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Mass Spectra of 5,5-Diphenyldithiohydantoin and Methylated Derivatives

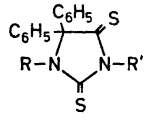
KÁROLY LEMPERT,[a] KÁROLY ZAUER,[a] JØRGEN MØLLER[b] and GUSTAV SCHROLL[c]

[a] *Department of Organic Chemistry, Technical University, Budapest, Hungary,* [b] *Physical Laboratory II, University of Copenhagen, The H. C. Ørsted Institute, DK-2100 Copenhagen Ø, Denmark and* [c] *Chemical Laboratory II (General and Organic Chemistry), University of Copenhagen, The H. C. Ørsted Institute, DK-2100 Copenhagen Ø, Denmark*

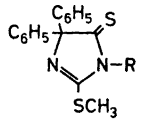
The mass spectra of 5,5-diphenyldithiohydantoin (I) and all possible mono- and dimethylated analogues (II–X) have been recorded and interpreted. High resolution mass measurements, metastable defocussing technique as well as deuterium labeling have been applied. It is shown, that it is possible to distinguish between the methylated isomers by mass spectrometry.

The present study deals with the mass spectra of 5,5-diphenyldithiohydantoin (I) and all possible mono- and dimethylated analogues (II–X). The mass spectra of more hydantoins and a few monothiohydantoins have previously been published and discussed,[2–5] whereas no work dealing with the mass spectra of dithiohydantoins has been made.

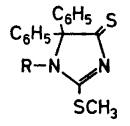
The structures of the compounds under investigation have been studied by IR and NMR spectroscopy,[6–8] and the structures of the compounds both in crystalline state and in solution are those listed below. One of the compounds (V) is found to be stable in two forms (V*a* and V*b*) in the crystalline state. While the compound exists as a mixture of its two tautomeric forms in solution, the conjugated form V*b* is transformed into the isolated form V*a* when subjected to sublimation in vacuum. The structures of the molecular ions formed upon electron impact, however, may differ to a large extent from the "ground state", due to the large amount of excess energy (normally believed to be of the order of 5 eV [9]), but it is not always evident from the mass spectra in which direction the distortions take place.[10–12]



I, R=R'=H
II, R=CH_3, R'=H
III, R=H, R'=CH_3
IV, R=R'=CH_3

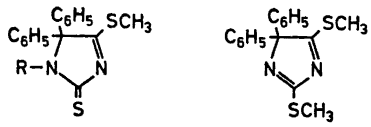


Va, R=H
VI, R=CH_3



Vb, R=H
VII, R=CH_3

* This paper is considered as Part 32 in the series Hydantoins, Thiohydantoins and Glyco-



VIII, R=H
IX, R=CH_3

X

Whereas the *N*-methylated derivatives (II – IV) have retained the double bond structure of the parent molecule (I), *S*-methylation requires migration of one or two double bonds.

