

The Mass Spectra of Phthalide and its Sulfur and Selenium Isologs

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The mass spectra of phthalide and its sulfur and selenium isologs have been determined. The fragmentation pattern of dithiophthalide shows some interesting differences from the fragmentation pattern of phthalide. The substitution of a sulfur or selenium for oxygen, or selenium for sulfur produces distinctive changes in the fragmentation schemes of these isologs when compared to phthalide and dithiophthalide. The mass spectra of the isomeric pairs with the group VI element located at either the carbonyl or alcohol portion are nearly identical indicating the location of the sulfur or selenium in the molecule does not significantly alter the fragmentation pathway.

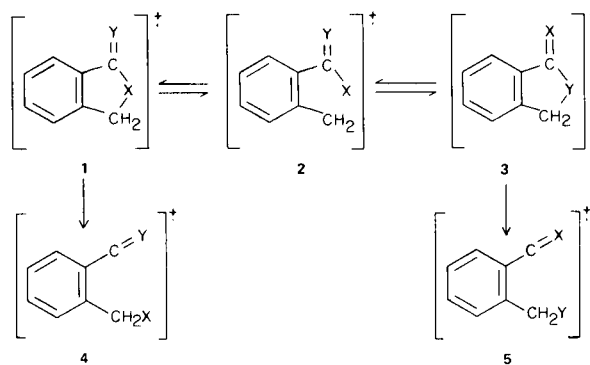
Results.

The mass spectra of phthalide (I) and its sulfur and selenium isologs (II-VIII) have been determined. The spectra are shown in Fig. 1 (a-e) and Fig. 2 (a-c) and their electron impact behavior summarized in Schemes 1-5 (1).

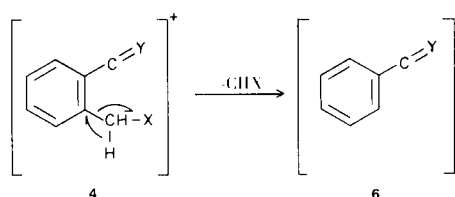
Discussion.

The molecular ions formed from phthalide and its sulfur and selenium isologs can be represented by **1-5**. The fragmentation patterns of these compounds (I-VIII) can be rationalized in terms of the formation of **2**, **4**, and **5** prior to or during the decomposition.

It is obvious from an examination of Fig. 1b, c, d, e and Fig. 2b, c that the mass spectra of the isomeric pairs thiophthalide (II) and thionophthalide (III), selenophthalide (IV) and selenocarbonylphthalide (V), and thionoselenophthalide (VI) and selenocarbonylthiophthalide (VII) are qualitatively identical, exhibiting only small variations in the relative intensities of their fragments. This electron impact behavior was not unexpected in the light of the reported interconversion of *N*-phenylphthalimide and *N*-phenylisophthalimide (2) and tendency of



sulfur-oxygen (3) and selenium-oxygen (4) compounds to rearrange under electron bombardment. This spectral similarity requires that the CH₂-X bond in **1** is broken to form **2** which permits the molecular ions formed from the less stable isomers III, V, and VII (represented by **1**) to rearrange prior to fragmentation to molecular ions similar in structure to those of the more stable isomers II, IV and VI (represented by **3**) respectively.



It can be seen from Schemes 1 and 2 and Fig. 1a and 2a that the spectrum of both phthalide and dithiophthalide (VIII) contain abundant M-CHX (X = O, S) fragments. Their formation from the molecular ion of I and VIII are confirmed by observation of the appropriate metastable ions. A small M-CS fragment is observed by the corresponding M-CO fragment is absent over the range 14-70 eV. The M-CHX (X = O, S) fragments are formed *via* **4** (**5** is identical to **4** when X = Y) after rearrangement of the

