

Mass Spectral Fragmentation Modes of Some New Pyrimidinethiones, Thiazolo[3,2-*a*]Pyrimidines and *Bis*-Pyrimidines

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Abstract Mass fragmentation pathways of a number of pyrimidinethiones, thiazolo[3,2-*a*] pyrimidines and bis-pyrimidines were investigated by electron impact mass spectrometry (EI-MS). The molecular ion peaks $M+2$ and M^+ were recorded at different intensities. Characteristic fragment ions were formed by successive loss of simple functional groups followed by decomposition of the heterocycles connected to pyrimidine ring.

Keywords Mass spectrometry, Fragmentation processes, Pyrimidines

1. Introduction

The pyrimidine ring is the building unit of DNA and RNA which explains the fact that pyrimidine derivatives exhibit diverse pharmacological activities, the most pronounced of which are anticancer, [1, 2] antiviral, [3, 4] anti-HIV, [5, 6] antiamoebic activity [3] and antimicrobial activities. [7] They also showed activity against gonadotropin releasing hormone receptors [8] as well herbicidal activity targeting acetohydroxyacid synthase, which catalyzed the first common step in branched-chain amino acid biosynthesis. [9] Mass spectrometry was applied to the characterization of the compounds using analysis of metastable ions by the collision induced dissociation technique and exact mass measurements. [10-14] However, to best our knowledge, there are some few mass spectral fragmentation studies for isolated and fused pyrimidines. [15-17] In continuation of our work on the mass fragmentation mechanisms of the heterocyclic compounds, [18-21] a detailed study on a number of pyrimidinethiones, thiazolopyrimidines and *bis*-pyrimidines, was performed to understand the fragmentation modes of these compounds. Thus, this paper reports a study on the fragmentation mechanisms under electron ionization conditions of some new pyrimidinethiones, thiazolopyrimidines and *bis*-pyrimidines.

It has been possible to make some generalizations regarding fragmentation modes of their molecular ions.

2. Experimental

2.1. Synthesis of the Studied Compounds

The studied compounds **1-8** were synthesized as shown in Schemes 1 and 2. Details of the synthetic methods are reported in our recent article. [22] Also, all the compounds were previously characterized by elemental analysis, MS, IR, ¹H, and ¹³C-NMR spectra [22].

2.2. MS Measurements

The electron ionization mass spectra were recorded on Shimadzu GCMS-QP-1000EX mass spectrometers at 70 eV in Microanalytical center at Cairo University, Giza, Egypt. The electron ionization ion source was kept at 200°C. The compounds were introduced with a probe which was ballistically heated to 250°C. The EI mass spectra were obtained over the range of m/z 50-650.

3. Results and Discussion

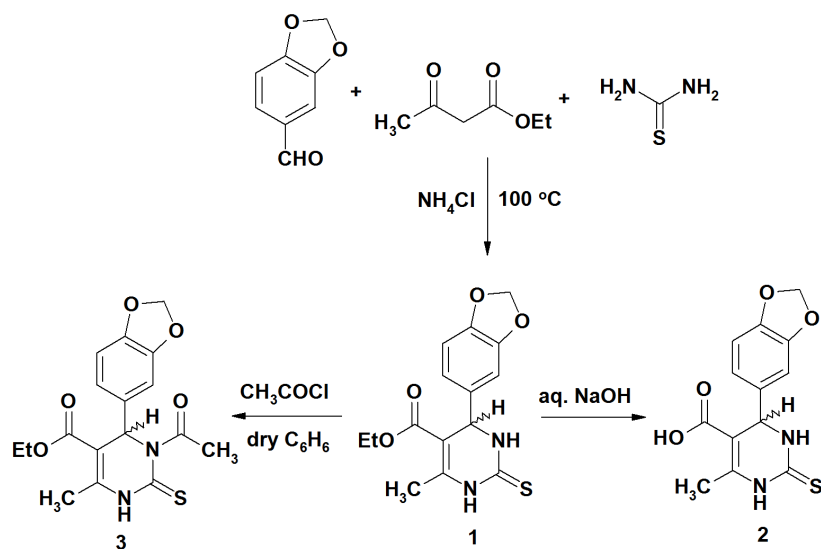
For a better understanding of mass fragmentation routes, the compounds under study were divided into three groups according to their structural patterns: **A** (*pyrimidinethiones*), **B** (*thiazolopyrimidines*) and **C** (*bis-pyrimidines*) (Figure 1).

