Electron Ionization Mass Spectrometric Studies of Methoxyphenylisocoumarins and their 3,4-Dihydroderivatives

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Summary: Electron ionization mass spectra of 3-methoxyphenylisocoumarins (**1-4**), 3-methoxyphenyl-3,4-dihydroisocoumarins (**5-8**) and synthetic intermediates namely, 2-benzoylmethylbenzoic acids (**9-12**) and methyl-2-(benzoylmethyl)benzoates (**13-16**) are discussed. The mass fragmentation patterns were designed with the help of EIMS. The molecular formulae were further confirmed by HREIMS.

Introduction

Isocoumarins and their dihydroderivatives are an important class of biologically active natural products. Several of these have been isolated from different natural sources and found to possess a variety of bioactivities. Some of these isocoumarins like hydrangenol, phyllodulcin, macrophylloside A and 8-hydroxy-3-(3',4'-dihydroxyphenyl)isocoumarin are found to possess antimicrobial activities [1-3]. Phyllodulcin is 400 times sweeter [4] than sugar and has also been used as a refrigerant [5]. Various routes have been developed for the synthesis of these compounds [6-10] which also highlight their importance. Recently, we have reported [11-12] the synthesis and biological activities of some 3-methoxyphenylisocoumarins and their dihydroderivatives. In the present paper, as a continuation of our previous studies [13-15], we wish to report the mass spectral behaviour of these 3-methoxyphenylisocoumrins (**1-4**), their dihydroderivatives (**5-8**) and synthetic intermediates (**9-16**).

The elemental compositions of molecular ion peaks have been confirmed by HREIMS data (Table-1).

Table-1: HREIMS of Molecular Ion Peaks

Compound	Mol. Formulae	M^+ (*m/z*)	
		Calculated	Found
1	$C_{16}H_{12}O_3$	252.0786	252.0795
2	$C_{17}H_{14}O_4$	282.0892	282.0902
3	$C_{18}H_{16}O_5$	312.0998	312.0990
5	$C_{16}H_{14}O_3$	254.0943	254.0955
6	$C_{17}H_{16}O_4$	284.1049	284.1031
7	$C_{18}H_{18}O_5$	314.1154	314.1165
9	$C_{16}H_{14}O_4$	270.0892	270.0885
10	$C_{17}H_{16}O_5$	300.0998	300.0502
11	$C_{18}H_{18}O_6$	330.1103	330.1095
13	$C_{17}H_{16}O_4$	284.1049	284.1071
14	$C_{18}H_{18}O_5$	314.1154	314.1165
15	$C_{19}H_{20}O_6$	344.1260	344.1275

Results and Discussions

The general fragmentation patterns were designed with the help of LREIMS and are depicted in Schemes **1-4**.

3-Methoxyphenylisocoumarins (1-4)

The EIMS of isocoumarins (**1-4**) afforded the radical cations corresponding to their molecular ions which are also the base peaks for these compounds. The loss of carbon monoxide molecule from the molecular ion gave the radical cations (**1a-4a**) followed by the removal of methoxy radical to generate the cations (**1b-4b**). The loss of substituent groups at position 3 of the isocoumarin nucleus in the form of radical gave the cations (**1c-4c**). Removal of carbon monoxide molecule was also observed from (**1c-4c**) to afford the cations (**1d-4d**). Loss of C_8H_5O radical from the molecular ions afforded the cations (**1e-4e**) followed by the loss of CO molecule to furnish the cations (**1f-4f**) corresponding to the substituents at position 3 of the nucleus. These same fragments can also be formed by the loss of $C_9H_5O_2$ radical from the molecular ions. The frag-mentation pattern of compounds (**1-4**) is presented in scheme-1.