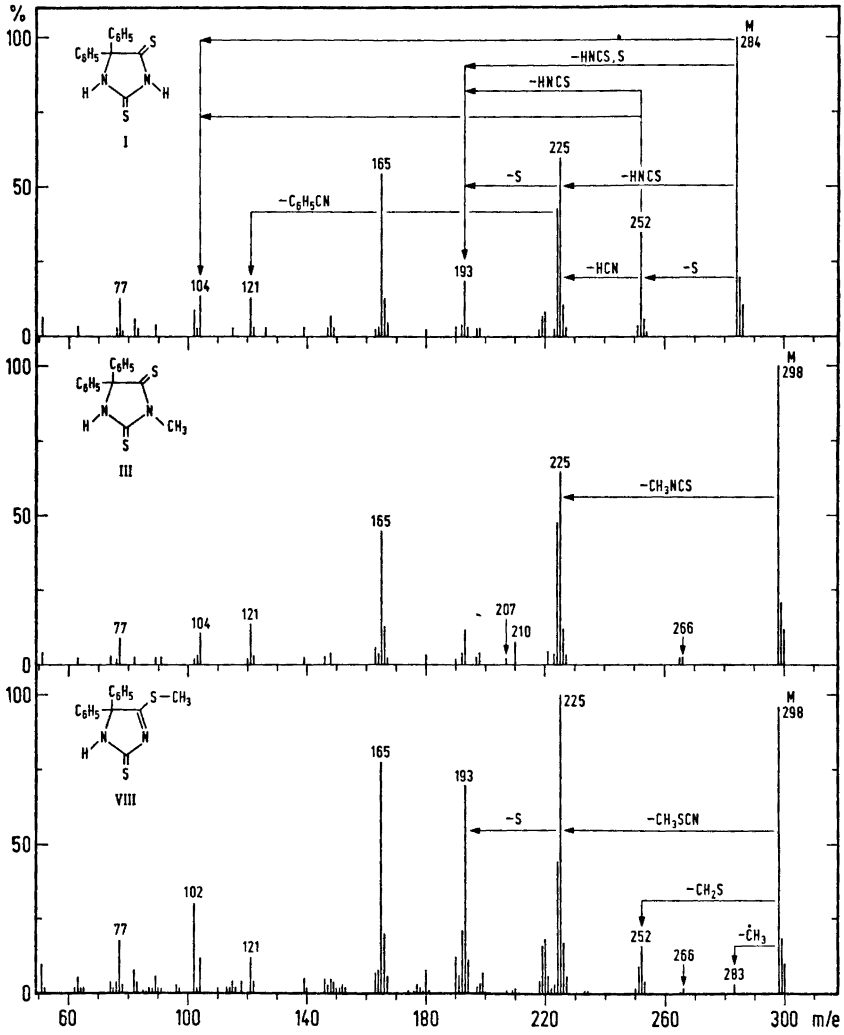


Fig. 1.

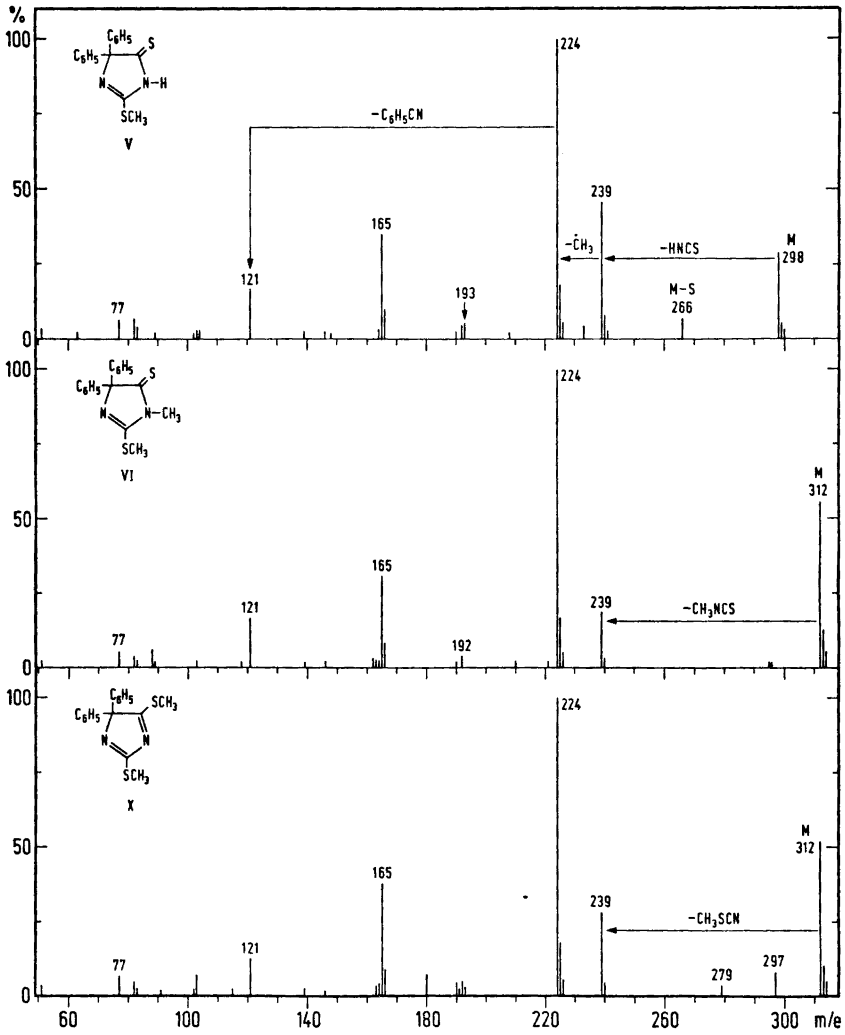

%
100
50
0
V
VI
X
224
239
165
121
193
77
M
298
M-S
266
-HNCS
-·CH3
-C6H5CN
312
192
-CH3NCS
279
297
-CH3SCN
60
100
140
180
220
260
300
m/e

Fig. 2.

