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3-Aroyl-5-hydroxyflavones: Synthesis and Mechanistic Studies by Mass Spectrometry

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The synthesis and mass spectra of three 3-aroyl-5-hydroxyflavones are reported. The interpretation of the mechanistic pathways for the fragmentation of the metastable molecular ions of these compounds was achieved through the analysis of their mass-analysed ion kinetic energy (MIKE) spectra and of the B^2/E spectra of a few fragment ions. Labelling of the hydroxyl proton with deuterium and the analysis of the MIKE spectra of a model compound with chlorine atoms in the 2′,6′- and 2″,6″-positions led to a mechanism for the losses of OH˙ and HCO˙ which involves hydrogen migration from the 2″- or 6″-position to the 4-carbonyl oxygen atom. A mechanism for the loss of a neutral molecule of anisole from the molecular ion of the 3-aroyl-5-hydroxyflavone with a methoxyl group in the 4′- and 4″-positions is also suggested. For the flavones with hydrogen or chlorine substituents at these positions, loss of a phenyl (or chlorophenyl) radical occurs instead. © **1997 by John Wiley & Sons, Ltd.**

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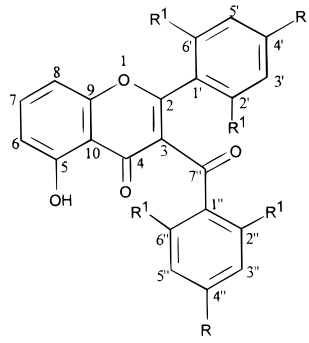
INTRODUCTION

Flavones are one of the most common classes of natural flavonoids[1] for which significant biocidal,[2–4] pharmacological[5–7] and antioxidant[5,8–10] activities have been reported. Owing to their importance, the synthesis and structural characterization of flavones, by NMR[11–13] and mass spectrometry,[14–19] have been the subject of many publications. Mass spectrometric studies have established the general modes of fragmentation of the ions of those compounds inside the ion source.

However, synthetic or spectroscopic studies on 3-aroylflavones have been scarce[20,21] and since these derivatives have shown significant antibacterial and antifungal activities,[21] we have studied the synthesis and mass spectral behaviour of the compounds shown in Scheme 1. Our mass spectrometric study was mainly concerned with the reactions occurring outside the ion source and with the elucidation of fragmentation mechanisms, rather than with the analysis of the normal mass spectrum. The synthesized 3-aroyl-5-hydroxyflavones **1a–c** were ionized by electron impact and the unimolecular fragmentations of their molecular ions, occurring in the third field-free region of the mass spectrometer, were studied through the analysis of their mass-analysed ion kinetic energy (MIKE) spectra. In order to understand the formation of some fragment ions, we used the information contained in the MIKE spectra of the molecular ions of 3-aroyl-5-hydroxyflavones **1a–c**, of 5-[^{2}H]hydroxy-4′-methoxy-3-(4″-methoxybenzoyl)flavone and of two model compounds, **1d** and **e**, and performed a few linked scans to ascertain the origin of the fragment ions.



1a. R = H R^1 = H
1b. R = Cl R^1 = H
1c. R = OCH_3 R^1 = H
1d. R = H R^1 = Cl

Scheme 1

EXPERIMENTAL

General methods

Melting points are uncorrected and were determined on a Reichert Thermovar apparatus fitted with a microscope.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 300 instrument at 300.13 and 75.47 MHz, respectively; chemical shifts are expressed in δ (ppm) values relative to tetramethylsilane (TMS) as internal reference. The proton and carbon resonances of the synthesized

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compounds were unambiguously assigned using several NMR techniques, such as (^{1}H/^{1}H) COSY, (^{1}H/^{13}C) HETCOR, HMBC and one-dimensional selective INEPT.

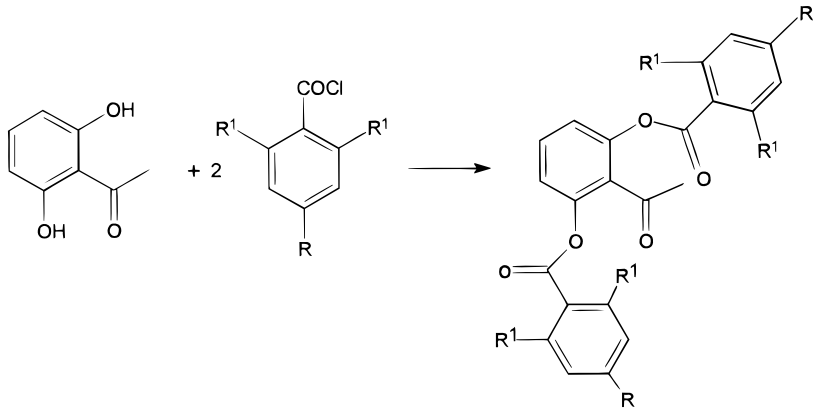
All chemicals and solvents were obtained from commercial sources and were used without further purification with the exception of pyridine, which was distilled from potassium hydroxide.

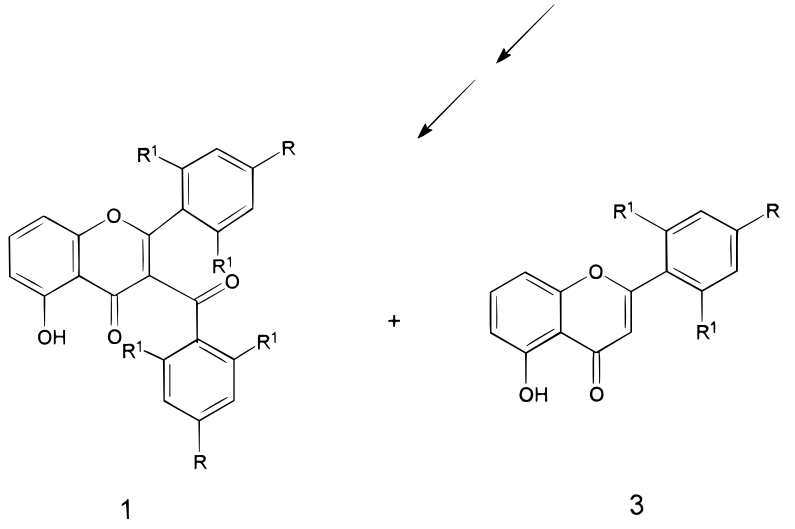
Preparative thin-layer chromatography was carried out on silica gel plates (Riedel-de Haën silica gel 60 DGF_{254}). Column chromatography was also performed on silica gel (Merck silica gel 60, 70–230 mesh).