3-Methoxyphenyl-3,4-dihydroisocoumarins (5-8)

The EIMS of the dihydroisocoumarins (**5-8**) afforded the radical cations corresponding to their

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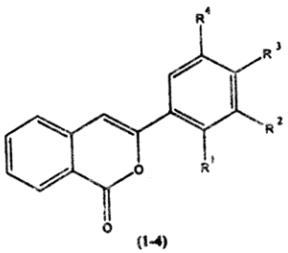
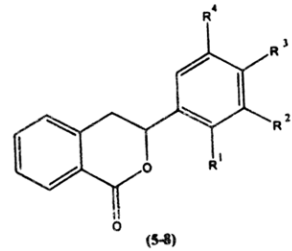
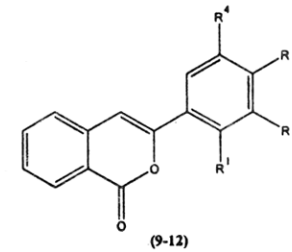


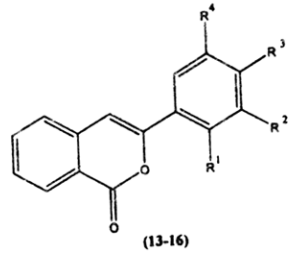
(1-4)



(5-8)



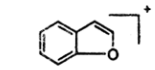
(9-12)



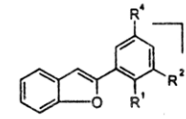
(13-16)

(1, 5, 9, 13)	$R_1 = R_2 = R_4 = H$, $R_3 = OMe$
(2, 6, 10, 14)	$R_1 = R_4 = H$, $R_2 = R_3 = OMe$
(3, 7, 11, 15)	$R_1 = H$, $R_2 = R_3 = R_4 = OMe$
(4, 8, 12, 16)	$R_1 = R_2 = R_3 = OMe$, $R_4 = H$

Figure 1



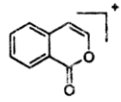
m / z = 117 (7.1%, 1d)
(11.2%, 2d)
(15.3%, 3d)
(12.1%, 4d)



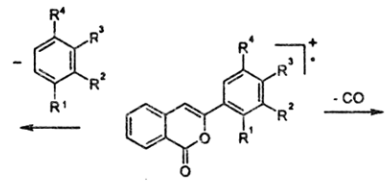
m / z = 193 (62.1%, 1b)
= 223 (49.4%, 2b)
= 253 (54.6%, 3b)
= 253 (57.7%, 4b)

- CO

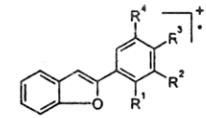
- $\dot{O}CH_3$



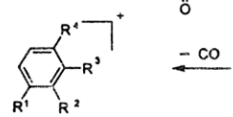
m / z = 145 (3.6%, 1c)
(6.9%, 2c)
(7.8%, 3c)
(6.9%, 4c)



m / z = 252 (100%, 1) $R^1 = R^2 = R^4 = H$; $R^3 = OCH_3$
= 282 (100%, 2) $R^1 = R^4 = H$; $R^2 = R^3 = OCH_3$
= 312 (100%, 3) $R^1 = H$; $R^2 = R^3 = R^4 = OCH_3$
= 312 (100%, 4) $R^1 = R^2 = R^3 = OCH_3$; $R^4 = H$

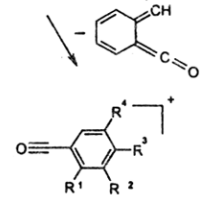


m / z = 224 (52.4%, 1a)
= 254 (59.5%, 2a)
= 284 (68.8%, 3a)
= 284 (66.7%, 4a)