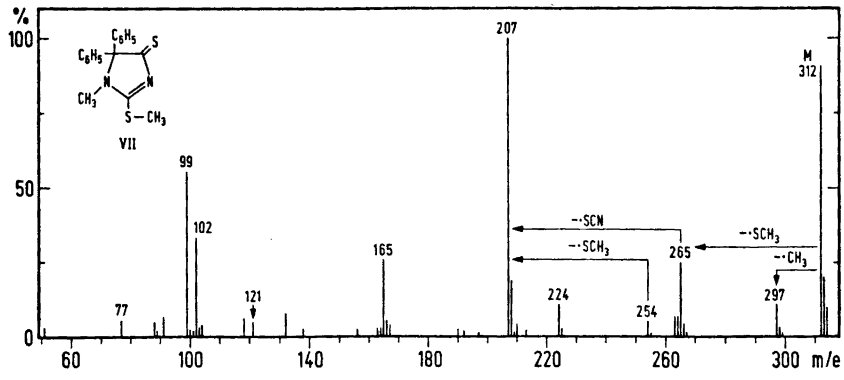

%
100
50
0
VII
207
M
312
99
102
165
121
77
224
254
265
297
-·SCN
-·SCH3
-·CH3
60
100
140
180
220
260
300
m/e

Fig. 3.

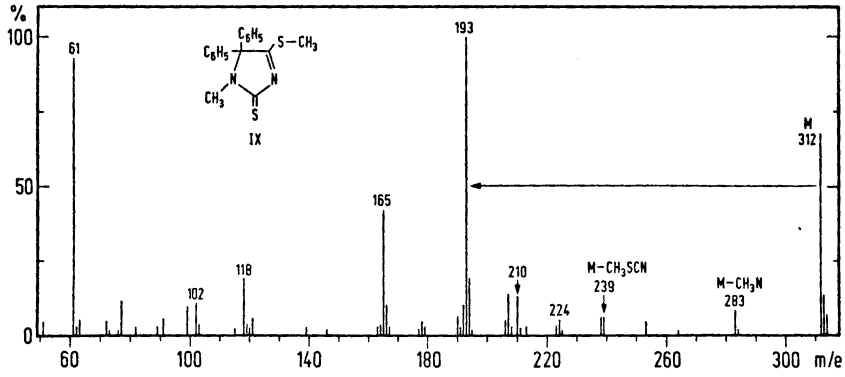


Fig. 4.

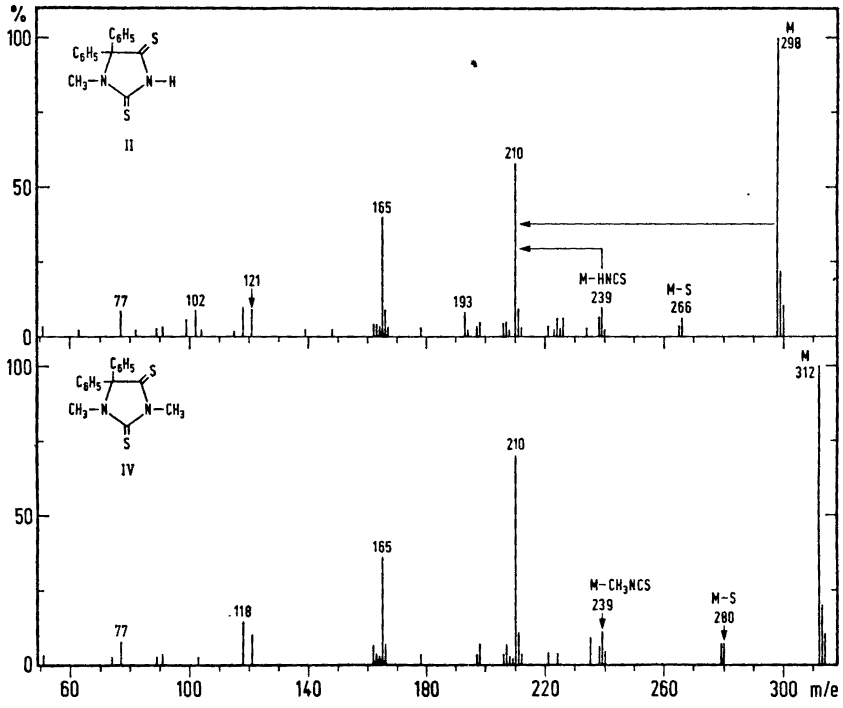


Fig. 5.