Synthesis

3-Aroyl-5-hydroxyflavones 1a–d (Scheme 2). Each synthesis was started by treatment of 2′,6′-dihydroxyacetophenone with the appropriate benzoyl chloride in pyridine for 2 h, to provide the corresponding 2′,6′-diaroyloxyacetophenones (**2**). Baker–Venkataraman rearrangement[22–24] of the latter compounds in the presence of potassium hydroxide in pyridine afforded the 2-aroyl-2′-aroyloxy-6′-hydroxyacetophenone and 2,2-diaroyl-2′,6′-dihydroxyacetophenone (and corresponding enolic forms) intermediates.[24] Final cyclization of these compounds, without further purification, was performed with sulphuric acid in acetic acid, affording a mixture of two compounds. This mixture, in each case, was dissolved in dichloromethane and chromatographed on preparative thin-layer chromatographic plates, eluting several times with light petroleum–dichloromethane (4:6). The following compounds, in increasing R_f order, were obtained: 3-aroyl-5-hydroxyflavones (**1**) (55–63%) and 5-hydroxyflavones (**3**) (15–16%). All the compounds were crystallized from ethanol and fully characterized by ^{1}H and ^{13}C NMR.

3-Benzoyl-5-hydroxyflavone (***1a***). M.p. 171–173 °C (lit.[20] 177–178 °C). ^{1}H NMR ($CDCl_3$): 6.86 (1H, d, J = 8.1





a. R^1= R R = H
b. R^1 = H R = Cl
c. R^1 = H R = OCH_3
d. R^1 = Cl R = H

Scheme 2

Hz, H-6), 7.04 (1H, d, $J = 8.1$ Hz, H-8), 7.33–7.47 (5H, m, H-3′,3″,4′,5′,5″), 7.56 (1H, t, $J = 7.4$ Hz, H-4″), 7.62 (1H, t, $J = 8.1$ Hz, H-7), 7.64 (2H, d, $J = 7.9$ Hz, H-2′, 6′), 7.93 (2H, d, $J = 7.9$ Hz, H-2″,6″), 12.18 (1H, s, O*H*-5). ^{13}C NMR ($CDCl_3$): 107.2 (C-8), 110.1 (C-10), 112.0 (C-6), 121.0 (C-3), 128.6 (C-2′,6′), 128.9 (C-3′,3″,5′,5″), 129.4 (C-2″,6″), 131.2 (C-1′), 131.9 (C-4′), 134.1 (C-4″), 136.8 (C-7), 136.8 (C-1″), 156.2 (C-9), 160.9 (C-5), 163.7 (C-2), 181.6 (C-4), 192.5 (C-7″).

4′-Chloro-3-(4″-chlorobenzoyl)-5-hydroxyflavone (***1b***). M.p. 163–165 °C. ^{1}H NMR ($CDCl_3$): 6.87 (1H, d, $J = 8.3$ Hz, H-6), 7.03 (1H, d, $J = 8.3$ Hz, H-8), 7.36 (2H, d, $J = 8.6$ Hz, H-3′,5′), 7.42 (2H, d, $J = 8.6$ Hz, H-3″,5″), 7.56 (2H, d, $J = 8.6$ Hz, H-2′,6′), 7.63 (1H, t, $J = 8.3$ Hz, H-7), 7.86 (2H, d, $J = 8.6$ Hz, H-2″,6″), 12.04 (1H, s, O*H*-5). ^{13}C NMR ($CDCl_3$): 107.1 (C-8), 110.2 (C-10), 112.3 (C-6), 121.0 (C-3), 129.4 (C-2′,6′), 129.4 (C-2″, 6″), 129.6 (C-1″), 129.9 (C-3″,5″), 130.7 (C-3′,5′), 135.2 (C-1′), 136.4 (C-7), 138.6 (C-4″), 140.9 (C-4′), 156.2 (C-9), 161.1 (C-5), 162.6 (C-2), 181.4 (C-4), 191.0 (C-7″).

5-Hydroxy-4′-methoxy-3-(4″-methoxybenzoyl)flavone (***1c***). M.p. 172–175 °C (lit.[20] 177–178 °C). ^{1}H NMR ($CDCl_3$): 3.79 and 3.84 ($2 \times OCH_3$, 2 s), 6.83 (1H, d, $J = 8.1$ Hz, H-6), 6.86 (2H, d, $J = 8.9$ Hz, H-3′,5′), 6.90 (2H, d, $J = 9.0$ Hz, H-3″,5″), 7.01 (1H, d, $J = 8.1$ Hz, H-8), 7.58 (1H, t, $J = 8.1$ Hz, H-7), 7.64 (2H, d, $J = 8.9$ Hz, H-2′,6′), 7.92 (2H, d, $J = 9.0$ Hz, H-2″,6″), 12.31 (1H, s, O*H*-5). ^{13}C NMR ($CDCl_3$): 55.4 and 55.5 ($2 \times OCH_3$), 107.0 (C-8), 110.0 (C-10), 111.7 (C-6), 114.2 (C-3″,5″), 114.3 (C-3′,5′), 120.0 (C-3), 123.4 (C-1′), 130.0 (C-1″), 130.4 (C-2′,6′), 131.9 (C-2″,6″), 135.8 (C-7), 156.1 (C-9), 160.6 (C-5), 162.4 (C-4′), 163.0 (C-2), 164.3 (C-4″), 181.6 (C-4), 191.4 (C-7″).

2′,6′-Dichloro-3-(2″,6″-dichlorobenzoyl)-5-hydroxyflavone (***1d***). M.p. 178–179 °C. ^{1}H NMR ($CDCl_3$): 6.88 (1H, dd, $J = 8.3$ and 0.6 Hz, H-6), 6.96 (1H, dd, $J = 8.3$ and 0.6 Hz, H-8), 7.24–7.28 (3H, m, H-3′,4′,5′), 7.40–7.42 (3H, m, H-3″,4″,5″), 7.60 (1H, t, $J = 8.3$ Hz, H-7), 12.08 (1H, s, O*H*-5). ^{13}C NMR ($CDCl_3$): 107.4 (C-8), 110.8 (C-10), 113.0 (C-6), 120.2 (C-3), 127.9 (C-3′,5′), 128.0 (C-3″,5″), 130.1 (C-4′), 131.2 (C-2′,6′), 131.7 (C-4″), 134.0 (C-1′), 134.0 (2″,6″), 136.5 (C-7), 139.5 (C-1″), 155.9 (C-9), 161.3 (C-5), 167.4 (C-2), 180.7 (C-4), 186.5 (C-7″).

