# STEREOSELECTIVE H₂O ELIMINATIONS IN 3- AND 4-ARYLCYCLOHEXANOLS UNDER ELECTRON IMPACT

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Abstract—The elimination of  $H_2O$  from the molecular ions of *trans*-4- and *trans*-3-arylcyclohexanols takes place to a greater extent than in the corresponding *cis* isomers. The remarkable differences in abundance, taken together with substituent effects and the results of deuterium labelling, show that configuration is retained in the molecular ions which undergo the elimination, and that this process is a *cis*-1,4 and *cis*-1,3 elimination in the *trans*-4- and *trans*-3-arylcyclohexanols, respectively. Possible mechanisms for the elimination in the *cis* isomers are discussed.

## INTRODUCTION

THE STERIC course of elimination of  $H_2O$  from the molecular ions of cyclohexanol and some substituted analogues has been studied in several laboratories. The 1,4 elimination is highly stereospecific, involving the *cis*-4-hydrogen atom.<sup>1</sup> This has been shown by the examination of stereospecifically deuterium labelled cyclohexanols.<sup>1</sup> The great difference between the mass spectra of stereoisomeric 4-*t*-butylcyclohexanols (both under electron impact and photoionization) is due to the stereospecific nature of this elimination.<sup>1-4</sup> On the other hand, the 1,3 elimination is nonstereospecific and it is consequently suggested to be preceded by ring opening of the molecular ion,<sup>1</sup> in contrast to the retention of configuration of the molecular ions of cyclohexanol which undergo the 1,4 elimination.

The difference between the mechanisms of the 1,3 and 1,4 eliminations of H<sub>2</sub>O has been suggested to stem from the ground state distance between hydroxyl oxygen and the 4- vs 3-H atom. In the twisted-boat conformation the distance of  $\sim 1.7$  Å between the oxygen and the *cis*-4-H atom allows the formation of a cyclic transition state for the elimination. The distance to the 3-H atom is larger ( $\sim 2.3$  Å) and, consequently, the 1,3 elimination occurs after ring opening.

Stereoisomeric 3-alkylcyclohexanols exhibit smaller differences in the elimination of  $H_2O$  than the 4-analogues.<sup>2,4–6</sup> In the case of 3-methylcyclohexanols, it has been shown that despite the similarity in the mass spectra of the stereoisomers, deuterium labelled analogues exhibit a partially stereospecific 1,3 elimination.<sup>4</sup> Stereospecific 1,3 elimination has also been reported in some polycyclic systems.<sup>7,8</sup> The apparently one-step 1,3 elimination in these cases has been attributed to the lower energy of activation for such a process when the cyclic transition state involves a tertiary hydrogen atom, despite the relatively large ground state distance between the relevant atoms.<sup>1,7</sup>

In the course of our studies of stereospecific eliminations involving activated hydrogen atoms,<sup>9-15</sup> it was of interest to examine the effect of configuration on the H<sub>2</sub>O elimination in stereoisomeric arylcyclohexanols. Two contrasting effects can be expected to be imposed by the aryl substituents. The tertiary hydrogen atom now has a benzylic character and may be expected to be more mobile in the elimination process, thus accelerating the process for the *trans* isomers and increasing the degree

of stereoselectivity. On the other hand, arylalkyl compounds may undergo rearrangements under electron impact through tropylium-type intermediates, which could lead to common structures from the *cis* and *trans* isomers, thus giving rise to similar mass spectra.

# 4-Arylcyclohexanols

Data listed in Table 1 (see also Figs. 1 and 2) show that elimination of  $H_2O$  from 4-arylcyclohexanols (1-5) is stereoselective, occurring to a greater extent in the



FIG. 1. Mass spectra of trans- and cis-4-p-nitrophenylcyclohexanols (1t and 1c).

trans isomers. The relative abundances column in Table 1 shows that the  $[M - H_2O]^{+}$  ions give rise to the most abundant peaks ('base peaks') in the mass spectra of the *trans* alcohols (with the exception of 5t) in contrast to the *cis*-analogues. It is evident from the values of the abundance ratios  $[M - H_2O]^{+}/[M]^{+}$  that there is a strong substituent effect in the elimination of water from the molecular ions of the *trans* isomers, accelerating it with the increase of the electron-withdrawing character of the substituent. No significant substituent effect is observed in the elimination of water from the *cis* isomers.

