12. Stereochemistry of Dehydrogenation of 1,4-Cyclohexadiene with 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone

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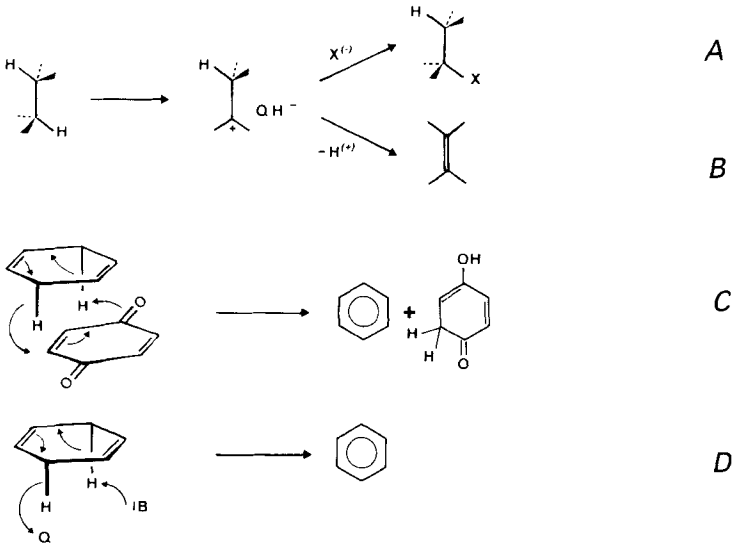
Summary

cis- and *trans*-(3,6-D_2)-1,4-cyclohexadienes **1a** and **1b** have been synthesized from *cis*-3,4-dichlorocyclobutene (**5**). Aromatization to benzene with DDQ is *cis*-stereospecific with an uncertainty of 5%. This result is discussed in relation to concerted or stepwise mechanisms for aromatization of 1,4-dihydroaromatics with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ).

Introduction. – Oxidation of hydrocarbons with quinones proceeds *via* hydride transfer from the substrate to the quinone (mechanism *A*, *Scheme 1*) [1]. In agreement with this description, reaction rates of substituted toluenes with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) correlate with σ giving a ρ-value of -4.3 [2]. Accordingly, substrates capable of forming stable carbenium ions upon hydride transfer exhibit enhanced reactivity. For example, cycloheptatriene reacts 200 times faster than 1,3-cycloheptadiene, and 1,2,3-triphenylcyclopropene *ca.* 10^5 times faster than triphenylmethane [3] [4]. Similarly, vicinal dehydrogenation is believed to proceed in a stepwise manner (mechanism *B*) involving sequential hydride and proton loss [5]. The partial *cis*-stereospecificity observed for dehydrogenation of acenaphthene has been ascribed to formation of an ion pair as reactive intermediate [6]. In contrast, dehydrogenation of 1,4-cyclohexadiene (**1**) and its benzannulated homologues does not fit this mechanistic picture. The reactivity of these compounds is usually about 100 times higher than that of 1,2-dihydroaromatics or similar model compounds, and it approaches that of cycloheptatrienes, provided that loss of two H-atoms from the allylic positions is possible [3–5]. The enhanced rate of 1,4-dihydroaromatics can be understood if it is assumed that part of the aromatic stabilization of the product is already reflected in the transition state of the reaction. This mechanistic hypothesis requires concerted loss of two H-atoms from the 1,4-positions, either in a cyclic mechanism *(C)* involving two *cis*-H-atoms, or in a *cis*- or *trans*-conjugate 1,4-elimination *(D)*. The cyclic mechanism *C* was proposed by *Stoos & Roček*, when they found that *cis*-3,6-dimethyl-1,4-cyclohexadiene (**2**) reacts *ca.* 20 times faster than the *trans*-isomer **3** and 700 times faster than the 3,3-dimethyl derivative **4** [4]. Although the preference for *cis*-