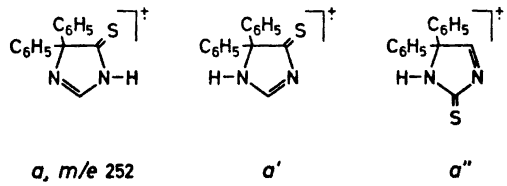
DISCUSSION

From the appearance of the mass spectra (Figs. 1 – 5) the ten compounds under scrutiny can be divided into the following five groups:

Group A: compounds I, III, and VIII
Group B: compounds V, VI, and X

Group C: compound VII
Group D: compound IX
Group E: compounds II and IV

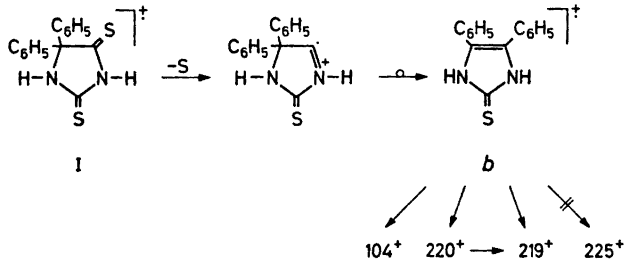
Group A. The mass spectra of the three compounds constituting this group (I, III, and VIII, Fig. 1) display abundant molecular ion peaks (96–100 %) as well as prominent peaks at *m/e* 225, 224, 193, and 165. The mass spectrum of (I) differs from those of III and VIII in the abundance of the M–S ion (35 %), whereas the corresponding ions from III and VIII are only 2.4 and 2.0 %, respectively. The mass spectrum of VIII, however, displays a fairly abundant peak at *m/e* 252 (16 %), corresponding to $M-CH_2S$ and with a composition identical with that of the M–S ions from (I). Peaks due to M–S ions are observed in most of the ten mass spectra studied, but it should be noted, that only (I) undergoes this process to an appreciable extent. Either sulfur atom may be lost in this process. If it is assumed that the desulfurization process takes place only with the migration of a hydrogen atom from one of the nitrogen atoms, the fragment ion can be formulated as any of the three structures *a*, *a'*, and *a''*.



a, *m/e* 252 *a'* *a''*

By the application of metastable defocussing technique (MDT) it was shown that the M–S ion decomposes further into ions of mass 225 (loss of HCN), 193 (loss of HNCS), and 104 ($C_6H_5CNH^+$). The latter processes (formation of 193^+ and 104^+) are most likely if the structure of the M–S ion is *a''*. This structure will also account for the unimportance of the desulfurization in the case of III.

If the sulfur is abstracted from the 4-position and the occurrence of a phenyl migration is assumed the M–S ion can be formulated as *b*.

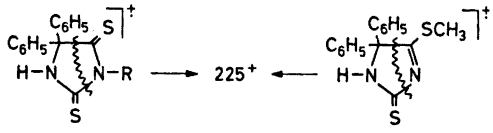


I *b*

The mass spectrum of *b* is known,[13] and it shows no peak at *m/e* 225 and 224, thus *b* can be ruled out as a precursor for these ions.

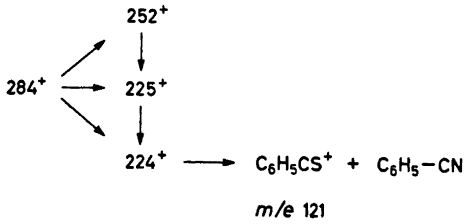
The structure *a''* is also the most likely assignment to the $M-CH_2S$ ion from VIII. Loss of CH_2S from the molecular ions of aromatic and heterocyclic compounds containing a methylthio group is well known.[11,14]

The abundant peaks at *m/e* 225 found in all three mass spectra are due to $M-HNCS$, $M-CH_3NCS$, and $M-CH_3SCN$, respectively. No peaks corresponding to $M-HNCS$ were observed in the mass spectra of III and VIII, indicating that the 1-N nitrogen atom is retained in this process. A plausible mechanism for these processes is depicted below.

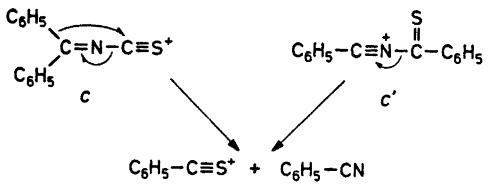


I, III VIII

The ion of mass 224 is formed from the molecular ion as well as from the ion of mass 225, and it decomposes further under the formation of thiobenzoylium ions and neutral benzonitrile, according to the Scheme (valid for (I) only).