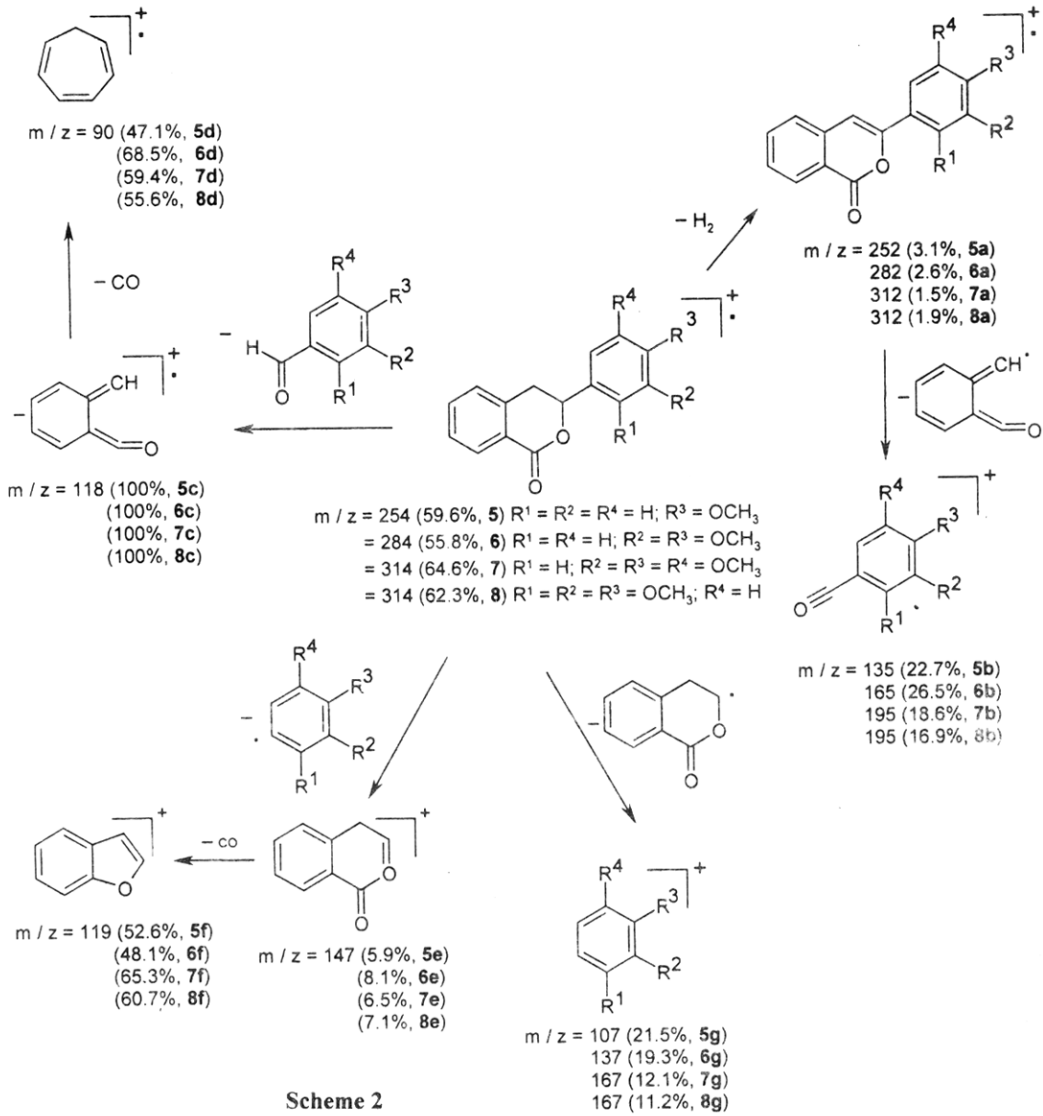
m / z = 107 (22.2%, 1f)
137 (31.7%, 2f)
167 (19.6%, 3f)
167 (19.8%, 4f)

- CO



m / z = 135 (7.1%, 1e)
165 (11.2%, 2e)
195 (15.3%, 3e)
195 (12.5%, 4e)