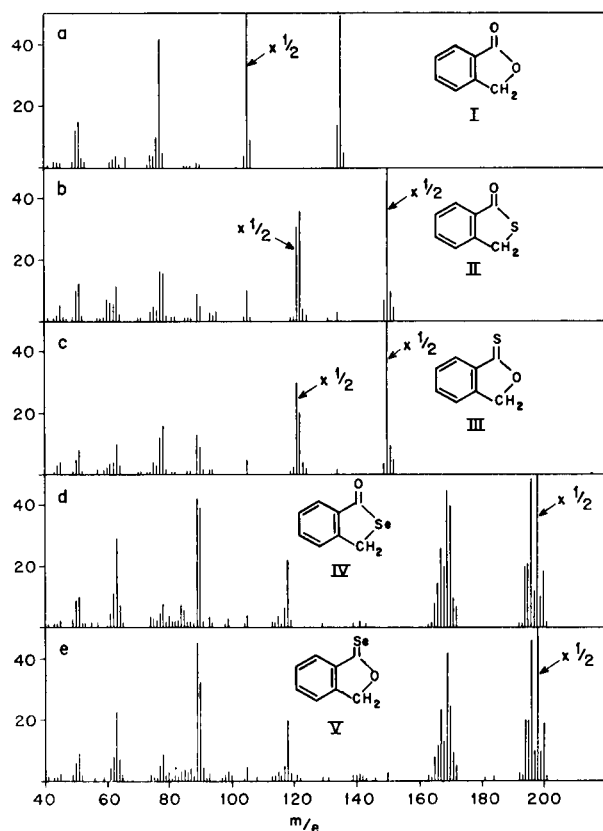


Figure 1.

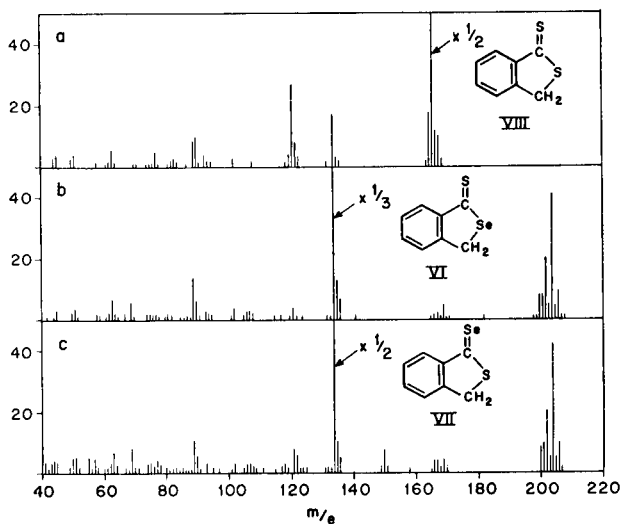
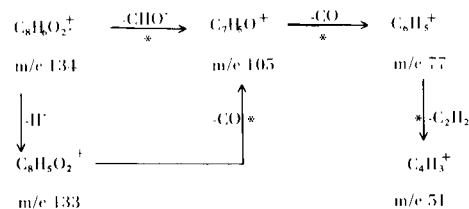


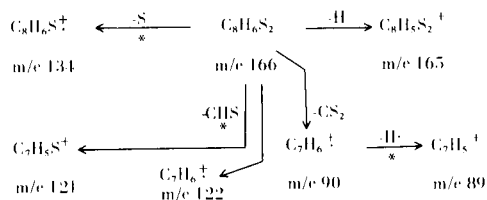
Figure 2.

benzylic hydrogen. This mode of fragmentation cannot be proven without the appropriate ^{13}C , ^{18}O or ^{34}S labeling. However, the fragments at m/e 77, 51 and 50, observed in the spectrum of I, together with the appropriate metastables are consistent with the benzoyl structure for the ion at m/e 105 (6, $\text{Y} = \text{O}$). Similar secondary