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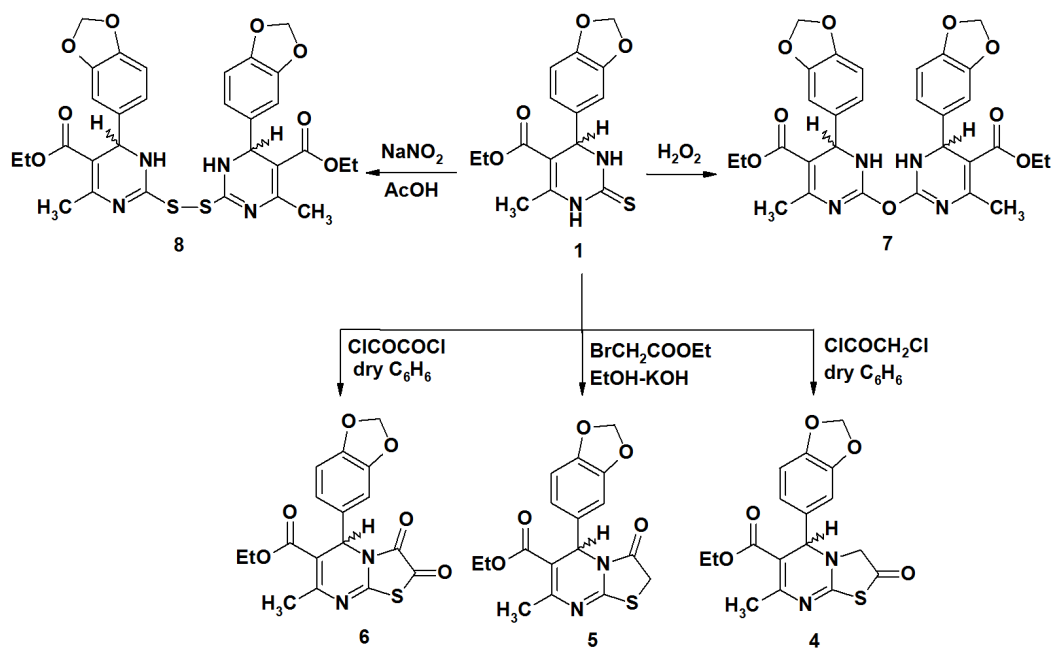
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Scheme 1.



Scheme 2.

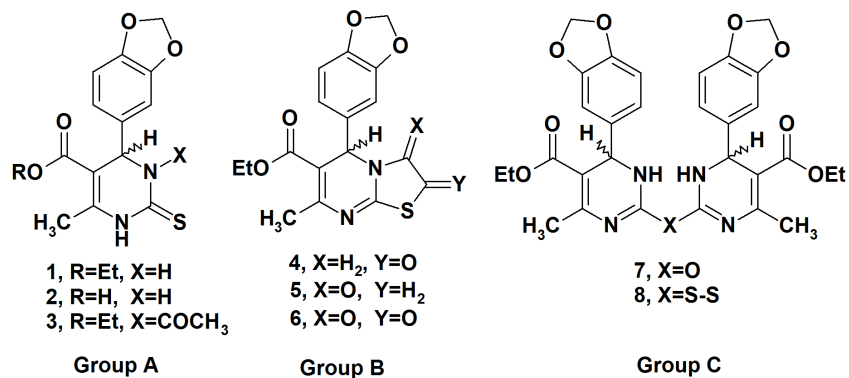


Figure 1.

As expected from the molecular formula $C_{15}H_{16}N_2O_4$, the molecular ion peak of ethyl 4-(1,3-benzodioxol-5-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (1) appeared as a base peak at m/z 320, which indicated to stability of compound 1. Also, the mass spectrum of compound 2 recorded its molecular ion peaks at m/z 294 ($M+2$, 1%) and 292 (M^+ , 18%). Both compounds 1 and 2 behave similar fragmentation routes. They lose ethyl and hydrogen radicals from their molecular ion peaks, respectively, generates the fragments cations m/z 291, which lose an oxygen radical [16] producing the acylium ions, m/z 275. The latter cations undergo the expected removal of CO molecules and methyl radicals bringing the fragments m/z 247 and m/z 232, respectively. Loss of SH radicals from the cation radicals m/z 232 affords the corresponding cations m/z 199. Decomposition of the latter cations into their components gives the corresponding fragments m/z 122 and m/z 77. The fragments m/z 122 lose the formaldehyde

