

## Mass Spectrometry of Substituted Phenylhydantoic Acids and Phenylhydantoins

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Recently Melvås<sup>1</sup> published results of a mass spectrometric investigation of phenylthiohydantoins, the main result of which was that strong peaks were found at  $m/e=M$ , at  $m/e=135$  (phenylisothiocyanate ion), and at  $m/e=77$  (phenyl ion). A peak at  $m/e=192$  was explained as representing the phenylthiohydantoin ion, formed by the substitution of hydrogen for the carbon chain linked to the  $\alpha$ -carbon atom of the amino acid.

Other minor peaks were explained as resulting from the splitting off of different  $C_nH_{2n+1}$ ,  $C_nH_{2n}$  and  $C_nH_{2n-1}$  fragments. As we had prepared 3-methyl-5-(4'-chlorophenyl)hydantoic acid (I), 3-methyl-5-(3',4'-dichlorophenyl)hydantoic acid (II) and the corresponding hydantoins for other purposes, we found it of interest to compare the fragmentation of these substances with the fragmentation of the phenylthiohydantoins. The mass spectra of the 4 compounds are shown in Figs. 1-4, in which the peak heights are given in a normalised scale, representing the ratios to the highest peak.

The main peaks are as indicated in Tables 1 and 2 where also the ions thought responsible for the peaks are indicated. Besides, a considerable number of very small peaks may be ascribed to a cleavage similar to that assumed by Melvås for the thiohydantoins.

It is seen that the hydantoic acids to some degree are transformed into the hydantoins before the fragmentation starts, most likely by a thermal reaction in the inlet-system (inlet temperature 70°C). However, a peak at  $m/e=88$ , corresponding to a  $CH_3NCH_2COOH$ -ion shows that also direct fragmentation of the hydantoic acids occurs. This also explains that both

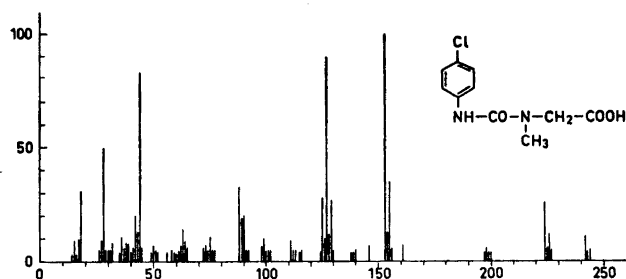


Fig. 1. 3-Methyl-5-(4'-chlorophenyl)hydantoic acid.

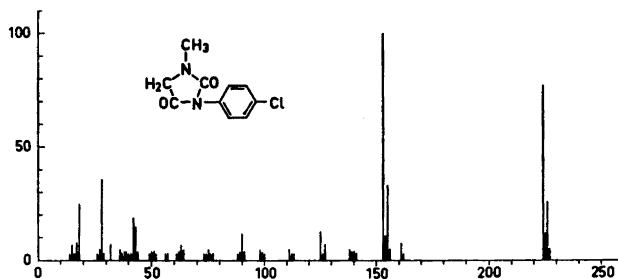


Fig. 2. 1-(4'-Chlorophenyl)-3-methylhydantoin.

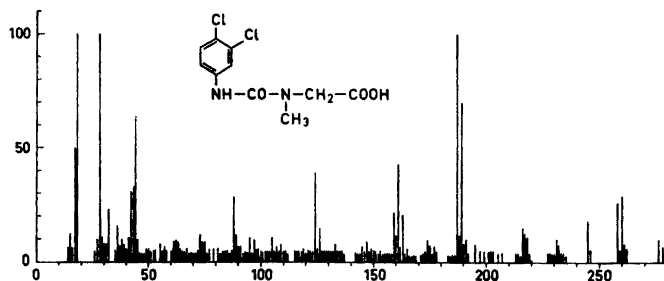


Fig. 3. 3-Methyl-5-(3',4'-dichlorophenyl)hydantoic acid.