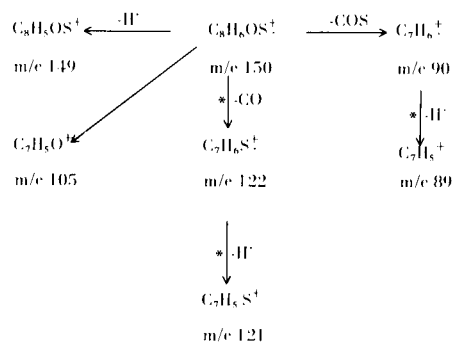
Scheme 1 Fragmentation of Phthalide



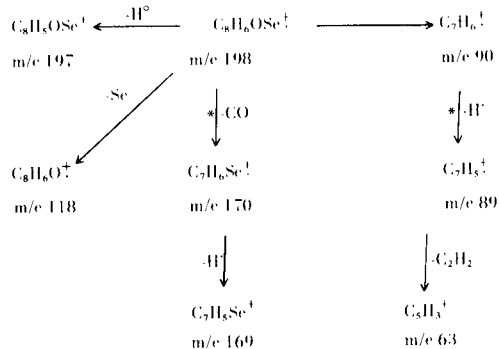
Scheme 2 Fragmentation of Dithiophthalide



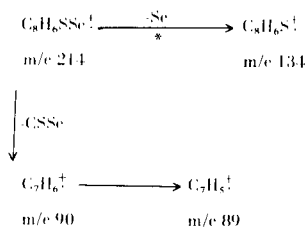
Scheme 3 Fragmentation of Thiophthalides



Scheme 4 Fragmentation of Selenophthalides



Scheme 5
Fragmentation of Selenothiophthalides



fragmentation of the m/e 121 fragment from VIII is not observed. In addition, dithiophthalide does show a relatively abundant peak due to loss of sulfur from the molecular ion for which no analogous M-O fragment is observed in the spectrum of phthalide. The instability of the diselenophthalide prevented its preparation and therefore, its inclusion in this spectral comparison.

It is of interest to compare and contrast the mass spectral behavior of this series of compounds in terms of the ability of the oxygen, sulfur and selenium atoms to influence the fragmentation of each molecule. A previous report on the influence of heteroatoms on the fragmentation of five-membered ring heterocycles included O, S, and Se in the study (5). Within the set where only one heteroatom, X or Y, is varied, the spectra exhibit distinctive fragmentations. These differences can be understood in terms of the influence of the heteroatom on the structure of the molecular ion.

The fragmentation of the thionophthalides, X = O, Y = S summarized in Scheme 3, is best understood by assuming the $\text{CH}_2\text{-X}$ bond in **1** is broken to form **2** which then recycles to form **3**. This conclusion is based on the low abundance of the M-COS and M-COS-H fragments and the high abundance of the M-CO and M-CO-H fragments. These latter fragments could only be formed *via* **5**. In both II and III, a metastable peak confirmed the genesis of m/e 122 (M-CO) from the molecular ion and m/e 121 from m/e 122. No metastable peak was observed to confirm the direct formation of m/e 121 from m/e 150 or m/e 149. Hence, the thiophthalides lose carbon monoxide while phthalide eliminates the formyl group. No fragments derived from loss of sulfur from the molecular ion are observed.

The mass spectra of the selenophthalides, as summarized in Scheme 4, show a marked increase in the fragments at m/e 89 (M-COSe-H), and m/e 90 (M-COSe). This suggests that more than 50% of the fragmentation occurs *via* **2**. The percentage of fragmentation proceeding *via* **2** is based on a comparison of the sum of the abundance of the M-CO and M-CO-H fragments and the M-COSe and M-COSe-H fragments. This means both the $\text{CH}_2\text{-X}$ bond and $\text{CH}_2\text{-Y}$ bond cleave to yield **2** which either recycles

to **3** or decomposes by loss of COSe. The abundant M-CO fragment for which a metastable is observed shows that substantial decomposition *via* **5** does occur. This behavior parallels that observed for the thiophthalides. In contrast to the thiophthalides in which no M-S fragment is observed, there is a fragment at m/e 118 derived by direct loss of Se from the molecular ion. This M-Se fragment (m/e 118) could be formed *via* either **2** or **5**. Therefore, we conclude that phthalide fragments exclusively *via* **4** (or **5**), and that the spectra of thiophthalide and selenophthalide show increasing tendency to fragment *via* **2**. This reluctance of the molecular ion to recycle may be due to the smaller bond angles formed by sulfur and selenium (6) and therefore the lower stability of these five membered heterocyclic systems when compared to oxygen containing heterocycles. The fragmentation must also reflect in part the greater stability of CO versus CS and CSe which will favor elimination of the former molecule over the latter pair. Finally, the ability of the heteroatom to stabilize the positive ion must contribute to the spectrum of the thio- and selenophthalides.

