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

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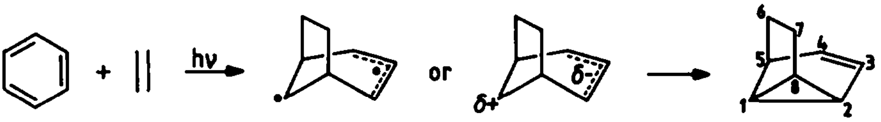
Abstract. The effect of substitution of hydrogen by deuterium in some aromatic compounds on product distributions in the meta photocycloaddition to alkenes was investigated. The isotope effects found are in agreement with a polar mechanism.

Introduction.

On the basis of a wide range of studies on the meta photocycloaddition of aromatic compounds to alkenes, it is generally accepted that the reaction proceeds via a pathway where formation of the two bonds between the alkene and the arene precedes closure of the three-membered ring[1,2,3,4]. Some authors propose an intermediate with biradicaloid character (I), whereas others assume a dipolar species (II).



I II

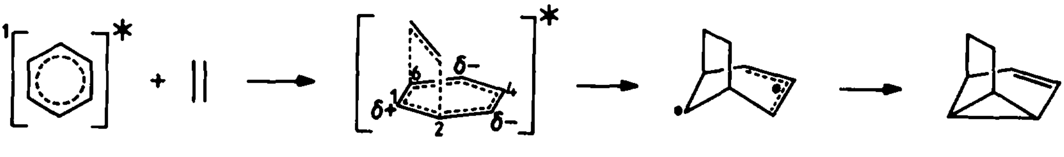
For both points of view strong arguments can be found :

The effect of electron-withdrawing and electron-releasing substituents on the mode of addition can only be accounted for in terms of a polarised species. Electron-withdrawing substituents such as cyano or trifluoromethyl are only found at positions 2 and 4 in the adduct [5], while electron-releasing substituents such as methoxy are exclusively found at position 1 [6].

Observations of Sheridan provide a strong argument for the occurrence of a biradical intermediate. He synthesized azo compounds from the meta adducts of ortho-xylene and meta-xylene with cyclopentene [4]. Such compounds are assumed to give a derivative of biradical I upon irradiation[7]. Closure of a three-membered ring then yields the meta adduct. The product ratios from these irradiations are equal to those found upon irradiation of the xylenes in the presence of cyclopentene.

Both postulated mechanisms are based on the observation of product ratios, but there is one important difference. The formation of a polarised species accounts for substituent effects on the addition step, while the conclusions from the experiment of Sheridan are based on substituent effects on closure of the three-membered ring.

It is tempting to try to combine the two intermediates in one mechanism in order to account for all observed effects. One can imagine that the electron cloud of the excited arene becomes polarized upon approach of the alkene. In this early stage bond formation between the alkene and the arene takes place if the substituents are in the right position to stabilize the polarized complex. If the bonds become fully formed the intermediate loses its polarization and attains biradicaloid character. In the second stage of the reaction substituents can only influence the direction of the closure of the three-membered ring. Such a mechanism is in agreement with semi-empirical calculations[8].



III

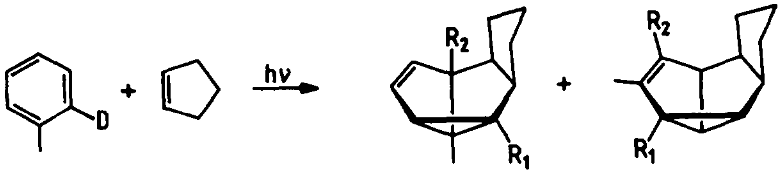
In an attempt to obtain experimental evidence for this mechanism we investigated some intramolecular deuterium isotope effects which could give information about the timing of bond formation. From a study of intermolecular isotope effects [9] we were not able to conclude which bond was formed in the rate determining step. Both 2,6-dideutero- and 3,5-dideuterotoluene exhibit an isotope effect in a competition experiment with toluene. From later studies on octadeuterotoluene we concluded that these isotope effects are mainly caused by energy transfer between the labeled and unlabeled arene [10]. After correction for this effect we find an inverse isotope effect of 0.93 for the meta photoaddition of cyclopentene to toluene and 2,6-dideuterotoluene and no effect for 3,5-dideuterotoluene.

This leads to the conclusion that the addition step is rate determining. Now we have a good basis for analysing the intramolecular isotope effects, reported here.

Results and discussion.