Group B: Ethyl 5-(1,3-benzodioxol)-7-methyl-2-oxo-2,3-dihydro-5H-1,3-thiazolo[3,2-a]pyrimidine-6-carboxylate (4), ethyl 5-(1,3-benzodioxol)-7-methyl-3-oxo-2,3-dihydro-5H-1,3-thiazolo[3,2-a]pyrimidine-6-carboxylate (5) and ethyl 5-(1,3-benzodioxol)-7-methyl-2,3-dioxo-2,3-dihydro-5H-1,3-thiazolo[3,2-a]pyrimidine-6-carboxylate (6).

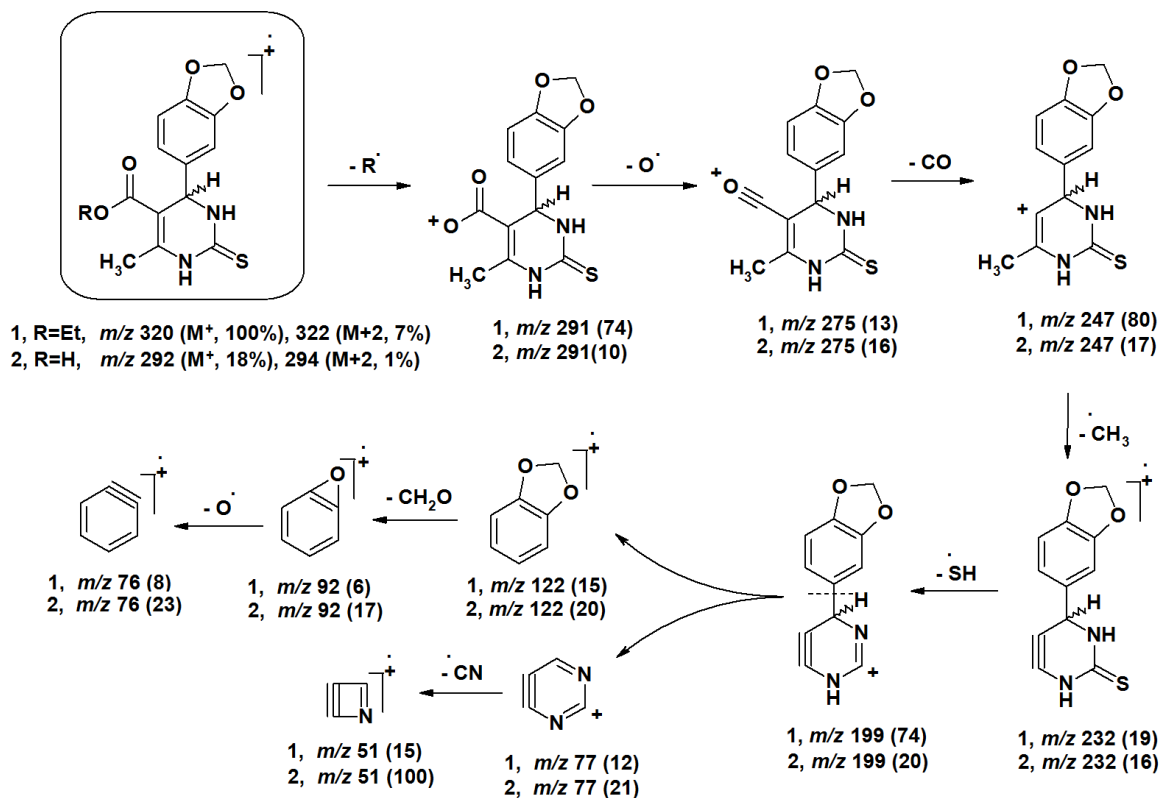


Figure 2.