The formation of the thiobenzoylium ion requires a phenyl migration. This skeletal rearrangement may take place in any of the four precursors. The *m/e* 224 ion can now be formulated as *c* and *c'*

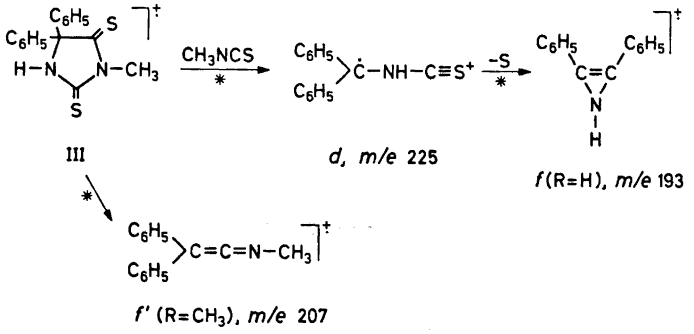


From this it is most likely that the ion of mass 225 has the structure *d* or (less probable) *d'*

The peak at *m/e* 193 in the mass spectrum of (I) is due to an ion formed by decompositions of M^+, M – S as well as M – HNCS, as shown by MDT. The product ion can be formulated as *f* or *f'* (R = H), depending on the structure of the precursors.

f *f'*

A minor peak in the mass spectrum of III at *m/e* 207 is believed to be due to *f* (or *f'*) (R = CH_3). If this is true it is most likely that the ion formed from the molecular ion contains the 3-N nitrogen atom whereas that formed from 225^+ contains the 1-N nitrogen atom. Further, it is most probable then that the 225^+ ion decomposes to *f* (R = H) and the molecular ion to *f'* (R = CH_3), as depicted below.



III *d*, *m/e* 225 *f*(R=H), *m/e* 193

f' (R=CH_3), *m/e* 207

The abundant peak at *m/e* 165 found in all ten mass spectra is due to $C_{13}H_9^+$. Ions of this composition is typically for diphenyl substituted compounds and the structure of these types of ions has recently been discussed.[15,16]

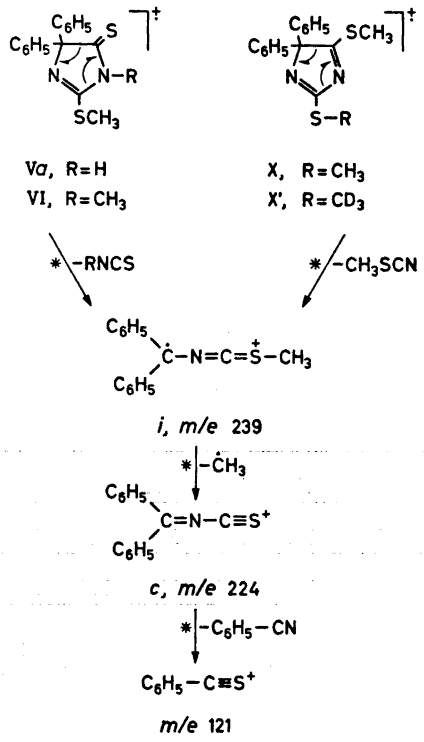
Protonated benzonitrile gives rise to peaks at *m/e* 104 in all three mass spectra. In the case of (I) metastable peaks indicate, that this ion can be formed from the molecular ion as well as from the M – S ions. Minor peaks are found at *m/e* 220 in the mass spectra of (I) and VIII. These are due to M – 2S and M – CH_2S – S, respectively. The peaks at *m/e* 102 are probably due to $C_6H_5-C{\equiv}CH^{+\cdot}$, as supported by high resolution mass measurements (H.R.).

Group B. S-Methylation leads to a changed double bond system and this might be the reason for the diminished abundance of the molecular ion of the three compounds constituting this group (V, VI, and X). Although compound V and VI contain a double bond system different from that of X all three mass spectra (Fig. 2) are very similar. The main process is initiated by the formation of the ion *i* (*m/e* 239) by loss of HNCS, CH_3NCS, and CH_3SCN, respectively, from the molecular ion. The elimination of a methyl radical from *i* leads to the formation of the ion *c* also known from the decomposition

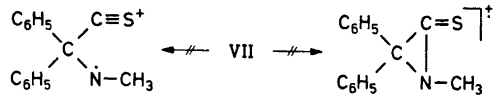
of the Group A compounds. In the mass spectrum of the deuterated derivative X′ the sequence M, $M-CH_3SCN$, $M-CH_3SCN-\cdot CD_3$ was observed, supporting the mechanism depicted below.