A. 2-d- and 3-d-toluene, and 2-d-para-xylene.

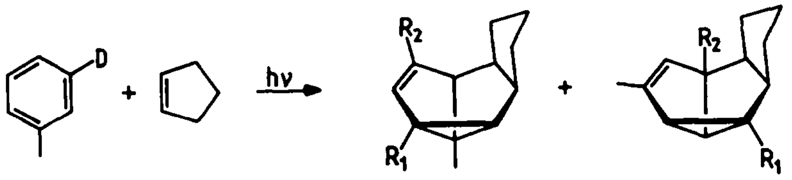
A mixture of 2-d-toluene and cyclopentene in cyclohexane was irradiated and two products 1 and 2 were formed in the ratio 12:1 and isolated by preparative gc. The deuterium distributions in the products were determined by deuterium NMR, and these ratios are listed in Table 1, entries a and b.



1a. R_1=H, R_2=D
1b. R_1=D, R_2=H

2a. R_1=H, R_2=D
2b. R_1=D, R_2=H

From the irradiation of 3-d-toluene the following products were observed:



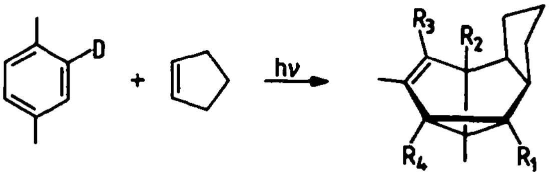
1c. R_1=H, R_2=D 2c. R_1=H, R_2=D
1d. R_1=D, R_2=H 2d. R_1=D, R_2=H

Ratios are listed in Table 1, entries c and d.

Table 1. Intramolecular competition experiments with ring-deuterated arenes.

	arene	product ratios
a	2-d-toluene	1a : 1b = 1.00
b		2a : 2b = 1.22
c	3-d-toluene	1c : 1d = 1.17
d		2c : 2d = 1.00
e	2-d-para-xylene	3a : 3b = 1.00
f		3c : 3d = 1.17
g		3c+3d : 3a+3b = 0.97

From the irradiation of 2-d-para-xylene one product (3) could be isolated. The deuterium NMR spectrum showed the four expected peaks. From the intensities of these peaks deuterium distributions were obtained (Table 1, entries e-g).



3a. R_1=D, R_2=R_3=R_4=H
3b. R_2=D, R_1=R_3=R_4=H
3c. R_3=D, R_1=R_2=R_4=H
3d. R_4=D, R_1=R_2=R_3=H

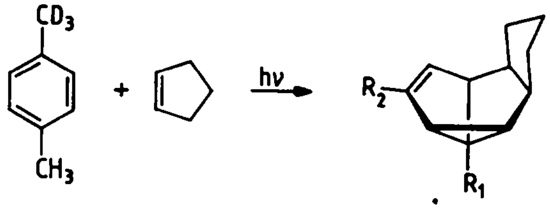
The effects a-f fall into two categories. The first category (entries a, d and e of Table 1) contains the effects of deuterium at the site of addition on the direction of closure of the three-membered ring (in all three cases the isotope effects are unity within experimental error). The inverse isotope effect on the addition reported earlier for 2,6-dideutero-4-ethyltoluene and 3,5-dideutero-4-ethyltoluene[9] implies that in the monodeuterated compound here, where deuterium is also at an addition site, formation of the bond towards the deuterated atom will run ahead of that to the carbon bearing hydrogen. If closure of the three-membered ring would occur before the bonds between the alkene and the arene are completely formed an isotope effect would result because the adduct would be formed from an asymmetric precursor. The absence of an isotope effect provides evidence for the (almost) complete formation of the two addition bonds prior to closure of the three-membered ring.

The second category of effects (entries b, c and f of Table 1) contains the effects that deuterium has if it is at one of the carbon atoms to which ring closure can take place. The observed effect is quite large and somewhat unexpected. Considering the intermediates I and II it would seem that the carbon to which ring closure takes place changes hybridisation to sp^3, whereas the other one remains sp^2. One would therefore expect an inverse isotope effect (i.e. preferential ring closure to the deuterated carbon atom). In this particular case, however, the carbon atom becomes a bridgehead in a tricyclic system with a three- and two five-membered rings. To predict the effect one has to calculate the difference in vibrational freedom of the C-H bond in the intermediate and the product. If this freedom increases one expects a normal isotope effect, otherwise an inverse one. Calculations on this effect are in progress.