Scheme 1

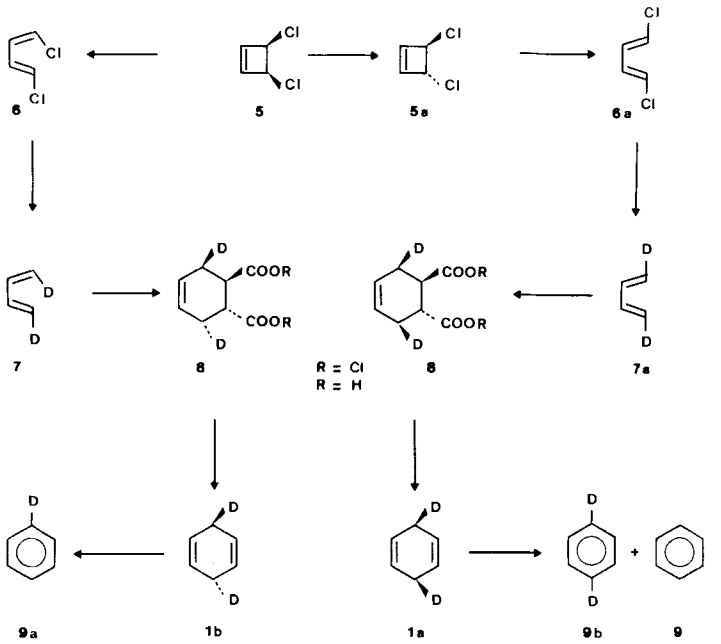


elimination with DDQ has also been reported for 9,10-diisopropyl-9,10-dihydroanthracenes [7], the cyclic mechanism has been contested [8] [9]. Indeed, the reactivity sequence of **2**, **3** and **4** could also be ascribed to steric hindrance by the CH_3-substituents which would block attack by the quinones from both sides in **3** and **4**, but only from one side in **2**. This argument is particularly important in connection with formation of charge-transfer (CT) complexes between substrate molecule and quinone, although the significance of these complexes for the oxidation mechanism remains still unclear [10] [11]. The objective of this work was to eliminate the potential steric effect by CH_3-substitution on the stereochemistry of 1,4-cyclohexadienes by investigation of the *cis*- and *trans*-3,6-dideuterated isotopomers (**1a** and **1b**).

Synthesis of *cis*- and *trans*-(3,6-D_2)-1,4-cyclohexadiene (1a) and (1b). – The *trans*-isomer **1b** has been synthesized by *Fleming & Wildsmith* starting from the *Diels-Alder* adduct of cyclooctatetraene to acetylene dicarboxylate [12]. However, the procedure appears not suitable for the *cis*-isomer **1a**. We therefore used an approach allowing synthesis of both stereoisomers from the same precursor, *cis*-3,4-dichlorocyclobutene (**5**) [13], and, with one exception, the same sequence of known reactions with full control of stereochemistry *(Scheme 2)*.

cis-3,4-Dichlorocyclobutene (**5**) was pyrolyzed at 180° for 36 h to afford (*Z*, *E*)-1,4-dichlorobutadiene **6** [14]. The comparison of ^{1}H-NMR data of **6** with the one in [15] showed no contamination by other stereoisomers within limits of detection (< 5%). Reduction of **6** with Cu/Zn in presence of D_2O/dioxane [16] was expected to afford **7** with only minor loss of stereochemistry [17]. However, in our hands substantial isomerization occurred. The analytical methods available to us (^{1}H-NMR, *Raman* spectroscopy [18]) did not allow determination of sample composition with the required accuracy. Therefore the sequence was completed by *Diels-Alder* addition of **7** to fumaroyl chloride, followed by hydrolysis to yield **8** as a mixture of diastereoisomers at C(4), C(5) [19]. Decarboxylation to **1b** was carried out according to the method of

Scheme 2



Wolfe & Campbell [19]. The same sequence applied to **5a** which is available by treatment of **5** with $AlCl_3$ [20] afforded **1a.** Pyrolysis of **5a** to **6a** occurred in 1 h at 90° [20] [21]. After reduction to **7a** as described above, ^1H- and ^2H-NMR spectra showed the presence of 20–30% contamination with the (*Z, E*)- and/or (*E, E*)-isomers but again exact sample composition could not be determined. In the context of this study the crucial point is the ratio **1a**/**1b**. This ratio can be determined from the relative amounts of di-, mono- and undeuterated benzene formed upon pyrolysis. It is known from kinetic [22] and stereochemical investigations [12], as well as from labelling studies [23], that 1,4-cyclohexadienes eliminate H_2 upon pyrolysis in a concerted stereospecific *cis*-fashion. *Table 1* summarizes the results for flash pyrolysis of the samples enriched in **1a** (A) and **1b** (B) at 400°. MS data were obtained using chemical ionization (isobutane, methane) and electron impact at 75 eV. Consistent results were obtained for both methods. The crude data (entry 2) are corrected for contamination of the cyclohexadienes with mono- and undeuterated material (entry 3). *Table 1* also contains data for (3-D)cyclohexadiene (**1c**), (3,3-D_2)cyclohexadiene (**1d**) and (3,3,6,6-D_4)cyclohexadiene (**1e**) for reference purposes. These compounds were synthesized in analogy to **1a** from the appropriate butadienes. The analysis reveals 38% contamination of the *cis*-isomer **1a** by **1b** (sample A), while sample B contains 30% of **1a** and 70% of **1b**. These results rely on the assumption of total stereospecificity in pyrolytic H_2-elimination of 1,4-cyclohexadienes. *Raman* spectroscopy used in the case of (*E, E*)-(1,4-D_2)butadiene (**7a**) gave a predicted ratio of *ca.* 66% *cis* and 34% *trans* in sample A.

