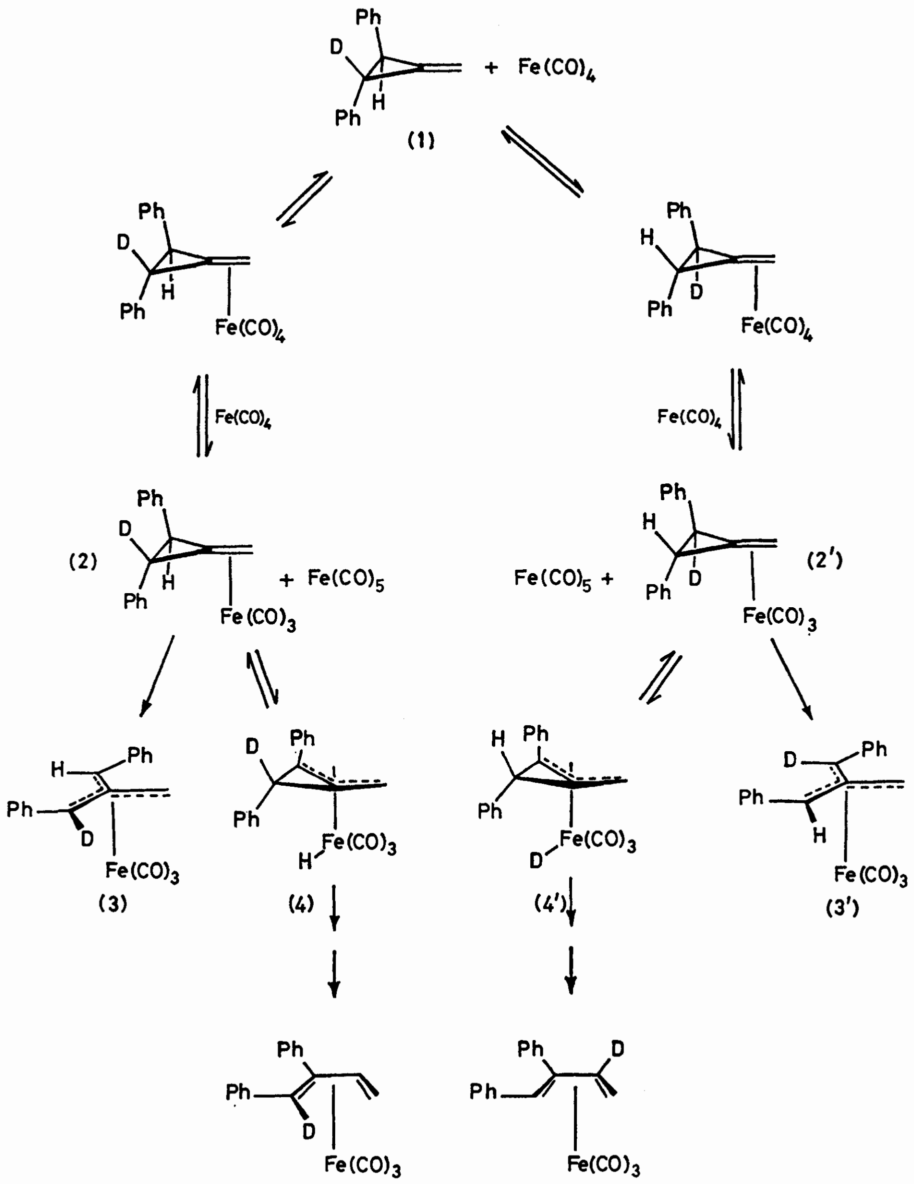
Observation of this kind of induced kinetic isotope effect (I.K.I.E.) requires that two reaction channels (formation of B and formation of C, in this example) share a reaction intermediate in such a way that one label-isomer of B is mechanistically linked to one label-isomer of C but that *B and B′ do not share a reaction intermediate* in the elementary step leading to their formation. Thus all mechanisms of the type in reactions (5)—(7) can be excluded upon detection of an I.K.I.E. Even if B, B′, C, and C′ are all formed from a single intermediate there can be no I.K.I.E. on the ratio [B′]/[B].