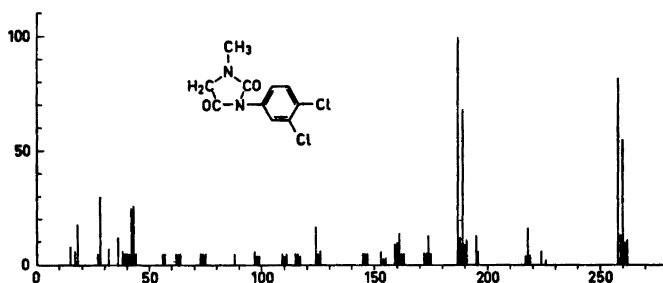
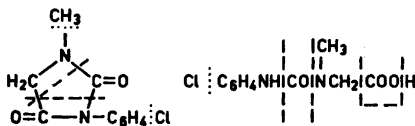


Fig. 4. 1-(3',4'-Dichlorophenyl)-3-methylhydantoin.

I and II show peaks at  $M-44$ , due to decarboxylation of the hydantoic acids, and strong peaks at  $m/e = 44$ , corresponding to  $\text{CO}_2^+$ . These peaks are not found in the hydantoin-spectra.

A strong peak at  $m/e = 127$  in I,  $m/e 161$  in II corresponds to  $\text{ClC}_6\text{H}_4\text{NH}_2^+$  and  $\text{Cl}_2\text{C}_6\text{H}_3\text{NH}_2^+$  formed when the fragments  $\text{ClC}_6\text{H}_4\text{N}$  or  $\text{Cl}_2\text{C}_6\text{H}_3\text{N}$  capture protons. These peaks are much more intense for the hydantoic acids than for the hydantoin.

This fragmentation can be explained as indicated below, ----- meaning the main fragmentation pattern, . . . . . minor fragmentation.



It is seen that the fragmentation follows the same pattern as that found for the phenylthiohydantoin.

*Experimental.* The hydantoic acids were prepared as indicated by Simonian *et al.*,<sup>2</sup> the only difference being that the isocyanates were dissolved in dioxan before adding them to the aqueous solution of the salt of the amino acid and that the temperature was allowed to rise during the reaction whereas Simonian *et al.* keep the temperature below 15°C by cooling.

*3-Methyl-5-(4'-chlorophenyl)hydantoic acid.*

To 36 g (0.4 mol) of sarcosine dissolved in 200 ml of 2 N sodium hydroxide was added a solution of 65 g (0.42 mol) of 4-chlorophenyl-isocyanate in 200 ml of dioxan, the addition causing a slight rise of temperature (to about 40°C). After 1 h 250 ml of water were added to precipitate bis(chlorophenyl)urea, formed by reaction of the isocyanate with water. After filtration the hydantoic acid was precipitated by addition of 130 ml of 4 N sulphuric acid, isolated by filtration and air-dried. Yield 87 g (90 %) with m.p. 121–122°C. Recrystallisation from 10 parts (by weight) of ethyl acetate raised the m.p. to 128–129°C (d). Gobeil *et al.*<sup>3</sup> indicate m.p. 140–141°C but Simonian *et al.*<sup>2</sup> m.p. 127–128.5°C. Just above the m.p.

Table 1. Main fragments of 3-methyl-5-(4'-chlorophenyl)hydantoic acid and of 1-(4'-chlorophenyl)-3-methylhydantoin.

3-Methyl-5-(4'-chlorophenyl)-hydantoic acid	1-(4'-Chlorophenyl)-3-methylhydantoin
<i>m/e</i> corresponding to ion of	<i>m/e</i> corresponding to ion of
242-244 Hydantoic acid	224-226 Hydantoin
224-226 Hydantoin	153-155 $\text{ClC}_6\text{H}_4\text{N}=\text{C}=\text{O}$
153-155 $\text{ClC}_6\text{H}_4\text{N}=\text{C}=\text{O}$	124-126 $\text{ClC}_6\text{H}_4\text{N}$
125-129 $\text{ClC}_6\text{H}_4\text{N}$ and $\text{ClC}_6\text{H}_4\text{NH}_2$	90 $\text{C}_6\text{H}_4\text{N}$
90 $\text{C}_6\text{H}_4\text{N}$	42-44 $\text{CH}_3\text{NCH}_2$ or $\text{CO}_2$
88 $\text{CH}_3\text{NCH}_2\text{COOH}$	
42-44 $\text{CH}_3\text{NCH}_2$ or $\text{CO}_2$	

Table 2. Main fragments of 3-methyl-5-(3',4'-dichlorophenyl)hydantoic acid and of 1-(3',4'-dichlorophenyl)-3-methylhydantoin.