A comparison of the mass spectra of VIII with VI and VII shows that the substitution of selenium for sulfur dramatically alters the mode of fragmentation. The M-CHS fragment observed in VIII is absent in the spectra of VI and < 9% in the spectrum of VII. The spectra of the latter two compounds is dominated by the M-Se fragment for which an analogous but less abundant M-S peak is observed in VIII. While the low abundance of the M-28 fragment and of the m/e 89, 90 peaks prevent any direct analysis, a comparison with the selenophthalides suggest that even though the M-Se can be formed from either **2** or **5**, it is most probably formed *via* **2**. It should be noted that spectrum of the dithiophthalide does contain an M-S fragment but those of the thiophthalides do not.

In conclusion, the replacement of one of the oxygen atoms of phthalide with one of the heavier atoms of group VI effects the electron impact behavior in an expected manner. The abundance of the molecular ion is increased and the subsequent mode of decomposition is altered by the heavier atom. If both oxygens are replaced by sulfur, the molecular ion is the base peak but the primary mode of fragmentation is similar to phthalide. If one of the sulfur atoms is replaced with selenium, the entire mode of fragmentation is radically changed. The largest effects on the spectrum are noted when the group VI atoms in the molecule are not the same. The fragmentation of phthalide and its sulfur and selenium isologs can be understood in terms of the effect of the heteroatoms on the structure of the molecular ions.

While we have noted that there are small differences in the intensities of the fragments of the isomeric pairs, the

question remains whether they are significant enough to allow each to be identified by mass spectrometry. From Figures 1b and 1c, it can be seen that there is a small difference in the ratio of m/e 121 to m/e 122 for the thiophthalides II and III. Since the factors which determine this ratio are unknown, it is marginal whether this difference could be used to distinguish II from III. The spectra of the selenophthalides IV and V, contain such small variations on the ratio of the M-28 to M-29 fragments that for practical purposes the spectra are identical. The M-Se fragment from the thioselenophthalides VI and VII are significantly different so that this pair could be distinguished by mass spectrometry.

EXPERIMENTAL

Phthalide was a commercial sample (Matheson, Coleman and Bell) and the phthalides isologs were prepared by known procedures (6,7) and were available from a previous study on their dipole moments (6).

The mass spectra were recorded on an A.E.I.-MS-9 at 70 eV with 100 μ a ionizing current at a resolution of \sim 1000. The samples were introduced directly into the ion source. The source temperature was 100-125°. The ion abundances reported represent the average from two or more scans.

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REFERENCES

- (1) The stable isotopes of selenium are ^{74}Se (0.87%), ^{76}Se (9.02%), ^{77}Se (7.58%), ^{78}Se (23.52%), ^{80}Se (49.82%) and ^{82}Se (9.19%). Beynon, J. H., "Mass Spectrometry and its Application to Organic Chemistry," Elsevier Publishing Company, New York, 1960, p. 558. Masses are reported relative to the most abundant isotope ^{80}Se .
- (2) C. M. Anderson, R. N. Warrenner and C. S. Barnes, *Chem. Commun.*, 166 (1968).
- (3) J. H. Bowie, D. H. Williams, S.-O. Lawesson, J. Madsen, C. Nolde and G. Schroll, *Tetrahedron*, **22**, 3515 (1966).
- (4) E. Rebane, *Acta Chem. Scand.*, **24**, 717 (1970).
- (5) A. M. Duffield, H. Budzikiewicz and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 2920 (1965).
- (6) I. Wallmark, M. H. Krackov, S. Chu and H. G. Mautner, *ibid.*, **92**, 4447 (1970).
- (7) M. Renson and R. Collienne, *Bull. Soc. Chim. Belg.*, **73**, 491 (1964).