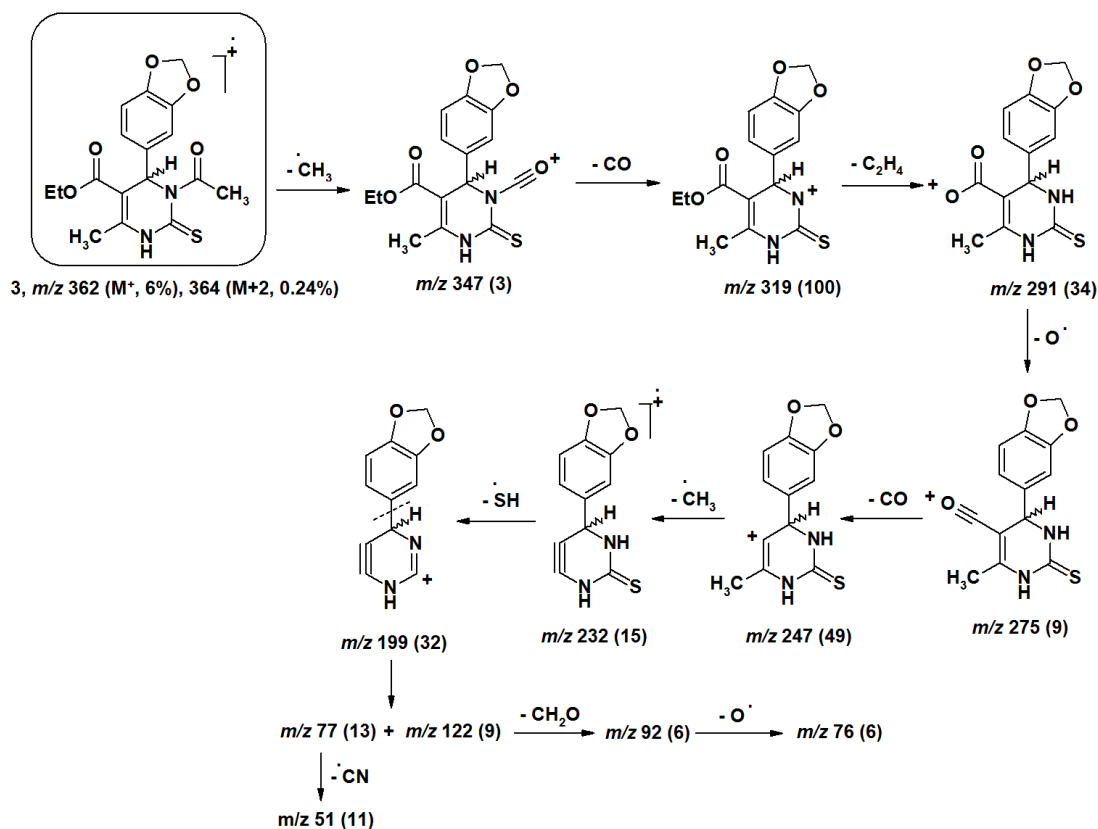


Figure 3.