Table 1. *Pyrolysis of Deuterated Cyclohexadienes* (Calculations were carried out using, as reference, experimental MS spectra of (D_0)cyclohexadiene and their extension to D_n, taking into account the statistical distribution of deuterium)

Sample	No.	Method	Cyclohexadiene; isotopic composition						Benzene, crude				Benzene, corr.[c])			
			D_0	D_1	D_2	D_3	D_4	D_5	D_0	D_1	D_2	D_3	D_0	D_1	D_2	D_3
cis-3,6-D_2	A	CI[a])	8	16	76	–	–	–	18	37	45	–	7	34	59	–
		EI[b])	0	14	86	–	–	–	10	45	45	–	6	42	52	–
trans-3,6-D_2	B	CI	7	14	79	–	–	–	14	60	26	–	3	74	23	–
		EI	0	16	84	–	–	–	12	65	23	–	8	64	27	–
3-D	**1c**	CI	5	95	–	–	–	–	47	53	–	–	44	56[d])	–	–
		EI	4	96	–	–	–	–	39	67	–	–	30	70[d])	–	–
3,3-D_2	**1d**	CI	9	3	88	–	–	–	18	75	7	–	9	81	10	–
		EI	0	7	93	–	–	–	2	86	12	–	0	87	13	–
3,3,6,6-D_4	**1e**	CI	–	–	–	2	90	8	–	4	94	2	0	2	98	0
		EI	–	–	–	4	95	1	–	0	96	4	0	0	97	3

[a]) Chemical ionization: isobutane for cyclohexadienes, methane for benzenes. [b]) Electron impact. [c]) After correction for isotopic composition in starting material (values below zero are set to zero). [d]) Used to estimate isotope effect for calculation of D_1-contamination.

Aromatization with DDQ. – Reactions of the cyclohexadienes with DDQ were carried out in dioxane. The benzene was analyzed by GC/MS under conditions identical to those used for the analysis after pyrolysis. Results are summarized in *Table 2*. For non-specific H_2-elimination we would expect the same pattern of D-content in the benzene produced from **1a** and **1b**. The crude MS data in *Table 2* shows that this is obviously not the case, *i.e.* the reaction shows stereospecificity. From comparison with *Table 1* we conclude that the stereochemical course of DDQ oxidation is almost identical to that of pyrolysis. This is shown graphically in the *Figure*. The MS data for DDQ oxidation plotted against those for pyrolysis of all labelled cyclohexadienes describe a straight line which is slightly different for chemical ionization (slope = 0.988) and electron impact (slope = 0.988). Correlation coefficients are *ca.* 0.989 and standard deviation *ca.* 5% in x and y. The correlation is somewhat less satisfactory for the **1a** and

Table 2. *Aromatization of Deuterated Cyclohexadienes with DDQ*

Sample	No.	Method	Benzene, crude				Benzene, corr.[c])			
			D_0	D_1	D_2	D_3	D_0	D_1	D_2	D_3
cis-3,6-D_2	A	CI[a])	20	34	46	–	9	30	61	–
		EI[b])	16	36	48	–	13	31	56	–
trans-3,6-D_2	B	CI	19	65	16	–	9	71	20	–
		EI	–	–	–	–	–	–	–	–
3-D	**1c**	CI	46	54	–	–	43	57	–	–
		EI	39	61	–	–	37	63	–	–
3,3-D_2	**1d**	CI	16	80	4	–	7	89	4	–
		EI	5	89	6	–	3	90	7	–
		CI	–	9	90	1	0	7	93	0
3,3,6,6-D_4	**1e**	EI	–	3	97	0	–	0	100	0

[a]), [b]), [d]) See *Table 1*.