$$\mathrm{I} \underset{k_1}{\overset{k_{-1}}{\rightleftharpoons}} \mathrm{A} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{J} \qquad (5)$$

$$\mathrm{B} \xleftarrow{k_3} \mathrm{I} \xrightarrow{k_3} \mathrm{B'} \qquad (6)$$

$$\mathrm{C} \xleftarrow{k_4} \mathrm{J} \xrightarrow{k_4/z} \mathrm{C'} \qquad (7)$$

Equation (4) reveals two further requirements for observation of an I.K.I.E.: namely that C and C′ should form a substantial fraction of the total product and that

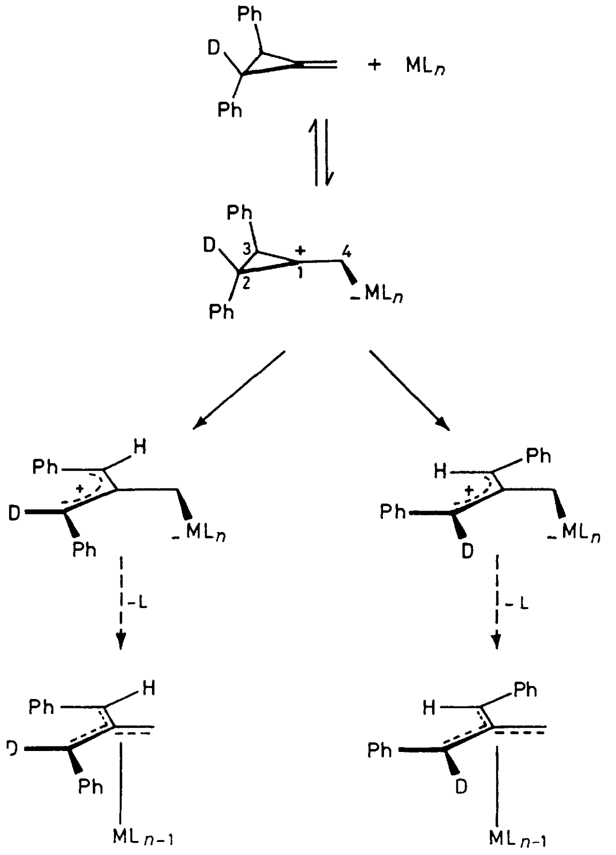


SCHEME 1. Mechanism for the formation of butadiene and trimethylenemethane complexes from (**1**) and a source of Fe(CO)$_4$.

product formation from I and I′ should occur at a rate comparable with or greater than the rate of interconversion of the intermediates. These requirements arise because the conditions $k_{-1} \gg k_3$ or $k_2 \gg k_3$ lead to $[B']/[B] \approx 1$.

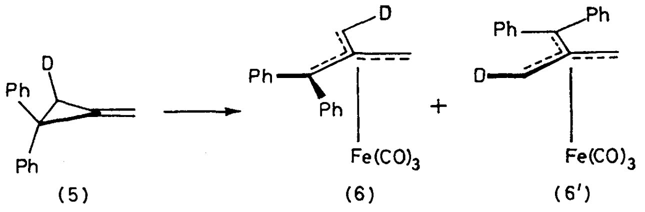
The utility of this type of I.K.I.E. can be illustrated by a study of the formation of tricarbonyl(diphenyltrimethylenemethane)iron (**3**) from *trans*-2,3-diphenylmethylenecyclopropane and $Fe_2(CO)_9$. This reaction is accompanied by the formation of tricarbonyl-(1,2-diphenylbutadiene)iron, a side product which turns out to be crucial for the present study. Previous work[1–3] has led us to propose a general mechanism for methylenecyclopropane–iron carbonyl reactions, illustrated in Scheme 1 for *trans*-2,3-diphenylmethylene[2-$^2H_1$]cyclopropane (**1**). However, recent studies on the reactions of $(MeCN)_2PdCl_2$[4] and $[C_5Me_5Mo(CO)_3]BF_4$[5] with methylenecyclopropanes have led to the proposal of a different ring-opening mechanism in these cases. Its application to (**1**) is illustrated in Scheme 2. We have considered the possibility that a similar mechanism could be operating in the $Fe_2(CO)_9$ reaction, noting in particular that the expected disrotatory ring opening of the cyclopropyl cation intermediate[4] would be consistent with our observed stereochemistry of tricarbonyl(trimethylenemethane)iron formation.[2,3] The generalised complex ML_n would be identified as $Fe(CO)_4$ in this case.