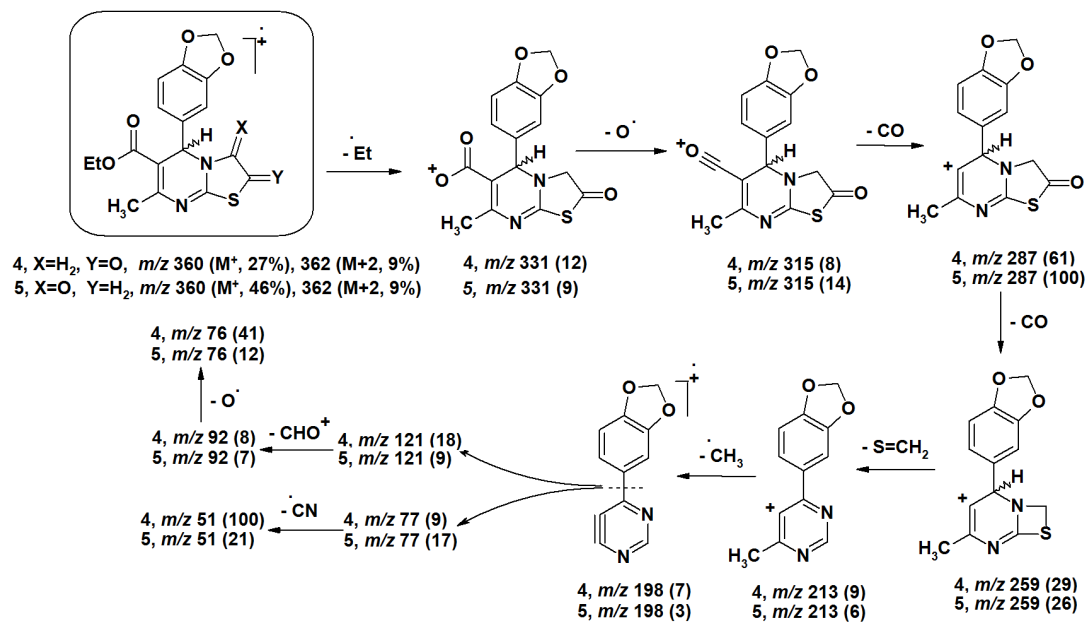


Figure 4.

As depicted in Figure 4, the molecular ion peaks of compounds 4 and 5 appeared as m/z 362 ($M+2$) and 360 (M^+). Because they have isomeric structures, their molecular ions m/z 360 eliminate ethyl radicals producing the fragment cations m/z 331, which remove an oxygen radical to give the acylium ions m/z 315. The presence of thiazolidinone rings

triggered the expected extrusion of CO molecules yielding the fragment cations m/z 287 and m/z 259, respectively. Another cleavage triggered by the presence of thiazetidine rings with loss of SCH₂, which generate the cations m/z 213. The fragments m/z 198 were formed via losing of methyl radicals from the cations m/z 213. The cation radicals m/z

198 undergo the same modes of fragmentation of the fragment m/z 199 in compounds **1-3** (Figures 4). On the other hand, the molecular ion peak of compound **6** undergoes two fragmentation routes. The first route is elimination of ethoxy radical and CO molecule to form the fragments cations m/z 329 and m/z 301, respectively. The presence of thiazolidine moiety triggered cleavage *via* loss of CO and SCO molecules to afford the corresponding cations m/z 273 as a base peak and m/z 213, respectively. The second route involves loss of two CO molecules generating the cation radical m/z 318. The latter ion radical undergoes the expected elimination of ethoxycarbonyl group bringing the ions m/z 273 and m/z 245, respectively. The cation m/z 245 eliminates sulfur radical [23] to produce the previous cation m/z 213, which loses methyl radical to give the cation radical m/z 198. Furthermore, some fragmentation behaviors of the fragment m/z 198 were also noted as shown in the previous compounds (Figure 5).

Group C: Bis{4-(1,3-benzodioxol-5-yl)-5-ethoxycarbonyl-6-methyl-1,2,3,4-tetrahydro-pyrimidin-2-yl}ether (7) and bis{4-(1,3-benzodioxol-5-yl)-5-ethoxycarbonyl-6-methyl-1,2,3,4-tetrahydropyrimidin-2-ylthio} (8). With a view to provide further support to the structures assigned to bis{4-(1,3-benzodioxol-5-yl)-5-ethoxycarbonyl-6-methyl-1,2,3,4-tetrahydropyrimidin-2-yl}ether (7) and bis{4-(1,3-benzodioxol-5-yl)-5-ethoxycarbonyl-6-methyl-1,2,3,4-tetrahydr

opyrimidin-2-ylthio} (8). Their mass spectra were also analyzed. The molecular ions invariably constituting the base peaks were in conformity with their molecular weights. In addition to locating the molecular ions, the mass spectra were also investigated to delineate the characteristic modes of fragmentation as expected from their molecular framework. The molecular ion peak of compound **7** which has the molecular formula $C_{30}H_{30}N_4O_9$ (M.Wt 590) was not recorded. It undergoes rapid partial oxidation to form the cation radical m/z 588. Also, the molecular ion decomposes into the fragments m/z 288 and m/z 287 in the same intensities with along loss of methyl radical. The fragment m/z 288 undergoes loss of the benzodioxol radical m/z 121 and ethoxycarbonyl group to give the cation m/z 167 and cation radical m/z 94, respectively. The 4-methyl-pyrimidine cation radical m/z 94 removes $CH_3-C\equiv CH$ molecule to give the diazetidine cation radical m/z 54. Also, the fragment m/z 287 loses ethylene molecule to give the carboxylic cation m/z 259 as a base peak. This base peak eliminates CO_2 molecule to form the cation m/z 215. The latter cation decomposes into the benzodioxol radical m/z 121 and the pyrimidinyl cation radical m/z 94 in moderate intensities. Each fragment of m/z 121 and m/z 94 behaves a regular fragmentation mode as mentioned in the previous compounds (Figure 6).