1b-enriched samples alone, mainly because corrections for contamination by D_0-**1** and D_1-**1** had to be applied to a small peak corresponding to (D_0)benzene (**9**) in the dehydrogenation products. Using a *t*-test to compare the slope of 0.931 for **1a** and **1b** ($r = 0.992$; chemical ionization) with the ideal slope of 1.000, we conclude that both are identical within a 95% confidence level. This leads to accept a similar *cis* stereochemical process. Although data from stereochemically pure samples of **1a** and **1b** would be more straightforward to analyze, the samples used here still lead to a consistent and unambiguous result.

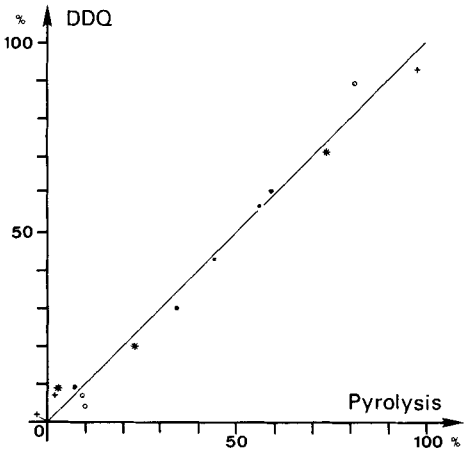
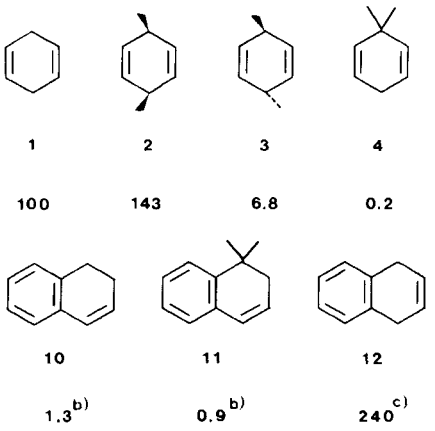


Figure. *Plot of MS data for cyclohexadiene DDQ oxidation* (y) vs. *pyrolysis* (x). Data from *Tables 1* and *2*. A ●; B ★; 1c ■; 1d ○; 1e +. The straight line represents the 100% correlation (slope = 1.0). The points are those for the corrected CI analysis.

Discussion. – The main argument advanced against the concerted mechanisms for aromatization of 1,4-cyclohexadienes was that the observed *cis/trans* rate ratio of 20 for **2** and **3** *(Scheme 3)* was due to steric effects [9]. In the light of our results, this argument is no longer valid. However, even if the reaction is stereospecific, this does not constitute proof for concertedness. Dehydrogenation could as well proceed stepwise; an intermediate ion-pair would also account for the observed stereospecificity [9]. We believe that the ion-pair mechanism does not satisfactorily explain the enhanced rates of 1,4-cyclohexadienes in comparison to other 1,4-dienes incapable of forming stable oxidation products, *i.e.* 1,4-pentadiene, 1,4-cycloheptadiene and **4**. The latter reacts 440 times slower than **1**. The difference should not be ascribed to steric hindrance alone, since introduction of a 1,1-dimethyl substitution in 1,2-dihydronaphthalene (**10**) reduces the rate only by a factor of 1.4 *(Scheme 3)*. We would expect steric hindrance to be more important in the naphthalene derivative **11** than in the cyclohexadiene **4**, because the hindering groups are closer to the reactive centre in **11**. Therefore the concerted mechanisms, although not proven, corresponds better with the experimental results than the stepwise process. Recently *Fleming* reported unpublished data in favour of full *cis*-stereospecific aromatization of **1b** with DDQ [25], but also presented evidence for a stepwise process in aromatization of a 3-trimethylsilyl-substituted 1,4-cyclohexadiene with DDQ where a 1,2-shift of the silyl group occurs.

We have attempted to obtain direct evidence for concertedness of the reaction, but so far without success. The high kinetic isotope effect of *ca.* 10 for perdeuterated 1,4-cyclohexadiene [8] and 1,4-dihydronaphthalene [26] could be taken as an indication for

Scheme 3



a) [4]. b) Extrapolated from chloranil, 100° [24]. c) [10].

a quasi-simultaneous breakage of two C–H bonds, but the argument is unconvincing in the light of isotope effects of 10 for hydride transfer from triphenylmethane dyes to quinones [27]. Some variations for isotope effects were found for **1a** and **1b**, but they are too small to allow definitive conclusions. The site of H-incorporation in the quinone should be significant with respect to concertedness of the reaction [4][28]. Transfer to the O- or C-atom is consistent with any of the mechanisms of *Scheme 1*, but with mechanism *C* transfer to C-atom *must* occur for reasons of conservation of orbital symmetry [4]. In the case of *N*-methylacridan, hydride is transferred to an O-atom of the quinone [28]. When (D_4)-1,4-cyclohexadiene (**1**) in (D_8)dioxane was heated to 180° with naphthoquinone in an NMR tube and the reaction examined at intervals by ^{1}H- and ^{2}H-NMR some evidence for initial transfer of D^- to O, followed by equilibration between O and C was obtained, but it was not entirely conclusive owing to partial decomposition of the hydroquinone. We are therefore forced to the conclusion that although the concerted mechanisms *C* and *D* are consistent with the experimental facts, concertedness is not definitely established, and although the cyclic mechanism *C* appears less likely than *D* it cannot be ruled out completely.