From the similarities of the mass spectra of V and VI the structure of V is most likely V*a* in agreement with the observation that V*b* on vacuum sublimation tautomerises to V*a* as mentioned previously.

As the only compound belonging to this group, V undergoes desulfurization. As in the case of Group A, methylation of 3-N seems to make this process unfavourable. Although the mass spectra of the isomeric compounds VI and X are very similar, minor differences (*e.g.* *m/e* 297, 279 and 180) allow the application of mass spectrometry in the identification of these isomers.



Group C. The only compound belonging to this group is VII, having a double bond distribution not found in any of the other compounds under scrutiny (V is believed to be found entirely as V*a*). This structure obviously impedes the elimination of RNCS or RSCN containing the 3-N and 4-C atoms being that important in most of the mass spectra discussed above. However, a 2-C 3-N elimination of CH_3-SCN might still be possible leading to an ion of structure *j* or *j*′ (*m/e* 239), but no peak was observed at *m/e* 239 in the mass spectrum of VII (Fig. 3).



j, *m/e* 239 *j'*

The fragment ion of highest mass is due to M – ·CH_3. Loss of a methyl radical from the molecular ion has not been observed in any of the mass spectra of the *N*-methylated compounds, but is present in the mass spectra of the *S*-methylated analogues VIII and X. It is therefore most likely that the methyl radical in this case is abstracted from the sulfur rather than from the nitrogen atom.

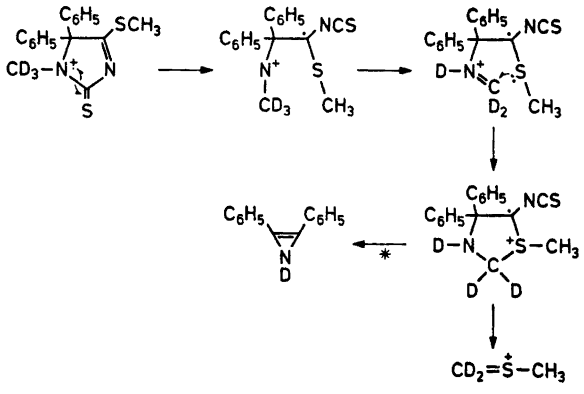
More important is the loss of CH_3S·. This process is also observed in the case of VIII although this compound to a larger extent undergoes elimination of CH_2S. The reason for this difference in decomposition mode is not evident from the present data.

A minor peak at *m/e* 254 is due to M – ·SCN. Together with the M – ·SCH_3 ion this ion constitutes the precursors for the *m/e* 207 ion (*f*, R = CH_3) giving rise to the base peak in the mass spectrum.

The structures of the ions responsible for the peaks at *m/e* 102 (C_2S_2N) and 99 (C_3H_3NS) are not fully understood. Application of MDT gave no reliable answer about the precursors for these ions.

Group D. Compound IX has been studied by deuterium labeling in order to investigate the reasons for this very surprising mass spectrum (Fig. 4). The *m/e*-values of the more important peaks in the mass spectra of IX of the deuterated analogues are found below.

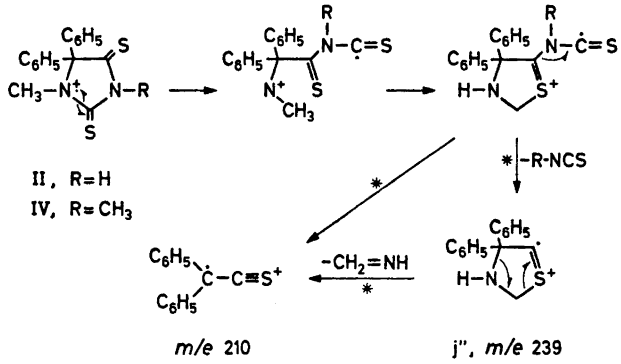
IX		312	283	239	238	224	210	207	193	102	99	61
IX′	*N*-CD_3	315	283	242	241	224	210	210	194	102	102	63
IX″	*S*-CD_3	315	286	239	238	224	210	207	193	102	99	64



The most important processes are formation of 193^+ and 61^+. The latter ion corresponds to $CH_2=\overset{+}{S}-CH_3$. The CH_2-group comes, as seen from the mass spectrum of the *N*-CD_3 analogue, from the *N*-methyl, whereas the CH_3-group comes from *S*-CH_3. The 193^+ ion contains one hydrogen from the *N*-methyl, and none from the *S*-CH_3. This ion can be assigned to the structure *f* (R=H). The formation of 193^+ and 61^+ is visualized above (for *N*-CD_3).