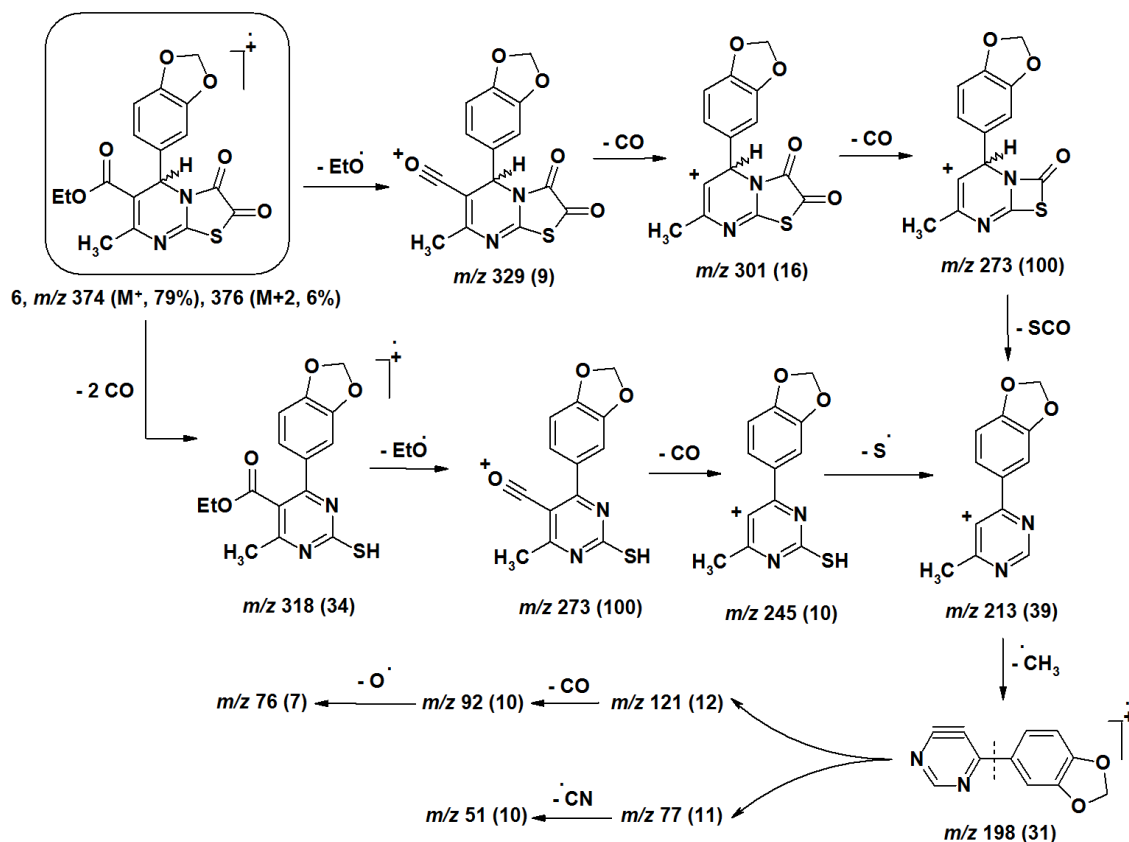


Figure 5.

