Stereospecific and Unspecific Pathways for Aromatization of 1,4-Cyclohexadienes***

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Abstract: The aromatization of *trans*-3,6-dideuterio-1,4-cyclohexadiene (**1-d$_2$**) to benzene (**2**) with chromic acid is slightly stereospecific with a diastereomeric excess of 25%. This result is ascribed to two competing mechanisms, a stereospecific 2-electron oxidation with Cr^{VI}, and a non-specific 1-electron oxidation with Cr^{IV}. In contrast, aromatization of **1-d$_2$** with lead tetraacetate exhibits no stereospecificity.

Alkenes have two reactive sites susceptible to attack by oxidating reagents, the olefinic π-system and the allylic C,H bonds. Some oxidants exhibit remarkable selectivities for one or the other of these functionalities, but often products originating from both modes of reaction are obtained. Chromic acid[1] is a typical oxidant of this latter class. In this case the different oxidation products can, in part, be ascribed to the intervention of (at least) two different chromium species: Chromium(VI) prefers to attack alkenes at the double bond[2], while reaction at the allylic position is usually ascribed to an intermediate chromium(IV)[3].

Reaction of chromium(VI) with C,H bonds is also possible provided the molecules in question are otherwise inert towards oxidation (alkanes[4], arylalkanes[5]), but normally with alkenes, double bond oxidation is much faster. Some time ago we reported two examples of alkenes where this trend is inverted[6]: Oxidation of 1,4-cyclohexadiene (**1**) to benzene (**2**) and that of tri-*tert*-butylcyclopropene to the corresponding cyclopropenium ion by chromium(VI) proceeds via attack at the allylic positions. Both educts exhibit unusually high reactivities for allylic oxidation, which fall in the rate range usually observed for reaction at the double bonds.

1,4-Cyclohexadiene (**1**) also shows enhanced reactivity in other allylic oxidations leading to benzene, for example with $Ph_3C^{\oplus}$[7], 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[8–10], and in pyrolytic hydrogen elimination[11]. The DDQ-induced and the pyrolytic aromatizations are stereospecific *cis*-eliminations[10–13]. We reasoned, that by analogy, stereospecificity might also occur in aromatization of **1** with chromic acid. Accordingly, a sample of *trans*-3,6-dideuterio-1,4-cyclohexadiene (**1-d$_2$**) was synthesized[14] from the adduct **3** of cyclooctatetraene to dimethyl acetylenedicarboxylate via *cis-trans*-1,4-dideuterio-1,3-butadiene (**4**) by a variation of the procedure originally described by *Fleming* et al.[12], and subjected to oxidation with excess chromic acid[6] (Scheme 1). For the purpose of comparison, aromatization of **1-d$_2$** was also investigated with $Pb(OAc)_4$[15]. For mechanistic reasons[16] this reaction is expected to show no stereospecificity.

The procedure of *Fleming*[12] for synthesis of **1-d$_2$** is not entirely satisfactory[13] because it leads at the same time to **1-d$_1$** and **1-d$_0$**; benzene is formed as a side-product and must be separated by preparative gas chromatography. Our sample, after purification, contained 6.0% of benzene (**d$_2$**: 34.3%, **d$_1$**: 30.0%, **d$_0$**: 35.7%); the isotopomeric composition of the cyclohexadiene (**1**), as determined by Raman[17] and high-resolution mass spectroscopy[18] was 82.4% **d$_2$**, 14.5% **d$_1$**, 3.1% **d$_0$**. The results of the analyses of the benzene product **2** are summarized in Table 1. The first two entries refer to the crude data

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*** *Acknowledgment:* This work was supported by the Swiss National Science Foundation (project No. 2.602-0.87 and previous grants). – The authors are indebted to Prof Dr. T. Gäumann, Swiss Federal Institute of Technology, Lausanne, for the mass-spectrometric determination of the isotopic composition of the samples, and to Ms. N. Jacquat for preparation of **1-d$_2$**.