The above results show clearly that the molecular ions of the stereoisomeric 4-arylcyclohexanols (1-5) do not undergo rearrangement to common structures prior to the elimination of water and that the elimination takes place by different mechanisms in the stereoisomers. The higher abundances of  $[M - H_2O]^{+}$  in the mass spectra of the *trans* alcohols suggest that this process is a 1,4 elimination in these isomers, involving the benzylic 4-hydrogen atom. The substituent effect observed in the *trans* isomers strongly supports this suggestion. The positive effect (linear



FIG. 2. Mass spectra of trans- and cis-4-phenylcyclohexanols (2t and 2c).



correlation with  $[\sigma]^+$ , see Fig. 3) indicates that there is a decrease in the positive charge density of the aromatic region in the transition state for the elimination. The lower abundances of  $[M - H_2O]^+$  ions and the lack of substituent effect in the *cis* isomers indicates that they undergo  $H_2O$  elimination by a mechanism which does not involve the benzylic hydrogen.

Deuterium labelling experiments, summarized in Table 2, prove the above conclusions for the *trans* isomers. Both *cis*- and *trans*-4-phenylcyclohexanols (2c and 2t) exhibit ~15% of 1,2 elimination, which can be attributed to thermal dehydration. Practically all the electron impact induced dehydration of the *trans* isomer 2t involves the 4-benzylic hydrogen. A similar result is observed in the case of *trans*-4-*p*-nitrophenylcyclohexanol (85% of  $[M - HOD]^+$  from the 4-*d*<sub>1</sub>-analogue). The *cis* isomers apparently undergo this elimination by more than one mechanism. The partial involvement of the 4-benzylic hydrogen in both 4-*d*<sub>1</sub>-4-*cis*-phenylcyclohexanol (33 and 24%, respectively) indicates ring opening prior to the elimination. A simple mechanistic description of these

			% Σ40		Relative :	abundance	[M—H	Ratio	
	Compound	Х	cis	trans	cis	trans	cis	trans	trans/cisª
ОН									
$\sim$	1	$NO_2$	2.5	14·8	29.4	100	<b>0</b> ∙45	123	270
	2	Н	4.3	14.2	21.4	100	0.56	18.7	33-4
$\rightarrow$	3	CH₃	3.0	12.3	21.4	100	<b>0</b> ·42	4.9	11.7
	4	$OCH_3$	5.5	13.7	47.7	100	0.51	1.7	3.3
	5	$\mathbf{NH}_{2}$	3.9	5.9	16.7	29.2	0.31	0∙45	1.5
x									
<u> </u>	OH 6	$NO_2$	5.9	15.6	85.7	100	1.35	22.4	16.6
	7	н	3.6	13.7	28.0	100	0.48	15.4	32.1
X	8	CH3	3.1	13.2	34.8	100	0.44	5.0	11.4
	9	OCH <sub>3</sub>	5.2	12.9	31.3	100	0.49	2.1	4-3
$\mathbf{\mathbf{Y}}$	10	NH <sub>2</sub>	3.7	7.8	19-3	44.4	0.28	0.60	2.1
Х									

Table 1. Abundance data for the elimination of  $\mathrm{H_2O}$  from 4- and 3-arylcyclohexanols

<sup>a</sup> { $[M-H_2O]^+$ ,  $[M]^+$ }<sub>trans</sub>/{ $[M-H_2O]^+$ ,  $[M]^+$ }<sub>cis</sub>.



FIG. 3. Log  $Z/Z_0(Z = [M - H_2O]^+/[M]^+, Z_0 = Z$  for the unsubstituted phenyl-cyclohexanol)<sup>2</sup> vs  $[\sigma]^+$  for stereoisomeric 4-arylcyclohexanols:  $\bigcirc$ -trans,  $\square$ -cis isomers.