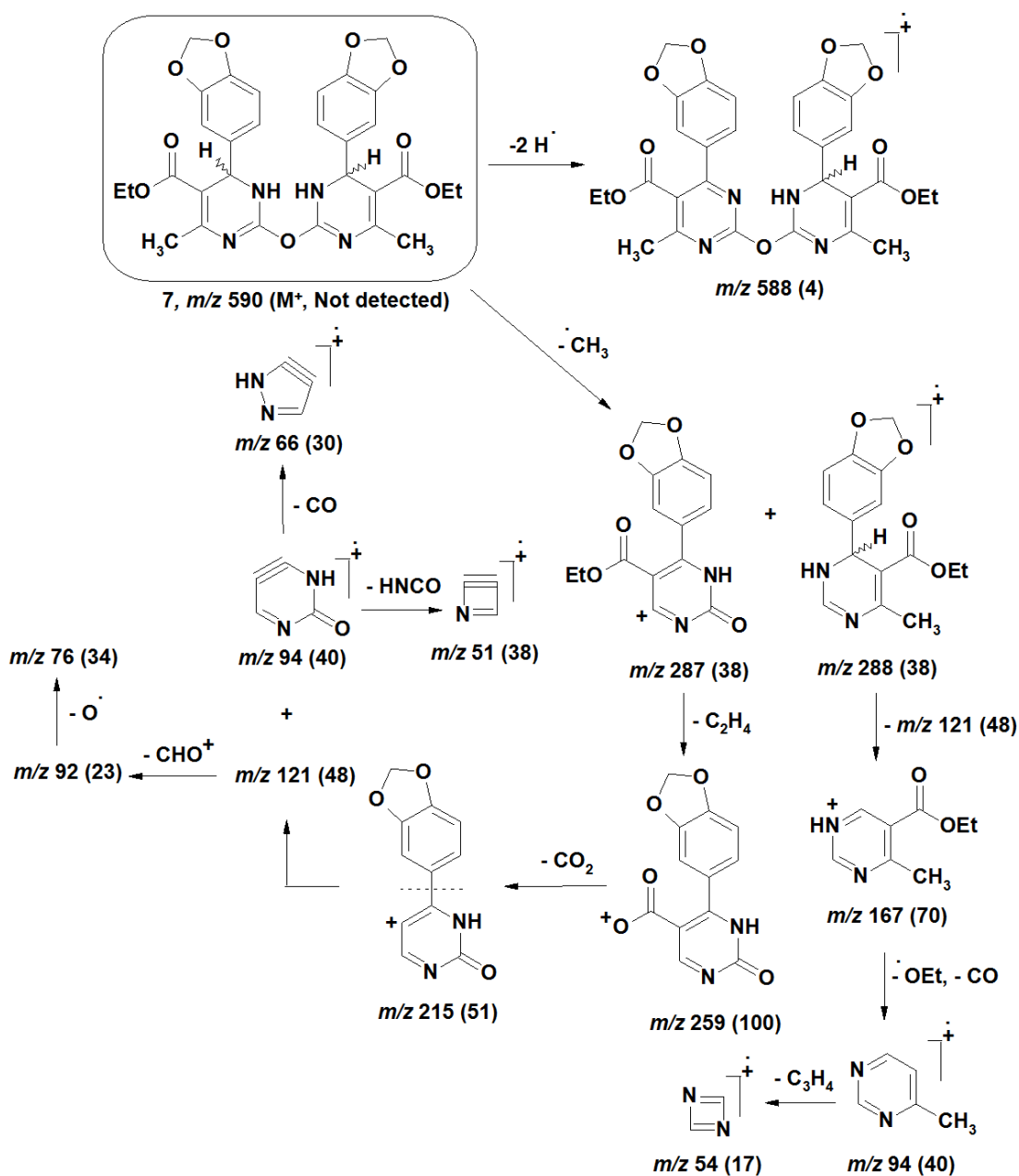


Figure 6.

Similarly, the molecular ion peak of compound **8** was not detected because of it undergoes rapid complete oxidation and elimination of ethoxy radical to give the recorded disulfide cation m/z 589. Fission of the latter cation across the disulfide bond and elimination of methyl radical followed by capture of hydrogen radical [24] resulted in the formation of the fragments m/z 303 and m/z 272. Both these fragments lose the side functional groups such as COOEt, CO and CH_3 to yield the same cation radical m/z 230.

Cleavage of the pyrimidinethione moiety in the fragment m/z 230 gives the moderately stable fragments m/z 147 and m/z 83. The benzodioxol-4-carbonitrile cation radical m/z 147 undergoes elimination of CO_2 molecule affording the cation radical m/z 103, which lose the nitrile radical to afford the phenyl cation m/z 77. The ethoxycarbonyl radical m/z 73 loses an oxygen radical to give the base peak at m/z 57 (Figure 7).