Scheme 1

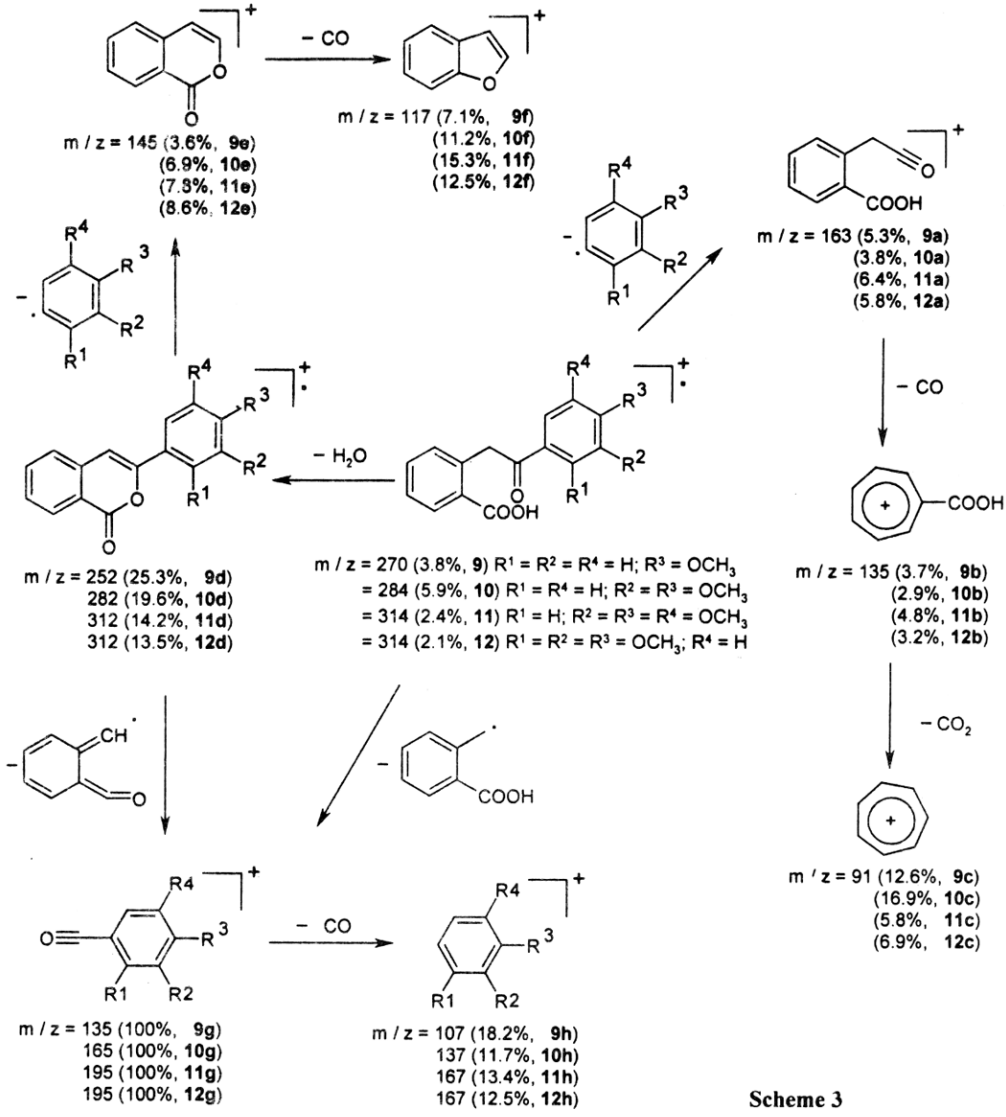


Scheme 2

molecular ions. The loss of a hydrogen molecule was observed resulting in the formation of radical cations (**5a-8a**) corresponding to the respective isocoumarins. The loss of a radical corresponding to C_8H_5O from the isocoumarins (**5a-8a**) generated the cations (**5b-8b**), the loss of this radical was also observed from the synthesized isocoumarins (**1-4**). The radical cations (**5c-8c**) were observed as the base peaks due to the loss of arylbenzaldehyde molecules from the molecular ions. This is a very typical fragment formed in case of