DEUTERIUM ISOTOPE EFFECTS IN THE *META* PHOTOCYCLOADDITION OF AROMATIC COMPOUNDS TO ALKENES

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Abstract. Secondary deuterium isotope effects were observed in the *meta* photocycloaddition
of several aromatic compounds to cyclopentene.

Although the *meta* photocycloaddition of aromatic compounds to alkenes has been the subject
of many investigations during the last decade, the mechanism of this reaction has not yet
been fully elucidated.[1-4]

Three mechanisms that have been proposed are: (I) formation of prefulvene from excited
benzene, followed by addition to the alkene[5,6]; (II) formation of a biradical or a zwitter-
ion from excited benzene and alkene, followed by closure of the three-membered ring[7]; and
(III) a concerted mechanism.[8]
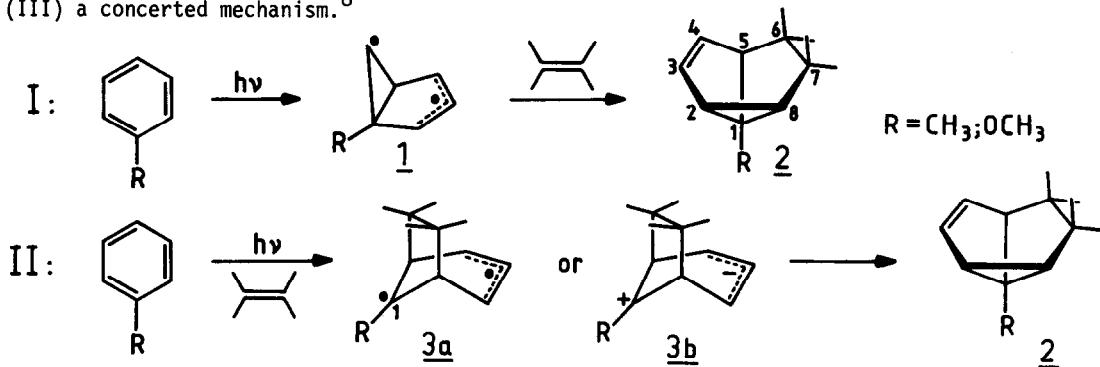
In order to determine which of these mechanisms is closest to reality it is important to
know which bond(s) is (are) formed in the primary step and which bond formation is rate
determining. We have investigated this by measuring deuterium isotope effects on the reaction
of derivatives of toluene and anisole with cyclopentene. It is known that electron donating
substituents such as alkyl and alkoxy appear at position 1 of the adduct.[4]

A. Photocycloaddition of 3,5-dideuterotoluene to cyclopentene

In order to determine a possible isotope effect on the closure of the three-membered ring,
we irradiated a mixture of toluene and 3,5-dideuterotoluene and measured the amount of deute-
rium in the products and the starting materials by means of mass spectrometry at several
times of irradiation. From these data we could calculate the isotope effect. The deuterium
content of the *meta* adduct was not determined from the ratio of the parent peaks, because the
intensities of those peaks were very low and because fragmentation to a fragment with a mass

equal to that of toluene (and toluene-d_2) took place with an isotope effect. However, this fragment constituted more than 95 % of the total intensity of the spectrum, and the deuterium contents could therefore be determined from this fragment. The spectra of starting materials and products were measured at low voltage to exclude the (m-1) peak. The isotope effect is presented in Table 1 (entry 1).

Table 1. Deuterium isotope effects from intermolecular competition experiments.

compound	k_H/k_D
3,5-dideuterotoluene	1.17 ± 0.02
2,6-dideuterotoluene	1.11 ± 0.02
4-deuteroanisole	1.01 ± 0.02
octadeuterotoluene	1.48 ± 0.04

*B. Photocycloaddition of 2,6-dideuterotoluene to cyclopentene*

The same method as in experiment A was applied to determine the effect of deuterium on the carbon atoms to which the addition takes place. The isotope effect measured by comparison of toluene and 2,6-dideuterotoluene is given in Table 1 (entry 2).

C. Photocycloaddition of 4-deuteroanisole to cyclopentene

The method used for experiments A and B was also applied to 4-deuteroanisole. In this case one expects no isotope effect because the *para* carbon atom does not undergo a change in hybridisation or steric interaction. This is indeed observed: within experimental error the measured value of k_H/k_D is unity (Table 1, entry 3).

D. Photocycloaddition of 2,6-dideutero- and 3,5-dideutero-4-ethyltoluene to cyclopentene

An accurate method of determining isotope effects is measuring the relative yields of a competition reaction from which two different products are formed. In the case of 4-ethyltoluene there are two modes of addition of the alkene (cyclopentene): 3,5-addition and 2,6-addition, leading to products 4 and 5, respectively.
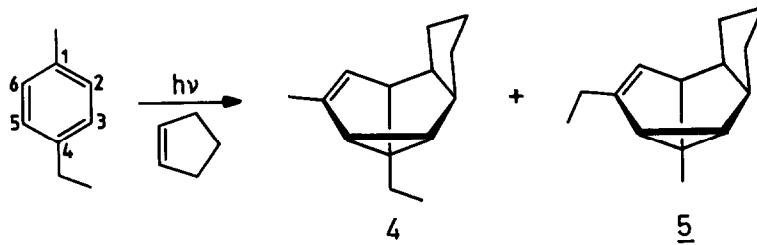
These products are formed in a ratio of 1.74 in favour of 5, presumably due to less steric hindrance if the alkene approaches to add in the 2,6 mode.