5-Hydroxyflavone (***3a***). M.p. 153–154 °C (lit.[20] 158–159 °C). ^{1}H NMR ($CDCl_3$): 6.76 (1H, s, H-3), 6.83 (1H, d, $J = 8.2$ Hz, H-6), 7.02 (1H, d, $J = 8.4$ Hz, H-8), 7.53–7.59 (4H, m, H-3′,4′,5′,7), 7.93 (2H, dd, $J = 7.8$ and 1.8 Hz, H-2′,6′), 12.59 (1H, s, O*H*-5). ^{13}C NMR ($CDCl_3$): 106.1 (C-3), 107.1 (C-8), 110.9 (C-10), 111.5 (C-6), 126.5 (C-2′,6′), 129.2 (C-3′,5′), 131.3 (C-1′), 132.1 (C-4′), 135.4 (C-7), 156.5 (C-9), 160.8 (C-5), 164.6 (C-2), 183.6 (C-4).

4′-Chloro-5-hydroxyflavone (***3b***). M.p. 186–187 °C. ^{1}H NMR ($CDCl_3$): 6.67 (1H, s, H-3), 6.80 (1H, dd, $J = 8.3$ and 0.8 Hz, H-6), 6.97 (1H, dd, $J = 8.3$ and 0.8 Hz, H-8), 7.49 (2H, d, $J = 8.7$ Hz, H-3′,5′), 7.53 (1H, t, $J = 8.3$ Hz, H-7), 7.82 (2H, d, $J = 8.7$ Hz, H-2′,6′), 12.46 (1H, s, O*H*-5). ^{13}C NMR ($CDCl_3$): 106.2 (C-3), 106.5 (C-8), 110.9 (C-10), 111.7 (C-6), 127.7 (C-2′,6′), 129.5 (C-3′,5′), 129.8 (C-1′), 135.5 (C-7), 138.4 (C-4′), 156.4 (C-9), 161.0 (C-5), 163.4 (C-2), 183.4 (C-4).

5-Hydroxy-4′-methoxyflavone (***3c***). M.p. 154–156 °C (lit.[20] 154–156 °C). ^{1}H NMR ($CDCl_3$): 3.88 (3H, OCH_3, s), 6.62 (1H, s, H-3), 6.78 (1H, dd, $J = 8.4$ and 0.9 Hz, H-6), 6.95 (1H, dd, $J = 8.4$ and 0.9 Hz, H-8), 7.00 (2H, d, $J = 9.1$ Hz, H-3′,5′), 7.51 (1H, t, $J = 8.4$ Hz, H-7), 7.84 (2H, d, $J = 9.1$ Hz, H-2′,6′), 12.69 (1H, s, O*H*-5). ^{13}C NMR ($CDCl_3$): 55.5 (OCH_3), 104.5 (C-3), 106.9 (C-8), 110.7 (C-10), 111.3 (C-6), 114.5 (C-3′,5′), 123.4 (C-1′), 128.1 (C-2′,6′), 135.1 (C-7), 156.3 (C-9), 160.8 (C-5), 162.7 (C-4′), 164.5 (C-2), 183.4 (C-4).

2′,6′-Dichloro-5-hydroxyflavone (***3d***). M.p. 142–146 °C. ^{1}H NMR ($CDCl_3$): 6.39 (1H, s, H-3), 6.86 (1H, dd, $J = 8.3$ Hz, H-6), 6.94 (1H, dd, $J = 8.3$ Hz, H-8), 7.42–7.48 (3H, m, H-3′,4′5′), 7.53 (1H, t, $J = 8.3$ Hz, H-7), 12.42 (1H, s, O*H*-5).

7-Hydroxy-5,4′-dimethoxy-3-(4″-methoxybenzoyl)flavone (1e). Treatment of 2′,4′,6′-trihydroxyacetophenone with *p*-methoxybenzoyl chloride in pyridine for 2 h provide 2′,4′,6′-tri(*p*-methoxybenzoyloxy)acetophenone. Baker–Venkataraman rearrangement[22–24] of this acetophenone with anhydrous potassium carbonate in pyridine at reflux for 3 h gave 2,2-di(*p*-methoxybenzoyl)-4′-(*p*-methoxybenzoyloxy)-2′,6′-dihydroxyacetophenone (and corresponding enolic forms) intermediates.[24] The cyclization of the latter compounds, without further purification, was performed with sulphuric acid in acetic acid. Usual work-up followed by purification of the crude product by column chromatography, using chloroform as solvent and eluent, afforded 3-(4″-methoxybenzoyl)-5,7-dihydroxyflavone (50%), which was crystallized from ethanol. This compound was benzylated with benzyl chloride, potassium carbonate and potassium iodide in acetone at reflux for 12 h. After filtration of inorganic salts, the crude product was purified by thin-layer chromatography, using chloroform as solvent and eluent. Crystallization of the residue from ethanol gave 7-benzylozy-5-hydroxy-4′-methoxy-3-(4″-methoxybenzoyl)flavone (73%). This flavone was methylated with methyl sulphate and sodium hydride in tetrahydrofuran at reflux for 3 h. Usual work-up followed by column chromatographic purification, using chloroform as solvent and eluent, yielded 7-benzylozy-5,4′-dimethoxy-3-(4″-methoxybenzoyl)flavone (70%), which was crystallized from ethanol. The hydrogenolysis of the 7-benzylic group of this flavone was carried out with Pd/C and ammonium formate in methanol at reflux for 3 h. Filtration of the reaction mixture through Celite followed by crystallization of the crude product from ethanol gave 7-hydroxy-5,4′-dimethoxy-3-(4″-methoxybenzoyl)flavone (**1e**) (60%).