3-Methyl-5-(3',4'-dichlorophenyl)-hydantoic acid	1-(3',4'-Dichlorophenyl)-3-methylhydantoin
<i>m/e</i> corresponding to ion of	<i>m/e</i> corresponding to ion of
276-278 Hydantoic acid	258-262 Hydantoin
258-262 Hydantoin	217-219 $\text{Cl}_2\text{C}_6\text{H}_3\text{N}(\text{CO})_2$
187-191 $\text{Cl}_2\text{C}_6\text{H}_3\text{N}=\text{C}=\text{O}$	187-191 $\text{Cl}_2\text{C}_6\text{H}_3\text{N}=\text{C}=\text{O}$
159-165 $\text{Cl}_2\text{C}_6\text{H}_3\text{N}$ and $\text{Cl}_2\text{C}_6\text{H}_3\text{NH}_2$	159-163 $\text{Cl}_2\text{C}_6\text{H}_3\text{N}$
124-126 $\text{ClC}_6\text{H}_4\text{N}$	124-126 $\text{ClC}_6\text{H}_4\text{N}$
89 $\text{C}_6\text{H}_3\text{N}$	42-43 $\text{CH}_3\text{NCH}_2$ or $\text{CO}_2$
88 $\text{CH}_3\text{NCH}_2\text{COOH}$	
42-44 $\text{CH}_3\text{NCH}_2$ or $\text{CO}_2$	

elimination of water with ring closure to the hydantoin takes place.

Titrated with 0.1 N sodium hydroxide  $E=243.3$  (calc. 242.7) was found.

*3-Methyl-5-(3',4'-dichlorophenyl)hydantoic acid* was prepared analogously from 36 g of sarcosin and 80 g of 3,4-dichlorophenylisocyanate. Yield 90 g (80 %); m.p. 147-148°C. Recrystallisation from 20 parts (by weight) of 50 % ethanol raised the m.p. to 153-154°C (d). Gobeil *et al.*<sup>3</sup> indicate m.p. 155-158°C. Just above the m.p. ring closure to the hydantoin takes place.

Titrated with 0.1 N sodium hydroxide  $E=278.1$  (calc. 277.2) was found.

*1-(4'-Chlorophenyl)-3-methylhydantoin*. 10 g of 3-methyl-5-(4'-chlorophenyl)hydantoic acid were refluxed for 30 min with 50 ml of 6 N hydrochloric acid. After cooling the hydantoin was isolated by filtration. Yield 8.8 g (95 %) with m.p. 118-120°C. Recrystallisation from 10-15 parts (w/v) of tetrachloromethane raised the m.p. to 121-122°C. Kroll<sup>4</sup> indicates m.p. 119-120°C.

*1-(3',4'-Dichlorophenyl)-3-methylhydantoin* was prepared analogously from the correspond-

ing hydantoic acid. Yield 97 % with m.p. 133-138°C which by recrystallisation from 15-20 parts (w/v) of tetrachloromethane was raised to 141-142°C. Kroll<sup>4</sup> indicates m.p. 140-152.5°C.

Thanks are due to Mrs. J. Borg Rasmussen for taking and drawing the mass spectra, using a Perkin-Elmer 270 instrument, solid inlet, ionisation potential 70 eV.

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2. Simonian, J. V., Kroll, H. and Peterson, J. (to Geigy Chemical Corp.), *U.S.P.* 3.205.258 (1965); *Chem. Abstr.* **64** (1966) 3417.
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