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New Fragmentation Pathways in the Electron Impact Mass Spectrometry of Derivatized Pyrano-1,3-diphenylprop-2-enones

Virinder S. Parmar,* Sunil K. Sharma, Anand Vardhan and Rakesh K. Sharma
Department of Chemistry, University of Delhi, Delhi 110007, India

Jørgen Møller and Per M. Boll
Department of Chemistry, Odense University, DK-5230 Odense M, Denmark

The fragmentation patterns of closely related chalcones, cinnamoylchromans and cinnamoylchromenes, are reported to be strikingly different. The mass spectra of the first group show peaks typical of the fragmentation of simple chalcones balanced by additional fragmentation routes competing effectively with the typical chalcone fragmentation. For the other group with the introduced double bond the fragmentation is considerably changed. Initial loss of a methyl group gives rise to formation of the base peak in three of four examples. The $[M - CH_3]^+$ ion decomposes further, eliminating a styrene yielding the *m/z* 187 ion. This process may be rationalized as a retro-Diels–Alder fragmentation of a flavanone formed on intramolecular rearrangement of the molecular ion.

INTRODUCTION

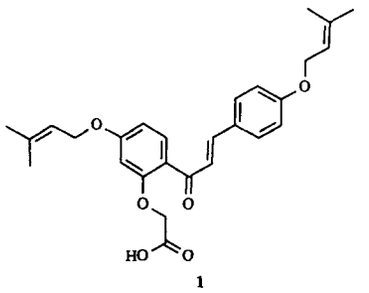
Chalcones (1,3-diphenylprop-2-enones) constitute an important group of natural products. The presence of a 3-methylbut-2-enyl unit on the chalcone moiety confers good biological activity to the compound, as a large number of chalcones having this unit or its cyclic analogues are found to show good physicochemical and biological activities, e.g. antibacterial,[1–4] antifungal,[1,4–8] anti-inflammatory,[9,10] antimicrobial,[9,11–15] antitumour,[16] anticancer,[17,18] as binders for prostaglandins[18] and as insect antifeedants.[19]

Kyogoku *et al.*[20] earlier prepared a few *O*-isopentenylated chalcones and found that they possess antipeptic ulcer activity. Subsequently they investigated the antiulcer effects of some isoprenylated chalcones isolated from *Sophora subprostrata*, and found these to be highly active.[21] Consequently, the same group[22] synthesized about 30 such chalcones, tested their antiulcer activities and a clinical compound (**1**) was developed.

Cyclic analogues of prenylated chalcones occur commonly in nature, and so far 15 cinnamoylchromans and 47 cinnamoylchromenes have been isolated from natural sources. We have synthesized a series of compounds which are analogues of naturally occurring species of this class to test their biological activities.

There have been sporadic reports on the mass spectra of such chalcones. However, in this paper we present a more detailed study of the mass spectra of four cinnamoyl chromans (**2–5**) and four correspondingly substituted cinnamoylchromenes (**6–9**). In spite of the close structural resemblance of the two types of compounds, their behaviours on electron impact are strikingly different.

Compounds **2** and **5** were prepared by the previously published procedures.[23,24] Compounds **3**, **4** and **6–9** were synthesized by us for the first time.



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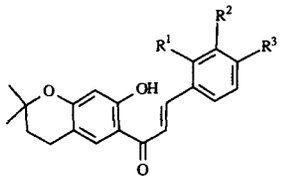

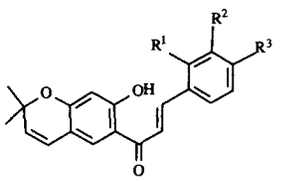

2	$R^1 = R^2 = R^3 = H$	**6**	$R^1 = R^2 = R^3 = H$
3	$R^1 = R^2 = OCH_3$; $R^3 = H$	**7**	$R^1 = R^2 = OCH_3$; $R^3 = H$
4	$R^1 = R^3 = OCH_3$; $R^2 = H$	**8**	$R^1 = R^3 = OCH_3$; $R^2 = H$
5	$R^1 = H$; $R^2 = R^3 = OCH_3$	**9**	$R^1 = H$; $R^2 = R^3 = OCH_3$

EXPERIMENTAL

All the cinnamoylchromans were synthesized by the base-catalysed $[Ba(OH)_2]$[25] Claisen–Schmidt reaction of the appropriate benzaldehyde and 6-acetyl-7-hydroxy-2,2-dimethylchroman,[26] while the cinnamoylchromenes were synthesized by the reaction between 6-acetyl-7-hydroxy-2,2-dimethylchromene[27] and the appropriate benzaldehyde. The purities of the compounds were checked by melting points and spectral data (UV, IR, ^1H NMR and ^{13}C NMR).