7-Hydroxy-5, 4′-dimethoxy-3-(4″-methoxybenzoyl)flavone (***1e***). M.p. 272–274 °C. ^{1}H NMR ($(CD_3)_2SO$): 3.75, 3.77 and 3.81 ($3 \times OCH_3$, 3 s), 6.45 (1H, s, H-6), 6.56 (1H, s, H-8), 6.97 (2H, d, $J = 8.5$ Hz, H-3′,5′), 6.98 (2H, d, $J = 8.4$ Hz, H-3″,5″), 7.52 (2H, d, $J = 8.5$ Hz, H-2′,6′), 7.83 (2H, d, $J = 8.4$ Hz, H-2″,6″), 10.97 (1H, s broad, O*H*-7). ^{13}C NMR ($(CD_3)_2SO$): 55.4, 55.6 and 55.9 ($3 \times OCH_3$), 95.2 (C-8), 96.7 (C-6), 106.3 (C-10), 114.2 (C-3″,5″), 114.3 (C-3′,5′), 121.8 (C-3), 123.4 (C-1′), 129.7 (C-2′,6′), 130.0 (C-1″), 131.4 (C-2″,6″), 157.7 (C-2), 159.0 (C-9), 160.9 (C-5), 161.3 (C-4′), 163.1 (C-7), 163.6 (C-4″), 174.2 (C-4), 192.4 (C-7″).

Mass spectra

All the mass spectrometric experiments were carried out with a VGAutospecQ mass spectrometer of EBEqQ geometry using an electron ionization (EI) source. The ion source was operated with accelerating voltage 8 kV, ionizing electron energy 70 eV and ion source temperature 200 °C. The MIKE spectra were obtained by selecting the precursor ion with the EB part of the instrument and scanning the second electric sector voltage. The compounds were introduced into the mass spectrometer with an unheated direct insertion probe.

DISCUSSION

In general, the EI mass spectra of flavones[14–19] are characterized by abundant molecular ions and by the presence of peaks due to a retro-Diels–Alder (RDA) reaction, the intensity of which depends on the nature and number of substituents. Other significant fragmentation modes of simple flavones include loss of H$^{\cdot}$, whose mechanism has been studied with some detail,[25] and CO. In the case of 3-aroylflavones used in our study, the analysis of the EI mass spectra presented in Fig. 1 show that the fragmentation of the molecular ions through an RDA reaction is a relatively unimportant process, since the intensities of the peaks originated by this reaction are very low. In the high-mass region of the EI mass spectra, the most intense peaks correspond to the molecular ions (base peaks for **1a** and **1b**), with losses of H$^{\cdot}$, CO, HCO$^{\cdot}$ and $C_6H_4R^{\cdot}$ (R = H, Cl, OCH_3). Together with the loss of the radical $C_6H_4OCH_3^{\cdot}$, a peak (*m/z* 294) due to the loss of a molecule of anisole is observed in the spectrum of **1c**. Low-intensity peaks due to the loss of a methyl radical (*m/z* 387) and a methyl radical followed by loss of CO (*m/z* 359) are also observed for **1c**.

Reactions of the metastable molecular ions

The most abundant ions observed in the MIKE spectra of the molecular ions of the three derivatives synthesized in our study are shown in Table 1. Losses of H$^{\cdot}$, HCO$^{\cdot}$ and OH$^{\cdot}$ radicals are common to the three compounds. Structurally specific losses of chlorine and methyl radicals are observed for **1b** and **1c**, respectively. Losses of $C_6H_5^{\cdot}$ and $C_6H_4Cl^{\cdot}$ radicals, by homolytic cleavage of the C-1″—C-7″ bond are observed for **1a** and **1b**, whereas for **1c** this fragmentation mode is completely absent and only loss of anisole is observed. Fragment ions originated by an RDA reaction of the molecular ion are completely absent in the three spectra. In order to establish the mechanisms involved in these fragmentations, we replaced the hydrogen atom of the hydroxyl group by deuterium, as confirmed by the disappearance of the 5-hydroxyl resonance in the ^{1}H NMR spectrum after shaking **1c** with D_2O, and recorded the MIKE spectrum of this deuterated analogue of **1c**. From the observation of the spectra shown in Fig. 2, we concluded that the peaks due to the losses of HCO$^{\cdot}$ (*m/z* 373) and OH$^{\cdot}$ (*m/z* 385) radicals are shifted, in the deuterated compound, by one mass unit, which means that the hydroxyl group is not involved in these fragmentations. The peak at *m/z* 294 in the original 3-aroyl-5-hydroxyflavone derivative **1c** is not shifted in the deuterated analogue, which means that in this case elimination of $C_6H_4DOCH_3$ occurs.

Since the hydroxylic proton is too far for a direct transfer to C-1″, two possible mechanisms (Scheme 3), both supported by the MIKE spectra shown in Fig. 2, for the loss of anisole can be envisaged. In mechanism (a), the reaction would be initiated by homolytic cleavage of the C-1″—C-7″ bond, followed by formation of an ion–neutral complex[27] between the radical and positive ion. The radical could then abstract a hydrogen (or deuterium) radical from the hydroxyl group to produce anisole. In mechanism (b), the reaction would be initiated by hydrogen transfer into the carbonyl group at C-4 and from there to C-1″ with simultaneous elimination of anisole (this mechanism was suggested by a referee as an alternative to the mechanism involving the formation of an ion–neutral complex as intermediate).

In order to test mechanism (a), we tried to synthesize a new analogue of **1c** with the hydroxyl group at C-7, since the elimination of anisole from the molecular ion of this compound would undoubtedly prove the intermediacy of an ion–neutral complex. Unfortunately, our attempts were not successful and, instead, we synthesized a model compound **1e**, shown in Scheme 4, with a hydroxy group at C-7 and replaced the hydroxyl group at C-5 by a methoxy group. We labelled this compound by replacing the hydroxylic proton by deuterium and measured the MIKE spectrum (Fig. 3) of the molecular ion of this deuterated compound. The peak at *m/z* 324 is due to the loss of $C_6H_5OCH_3$ from $M^{+\cdot}$ (*m/z* 432), which is more consistent with the classical mechanism (b).

The observation of this fragmentation for **1c** only may be tentatively explained by the presence of a methoxy group in a position *para* to the carbon to

Table 1. Partial MIKE spectra of 3-aroyl-5-hydroxyflavone derivatives[a]

Ion	1a	1b	1c
$[M - H^{\cdot}]^+$	47 *m/z* 341	4 *m/z* 409	26 *m/z* 401
$[M - CH_3^{\cdot}]^+$	—	—	44 *m/z* 387
$[M - OH^{\cdot}]^+$	17 *m/z* 325	15 *m/z* 393	41 *m/z* 385
$[M - HCO^{\cdot}]^+$	100 *m/z* 313	100 *m/z* 381	100 *m/z* 373
$[M - Cl^{\cdot}]^+$	—	39 *m/z* 375	—
$[M - C_6H_4R^{\cdot}]^+$	28 *m/z* 265	14 *m/z* 299	—
$[M - C_6H_5R]^{+\cdot}$	—	—	38 *m/z* 294

[a] Ion abundances are expressed as a percentage of the base peak.

