The Substituent Effect in the Fragmentation of Phenylcyclohexanols

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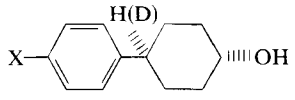
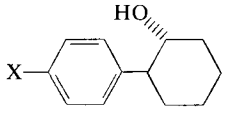
All the main fragmentation pathways undergone by *trans*-4- and *trans*-2-*p*-substituted phenylcyclohexanols have been studied, and the ionic abundances have been correlated with the σ constants. This analysis shows that electron withdrawing substituents, increasing the fraction of molecular ions having sufficient energy to decompose, favour all fragmentations. However, along with this 'non-specific' substituent effect, there is a 'specific' effect, in the opposite sense, increasing the formation of the $[M-59]^+$ and $[M-85]^+$ ions with increasing electron releasing power of the substituents. The loss of water, although it is almost exclusively a 1,4 elimination in the case of *trans* phenyl cyclohexanols, is not *specifically* influenced by the substituents.

The elimination of water from alcohols under electron impact is a long studied process. Acyclic and cyclic alcohols[1] have been subjected to extensive investigations. Stereochemical[2] and other subtle aspects[3] have been studied.

However, the influence of other functional groups or atoms on the abundance of the $[M-18]^+$ ions has not been investigated extensively. In order to investigate this, we have studied[4] the behaviour under electron impact of *p*-substituted phenylcyclohexanols. The publication of a study on the stereochemical aspects of this fragmentation in 4- and 3-phenylcyclohexanols[5] prompted us to record our conclusions, which differ from those reported in the abovementioned paper. Our work concerns a series (**1–13**) of *trans*-4- and 2-phenylcyclohexanols and some deuterated analogues (**1**-4-d_1, **2**-4-d_1, **7**-4-d_1).





1: X = H
1-4-d_1: X = H
2: X = NH_2
2-4-d_1: X = NH_2
3: X = OCH_3
4: X = OH
5: X = I
6: X = CN
7: X = NO_2
7-4-d_1: X = NO_2

8: X = H
9: X = NH_2
10: X = OCH_3
11: X = OH
12: X = I
13: X = NO_2

Mass spectra

The fragmentation of these *trans*-4-phenylcyclohexanols (Table 1) is similar to that of cyclohexanol.[6] Two main pathways are operative: (i) water elimination, followed by loss of methyl, ethyl or ethylene (losses supported by appropriate metastables); (ii) ring cleavage, with formation of the $[M-59]^+$, $[M-72]^+$ and $[M-85]^+$ ions.

The existence of these two paths is supported by the behaviour of the deuterated analogues **1**-4-d_1, **2**-4-d_1 and **7**-4-d_1. In their spectra (see Table 2) there is an almost exclusive loss of DHO, whereas the peaks due to the ring cleavage appear as doublets in all compounds considered. Additionally, the signals corresponding to losses of methyl, ethyl or ethylene from $[M-DHO]^+$ are single peaks, thus indicating their unique origin. The pre-eminent participation of benzylic hydrogen in this process is also demonstrated by a lower $[M-H_2O]^+/[M]^+$ intensity ratio in the spectrum of *cis*-4-phenylcyclohexanol, compared with the *trans* isomer. The occurrence almost exclusively of 1,4 elimination, which is different to the behaviour of cyclohexanol,[6] may be related to the tertiary (and/or benzylic) nature of the hydrogen atom. This also appears to be the lowest energy process: at 12 eV (nominal) only the $[M]^+$ and $[M-H_2O]^+$ ions are detectable.

The relative intensities of the same fragment ions in the *trans*-2-phenylcyclohexanols (Table 1) are very different. Elimination of water is an unimportant process here and does not predominate at low eV. The $[M-85]^+$ ions are more important, and their formation from $[M]^+$ is in some instances supported by appropriate metastables.

Substituent effect

The abundances of some of the abovementioned ions in each series, when treated according to the 'kinetic'[7] and the 'Chin and Harrison'[8] methods, show correlations with σ_{IP}[9] and σ_p^+, respectively. However, in several cases the slopes (corresponding to ρ) for the same process are *positive* in the 'kinetic' treatment and *negative* in the Chin and Harrison treatment (see Table 3).

It has been stated[10] that two different aspects of the substituent effect must be considered: (i) effect on the internal distribution of energy in the decomposing parent (molecular) ion and (ii) effect on the rate of the process considered.