The mass spectra were obtained with a Varian MAT 311A mass spectrometer/SS200 data system using the

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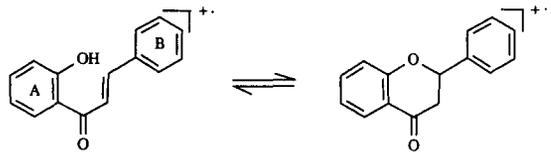
direct sample insertion system with the lowest feasible sample temperature and ionization by electron impact (70 eV). All the elemental compositions given were obtained by exact mass measurements carried out by the peak-matching method and the decompositions were supported by metastable analyses performed by scanning the electric sector voltage with fixed accelerating voltage and fixed magnetic field.

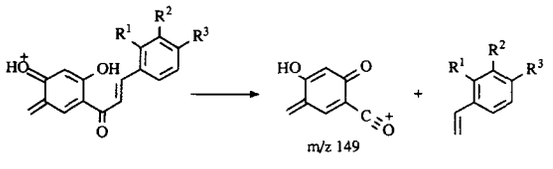
RESULTS AND DISCUSSION

The mass spectra (Table 1) of compounds **2–5** show peaks typical of the fragmentation of simple chalcones, i.e. α-cleavage next to the carbonyl group, loss of a hydrogen radical (from *ortho* positions of the B-ring)[28] and loss of the B-ring reflecting the intramolecular equilibrium between the chalcone-type molecular ion and a flavanone-type molecular ion, as discussed in detail by Van de Sande *et al.*[29] for 2′-hydroxychalcone and -flavanone:



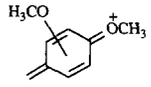
However, the presence of the condensed pyrano ring gives rise to additional fragmentation routes which compete effectively with the above-mentioned fragmentations.

Initial loss of C_4H_7 with hydrogen rearrangement probably to the oxygen atom is followed by formation of *m/z* 149 (Scheme 1). Both processes may well be rationalized through prior isomerization to the corresponding flavanone molecular ion.[29]



Scheme 1

Charge retention on the opposite fragment (Scheme 1) with formation of ions (*m/z* 164 in the spectra of **4** and **5**) with a styrene structure may also occur, but their abundances depend very much on the substituent pattern of the B-ring. The same is the case for the ion of *m/z* 151, which are formed as abundant ions in the spectra of **4** and **5**. These ions are formed directly from the molecular ions and may be formulated as



m/z 151

The corresponding ion of *m/z* 91 in the spectrum of **2** has an abundance of only 10%.

The normally observed facile loss of a hydrogen radical from the *ortho* position of the B-ring of the molecular ions of chalcones, often giving rise to ions with abundances comparable to those of the molecular ions, is diminished considerably in the spectra of these compounds. However, loss of *ortho*-methoxy groups is a favourable process which in the case of **3** almost completely suppresses the formation of the ions of *m/z* 164 and 151. Similar loss of OH and OAc from the *ortho* position of the B-ring of chalcones has been reported and found to be accompanied by cyclization to the stable flavylium ion.[30] The intense $[M - OCH_3]^+$ fragment ion in the spectra of **3** and **4** probably results from an intramolecular aromatic substitution of this kind.

Introduction of the double bond completely changes the fragmentation of compounds **6–9** (Table 2) as compared with **2–5** (Fig. 1). Now loss of a methyl group from the molecular ions is predominant, yielding a stable $[M - CH_3]^+$ ion, which gives rise to the base peak in the spectra of **6**, **7** and **9**. Elimination of CH_3 from the molecular ions of **2–5** gives rise to peaks with intensities of only 3–4%.