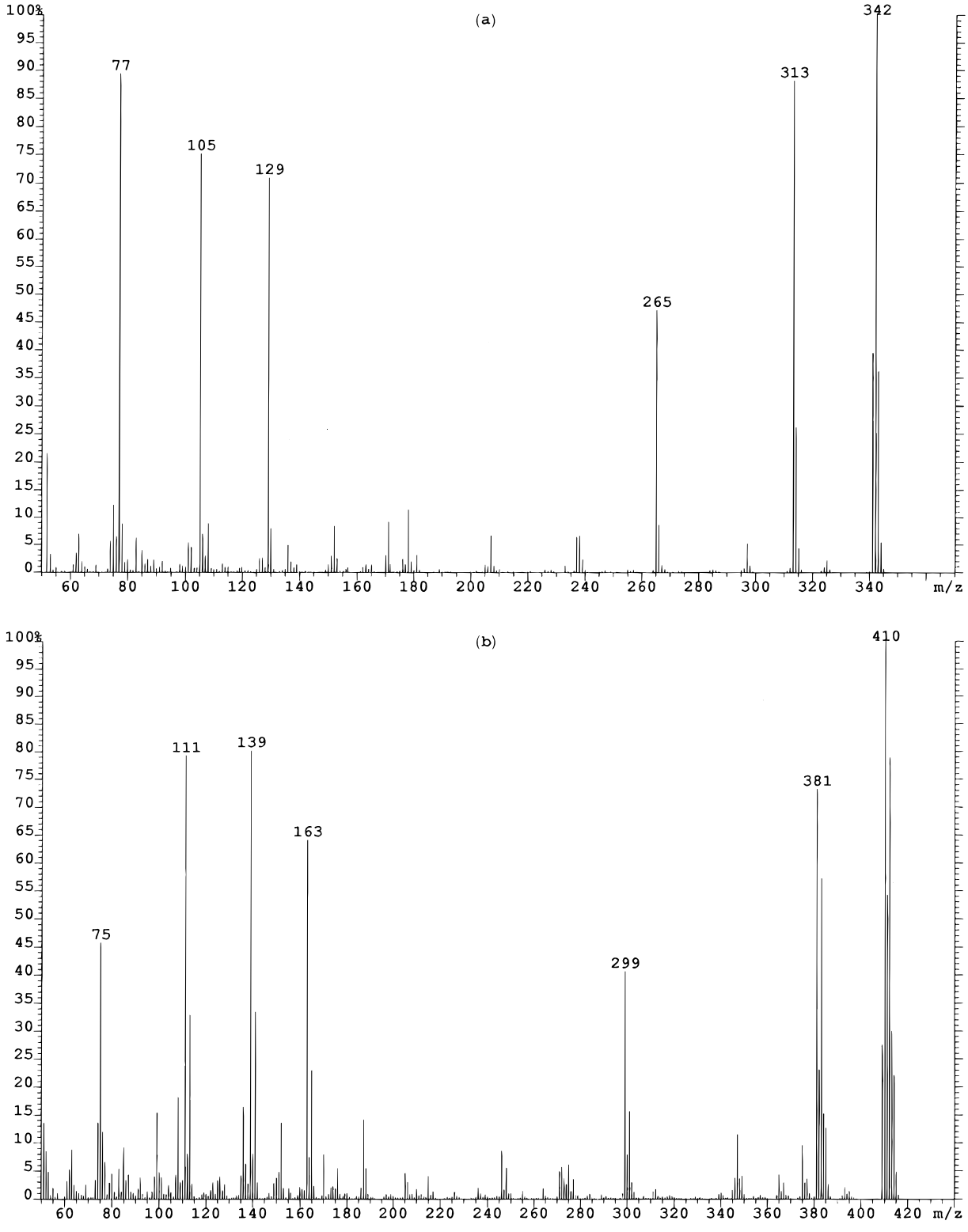


Figure 1. Electron impact mass spectra of (a) 3-benzoyl-5-hydroxyflavone, (b) 4′-chloro-3-(4″-chlorobenzoyl)-5-hydroxyflavone and (c) 5-hydroxy-4′-methoxy-3-(4″-methoxybenzoyl)flavone.

which the proton is transferred, and by an increased resonance stabilization of the product ion formed when $R = OCH_3$.

The mechanisms proposed for the loss of $HCO^{\cdot}$ and $OH^{\cdot}$ are shown in Scheme 5 and both involve hydrogen abstraction from the 2″- or 6″-position. To test this hypothesis, we synthesized a model compound, 2′,6′-dichloro-3-(2″,6″-dichlorobenzoyl)-5-hydroxyflavone (**1d**), in which the 2′,6′- and 2″,6″-positions of the aromatic rings are blocked by replacing the hydrogen atoms by chlorine. In the MIKE spectrum of the molecular ion (*m/z* 478) of this model **1d**, shown in Fig. 4, the