Compound	% [M − H₂O]+·	% [M – DOH]+·		
2,2,6,6-d <sub>4</sub> -cis-4-Phenylcyclohexanol	85	15		
2,2,6,6-d <sub>4</sub> -trans-4-Phenylcyclohexanol	87	13		
4-d <sub>1</sub> -cis-4-Phenylcyclohexanol	67	33		
4-d <sub>1</sub> -trans-4-Phenylcyclohexanol	16	84		
4-d <sub>1</sub> -cis-4-p-Nitrophenylcyclohexanol	76	24		
4-d1-trans-4-p-Nitrophenylcyclohexanol	15	85		

Table 2. Loss of  $H_2O$  and DOH from molecular ions of deuterium labelled 4-arylcyclohexanols

processes is given in Scheme 1. In intermediate a the benzylic hydrogen as well as



the 3-hydrogens are activated and may be expected to be transferred to the oxygen atom in the course of  $H_2O$  elimination.

# 3-Arylcyclohexanols

Data listed in Table 1 (see also Fig 4 and 5) for 3-arylcyclohexanols (6-10) show that these compounds undergo elimination of  $H_2O$  under electron impact in a similar way to the 4-arylcyclohexanols. With the exception of the 3-*p*-nitrophenylcyclohexanols (6), even the values of the abundance ratios  $[M - H_2O]^+/[M]^+$ are of the same order of magnitude. In all cases the *trans* isomers have a larger  $[M - H_2O]^+/[M]^+$  ratio which is subject to a strong substituent effect (linear correlation with  $[\sigma]^+$ , see Fig. 6). This similar behaviour indicates that the elimination of water in the *trans*-3-arylcyclohexanols takes place via a true (i.e. not preceded by a ring opening) 1,3 elimination involving the 3-benzylic hydrogen atom.

This conclusion is confirmed by the examination of deuterium labelled 3phenylcyclohexanols (see Table 3). Here again all the electron impact dehydration (85%) of the total) of the *trans* alcohol involves the benzylic hydrogen atom. The surprising point is the dehydration of the *cis* isomer, which does not involve the 3-hydrogen, in contrast to the 4-arylcyclohexanols where a partial involvement was observed. This result may perhaps indicate that the *cis*-3-arylcyclohexanols undergo



FIG. 4. Mass spectra of trans- and cis-3-p-nitrophenylcyclohexanols (5t and 5c).

a cis-1,4 elimination (ion e in Scheme 2). Partial elimination which involves a ring opening (four possibilities) cannot be eliminated, although two such ions (h and i) would require a partial involvement of the benzylic 3-hydrogen (similar to the cis-4-arylcyclohexanols, transition states a and b in Scheme 1).

It has been noted before that, despite the occurrence of a *cis*-1,3 elimination (as evidenced by deuterium labelling), the mass spectra of stereoisomeric 3-alkylcyclohexanols exhibit relatively small differences if any. It is noteworthy that the stereoisomeric 3-arylcyclohexanols give rise to different mass spectra, which parallel the behaviour of 4-arylcyclohexanols both qualitatively and quantitatively. Evidently the benzylic nature of the 3-hydrogen atom is responsible for this remarkable difference between the 3-alkyl and 3-arylcyclohexanols.

All the mass spectral data presented in this paper have been obtained at 70 eV. Similar stereoselectivity has been observed also at low electron energies. Substituent effects showed similar trends at low voltages, but correlation was difficult because of different ionization potentials and activation energies for the differently substituted compounds.

#### **Synthesis**

Phenyl-, p-nitrophenyl- and p-aminophenylcyclohexanols 1, 2, 5, 6, 7 and 10 were prepared by route shown in Scheme 3. The p-tolyl- and p-methoxyphenylcyclohexanols 3, 4, 8 and 9 were synthesized by a series of reactions as shown in Scheme 4.

Separation of stereoisomers was achieved by column chromatography, preparative t.l.c. or gas chromatography. Configuration was assigned by n.m.r. spectroscopy



FIG. 5. Mass spectra of trans- and cis-3-phenylcyclohexanols (6t and 6c).