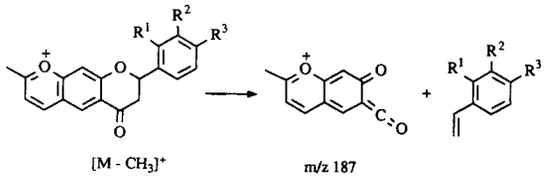
The $[M - CH_3]^+$ ion decomposes further by elimination of a styrene, yielding an ion of *m/z* 187 in a process which may be rationalized as a retro-Diels–Alder type of fragmentation of the corresponding flavanones formed by the intramolecular rearrangements of the molecular ions (Scheme 2). On introduction of methoxy groups into the B-ring, charge retention in the eliminated styrene part is observed to some extent, yielding the *m/z* 164 ion.

Table 1. EI mass spectra (70 eV) of compounds 2–5

				m/z (relative intensity, %)				
Compound	$M^{+\cdot}$	$[M - OCH_3]^+$	$[M - H]^+$	$[M - CH_3]^+$	$[M - C_4H_7]^+$	[M − B-ring]$^+$	(α-cleavage)	$[M - styrene]^{+\cdot}$
2	308 (100)	—	307 (47)	293 (4)	253 (54)	231 (65)	205 (13)	204 (20)
3	368 (43)	337 (100)	367 (5)	353 (4)	313 (3)	231 (10)	205 (6)	204 (3)
4	368 (88)	337 (100)	367 (15)	353 (4)	313 (8)	231 (6)	205 (9)	204 (5)
5	368 (100)	337 (3)	367 (25)	353 (3)	313 (7)	231 (10)	205 (4)	204 (5)

	m/z (relative intensity, %)			
	Styrene ion			Other important ions
2	104 (4)	151 (6)[a]	149 (98)[b]	291 (5), 260 (3), 189 (12), 165 (18), 131 (21), 103 (38), 77 (40), 69 (29)
3	164 (5)	151 (2)	149 (25)[b]	351 (1), 295 (2), 281 (5), 141 (6), 121 (3), 77 (3), 69 (7)
4	164 (84)	151 (72)	149 (73)[c]	351 (4), 295 (2), 281 (4), 170 (10), 138 (13), 133 (7), 121 (22), 77 (8), 69 (16)
5	164 (98)	151 (65)	149 (54)[c]	351 (3), 295 (3), 281 (1), 138 (5), 133 (3), 121 (11), 103 (9), 91 (11), 77 (10), 69 (14)

[a] Not a B-ring fragment in **2**.
[b] *m/z* 149: $C_8H_5O_3$.
[c] *m/z* 149: doublet of $C_9H_9O_2$ and $C_8H_5O_3$ (1 : 1).



Scheme 2

When present in the *ortho* position of the B-ring, the methoxy group introduces another rearrangement process resulting in elimination of a molecule of methanol from the $[M - CH_3]^+$ ion. Loss of the methoxy group from the molecular ions is also observed in these cases (**7** and **8**), but to a much smaller extent than in **3** and **4**.

Table 2. EI mass spectra (70 eV) of compounds 6–9

	m/z (relative intensity, %)							
Compound	$M^{+\cdot}$	$[M - OCH_3]^+$	$[M - H]^+$	$[M - CH_3]^+$		$[M - B\text{-ring}]^+$	(α-cleavage)	$[M - \text{styrene}]^{+\cdot}$
6	306 (51)	—	305 (1)	291 (100)	187 (57)	229 (2)	203 (1)	202 (2)
7	366 (57)	335 (35)	365 (2)	351 (100)	187 (97)	229 (—)	203 (3)	202 (3)
8	366 (81)	335 (8)	365 (3)	351 (95)	187 (100)	229 (0.5)	203 (3)	202 (2)
9	366 (65)	335 (1)	365 (2)	351 (100)	187 (90)	229 (1)	203 (1)	202 (3)

	m/z (relative intensity, %)			
	Styrene ion			Other important ions
6	104 (0.5)	151 (—)	149 (—)	153[a] (3), 145.5[b] (6), 145 (21), 131 (7), 103 (7), 91 (2), 77 (7)
7	164 (3)	151 (—)	149 (2)	319[c] (15), 175.5[b] (6), 160 (34), 131 (5), 103 (3), 91 (4), 77 (7)
8	164 (26)	151 (6)	149 (8)	319[c] (7), 183[a] (5), 175.5[b] (10), 160 (15), 131 (7), 121 (6), 103 (3), 91 (4), 77 (6)
9	164 (16)	151 (3)	149 (2)	319 (0.2), 183[a] (1), 175.5[b] (14), 160 (8), 131 (6), 103 (3), 91 (3), 77 (4)

[a] M^{2+}.
[b] $[M - CH_3]^{2+}$.
[c] $M - CH_3 - CH_3OH$.