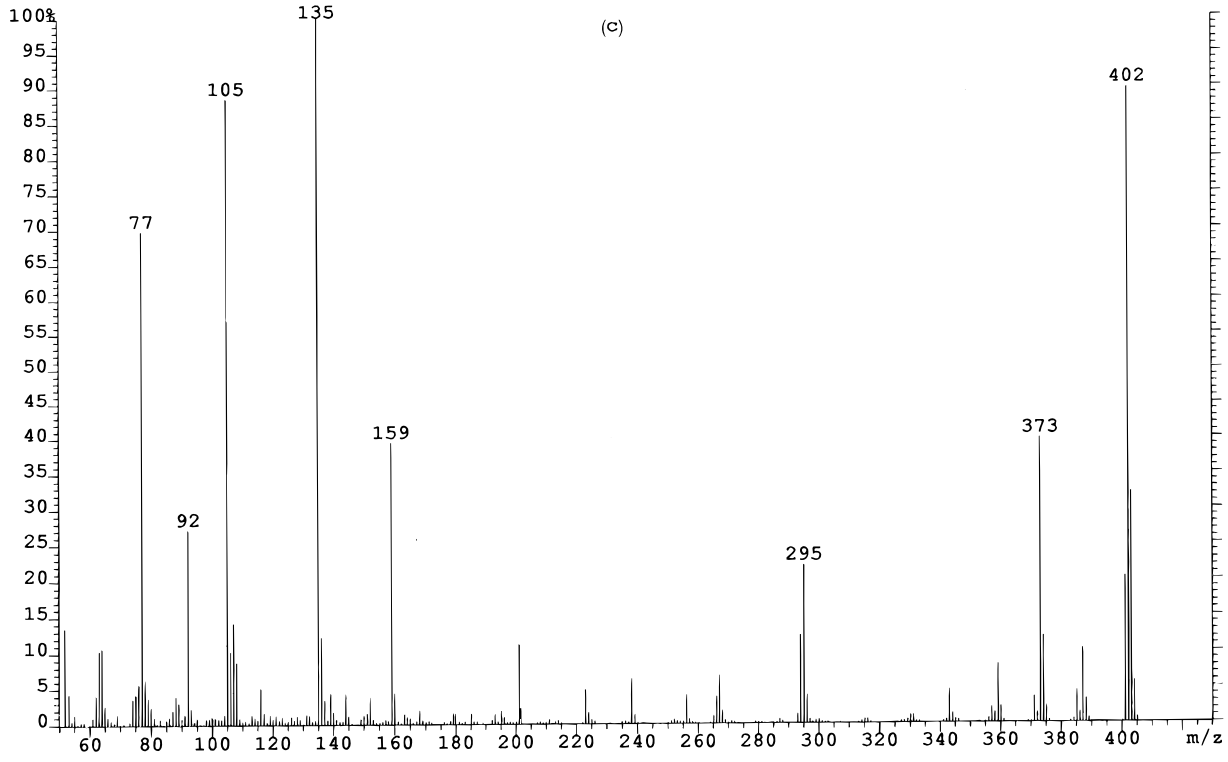


Figure 1. *Continued*

losses of 17 and 29 mass units are completely absent, the spectrum being dominated by the los of chlorine radical, which supports the mechanism proposed in Scheme 5.

In addition to the ions described above, we also observed in the MIKE spectra a few peaks (*m/z* 105 and 129 for **1a**, *m/z* 139 and 163 for **1b** and *m/z* 135 and 159 for **1c**) of low intensity (1% of the base peak) whose

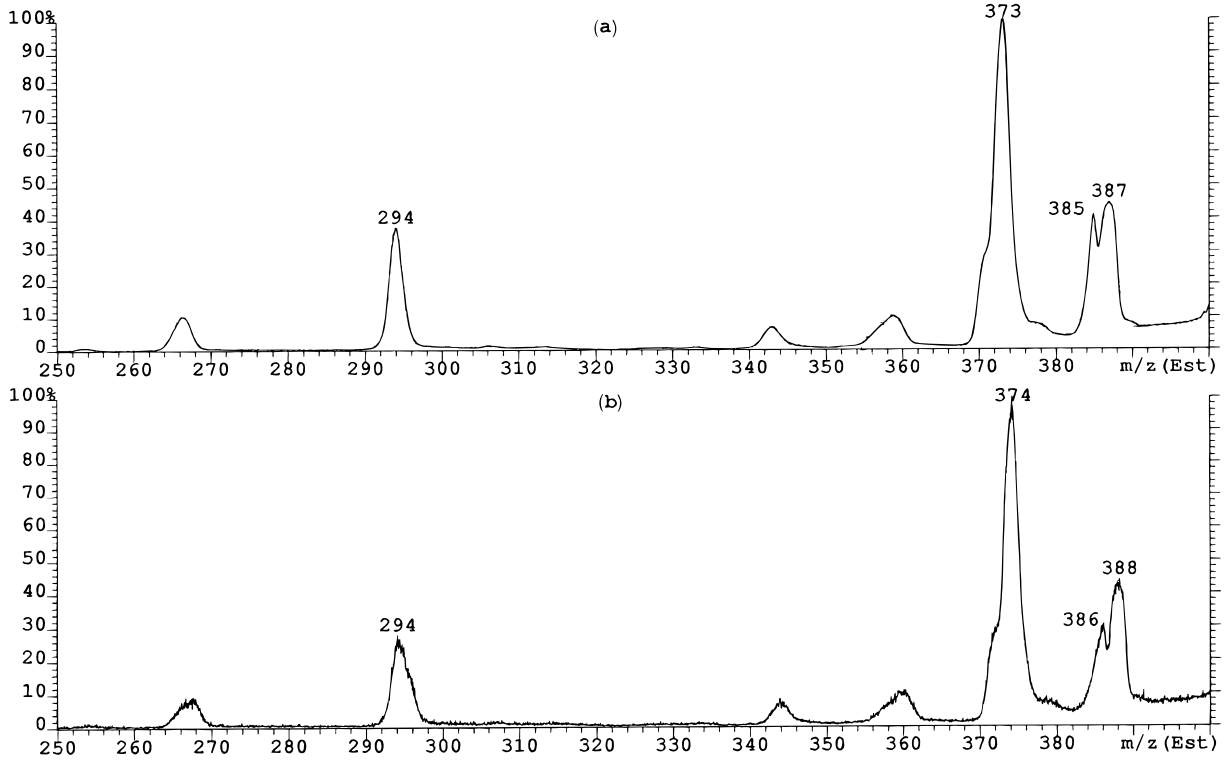
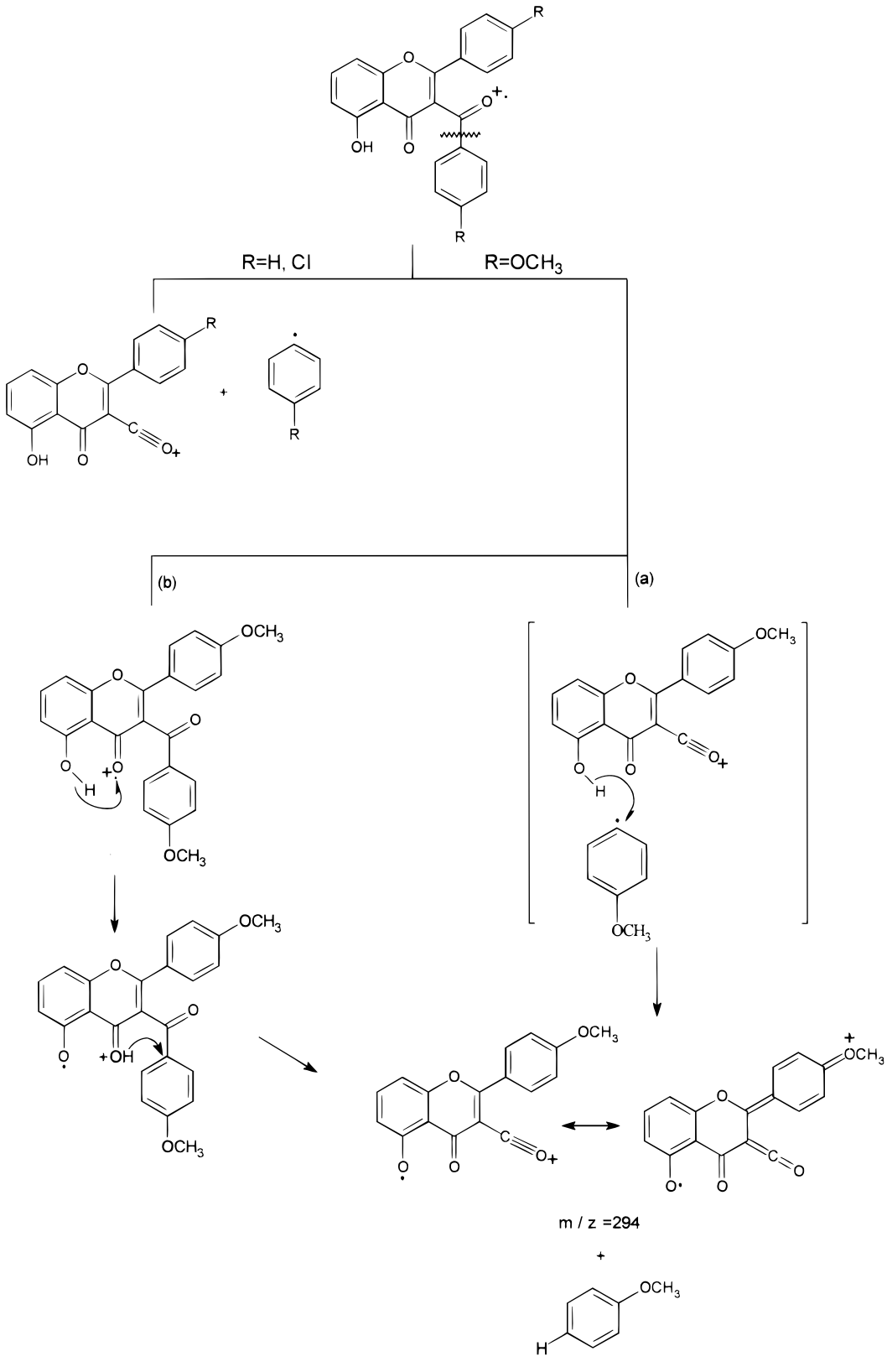