Scheme 1

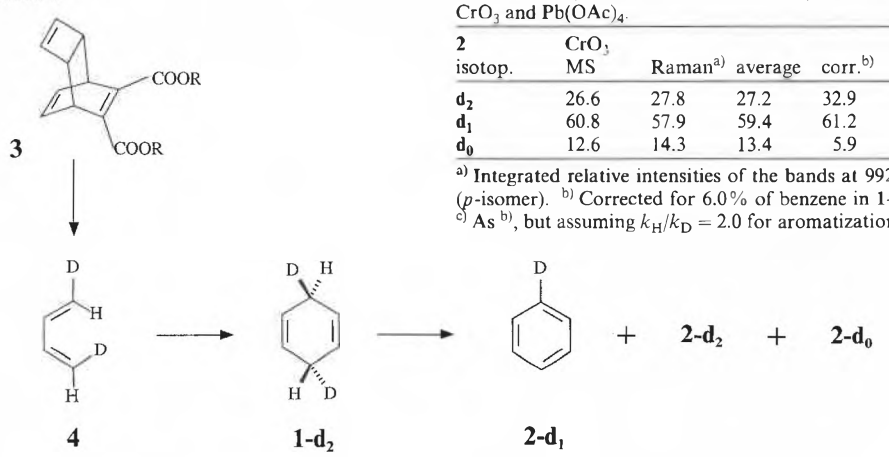


Table 1. Isotopomers of benzene (**2**) (in %) in aromatization of *trans*-3,6-dideuterio-1,4-cyclohexadiene (**1-d$_2$**) with CrO_3 and $Pb(OAc)_4$.

2 isotop.	CrO_3 MS	Raman[a]	average	corr.[b]	corr.[c]	$Pb(OAc)_4$ MS	Raman[a]	average	corr.[b]	corr.[c]
d_2	26.6	27.8	27.2	32.9	32.9	34.9	35.7	35.3	43.5	43.5
d_1	60.8	57.9	59.4	61.2	62.7	47.4	45.5	46.5	44.2	45.8
d_0	12.6	14.3	13.4	5.9	4.4	17.7	18.9	18.3	12.3	10.7

[a] Integrated relative intensities of the bands at 992, 981, and 978 cm^{-1} characteristic for benzene d_0, d_1, and d_2 (*p*-isomer). [b] Corrected for 6.0% of benzene in **1-d$_2$**, and with assumed $k_H/k_D = 1.0$ for aromatization of **1-d$_1$**. [c] As [b], but assuming $k_H/k_D = 2.0$ for aromatization of **1-d$_1$**.

as obtained directly from the Raman[17] and mass spectra[18], and the third column is the average from these data. The average discrepancy between Raman and MS analysis is ca. 1.0%. In the next column the data are corrected for the benzene contamination in the starting **1-d$_2$** and, additionally, the isotopic composition of the sample. The results given are obtained on the assumption of statistical loss of H and D ($k_H/k_D = 1$) from the monodeuterated 1,4-cyclohexadiene (**1-d$_1$**), i.e. one out of four molecules of **1-d$_1$** reacting to undeuterated benzene (**2-d$_0$**), and three to **2-d$_1$**. In the last entry of Table 1, apart from the correction due to the contamination of **1-d$_2$** with benzene, it is assumed that one out of three **1-d$_1$** isotopomers reacts to **2-d$_0$**, while two become **2-d$_1$**. This corresponds to the experimental result in the dehydrogenation of **1** with DDQ[13]. As Table 1 shows, the corrections and assumptions are of little consequences with respect to the trends in the data.

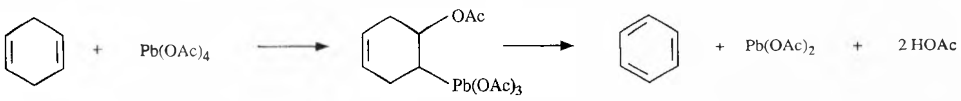
Starting from **1-d$_2$**, *cis*-elimination leads to **2-d$_1$** and *trans*-elimination to a mixture of **2-d$_2$** and **2-d$_0$**. In the oxidation with $Pb(OAc)_4$, *cis*- and *trans*-elimination contribute to about the same extent to the overall result, with a slight preference for *trans*. This is consistent with a reaction mechanism involving (unspecific) reaction at the double bond, followed by (unspecific) elimination of HOAc and $Pb(OAc)_2$[16] (Scheme 2). The slight excess of *trans*- over *cis*-elimination can be ascribed to isotope effects occurring in the second step of the reaction (elimination of HOAc and Pb^{II}).

With chromic acid, however, we find a significant, although small, preference for *cis*-elimination (diastereomeric excess 25%). We interpret this result as being due to two competing pathways, namely stereospecific *cis*-elimination of HD by chromium(VI), and non-specific aromatization by chromium(IV) (Scheme 3).