The effect reported in Table 1 as entry g is a measure of the relative ease of addition to deuterated and undeuterated carbon. Such an effect was reported earlier by us in the case of 2,6-dideutero-4-ethyltoluene. The value of $k_H/k_D = 0.93$ for two deuteriums found in that case is in agreement with the value of 0.97 for one deuterium in the present case.

B α,α,α-trideuteroxylenes.

To get more evidence for the polarised structure in the first step of the mechanism we investigated several methyl deuterated xylenes. α,α,α-Trideutero-para-xylene was irradiated in cyclohexane in the presence of cyclopentene. The meta adduct was isolated by means of preparative GC and the deuterium distribution measured with deuterium NMR. The result is presented in Table 2, entry a.

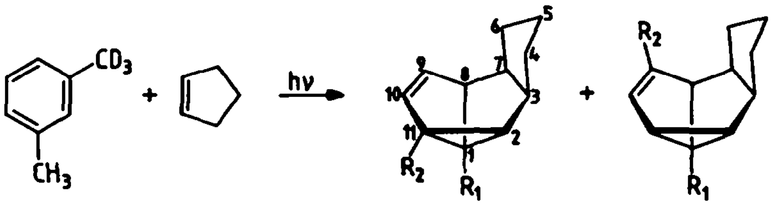


3e. $R_1=CH_3$, $R_2=CD_3$
3f. $R_1=CD_3$, $R_2=CH_3$

Table 2. Intramolecular competition experiments with methyl-deuterated xylenes.

	arene	product ratio
a	α,α,α d_3-para-xylene	3e : 3f = 1.06
b	α,α,α d_3-meta-xylene	4a : 4b = 1.00
c		5a : 5b = 1.00
d	α,α,αd_3-ortho-xylene	6a : 6b = 0.97
e		7a : 7b = 0.97

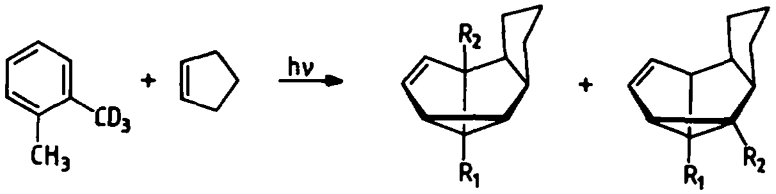
From α,α,α-trideutero-meta-xylene and cyclopentene four adducts were isolated, of which only two could be obtained in pure form. The deuterium distributions were determined by deuterium NMR (Table 2, entries b and c). One of the other products has the methyl groups on positions 8 and 10, and the fourth product is presumably the 2,10-dimethyl adduct.



4a. $R_1=CH_3$, $R_2=CD_3$ 5a. $R_1=CH_3$, $R_2=CD_3$

4b. $R_1=CD_3$, $R_2=CH_3$ 5b. $R_1=CD_3$, $R_2=CH_3$

From α,α,α-trideutero-ortho-xylene two products were isolated and the deuterium distributions determined (Table 2, entries d and e).



6a. $R_1=CH_3$, $R_2=CD_3$ 7a. $R_1=CH_3$, $R_2=CD_3$

6b. $R_1=CD_3$, $R_2=CH_3$ 7b. $R_1=CD_3$, $R_2=CH_3$

The isotope effects found in these cases where the methyl group is deuterated are of the beta secondary type. One of the main factors causing such effects is the difference in hyperconjugative stabilisation by hydrogen and deuterium[11]. In the case of a dipolar intermediate with some (positive) charge at carbon 1 one expects the reaction to go faster with a CH_3 group than with a CD_3 group at that position. Such an effect, $k_H/k_D = 1.06$, was found earlier in the case of 4-ethyltoluene deuterated in the methyl group[9]. The experiment with trideutero-para-xylene is expected to give the same value, which is indeed found.

The results obtained with α,α,α-trideutero-ortho-xylene allow us to discriminate between the intermediates II and III. In this compound addition can take place across the CH_3-group or the CD_3-group. From the para-xylene experiment it is known that addition across the latter is favoured by a factor 1.06. If only this effect would play a role in the case of ortho-xylene we would expect 6a:6b = 1.06. The ratio found is 0.97 indicating that there is also an isotope effect of the methyl group at the position of addition : $k_{CH3}/k_{CD3} = 1.08$. This implies that the carbon atoms to which the addition takes place bear charge at the stage of the reaction in which the mode of addition is determined. This is possible with a mechanism proceeding via III and not via II.