Figure 2. MIKE spectra of the molecular ions of (a) 5-hydroxy-4′-methoxy-3-(4″-methoxybenzoyl)flavone (*m/z* 402) and (b) 5-[^{2}H]-hydroxy-4′-methoxy-3-(4″-methoxybenzoyl)flavone (*m/z* 403).



Scheme 3

origin was ascertained by linked scans (B^2/E) of these fragment ions. It is worth mentioning that in the EI spectra these ions have relative abundances between 40 and 100%. The main route for ions of m/z 129 (**1a**), 163 (**1b**) and 159 (**1c**) is the RDA reaction shown in Scheme 6. However, in the MIKE spectra of the fragment ion $[M - C_6H_5OCH_3]^{+\cdot}$ a very intense peak corresponding to the formation of an ion of m/z 159 is also observed, which indicates the occurrence of the same type of the RDA reaction for that precursor ion.

The B^2/E spectra of ions $C_6H_4RCO^+$ (R = H, Cl, OCH_3 and m/z 105, 139 and 135, respectively) show

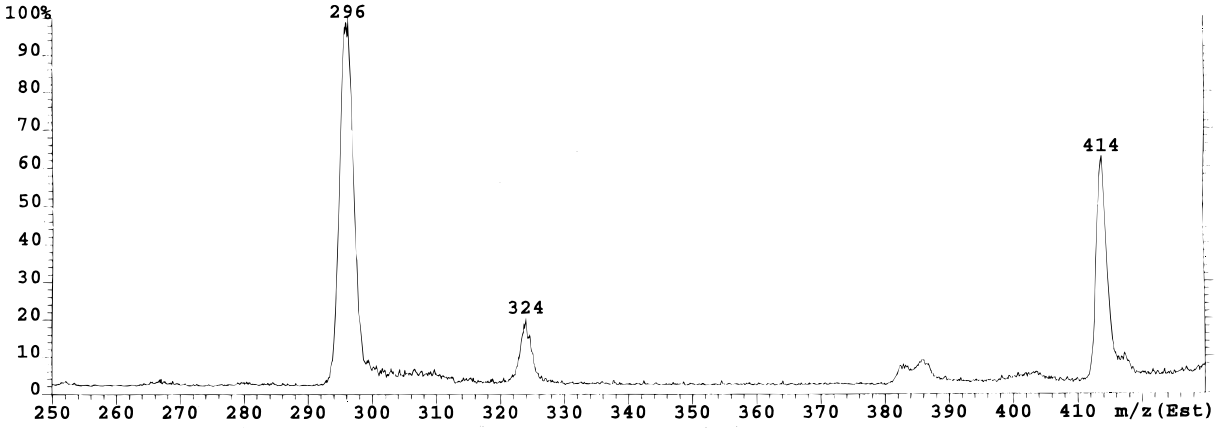


Figure 3. MIKE spectrum of the molecular ion of 7-hydroxy-5,4′-dimethoxy-3-(4″-methoxybenzoyl)flavone (*m/z* 432).

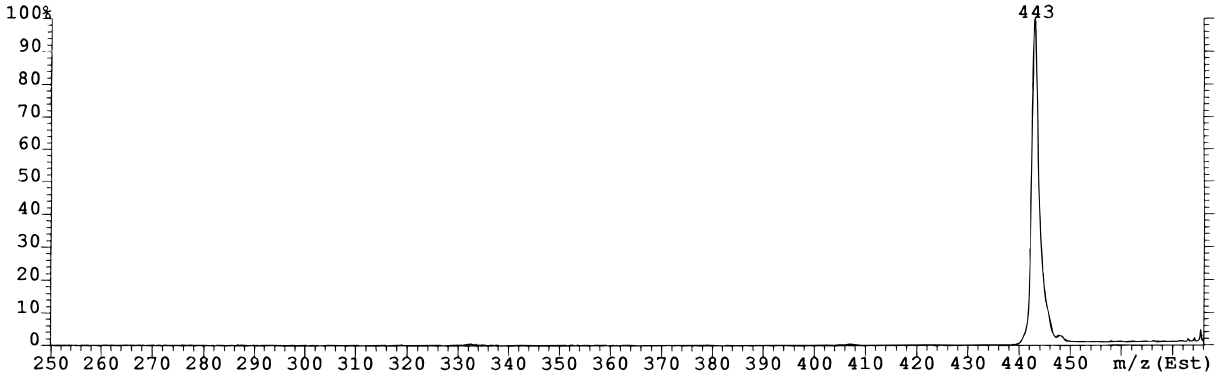
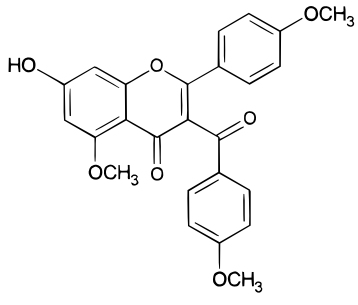