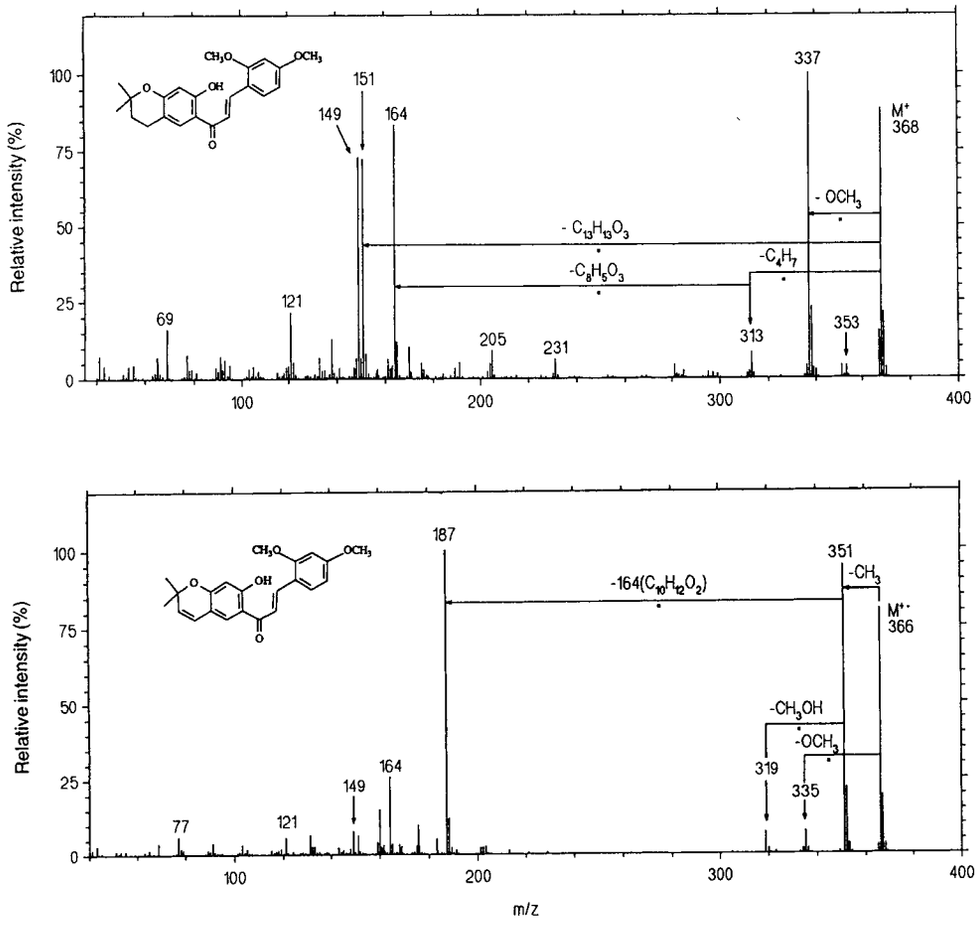


Figure 1. Mass spectra of **4** (top) and **8** (bottom).