Group E. This group of compounds (II and IV) display abundant molecular ion peaks (100 %). The fragmentation pattern observed for the Group A compounds is also observed here, but with the exception of $C_{13}H_9^+$, the resulting ions are much less intense.

The mass spectra of these two compounds (Fig. 5) exhibit high peaks at *m/e* 210, whereas the mass spectra of the remaining compounds only display peaks at *m/e* 210 of insignificant abundance, if present at all. These peaks correspond to $(C_6H_5)_2C=C=S^{+\cdot}$. The application of MDT in the case of II revealed that the 210^+ ion can be formed from the molecular ion as well as from the M – HNCS ion. The latter process involves the expulsion of a fragment with the composition CH_3N. Based on the observations of the decomposition of compound IX the following mechanism is proposed:



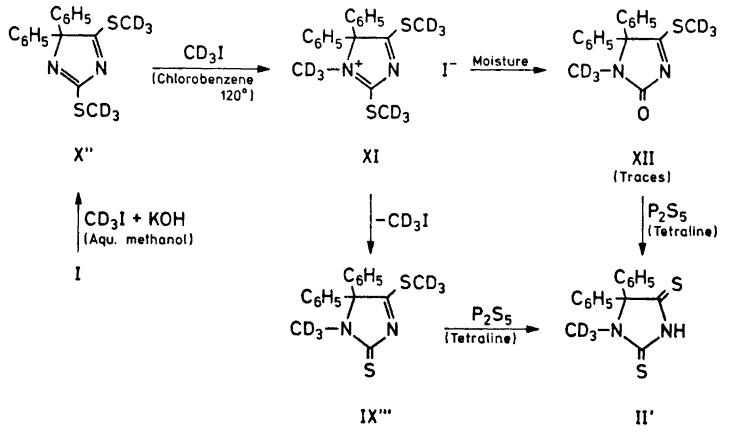
Preparation of the dithiohydantoins

The non-deuterated dithiohydantoin derivatives have, with the exception of V and VII, been synthesised by known methods (see Refs. 17 and 18 and earlier literature cited therein). Compounds V and VII have been obtained by a new method [19] developed for the selective methylation of dithiohydantoins at the 2-S atom, consisting in the treatment of the dithiohydantoins by boron trifluoride dimethyl etherate in boiling benzene or chlorobenzene.

5-Methylthio-4,4-diphenyl-2-trideuteromethylthio-4*H*-imidazole (X′) and 1-methyl-5,5-diphenyl-4-trideuteromethylthio-3-imidazoline-2-thione (IX″) have been prepared by reacting VIII and II, respectively, with trideuteromethyl iodide in the presence of base, as described [17] for the preparation of the their non-deuterated analogues.

4-Methylthio-5,5-diphenyl-1-trideuteromethyl-3-imidazoline-2-thione (IX′) was obtained by methylation of 5,5-diphenyl-1-trideuteromethyldithio-

hydantoin (II′). The latter, in turn, was prepared starting with (I) by a newly developed four step process shown in the Scheme below.



The non-deuterated methosulfate, analogous to XI, has been known for some time.[18] While the methosulfate proved rather stable, XI (as well as the non-deuterated iodide) easily decompose, *e.g.* on heating *in vacuo* to yield IX‴ (and IX, respectively). Although treatment of XI by ethanolic potassium hydrogen sulfide would directly lead to II′ (*cf.* Ref. 18), the two step process is more favourable because phosphorus pentasulfide transforms not only compound IX‴ into the desired II′, but also the oxo derivative XII, always present as a contaminant of XI and, consequently, of IX‴.

At first sight it would seem that II′ could be prepared through the non-deuterated compound X as the intermediate as well. However, under the conditions of the preparation of XI there exists an equilibrium between XI and IX‴ and, as a consequence, a product containing partly *N*-methylated and partly *N*-trideuteromethylated molecules rather than IX‴ would be obtained in this case.

Another, apparently more simple method for the preparation of IX′, using X′ as the starting substance and isomerising the latter directly to IX′ in the same way as X″ had been isomerised to IX‴ is none the less inpracticable. Thus, when X′ was quaternized with trideuteromethyl iodide, and the intermediate subsequently heated *in vacuo*, a product partly methylated and trideuteromethylated at 1-N and 4-S was obtained rather than IX′ demonstrating that, in the course of the preparation of XI (and its partly and non trideuteromethylated analogs) the methyl and trideuteromethyl groups at 5-S also enter into some kind of exchange process.