Figure 4. MIKE spectrum of the molecular ion of 2′,6′-dichloro-3-(2″,6″-dichlorobenzoyl)-5-hydroxyflavone (*m/z* 478).



1e

Scheme 4

that they can be formed via several fragmentation pathways, namely (in order of decreasing abundance): (a) from the fragment ions of *m/z* 207 (**1a**), 275 (**1b**) and 267 (**1c**) which probably arise from an RDA reaction in the molecular ion with hydrogen transfer to the fragment bearing the charge, (b) from the fragment ions $[M - C_6H_4R^{\cdot}]^+$ (R = H, Cl) and $[M - C_6H_5OCH_3]^+$ and (c) by heterolytic cleavage of the C-3–C-7″ bond of the corresponding molecular ions.

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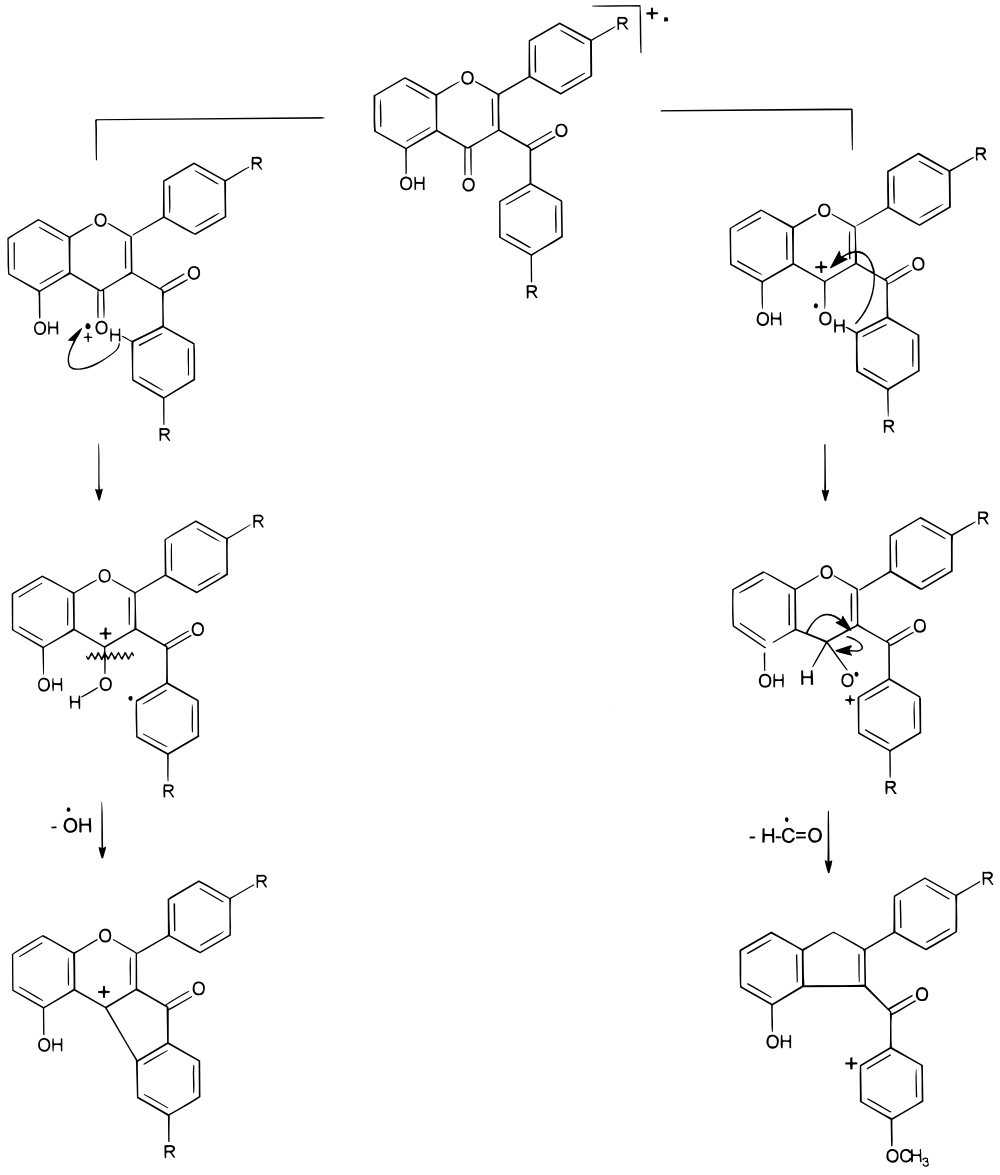
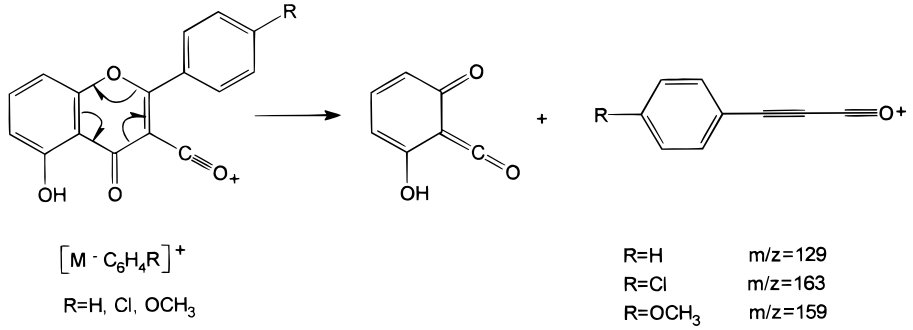


Scheme 5



Scheme 6

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