On the basis of the results of experiments A and B we expect that in the cases of 2,6- and 3,5-dideutero-4-ethyltoluene two competing isotope effects will play a role, resulting in a change of the ratio of 5 to 4. The overall effect is the quotient of the effects measured in experiments B and A: 1.11/1.17 = 0.95.

As can be seen from Table 2 (entries 1 - 3), the measured isotope effects in 2,6- and 3,5-dideutero-4-ethyltoluene are in agreement with this calculated value. The ratios of 5 and 4 were determined by means of gas chromatography.

Table 2. Deuterium isotope effects from intramolecular competition experiments.

compound	ratio 5/4	k_H/k_D
4-ethyltoluene	1.74	
2,6-dideutero-4-ethyltoluene	1.84	0.94 ± 0.01
3,5-dideutero-4-ethyltoluene	1.61	0.93 ± 0.01
α,α,α-trideutero-4-ethyltoluene	1.64	1.06 ± 0.005

E. Photocycloaddition of α,α,α-trideutero-4-ethyltoluene to cyclopentene

In the case of methyl deuterated 4-ethyltoluene an isotope effect may be expected due to better hyperconjugative interaction of an unfilled or partly filled orbital on carbon 1 with β C-H bonds than with C-D bonds.[9] This will only be the case in mechanism II. In intermediate 3 there are five hyperconjugative hydrogens if there is a methyl group at position 1: the three methyl hydrogens and the two hydrogens on the carbon atoms to which the addition takes place. The latter are less important because their C-H orbitals have little overlap with a vacant or singly occupied orbital on carbon atom 1.

The ratio of the adducts 5 and 4 from α,α,α-trideutero-4-ethyltoluene, as determined by means of GC, and the corresponding isotope effect are given in Table 2 (entry 4).

F. Photocycloaddition of octadeuterotoluene to cyclopentene

In octadeuterotoluene all the above mentioned effects operate simultaneously and they should give rise to a cumulative isotope effect of 1.39 ± 0.04. The measured value (same procedure as in experiments A, B and C) is presented in Table 1 (entry 4).

Discussion

If we consider the above mentioned mechanisms in connection with the measured isotope effects we can observe the following:

1. The isotope effect observed when the methyl hydrogens are replaced by deuteriums cannot be rationalized in terms of mechanism I, but it is in agreement with mechanism II.

2. For the normal effects observed with 3,5-deuteration and with 2,6-deuteration no easy explanation can be found. The normal isotope effect from 2,6-deuteration is very surprising because one expects an inverse effect on the addition step as is observed in many examples of cycloaddition reactions[10-12] when the carbon atom changes its hybridisation from sp^2 to sp^3.

For the normal effect observed with 3,5-deuteration there is some precedent. In the second step of mechanism II the carbon atom towards which ring closure will take place has to be twisted in order to obtain good overlap between its p-orbital and the p-orbital of carbon 1. A normal isotope effect of this kind has been observed earlier.[13]

Without knowing the exact cause of this effect we can already say that it arises in the step in which the three-membered ring is closed. The fact that this effect can be measured in an intermolecular competition experiment leads to the conclusion that closure of the three-membered ring is the rate determining step.

3. In order to determine the cause of the effect of 2,6-deuteration and to ascertain our conclusion from the effect of 3,5-deuteration we will have to measure the isotope effects in the corresponding monodeutero compounds.

Investigations with 2- and 3-deuterotoluene and with deuterated alkenes are in progress.

Experimental

All irradiations were carried out with light of 254 nm, using solutions of ca. 1 M aromatic compound and 2.5 M cyclopentene in cyclohexane.

The intermolecular competition experiments were carried out with approximately 1 : 1 mixtures of deuterated and undeuterated compound. Samples were taken at several times of irradiation at low conversion and separated by means of preparative GC (6 m SE-30 column, 140 °C, H_2). The deuterium content of starting material and product was measured with mass spectrometry (AEI, MS 902s double focusing mass spectrometer, at 12.5 eV).

The irradiation mixtures of the 4-ethyltoluenes were analysed by means of analytical GC (25 m × 0.25 mm fused silica capillary column with chemically bonded polydiphenyldimethyl-siloxane phase, 105 °C, H_2). Each sample was analysed at least 20 times.

All deuterated species except 4-deuteroanisole and octadeuterotoluene were synthesized via essentially the same procedure, as outlined below. Octadeuterotoluene was obtained from Aldrich Chemie b.v., Belgium, and 4-deuteroanisole was synthesized by quenching 4-methoxy-phenylmagnesium bromide with deuterium oxide.

The *ortho* hydrogens of 4-ethyl- and 4-methylaniline hydrochloride were exchanged by refluxing the compounds 3 to 4 times in deuterium oxide during 24 hours.[14]

4-Ethyl- and 4-methylaniline were diazotised and treated with copper(I)chloride to give the corresponding 4-alkylchlorobenzenes. These were treated with sodium and dimethyl or diethyl sulfate, respectively, to give 4-ethyltoluene.

Via this method 2,6-dideutero-4-ethyltoluene was prepared from 2,6-dideutero-4-ethyl-aniline, 3,5-dideutero-4-ethyltoluene from 2,6-dideutero-4-methylaniline, and α,α,α-tri-deutero-4-ethyltoluene from 4-ethylaniline and hexadeuterodimethyl sulfate.

3,5-Dideuterotoluene was prepared from 2,6-dideutero-4-methylaniline by means of diazoti-sation and reduction with hypophosphoric acid.

2,6-Dideuterotoluene was synthesized as follows. 4-Nitrotoluene was treated 3 times with deuterium sulfate at 90 °C during 24 hours[15] and then reduced with tin and hydrochloric acid to the corresponding aniline. This was then diazotised and reduced with hypophosphoric acid.

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