dihydroisocoumarins [16-17]. Removal of CO molecule from the base peak afforded the radical cations (**5d-8d**). The loss of the substituent groups at position 3 of the molecular ions in the form of a radical furnished the cations (**5e-8e**) followed by the loss of a carbon monoxide molecule to yield the cations (**5f-8f**). The cations (**5g-8g**) corresponding to the substituents were also observed due to the loss of dihydroisocoumarin nucleus in the form of a radical. The fragmentation pattern of these compounds is shown in scheme-2.

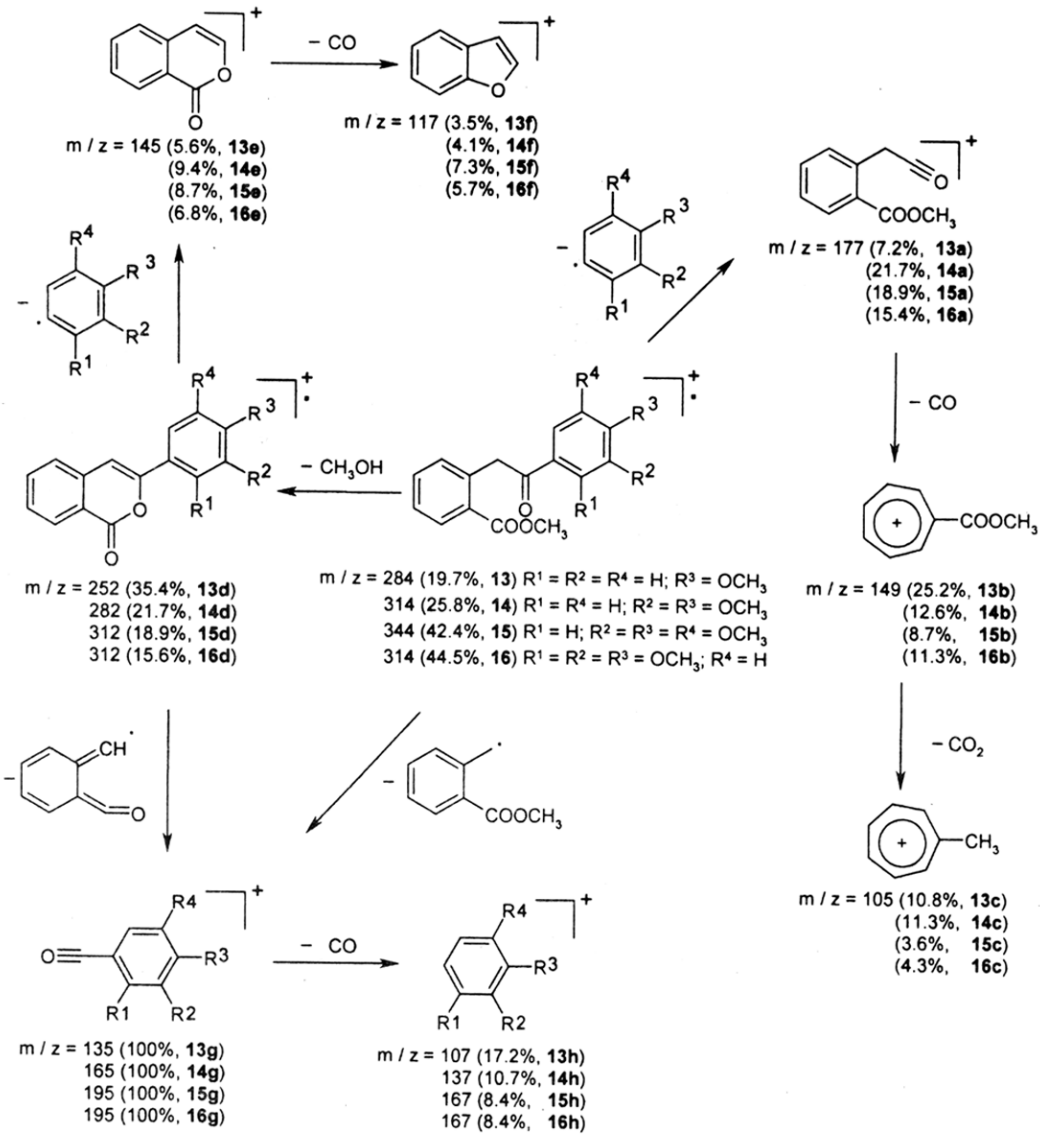
2-(Benzoylmethyl)benzoic acids (9-12)