Of course, the overall substituent effect is the result

Table 1[a]. Principal ions in the fragmentation of *trans*-4-(*p*-substituted) phenylcyclohexanols, *trans*-2-(*p*-substituted) phenylcyclohexanols and *cis*-4-phenylcyclohexanol

Compound		$[M]^{\ddagger}$	$[M-18]^{\ddagger}$	$[M-33]^{+}$	$[M-46]^{\ddagger}$	$[M-47]^{+}$	$[M-59]^{+}$	$[M-72]^{\ddagger}$	$[M-85]^{+}$	Other peaks (relative abundance ≥20%)			
trans-4-Phenyl-cyclohexanol	(1)	1.33	14.08	8.95	6.71	4.81	5.30	11.27	7.21	3.23	—	—	—
		(176)	(158)	(143)	(130)	(129)	(117)	(104)	(91)	(115)			
p-NH_2	(2)	10.91	6.13	3.06	0.86	1.47	21.45	8.58	5.76	5.76	—	—	—
		(191)	(173)	(158)	(145)	(144)	(132)	(119)	(106)	(133)			
p-OCH_3	(3)	9,06	16.27	7.22	2.23	2.76	8.14	7.48	3.94	3.94	3.94	—	—
		(206)	(188)	(173)	(160)	(159)	(147)	(134)	(121)	(148)	(91)		
p-OH	(4)	5.42	13.32	9.33	4.09	3.64	5.86	7.02	4.35	2.84	2.66	3.02	—
		(192)	(174)	(159)	(146)	(145)	(133)	(120)	(107)	(134)	(91)	(43)	
p-I	(5)	3.92	10.66	1.71	0.66	—	—	2.04	0.94	6.96	4.48	3.09	4.81
		(302)	(284)	(269)	(256)	(255)	(243)	(230)	(217)	(158)	(129)	(104)	(91)
p-CN	(6)	0.38	16.43	11.0	7.08	3.41	3.54	7.84	4.42	3.54	3.29	—	—
		(201)	(183)	(168)	(155)	(154)	(142)	(129)	(116)	(182)	(130)		
p-NO_2	(7)	0.16	13.27	4.17	1.14	—	—	1.90	0.63	3.41	4.30	3.27	4.17
		(221)	(203)	(188)	(175)	(174)	(162)	(149)	(136)	(116)	(107)	(91)	(77)
trans-2-Phenyl-cyclohexanol	(8)	11.93	1.92	1.38	5.75	3.09	5.64	6.18	13.31	6.92	2.77	—	—
		(176)	(158)	(143)	(130)	(129)	(117)	(104)	(91)	(92)	(57)		
p-NH_2	(9)	19.08	0.15	—	—	0.72	14.98	2.66	28.99	5.80	6.52	—	—
		(191)	(173)	(158)	(145)	(144)	(132)	(119)	(106)	(192)	(107)		
p-OCH_3	(10)	18.84	0.78	—	1.05	—	11.51	2.62	32.97	—	—	—	—
		(206)	(188)	(173)	(160)	(159)	(147)	(134)	(121)				
p-OH	(11)	16.27	0.59	—	1.76	0.99	10.20	3.53	30.59	—	—	—	—
		(192)	(174)	(159)	(146)	(145)	(133)	(120)	(107)				
p-I	(12)	21.93	0.71	—	—	—	—	2.50	7.84	4.99	6.06	—	—
		(302)	(284)	(269)	(256)	(255)	(243)	(230)	(217)	(116)	(91)		
p-NO_2	(13)	2.49	1.31	0.20	0.65	0.26	0.10	0.65	0.65	2.22	1.70	8.70	5.30
		(221)	(203)	(188)	(175)	(174)	(162)	(149)	(136)	(159)	(148)	(137)	(121)
cis-4-Phenyl-cyclohexanol		13.06	4.01	3.56	3.26	2.67	6.53	15.43	7.12	9.06	—	—	—
		(176)	(158)	(143)	(130)	(129)	(117)	(104)	(91)	(118)			

[a] Relative intensities are expressed as % of the total ion current; the corresponding *m/e* values are given in parentheses.