FIG. 6.  $\lg Z/Z_0 (Z = [M - H_2O]^{+}/[M]^{+})$  vs  $[\sigma]^+$  for stereoisomeric 3-arylcyclohexanol  $\bigcirc$  trans-,  $\Box$ -cisisomers.

TABLE 3.	Тне	LOSS	OF	H <sub>2</sub> O	AND	DOH	FROM	THE	MOLECULAR	IONS	OF	3-PHENY	L-
CYCLOHEXANOLS													

	Compound	% $[M - H_2O]^+$ .	% [M – DO	H]+·
	2,2,6,6-d <sub>4</sub> -cis-3-Phenylcyclohexanol 2,2,6,6-d <sub>4</sub> -trans-3-Phenylcyclohexanol 3-d <sub>1</sub> -cis-3-Phenylcyclohexanol 3-d <sub>1</sub> -trans-3-Phenylcyclohexanol	82 84 97 15	18 16 3 85	
6t-10t	$\rightarrow \boxed{ \begin{array}{c} H \\ H \\ Ar \\ d \end{array}}^{+} \longrightarrow [M - H_2]$	O]+.	С	is-1,3 elimination
	$\begin{bmatrix} Ar & & \\ H & & \\ H & & \\ H & & \\ H & & \\ C &$	O]+.	с	is-1,4 elimination
	$ \begin{array}{c} Ar \xrightarrow{} OH \\ & & & \\ H \end{array} \longrightarrow \begin{bmatrix} M - \\ H \end{bmatrix} $	H <sub>2</sub> O] <sup>+-</sup>	1	,3 elimination
6	$ac-10c \rightarrow Ar \rightarrow H$	→ [M−H <sub>2</sub> O] <sup>+.</sup>	1	,3 or 1,4 elimination
	Ar - H + Ar - h	$\left( \begin{array}{c} H \\ H \end{array} \right)^{\circ} H \longrightarrow I$	$[M-H_2O]^{+}$ t	hould involve also he benzylic hydrogen
	$\begin{array}{c} \text{OH} \\ & & \text{OH} \\ & & & \text{OH} \\ & & & \text{OH} \\ & & & \text{H}_2/\text{RaNi} \\ & & & \text{R}_1 \\ & & & \text{R}_2 \end{array}$	EME 2 (1) $Ac_20/Pyr$ (2) $Cu(NO_3)_2 - Ac_20$		2
11 H 12 H	$R_1 = C_6H_5, R_2 = H$ $R_1 = C_6H_5, R_2 = H$ $R_1 = C_6H_5;$ $R_1 = H; R_2$	$R_{i} = H(c + t)$ $= C_{6}H_{5}(c + t)$ (1) H <sub>2</sub> /RaNi (2) OH <sup></sup>	<b>15</b> $R_1 = p - NO_2$ <b>16</b> $R_1 = H; R_2$	$C_6H_4; R_2 = H_2 = p - NO_2C_6H_4$
	1	<b>5</b> $(c+t)$ <u>H<sub>2</sub>/RaNi</u> <b>0</b> $(c+t)$	$     \downarrow     1 (c+t)     6 (c+t) $	

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SCHEME 4

and by the comparison of the retention times in gas chromatography. In n.m.r. spectra use was made of the higher field absorption of axial carbinol protons. The retention times in g.c. were longer for those compounds which had both substituents in equatorial conformation (*trans*-4-aryl and *cis*-3-arylcyclohexanols).<sup>16</sup> In all cases both methods led to identical assignments. It is worth mentioning that the diequatorial compounds (*cis*-1,3- and *trans*-1,4-arylcyclohexanols) had higher melting points.

Deuterium labelling at positions 2 and 6 was achieved by acid-catalysed exchange of the  $\alpha$ -H atoms in 4-phenylcyclohexanone (by DCL + D<sub>3</sub>PO<sub>4</sub><sup>17</sup>), followed by reduction. Deuterium labelling at position 4 was accomplished by a strong basecatalysed exchange (heating with sodium hydride in dimethyl sulphoxide- $d_6$ ).<sup>18</sup>

#### EXPERIMENTAL

Mass spectra were measured with an Atlas CH 4 mass spectrometer fitted with an EB-4 ion source and direct inlet system, operated without heating. The measurements were made as soon as possible after the sample had been introduced into the ion source.