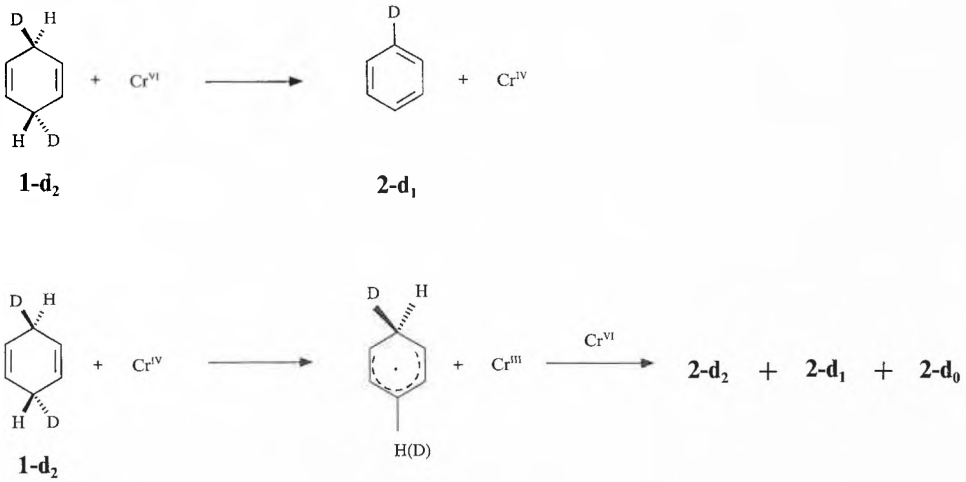
This scheme is formulated in analogy to that generally recognized for chromic acid oxidations of alcohols[19] and alkenes[3]. It ascribes stereospecificity to the oxidation step involving a two-electron transfer. Two-electron transfer takes place in all stereospecific aromatizations of **1** reported so far. As exemplified by Cr^{IV}, one-electron oxidations, even when occurring via hydrogen abstraction from the allylic position, should not exhibit stereospecificity, because the intermediate radicals are symmetrical except for the H or D substituent. Although oxidations of hydrocarbons usually take place via non-specific sequential 1-electron transfer processes[1], some cases of molecules reacting via hydride transfer to chromium(VI) have already been reported[5]. Since Cr^{V} disproportionates rapidly to Cr^{VI} and Cr^{IV}[20], a stereospecific aromatization by which Cr^{V} is reduced to Cr^{III} appears less likely. The contributions of the Cr^{VI}- and Cr^{IV}-pathways to the overall result may vary between $\frac{1}{3}$ and $\frac{2}{3}$[21] but cannot actually be predicted more precisely, since the subsequent steps of the mechanism are not known. It is clear from our result, however, that even if the Cr^{VI}-pathway contributes only to $\frac{1}{3}$, it cannot be totally stereospecific. This is also true for aromatization of *trans*-**1-d$_2$** with DDQ[13].

The stereospecificity in aromatization of **1** has been ascribed to various causes. For the thermal reaction, conservation of orbital symmetry is the generally accepted hypothesis[12]. For DDQ we have proposed a concerted one-step dihydrogen elimination, where *cis*-stereospecificity should be due to stereoelectronic reasons[7-9]. The aromatization of **1** with chromic acid shows some similarities to that with DDQ. With both oxidants, **1** reacts much faster than simple alkenes or 1,4-dienes, which cannot aromatize in a single step. With both the kinetic isotope effects are clearly above the normal range, 12.2 with DDQ and 8.5 with chromic acid. This suggests that the reason for stereospecificity might be also the same. However, other authors have criticized the concerted mechanism for DDQ aromatization and proposed a two-step mechanism, in which stereospecificity was ascribed to successive hydride and proton abstraction from the same side of **1**. Formation of an intermediate ion pair was meant responsible for the occurrence of stereospecificity[13,22]. Moreover, it was argued recently, that the high isotope effect observed upon oxidation of **1-d$_8$** with

Scheme 2



Scheme 3



DDQ is not indicative for a concerted mechanism, but should be ascribed to tunnelling[13]. This is an interesting alternative, but at present, it is nothing more than a hypothesis. To our knowledge, no detailed investigations in this direction have been made in the context of oxidations with chromic acid or DDQ, and the available evidence, although limited, does not support the idea of tunnelling. In fact tunnelling is most often observed when the reaction suffers some steric constraints[23]. This is certainly not the case with **1**. In contrast, the kinetic isotope effect for reaction of DDQ with the highly crowded 1,2,3-triphenylcyclopropene, where tunnelling is much more likely to occur than with **1**, amounts only to 6.9[7], i.e. about half of that measured with **1**. A similar situation prevails in the oxidation with chromic acid. The value of k_H/k_D for 1,2,3-tri-*tert*-butylcyclopropene measures 4.6, again about half of that for **1** ($k_H/k_D = 8.5$, measured with **1-d$_8$**[6]). Thus, with both oxidants, the isotope effect is much lower for the sterically hindered molecules which, for structural reasons, *must* react via hydride transfer, than for the less hindered ones, which can aromatize by a concerted mechanism. Although one might argue about the significance of the high k_H/k_D for aromatization of cyclohexadienes, the available evidence does not support the tunnelling hypothesis. Another disturbing failure of the ion pair mechanism is that it does not take into consideration the enhanced reactivity of cyclohexadienes in comparison to other alkenes or dienes. We believe therefore that the concerted mechanism for aromatization of cyclohexadienes with DDQ and chromic acid, although not proven, cannot be ruled out on the grounds of the existing experimental results.

Received: November 25, 1988 [FC 153]

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