Table 2[a]. Principal ions in the fragmentation of *trans*-4-(*p*-substituted) phenylcyclohexanols-4-d_1

Compound	$[M]^{\ddagger}$	$[M-18]^{\ddagger b}$	$[M-19]^{\ddagger}$	$[M-34]^{+}$	$[M-47]^{\ddagger b}$	$[M-48]^{+}$	$[M-59]^{+b}$	$[M-60]^{+c}$	$[M-72]^{\ddagger b}$	$[M-73]^{\ddagger c}$	$[M-85]^{+b}$	$[M-86]^{+}$
trans-4-Phenyl-	13.6	8.1	100.0	60.0	50.0	27.3	22.5	11.1	30.8	12.0	21.5	22.7
cyclohexanol-4-d_1	2.17	1.28	15.91	9.65	7.96	4.34	3.60	1.77	4.90	1.91	3.42	3.65
(1-4-d_1)	(177)	(159)	(158)	(143)	(130)	(129)	(118)	(117)	(105)	(104)	(92)	(91)
	67.5	4.5	37.3	17.5	6.3	7.1	100.0	20.0	44.3	5.7	22.8	11.1
p-NH_2	9.67	0.64	5.35	2.50	0.91	1.02	14.33	2.86	6.35	0.82	3.27	1.59
(2-4-d_1)	(192)	(174)	(173)	(158)	(145)	(144)	(133)	(132)	(120)	(119)	(107)	(106)
	1.6	8.8	100.0	29.4	8.2				5.2	5.6		
p-NO_2	0.26	1.39	15.91	4.68	1.31	—	—	—	0.82	0.92	—	—
(7-4-d_1)	(222)	(204)	(203)	(188)	(175)	(174)	(163)	(162)	(150)	(149)	(173)	(136)

[a] Relative intensities are expressed as % of total ion current; the corresponding *m/e* values are given in parentheses.
[b] Relative intensities are corrected for the isotopic contribution of the preceding peak.
[c] Relative intensities are corrected for contribution of alternative fragmentations observed in the d_0-analogues.

Table 3. Peak intensities correlations in the fragmentation of *trans*-4- and 2-(*p*-substituted) phenylcyclohexanols

Fragment ion	Correlation coefficient	Log Z/Z_0 vs σ_{IP} ρ	eV	Comments[a]
trans-4-(*p*-Substituted) phenylcyclohexanols:				
$[M-18]^+$	0.99	1.15	20	
$[M-18]^+$	0.99	1.16	70	
$[M-33]^+$	0.97	1.17	20	
$[M-33]^+$	0.96	1.09	70	
$[M-46]^+$	0.97	1.60	20	n.c. NO_2
$[M-46]^+$	0.99	1.38	70	n.c. NO_2; I
$[M-47]^+$	0.97	1.25	20	
$[M-47]^+$	0.99	1.07	70	
$[M-59]^+$	0.92	0.70	70[d]	abs. NO_2; I
$[M-72]^+$	0.97	0.93	20	
$[M-72]^+$	0.90	0.81	70	
$[M-85]^+$	0.90	0.74	20	abs. NO_2
$[M-85]^+$	0.83	0.73	70	
trans-2-(*p*-Substituted) phenylcyclohexanols:[c]				
$[M-18]^+$	0.99	0.69	16	
$[M-18]^+$	0.97	0.72	70	
$[M-46]^+$	0.73	0.42	70[d]	
$[M-47]^+$	0.66	0.27	70[d]	
$[M-59]^+$	0.98	−0.35	16	abs. I
$[M-59]^+$	0.89	−0.55	70	n.c. I
$[M-85]^+$	0.64	0.15	70[d]	n.c. I

Fragment[b] ion	Correlation coefficient	$\text{Log}\frac{[A]}{[M_0]^+(1-f)}$ vs σ_p^+ Slope	eV	Comments[a]
trans-4-(*p*-Substituted) phenylcyclohexanols:				
$[M-18]^+$	0.76	0.15	20[e]	
$[M-59]^+$	0.82	−0.43	20	
$[M-59]^+$	0.84	−0.34	70	abs. NO_2; I
$[M-85]^+$	0.83	−0.24	20[e]	abs. NO_2
trans-2-(*p*-Substituted) phenylcyclohexanols:[f]				
$[M-59]^+$	0.97	−0.92	16	abs. I
$[M-59]^+$	0.97	−0.33	70	abs. NO_2; I
$[M-85]^+$	0.95	−0.33	70[d]	n.c. I

[a] abs. = the corresponding peak is absent in the spectrum. n.c. = the corresponding value has not been considered.
[b] correlation parameters for $[M-33]^+$, $[M-46]^+$, $[M-47]^+$, $[M-72]^+$ fragment ions are not given because they do not show any correlation (correlation coefficient lower than 0.60).
[c] Only processes showing significant correlations are considered.
[d] No correlation at 16 eV.
[e] No correlation at 70 eV.
[f] No correlation for $[M-H_2O]^+$.

of these two factors, which often work in opposite directions: electron withdrawing substituents enhance *any* fragmentation, that is, when the ionization potential increases the fraction of ions having sufficient energy to decompose also increases.[11] In terms of the 'kinetic' correlation[7] (if it exists) then ρ should be positive.