Of particular relevance to the present communication is the observation that the expected primary isotope effect[3] on the step (**2′**) → (**4′**) (Scheme 1) should cause an I.K.I.E. on the ratio [(**3′**)]/[(**3**)]. By contrast the mechanism shown in Scheme 2 could not exhibit an I.K.I.E., regardless of the mechanism of formation of the butadiene complex, since (**3**) and (**3′**) come from a common intermediate.† The latter mechanism could therefore give a ratio [(**3′**)]/[(**3**)] that differed from unity only by the magnitude of a possible steric isotope effect. Accordingly we have synthesised (**1**) and subjected it to the $Fe_2(CO)_9$ reaction. The ratio [(**3′**)]/(**3**)] was determined from the ^{1}H n.m.r. spectrum and found to be 1·22 ± 0·03.



Scheme 2. Alternative mechanism for methylenecyclopropane ring opening by an electron-deficient metal complex (*cf.* refs. 5 and 6).

In order to assess the magnitude of the steric isotope effect we have also synthesized 2,2-diphenylmethylene[3-$^{2}H_{1}$]-cyclopropane (**5**). Previous studies[3] have shown that this methylenecyclopropane gives a trimethylenemethane complex but no detectable amount of tricarbonyl-(1,1-diphenylbutadiene)iron upon reaction with $Fe_2(CO)_9$. Consequently the ratio of the trimethylenemethane complexes [(**6′**)]/[(**6**)] (Scheme 3) could not be subject to an I.K.I.E. even if a mechanism analogous to that shown in Scheme 1 were operating. It is assumed that disrotatory ring openings of (**1**) and (**5**) should exhibit steric isotope effects of similar magnitude regardless of the mechanism. ^{1}H N.m.r. analysis of the products from reaction of (**5**) with $Fe_2(CO)_9$ revealed that (**6**) and (**6′**) were formed in a ratio of (1·02 ± 0·02) : 1. If the assumption of similar magnitudes for the steric isotope effects in (**1**) and (**5**) is valid, then it appears that the isotope effect on the ratio [(**3′**)]/[(**3**)] is largely due to an I.K.I.E., thereby ruling out the mechanism shown in Scheme 2 as a viable pathway in the $Fe_2(CO)_9$ reaction. The results can also be used to rule out a mechanism involving direct insertion of $Fe(CO)_4$ into the C(2)–C(3) bond of the methylenecyclopropane since this too would give a common intermediate leading to the two label-isomeric trimethylenemethane complexes.



Scheme 3. Control experiment to estimate the magnitude of the steric isotope effect.

It is particularly interesting to note that the excess of (**3′**) over (**3**) is consistent with a disrotatory-away[1–3] ring opening of (**2**) and (**2′**). A disrotatory-towards ring opening would have given [(**3′**)]/[(**3**)] < 1. The observed stereochemistry is in accord with previous theoretical[1] and experimental studies.[2,3]

The design of experiments to employ the I.K.I.E. phenomenon for mechanistic discrimination is, of course, not limited to the realm of organometallic chemistry. We expect that it could be of value in searching for common biradicals in thermal rearrangements of hydrocarbons and common electronic excited states in organic photochemistry.

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† Free rotation about the C(1)—C(4) bond is assumed (Scheme 2).

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