The radical cations observed for these acids (**9-12**) corresponding to the molecular ions were of considerably low intensity. The loss of the substituted



Scheme 3

phenyl radical from the molecular ions gave the cations (**9a-12a**) at *m/z* 163, followed by the loss of carbon monoxide molecule to generate the cations (**9b-12b**) at *m/z* 135. These cations in turn lose a molecule of carbon dioxide to produce the respective cations (**9c-12c**) at *m/z* 91 corresponding to the tropyllium cation. The loss of water molecule from the molecular ions gave the radical cations (**9d-12d**) corresponding to the isocoumarin molecules. This is a typical behaviour of such carboxylic acids. The formation of the cations (**9e-12e**) corresponding to the isocoumarin nucleus at *m/z* 145 was observed from the cations (**9d-12d**) followed by the loss of a carbon monoxide molecule to afford the cations (**9f-12f**) at *m/z* 117. The loss of $C_8H_7O_2$ radical from the molecular ions resulted in the formation of the cations (**9g-12g**) also observed for compounds (**1-4**). These are also the base peaks for the acids. The removal of a carbon monoxide molecule from (**9g-12g**) furnished the cations (**9h-12h**).



Scheme 4

Methyl 2-(benzoylmethyl)benzoates (13-16)

The EIMS of (**13-16**) afforded the radical cations at their corresponding molecular masses. The loss of substituted phenyl radical from the molecular ion through α cleavage of the ketone gave the cations (**13a-16a**) at *m/z* 177. This cation looses a molecule of carbon monoxide to generate the cations (**13b-16b**) at *m/z* 149 followed by the loss of carbon dioxide molecule to afford the cations (**13c-16c**) at *m/z* 105. The removal of methanol molecule from the molecular ions gave the radical cations (**13d-16d**) corresponding to the 3-substituted isocoumarins. The loss of the substituents at position 3 in the form of a radical from (**13d-16d**) afforded the cations (**13e-16e**) at *m/z* 145 corresponding to the isocoumarin nucleus followed by the loss of a carbon monoxide molecule to furnish the cations (**13f-16f**) at *m/z* 117. The loss of $C_9H_9O_2$ radical from the molecular ions yielded the cations (**13g-16g**) which also serve as the

base peaks. These cations corresponding to the base peaks also lose a molecule of carbon monoxide to generate the corresponding cations (**13h-16h**).

Experimental

The compounds were prepared according to the literature procedures [13]. All of them were characterized by IR, ^{1}H-NMR and high resolution mass spectral data. The EIMS were recorded on mAT-311 instrument with an accelerating voltage of 3kv and ionization energy of 70 *eV*. The temperature of the ion source was maintained at 250 °C and inlet temperature was 110 °C.

Conclusions

The isocoumarins (**1-4**) appeared as the base peaks in their mass spectra. A fragment at *m/z* 145 was observed in all these compounds corresponding to the isocoumarin nucleus and is a typical one for isocoumarins [14-15]. A typical fragment reported in the literature [16-17] for dihydroisocoumarins appeared at *m/z* 118 for compounds (**5-8**) and is also the base peak. The carboxylic acids (**9-12**) and their methyl esters (**13-16**) show similar behaviour in their mass spectra.

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