The n.m.r. spectra were measured with a Varian T-60 spectrometer in  $CDCl_3$  with TMS as internal reference compound.

Gas chromatographic analyses and collections were performed on a Varian Aerograph 90-P instrument using 3% SE-30 or 3% XE-60 columns on Chromosorb Q ( $1.8 \text{ m} \times 1/4 \text{ in}$ ).

#### Materials

4-Phenylcyclohexanols (2c and 2t) and 3-phenylcyclohexanols (7c and 7t). These compounds were prepared by hydrogenation of p- and m-phenylphenol on RaNi W-2 (2-3 week old) in dry methanol at 100 °C and 150 atm. of H<sub>2</sub>.<sup>19</sup> Stereoisomers were separated by careful chromatography on a Florisil column (60:1 to material ratio) with hexane + chloroform 235:15 v/v.

2c, m.p. 74-76 °C (pentane) (Lit.19 76-77 °C); n.m.r. (carbinol-H), 4.15 ppm.

2t, m.p. 115-117 °C (pentane) (Lit.<sup>19</sup> 119-120°C); n.m.r. (carbinol-H), 3.65 ppm.

7c, m.p. 76-78 °C (pentane) (Lit.20 79-80 °C); n.m.r. (carbinol-H), 3.8 ppm.

7t, m.p. 62-63 °C (pentane) (Lit.<sup>20</sup> 63-64 °C); n.m.r. (carbinol-H), 4.3 ppm.

p-Nitrophenylcyclohexanols (1c, 1t, 6c and 6t). The corresponding phenylcyclohexanol was acetylated by acetic anhydride in pyridine (yields 80-97%). The acetate (0.5 mmol) dissolved in acetic anhydride (6 ml) was treated with cupric nitrate (Cu(NO<sub>2</sub>)<sub>2</sub>4H<sub>2</sub>O, 500 mg) at 0 °C. After stirring at room temp. for 45 min the mixture was treated with water until acetic anhydride was hydrolysed and extracted with chloroform. The organic solution was washed with Na<sub>2</sub>CO<sub>3</sub> solution

and water, dried and evaporated off. The resulting oil yielded the corresponding p-nitrophenylcyclohexyl acetate after chromatography on neutral alumina.

cis-4-p-nitrophenylcyclohexylacetate (15c), m.p. 44.46 °C (hexane); anal.: found N, 5.31%, calc. N, 5.32%; n.m.r. (carbinol-H) 5.1 ppm; yield, 38%.

trans-4-p-nitrophenylcyclohexylacetate (15t), m.p. 126–128 °C (hexane); anal.: found N, 5·45%, calc. N, 5·32%; n.m.r. (carbinol-H), 4·8 ppm; yield, 41%.

cis-3-p-nitrophenylcyclohexylacetate (16c), m.p. 63-65 °C (pentane); anal.: found N, 5.62%, calc. N, 5.32%; n.m.r. (carbinol-H), 4.8 ppm; yield, 52%.

trans-3-p-nitrophenylcyclohexyl acetate, (16t), m.p. 57-59 °C (pentane); anal.: found N, 5.24%, calc. N, 5.32%; n.m.r. (carbinol-H), 5.1 ppm; yield, 35%.

Hydrolysis of the nitrophenylcyclohexyl acetates by NaOH 10% in aqueous methanol (2 h reflux under  $N_2$ ) yielded the corresponding nitrophenylcyclohexanols.

*cis*-4-*p*-nitrophenylcyclohexanol, (1*c*), m.p. 89-91 °C (hexane + methylene chloride); anal.: found N, 6·21 %, calc. N, 6·33 %; n.m.r. (carbinol-H), 4·2 ppm; yield, 75 %.