EXPERIMENTAL

Mass spectra were obtained with an MS902 mass spectrometer at an ionizing potential of 70 eV with direct sample insertion system and an ion source temperature of approximately 200°C. High resolution mass measurements were carried out under the same conditions and with an accuracy within ± 3 ppm.

5-Methylthio-4,4-diphenyl-2-trideuteromethylthio-4H-imidazole (X'). Trideuteromethyl iodide (0.3 ml; 4.7 mmol), was added to a mixture of VIII (1.1 g; 3.7 mmol), potassium hydroxide (0.3 g; 5.4 mmol) methanol (30 ml) and water (4 ml) at room temperature. Crystallization started within a few minutes. The mixture was kept overnight in a refrigerator to yield 1.05 g (90 %) of almost pure X', m.p. 138°C (lit.[17] m.p. of X: 140°C) which was recrystallized from methanol.

1-Methyl-5,5-diphenyl-4-trideuteromethylthio-3-imidazoline-2-thione (IX''). Trideuteromethyl iodide (0.5 ml; 8 mmol) was added to a mixture of II (2.0 g; 6.7 mmol), potassium hydroxide (0.4 g; 7.2 mmol), methanol (60 ml) and water (2 ml). The mixture was worked up as described above for the preparation of X' to yield 1.35 g (64 %) of almost pure IX'', m.p. 206–207°C (ethanol), (lit.[17] m.p. of IX: 205°C). NMR ($CDCl_3$): N-CH_3 3.05 δ, S-CH_3-, (IX: N-CH_3 3.05 δ, S-CH_3 2.60 δ[8]).

2,5-Bis(trideuteromethylthio)-4,4-diphenyl-4H-imidazole (X''). Trideuteromethyl iodide (1.9 ml; 30 mmol) was added dropwise under stirring within about 2 min to a mixture of (I) (3.8 g; 13.6 mmol), potassium hydroxide (2.0 g; 36 mmol), methanol (50 ml) and water (5 ml). Crystallization of the product started soon. The mixture was kept overnight in a refrigerator and diluted with water (50 ml) to yield 3.8 g (88 %) of pure X'', m.p. 140°C.

5,5-Diphenyl-1-trideuteromethyl-4-trideuteromethylthio-3-imidazoline-2-thione (IX'''). The above product (1.8 g; 5.8 mmol) was, without further purification, dissolved in dry chlorobenzene (20 ml), trideuteromethyl iodide (0.3 ml; 4.7 mmol) was added; the mixture was heated in a sealed tube for 30 h to 120°C and evaporated to dryness *in vacuo*. The residue was triturated with petroleum ether (b.p. 40–70°C; 10 ml), filtered by suction and washed with petroleum ether to yield 1.5 g (about 80 %) of crude IX''', m.p. 185–190°C, contaminated according to its IR spectrum by XII.

5,5-Diphenyl-1-trideuteromethyldithiohydantoin (II'). A mixture of crude IX''' (2.4 g; about 7.6 mmol), phosphorus pentasulfide (2.0 g) and dry tetraline (15 ml) was refluxed for 2 h under continuous stirring. The red solution was decanted from the insoluble gummy residue while still hot, the residue was washed with tetraline (2 ml) and the product was precipitated from the combined tetraline solutions by slowly adding under scratching 30 ml of gasoline (b.p. about 140°C) to it. The yellow powder obtained was filtered on the next morning and thoroughly washed with gasoline and petroleum ether to yield 2.25 g of crude II', m.p. 200–206°C. This product was triturated with a mixture of water (15 ml) and conc. ammonia (0.5 ml) in order to remove any (thio)phosphoric acid. After acidification (pH = 6) of the mixture with acetic acid, the product was filtered, washed with water and recrystallized from aqueous acetone to yield 1.6 g (71 %) of II', m.p. 214°C (methanol); lit.[17] m.p. of II: 217°C.

4-Methylthio-5,5-diphenyl-1-trideuteromethyl-3-imidazoline-2-thione (IX'). The above product (0.8 g; 2.7 mmol) was methylated with methyl iodide similarly as described for the preparation of IX'' to yield 0.75 g (90 %) of crude IX', m.p. 198–200°C, contaminated with a small amount of the corresponding 3-imidazolin-2-one. The crude product was dissolved in chloroform (6 ml) and chromatographed through a column of Brockmann alumina (neutral, grade II), the yellow fractions being combined and the dry residue (0.6 g) being recrystallized from methanol-acetone (3 : 2). M.p. 206–206.5°C; lit.[17] m.p. of IX: 205°C. NMR ($CDCl_3$): S-CH_3 2.60 δ, N-CH_3–.

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