The stereochemical result should be appreciated in the context of other 1,4-eliminations on cyclohexenes and cyclohexadienes. There is evidence that concerted 1,4-eliminations occur predominantly or exclusively with *cis*-stereospecificity [29] in these systems. In the case of an elimination proceeding *via* an E_1cB mechanism it was found that even unconcerted eliminations may be stereospecific [30] while solvolytic eliminations with cyclohexene derivatives proceeding *via* allylic carbenium ions are non-stereospecific [29]. Unfortunately, no solvolytic eliminations with cyclohexadienyl derivatives have been investigated, so that direct comparison with the DDQ-promoted aromatization is not possible.

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Experimental Part

General. See [31]. GC/MS analyses were carried out with a *Finnigan 4000* spectrometer using a 2 m 3% *GESE-30* packed column. An isothermal temperature of 50° was used. All EI spectra were recorded at 70 eV and CI studies were operated with a reactant gas pressure of 0.30 Torr.

Synthesis of Deuterated 1,4-Cyclohexadienes. – trans-*3,4-Dichlorocyclobutene* (**5a**) [20]. To the *cis*-isomer **5** (6.2 g, 50 mmol) was added at 0° under Ar a catalytic quantity of $AlCl_3$. The blue solution was stirred during 2 h. It was decomposed by addition of Ph_3P, until the colour changed to yellow. Flash distillation afforded pure **5a** (3.7 g, 60%). The distillation residue contained polymeric material.

(Z, E)-*and* (E, E)-*1,4-Dichlorobutadiene* (**6** and **6a**). *cis*-3,4-Dichlorocyclobutene (**5**) (6.4 g, 52 mmol) was heated in triglyme (10 ml) under Ar to 180° for 36 h. After completion of the reaction, the diene **6** (35 mmol, 67%) was separated by flash distillation. The ^{1}H-NMR of **6** was identical with that described in [15] [32]. The *trans*-isomer **5a** (3.7 g, 30 mmol) in dioxane was heated to 90° during 1.5 h. The crude product **6a** was used without purification for the next step. The ^{1}H-NMR of **6a** was identical to the spectrum reported [15] [32] and showed no contamination with **5a** and **6**.

Deuterated Butadienes by Reaction of Halogenobutadienes. Reductions were carried out with Zn/Cu-couple, prepared according to *Stephenson et al.* [17], and with the reduction procedure of *Craig & Fowler* [16] also applied by *Stephenson et al.* The same method was used for preparation of (1,1-D_2butadiene from the dibromo-derivative [33] and (1-D)butadiene from 1-chlorobutadiene [34]. (1,1,4,4-D_4)butadiene was prepared by base-catalyzed H/D-exchange of sulfolene [35] followed by pyrolysis at 160° in triglyme [19].

Deuterated Cyclohexadienes (**1**). The deuteriobutadienes reacted with fumaroyl chloride to afford the stereoisomeric cyclohexene derivatives of structure **8** [19]. Hydrolysis followed by oxidative bis-decarboxylation led to the various cyclohexadienes [19]. Their isotopic composition is given in *Table 1*, and the stereochemical purity of the samples enriched in **1a** (sample A) and **1b** (sample B) is discussed in the text.

Pyrolysis of Deuterated Cyclohexadienes (1) to Benzene (9). – The diene (5 µl) is placed at the entrance of a quartz pyrolysis tube (volume of the heated zone 62.8 cm^3) heated to 400°. The sample is swept through the hot tube by means of a slow stream of Ar. The pyrolysis products are collected at −78°, diluted with Et_2O and analyzed by GC/MS. Under these conditions conversion is 100%.

Aromatization of Deuterated Cyclohexadienes with DDQ. – The diene (3–4 mg) in dioxane (1 ml) was saturated with DDQ, then allowed to stand in the dark overnight. After centrifugation the liquid fraction was submitted to GC/MS analysis.

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