*trans*-4-*p*-nitrophenylcyclohexanol (1*t*), m.p. 94–96 °C (hexane + methylene chloride); anal.: found N, 6·21 %, calc. N, 6·33 %, n.m.r. (carbinol-H), 3·7 ppm; yield, 62%.

cis-3-p-nitrophenylcyclohexanol (6c) m.p.  $105-107 \,^{\circ}C$  (hexane + methylene chloride); anal.: N, 6.47%, calc. 6.33%; n.m.r. (carbinol-H) 3.7 ppm; yield, 65%.

trans-3-p-nitrophenylcyclohexanol (6t) m.p. 79-81 °C (hexane); n.m.r. 4.35 ppm; yield, 73%.

p-Aminophenylcyclohexanols (5 and 10). Hydrogenation of p-nitrophenylcyclohexyl acetates 15 and 16 at atm. pressure on Pd + C 10% yielded the corresponding p-aminophenylcyclohexyl acetates. Hydrolysis with NaOH 10% in aqueous methanol (2 h reflux under  $N_2$ ) gave the corresponding p-aminophenylcyclohexanols.

cis-4-p-aminophenylcyclohexanol (5c), m.p. 139-141 °C (benzene); anal.: found N, 7.32%, calc. N, 7.32%; n.m.r. (carbinol-H), 4.15 ppm.

trans-4-p-aminophenylcyclohexanol (5t), m.p. 196-198 °C (benzene); anal.: found N, 7.42%, calc. N, 7.32%; n.m.r. (carbinol-H), 3.65 ppm.

cis-3-p-aminophenylcyclohexanol (10c) m.p. 122-124 °C (benzene); anal.: found N, 7.52%, calc. N, 7.32%; n.m.r. (carbinol-H), 3.65 ppm.

trans-3-p-aminophenylcyclohexanol (10t), m.p. 101-103 °C (hexane); anal.: found N, 7.40%, calc. N, 7.32%; n.m.r. (carbinol-H), 4.25 ppm.

p-Tolylcyclohexanols (3 and 8) and p-anisylcyclohexanols (4 and 9). Ether solution (5 ml) of cyclohexan-1,4- or 1,3-dione monoethylene ketal (1 mmol, prepared from the corresponding diones with ethylene glycol in benzene and p-toluenesulphonic acid<sup>21</sup>) was added to a cooled ether solution of the appropriate arylmagnesium bromide (10 mmol). After reflux for several h water was added, the ether solution was separated, dried and evaporated off. The residual oil was hydrogenated in methanol (30 ml) at room temp. and atm. pressure on Pd + C 30% (20 mg) until the calculated volume of H<sub>2</sub> was absorbed (several h to several days, dependent on the quality of the catalyst). The resulting ketals were hydrolysed to the corresponding arylcyclohexanones in 10% HCl (5 ml) and THF (30 ml) at room temp. or by refluxing in acetone containing p-toluenesulphonic acid. The crude arylcyclohexanones were hydrogenated in methanol (30 ml) at room temp. or by refluxing in acetone containing p-toluenesulphonic acid. The crude arylcyclohexanones were hydrogenated in methanol (30 ml) at room temp. or by refluxing in acetone containing p-toluenesulphonic acid. The crude arylcyclohexanones were hydrogenated in methanol (30 ml) at room temp. and atm. pressure on RaNi. The resulting stereoisomeric alcohols were separated by preparative t.l.c. on 1 mm thick alumina 20 × 20 cm plates.

cis-4-p-tolylcyclohexanol (3c), m.p. 59-61 °C (pentane); anal.: found C, 81.75, H, 9.09%, calc. C, 82.06, H, 9.54%; n.m.r. (carbinol-H), 4.15 ppm.

*trans*-4-*p*-tolylcyclohexanol (3*t*), m.p. 108–110 °C (pentane); anal.: found C, 81·83, H, 9·10%, calc. C, 82·06, H, 9·54%; n.m.r. (carbinol-H), 3·65 ppm.

cis-4-p-anisylcyclohexanol (4c), m.p. 62-64 °C (pentane) (Lit.<sup>22</sup> 65-66 °C); n.m.r. (carbinol-H), 4·15 ppm.