REFERENCES

1. V. K. Ahluwalia, N. Kaila and S. Bala, *Indian J. Chem.* **25B**, 663 (1986).
2. N. B. Poppano, O. P. de Centorbi, N. B. Debattist, C. C. de Milan, E. J. Browkowski and F. H. Feretti, *Rev. Argent. Microbiol.* **17**, 27 (1985).
3. J. Mathew, A. V. Subba Rao and S. Rambhav, *Curr. Sci.* **53**, 576 (1984).
4. V. K. Ahluwalia, R. R. Manu and S. Bala, *Indian J. Chem.* **28B**, 608 (1989).
5. S. Mizobuchi and Y. Sato, *Agric. Biol. Chem.* **48**, 2771 (1984).
6. D. S. Bhakuni and R. Chaturvedi, *J. Nat. Prod.* **47**, 585 (1984).
7. A. Chowdhury, N. Mukherjee and N. Adityachoudhury, *Experientia* **30**, 1022 (1974).
8. A. K. Bhat, R. P. Bhamaria, M. R. Patel, R. A. Bellare and C. V. Deliwala, *Indian J. Chem.* **10**, 694 (1972).
9. E. T. Oganesyan, V. I. Yakavenko, M. M. Khatryan, S. R. Preshkov and V. S. Cherevatyi, *Khim.-Farm. Zh.* **20**, 696 (1986); *Chem. Abstr.* **105**, 126832 (1986).
10. V. Dauksas, P. Gaidelis, E. Udrenaite, O. Petrauskas and A. Brukstus, *Khim.-Farm. Zh.* **19**, 1069 (1985); *Chem. Abstr.* **104**, 129843 (1986).
11. M. Sazada and B. Kedzia, *Pharmazie* **44**, 190 (1989).
12. M. H. Jagdale, J. G. Deshmukh, M. M. Salunkhe, S. S. Swami and Y. B. Vibhute, *Natl. Acad. Sci. Lett. (India)* **9**, 39 (1986); *Chem. Abstr.* **105**, 222529 (1986).
13. P. Biswas, A. Bhattacharya, P. C. Bose, N. Mukherjee and N. Adityachaudhury, *Experientia* **37**, 397 (1981).
14. Y. B. Vibhute and S. S. Wadje, *Indian J. Exp. Biol.* **14**, 739 (1976).
15. V. K. Ahluwalia, L. Nayal, N. Kaila, S. Bala and A. K. Tahim, *Indian J. Chem.* **26B**, 384 (1987).
16. J. C. Dore and C. Viel, *J. Pharm. Belg.* **29**, 341 (1974).
17. M. Gschwendt, W. Kittstein, G. Fuerstenberger and F. Mark, *Cancer Lett.* **25**, 177 (1984); *Chem. Abstr.* **102**, 216605 (1985).
18. J. R. Sinythies, *Psychoneuroendocrinology* **4**, 177 (1979).
19. M. S. J. Simmonds, W. M. Blaney, F. D. Monache and G. B. Marini-Bettolo, *J. Chem. Ecol.* **16**, 365 (1990).
20. K. Kyogoku, K. Hatayama, S. Yokomori and T. Seki, *Jpn. Kokai* 75, 140, 430 (1975); *Chem. Abstr.* **84**, 121467 (1976).
21. M. Sasajima, S. Nakane, R. Saziki, H. Saotome, K. Hatayama, K. Kyogoku and I. Tanaka, *Nippon Yakurigaku Zasshi* **74**, 897 (1978); *Chem. Abstr.* **90**, 197536 (1979).
22. K. Kyogoku, K. Hatayama, S. Yokomori, R. Saziki, S. Nakane, M. Sasajima, J. Sawada, M. Ohzeki and I. Tanaka, *Chem. Pharm. Bull.* **27**, 2943 (1979).
23. R. V. Suresh, C. S. R. Iyer and P. R. Iyer, *Heterocycles* **24**, 1925 (1986).
24. R. V. Suresh, C. S. R. Iyer and P. R. Iyer, *Indian J. Chem.* **24B**, 254 (1985).
25. S. Sathyanarayana and H. G. K. Murty, *Curr. Sci.* **57**, 1114 (1988).
26. V. K. Ahluwalia and K. K. Arora, *Tetrahedron* **37**, 1437 (1981).
27. T. Anthonsen, *Acta Chem. Scand.* **23**, 3605 (1969).
28. C. Van de Sande, J. W. Serum and M. Vandewalle, *Org. Mass Spectrom.* **6**, 1333 (1972).
29. J. Ronayne, D. H. Williams and J. H. Bowie, *J. Am. Chem. Soc.* **88**, 4980 (1966).
30. R. Mentleim and E. Vowinkel, *Org. Mass Spectrom.* **19**, 330 (1984).