Correlations of this type, which are often observed, can be due to the well known correlation of the ionization potentials with σ_p^+.[12] In this respect it appears reasonable to use the σ_{IP}[9] values here.

In contrast, when a specific fragmentation leading to a certain ion *retaining the substituent* is considered, an electron withdrawing substituent ought to reduce the importance of this process, since it generally interacts more strongly with the positive charge in the daughter ion, as compared to the parent, so giving rise to a substituent effect on the rate of the process considered. In this connection a *negative* ρ value reflects a 'specific' substituent effect which means that the second of two factors mentioned above is pre-eminent with respect to the first.

As far as the Chin and Harrison method is concerned, the ratio considered

$$\frac{[A]^+}{[M_o]^+(1-f)} = f' \frac{k_1}{k_t}$$

reflects the abundance of a certain fragment ion with respect to the abundances of all fragment ions. In contrast to the 'kinetic' method, in which both terms of the ratio $(Z=[A]^+/[M]^+)$ considered vary considerably, here only the term $[A]^+$ varies to a great extent, while the term $[M_o]^+(1-f)$ can be considered roughly constant. Therefore, whereas the extent of total fragmentation (which depends on the internal distribution of energy in the molecular ion, that is on the ionization potential) strongly affects the result in the 'kinetic' method, it does not have the same influence in the Chin and Harrison method where the process leading to a single fragment assumes much more importance.

However, when more competitive pathways are influenced by the substituent, the term k_t includes other processes, whose rate can vary in the same direction. In these cases, as suggested by Brown,[13] an inversion of the sign in a slope of a certain fragmentation does not mean a different substituent effect: probably it simply means a weaker substituent effect. Therefore, it appears necessary to consider *all the main fragmentation pathways* in a spectrum and their relative importance, before drawing any conclusions.

The correlations presented in Table 3 can be discussed in terms of the above considerations. With one exception, *all* the fragmentation pathways show 'kinetic' correlations with positive ρ. Such trends are due to the internal distribution of energy of decomposing molecular ions and no effect on the rate of the single process is recognizable from them.

As far as the Chin and Harrison treatment is concerned, only the slopes for the $[M-59]^+$ and $[M-85]^+$ ions are negative in both series. This suggests a specific substituent effect, due to a strong stabilization effect on these ions (with respect to the molecular ions), exerted by electron releasing groups.

In the case of 2-substituted isomers, the $[M-59]^+$ ions exhibits the (negative) slope with the highest value: the corresponding ρ from the kinetic treatment is the only negative one. A strong 'negative' substituent effect is recognizable with both methods.

The slope from the Chin and Harrison method for the $[M-18]^+$ ions of the 4-phenylcyclohexanols, whose study was the main purpose of our work, shows a small positive value. As a first approximation we can conclude that there is not a sharp substituent effect on the water elimination. A more detailed analysis would suggest that the slight positive value of the slope is a result of the existence of two concurrent processes

($[M-59]^+$ and $[M-85]^+$) which have quite high negative slopes.

From this analysis, which includes all the main processes occurring, we are able to conclude that in phenylcyclohexanols a 'true' substituent effect is recognizable on the rates of the processes leading to $[M-59]^+$ and $[M-85]^+$ ions. Other paths are actually influenced by substituents, but this is a consequence of the different energy distribution in the molecular ions.

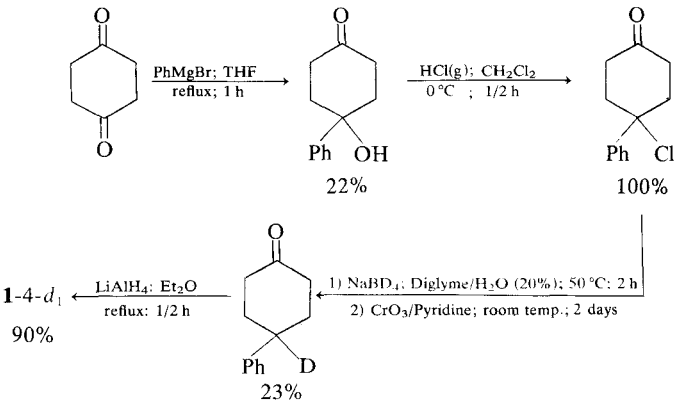
EXPERIMENTAL

Mass spectra were obtained using an A.E.I. MS-12 at 70, 20 and 16 eV, in each case choosing a value in which the fragmentation was simplified but still abundant enough to apply the Chin and Harrison method. The filament current was 100 μA; an all-glass heated inlet system was used for 2-phenylcyclohexanols and the direct inlet system for 4-phenylcyclohexanols; the source temperature was maintained at about 150 °C.