*trans*-4-*p*-anixylcyclohexanol (4*t*), m.p. 141–142·5 °C (hexane + methylene chloride) (Lit.<sup>22</sup> 140–141 °C); n.m.r. (carbinol-H), 3·65 ppm.

cis-3-p-tolylcyclohexanol (8c), m.p. 72-74 °C (pentane); anal.: found C, 81.96, H, 9.41%, calc. C, 82.06, H, 9.54%, n.m.r. (carbinol-H), 3.8 ppm.

trans-3-p-tolylcyclohexanol (8t), m.p. 67-69 °C (pentane); anal.: found C, 82·12, H, 10.00%, calc. C, 82·06, H, 9·54%; n.m.r. (carbinol-H), 4·3 ppm.

*cis*-3-*p*-anisylcyclohexanol (9*c*), m.p. 80–82 °C (hexane); anal.: found C, 75.52, H, 9.01%, calc. C, 75.69, H, 8.80%; n.m.r. (carbinol-H), 3.75 ppm.

trans-3-p-anisylcyclohexanol (9t), m.p. 80-82 °C (hexane); anal.: found C, 76.07, H, 8.98%, calc. C, 75.69, H, 8.80%, n.m.r. (carbinol-H), 4.25 ppm.

2,2,6,6-d<sub>4</sub>-*Phenylcyclohexanols*. The corresponding 3- or 4-phenylcyclohexanone was treated with DCl–D<sub>8</sub>PO<sub>4</sub> (prepared from phosphorus pentoxide and D<sub>2</sub>O<sup>17</sup>) at room temp. three times. The resulting 2,2,6,6-d<sub>4</sub>-phenylcyclohexanones were reduced with lithiumaluminium hydride. Stereo-isomeric alcohols were separated by preparative t.l.c. on 1 mm thick 20 × 20 cm alumina plates (eluent chloroform benzene 2:3 v/v). The isotopic compositions were measured from the mass spectra.

2,2,6,6- $d_4$ -4-phenylcyclohexanols,  $d_4$ , 75%,  $d_3$ , 23%;  $d_2$ , 2%.

2,2,6,6- $d_4$ -3-phenylcyclohexanols,  $d_4$ , 80%;  $d_3$ , 17%;  $d_2$ , 3%.

4-d<sub>1</sub>-4-*Phenylcyclohexanols and* 3-d<sub>1</sub>-3-*phenylcyclohexanols.* The exchange of the benzylic hydrogen was achieved by heating of the mixtures of stereoisomers (200 mg) in dry hexadeuterodimethyl sulphoxide (1 ml) with sodium hydride (70 mg) for 24 h at 165–170 °C.<sup>18</sup> Addition of D<sub>2</sub>O (1 ml), extraction with benzene, drying and solvent evaporation yielded mixtures of the stereoisomers. After four such treatments the stereoisomers were separated by preparative t.l.c. The yields were low (40–50%) and the materials were also deuterated to some extent at the aromatic ring. The following isotopic compositions were found.

4- $d_1$ -cis-4-phenylcyclohexanol:  $d_0$ , 46%;  $d_1$ , 32%;  $d_2$  1%;  $d_3$ , 3%;  $d_4$ , 9%;  $d_5$ , 7%;  $d_6$ , 2%. 4- $d_1$ -trans-4-phenylcyclohexanol:  $d_0$ , 47%;  $d_1$ , 23%;  $d_2$ , 6%;  $d_3$ , 5%;  $d_4$ , 7%;  $d_5$ , 6%;  $d_6$ , 6%. 3- $d_1$ -cis-3-phenylcyclohexanol:  $d_0$ , 60%;  $d_1$ , 13%;  $d_2$ , 6%;  $d_3$ , 3%;  $d_4$ , 10%;  $d_5$ , 8%.

3- $d_1$ -trans-3-phenylcyclohexanol:  $d_0$ , 24%;  $d_1$ , 32%;  $d_2$ , 13%;  $d_3$ , 10%;  $d_4$ , 4%;  $d_5$ , 15%;  $d_6$ , 2%.

 $4-d_1-4-p-Nitrophenylcyclohexanols$ . The corresponding  $4-d_1-4-phenylcyclohexanols$  were nitrated with cupric nitrate in acetic anhydride as described above. No change in isotopic composition was observed.

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