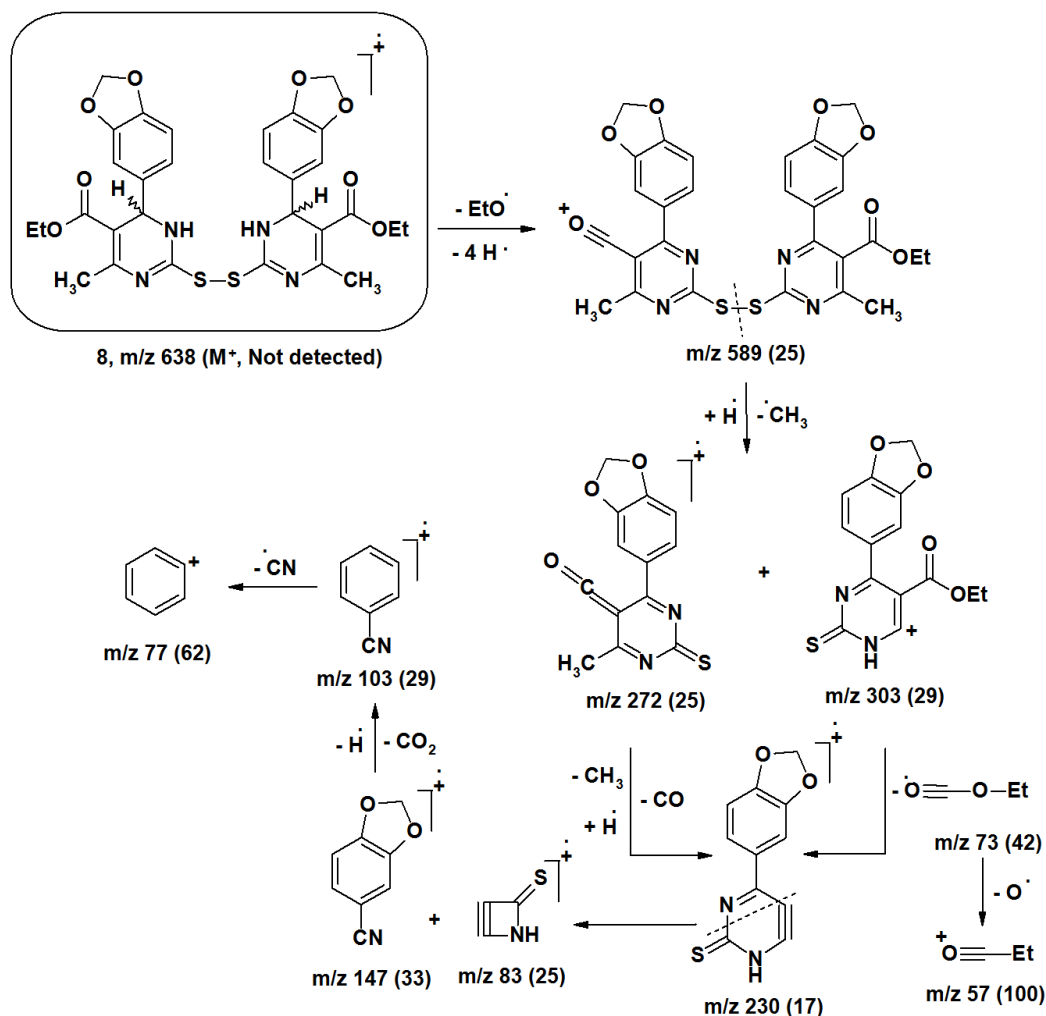


Figure 7.

4. Conclusions

The $[M+\bullet]$ ion of compounds **1–6** are low to high intensities (relative abundances 6–100%). Compounds **7** and **8** did not record their molecular ions. They underwent oxidation process followed by decomposition due to easy breakage of ether and dithioether bonds. Most of the studied compounds recorded the molecular ion peaks $M+2$ due to presence of sulfur isotopes. Compounds of each group take nearly the same fragmentation modes to give the corresponding fragments in similar relative abundance. The fragments obtained from compounds **1–3** are produced by elimination of side functional groups followed by fragmentation of the pyrimidine ring. The compounds **4–6** undergo fragmentation of the thiazole rings followed by fragmentation of the pyrimidine rings. This means the pyrimidine rings are more stable than the thiazole rings during the fragmentation process. Because of the difficult decomposition of the pyrimidinethione moieties in all compounds **1–8**, they appear in the formation of the fragments that have molecular weight larger than m/z 77.

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