Normalization of mass spectra and calculation of metastable transitions were carried out on a UNIVAC 1108 computer. Correlations were made using the least squares method.

Samples

Compounds **7** and **13** were prepared by nitration of the acetoxy derivatives of *trans*-4-phenylcyclohexanol (**1**)[14] and *trans*-2-phenylcyclohexanol (**8**).[15] The nitro derivatives **7** and **13** were converted to products **2–6** and **9–12**, respectively, by standard methods. *cis*-4-Phenylcyclohexanol was prepared according to the method of Ungnade.[14] Compound **1**-4-d_1 was obtained according to the following scheme:



The second and third steps of the above synthesis were carried out introducing some modifications to the methods reported in literature.[16,17] Compounds **2**-4-d_1 and **7**-4-d_1 were prepared from **1**-4-d_1 following the standard procedures. Structures of all compounds were established by i.r., n.m.r. and mass spectra. Purity of the samples was routinely checked by t.l.c., g.l.c. and their melting points. The n.m.r. and mass spectra of the deuterated compounds showed an isotopic purity better than 99%. Melting points are uncorrected and their values are:

Compound	**1**	**2**	**3**	**4**	**5**
m.p., °C	118–120	193–194	136–138	220–221	153–155
Compound	**6**	**7**	**8**	**9**	**10**
m.p., °C	120–121	76–78	56–57	101–102	68–69
Compound	**11**	**12**	**13**		
m.p., °C	168–170	115–117	126–127		

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REFERENCES

1. H. Budzikiewicz, C. Djerassi and D. H. Williams, *Mass Spectrometry of Organic Compounds*, p. 94 ff. Holden-Day, San Francisco (1967).
2. C. C. Fenselau and C. H. Robinson, *J. Am. Chem. Soc.* **93**, 3070 (1971).
3. J. L. Holmes, D. McGillivray and R. T. B. Rye, *Org. Mass Spectrom.* **7**, 347 (1973).
4. F. De Angelis, M. L. Forcellese, A. Gambacorta and R. Nicoletti, Società Chimica Italiana, Atti del XII Congresso Nazionale, 295 (1975).
5. J. Sharvit and A. Mandelbaum, *Org. Mass Spectrom.* **11**, 488 (1976).
6. H. Budzikiewicz, C. Djerassi and D. H. Williams, *Mass Spectrometry of Organic Compounds*, pp. 107–113 Holden-Day, San Francisco (1967) and references therein.
7. F. W. McLafferty, *Anal. Chem.* **31**, 477 (1959). I. Howe, in *Mass Spectrometry*, Vol. 1, D. H. Williams (Senior Reporter), p. 66 ff. Specialist Periodical Reports, The Chemical Society, London (1970).
8. M. S. Chin and A. G. Harrison, *Org. Mass Spectrom.* **2**, 1073 (1969).
9. T. W. Bentley and R. A. W. Johnstone, *J. Chem. Soc. B*, 263 (1971).
10. F. W. McLafferty, *Chem. Commun.* 956 (1968). R. G. Cooks, I. Howe and D. H. Williams, *Org. Mass Spectrom.* **2**, 137 (1969); F. W. McLafferty, T. Wachs, C. Lifshitz, G. Innorta and P. Irving, *J. Am. Chem. Soc.* **92**, 6867 (1970).
11. T. W. Bentley, R. A. W. Johnstone and D. W. Payling, *J. Am. Chem. Soc.* **91**, 3978 (1969). T. W. Bentley and R. A. W. Johnstone in *Advances in Physical Organic Chemistry*, edited by V. Gold, Vol. 8, p. 229 ff. Academic Press, London (1970).
12. T. W. Bentley, R. A. W. Johnstone and D. W. Payling, *J. Am. Chem. Soc.* **91**, 3978 (1969).
13. P. Brown, *Org. Mass Spectrom.* **4**, 519 (1970).
14. H. E. Ungnade, *J. Org. Chem.* **13**, 361 (1948).
15. H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.* **83**, 2544 (1961).
16. S. R. Sandler and W. Karo, *Organic Functional Group Preparation*, Vol. I, p. 120. Academic Press, New York (1968).
17. H. C. Brown and H. M. Bell, *J. Org. Chem.* **27**, 1928 (1962).

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