In the case of meta-xylene the same kind of reasoning leads to the conclusion that the carbon atoms 3 and 5 in III also bear charge leading to a relatively small isotope effect. This charge is assumed from substituent effects to be negative which implies that the isotope effect in this case is of anionic hyperconjugative origin.

Experimental.

Irradiation conditions and work-up.

All irradiations were carried out in a Rayonet RPR200 Photochemical reactor fitted with seven 254 nm lamps, using a quartz tube containing 25 ml of a solution of 1 M arene and 2 M cyclopentene in cyclohexane. After 24-48 hours irradiation the solvent was evaporated and the mixture separated by preparative GC using a Varian Aerograph Model 90-P gaschromatograph fitted with a 6 m x 8 mm column packed with 17% SE 30 on Chromosorb WAW 40-60 mesh, oven temperature 130 °C.

NMR Spectroscopy.

All deuterium distributions in the products were determined by means of recording their deuterium NMR spectra and integrating the corresponding peaks. Deuterium NMR spectra were recorded on a Bruker WM 300 spectrometer at 46 MHz, using a broad band preamplifier and a deuterium matching unit, a sweep width of 920 Hz, 500-2000 scans and a relaxation delay of 4 s to obtain maximum accuracy of peak integrals.

Preparation of deuterated compounds.

The ring deuterated arenes were prepared by quenching their corresponding Grignard reagents with deuterium oxide. For example 2-d-toluene was prepared as follows :

2.6 g (0.11 mol) Magnesium turnings were put in a dry 250 ml three-necked bottle fitted with a reflux condenser and a dropping funnel containing 100 ml dry ether. To the solution was added 1 g methyl iodide in 5 ml ether. When the mixture started to reflux a solution of 17 g (0.1 mol) 2-bromotoluene in 20 ml ether was added dropwise through the funnel. After 2 hours 3 ml deuterium oxide was added slowly. The solution was extracted with water, the ether layer dried over magnesium sulfate and the product distilled after evaporation of the ether. A typical yield was 60% of the arene, containing 80-95% deuterium.

The preparation of the methyl-deuterated xylenes was carried out by adding hexadeuterodimethyl sulfate to the corresponding lithiumarene. For example α,α,α-trideuteropara-xylene was prepared as follows :

In a 250 ml three-necked bottle fitted with a reflux condenser, dropping funnel and nitrogen inlet, the 4-lithiotoluene was prepared by adding dropwise 17.1 g (0.1 mol) of 4-bromotoluene in 25 ml ether to 0.6 g (0.1 mol) of lithium shavings in 100 ml dry ether under nitrogen atmosphere. After 2 hours a solution of 13.2 g (0.1 mol) hexadeuterodimethyl sulfate in 5 ml hexane was added dropwise. Extraction with water, drying and distillation yielded 50-80% of the xylene, with a deuterium incorporation of at least 98% D_3.

References and notes.

1. E.M. Osselton, J. Cornelisse and J. Mattay, J.Photochem. 31 (1985), 381.
2. J. Mattay, J. Runsink, J. Gersdorf, T. Rumbach and C. Ly, Helv.Chim.Acta 69 (1986), 442.
3. M.G.B. Drew, A. Gilbert, P. Heath, A.J. Mitchell and P.W. Rodwell, J.Chem.Soc.,Chem.Commun. (1983),750.
4. D.E. Reedich and R.S. Sheridan, J.Am.Chem.Soc., 107 (1985), 3360.
5. E.M. Osselton and J. Cornelisse, Tetrahedron Lett. 26 (1985), 527.
6. R. Srinivasan and J.A. Ors, Chem.Phys.Lett. 42 (1976), 506.
7. H.E. Zimmerman,R.J. Boettcher, N.E. Buehler, G.E. Keck and M.G. Steinmetz, J.Am.Chem.Soc. 98 (1976), 7680.
8. J.A. van der Hart, J.J.C. Mulder and J. Cornelisse, to be published.
9. P. de Vaal, G. Lodder and J. Cornelisse, Tetrahedron Lett. 26 (1985), 4395.
10. P. de Vaal, G. Lodder and J. Cornelisse, to be published.
11. D.J. DeFrees, M. Taagepera, B.A. Levi, S.K. Pollack, K.D. Summerhays, R.W. Taff, M. Wolfsberg and W.J. Hehre, J.Am.Chem.Soc. 101 (1979), 5532.