Mass Spectra of Isothiocyanates

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The mass spectra of 40 diversely substituted isothiocyanates have been examined and a number of characteristic features noted, which should prove helpful in the micro-identification of naturally derived or synthetic isothiocyanates. Thus all of the alkyl isothiocyanates exhibit a peak at m/e 72 corresponding to the ion CH₃NCS⁺. Lower alkyl isothiocyanates exhibit an m/e 59 ion (NCSH⁺), while higher ones (beyond pentyl) show M−33 (loss of SH) and m/e 115 fragments. Branching in the α- or β-positions as well as introduction of unsaturation into the alkyl portion are easily detected by mass spectrometry. Introduction of a methylthio substituent — so common among naturally derived isothiocyanates — drastically changes the mass spectral behavior, which can again be correlated with the size of the alkyl fragment separating the methylthio substituent from the isothiocyanate grouping. The mass spectra of some isothiocyanates containing aromatic substituents are also reported.

Isothiocyanates derived from glucosidic progenitors in higher plants have been studied extensively in recent years (cf. Ref.¹) and their fast and reliable identification is a matter of considerable interest. Micro-identification procedures would be highly desirable for this purpose and since mass-spectrometry would satisfy these criteria, the mass spectra of an extensive series of naturally derived as well as synthetic isothiocyanates were measured. Bailey et al.² reported previously the mass spectrum of allyl isothiocyanate in connection with a study of flavour constituents in cabbage, and one of the present authors recently utilized mass spectra for the identification of a naturally


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derived keto-isothiocyanate; otherwise, mass spectra of mustard oils do not seem to have been recorded. As shown below, several correlations between mass spectral fragmentation behaviour and structure could be made and there is little doubt that this physical tool, possibly combined with vapour phase chromatography, may prove to be uniquely useful for the rapid characterization of naturally occurring isothiocyanates. In a number of instances, hydrogen rearrangements were observed, for which plausible paths are postulated. A detailed examination of such hydrogen transfers is reserved for a subsequent paper, where the synthesis and mass spectra of suitably deuterated isothiocyanates will be considered.

STRAIGHT CHAIN ALKYL ISOThIOcyanATES

The normal alkyl isothiocyanates comprise the largest single group of the compounds studied, and these shall be considered first. In this consideration it is possible to make comparisons with the published spectra of a large number of monofunctional derivatives of the aliphatic hydrocarbons. Among those compounds whose spectra are reported the most common processes are fissions of the bonds $\alpha$ or $\beta$ to the functional group as follows.

$$\text{R-CH}_2\text{CH}_2\text{CH}_2\text{X} \rightarrow \text{R-CH}_2\text{CH}_2\text{CH}_2^+ + \text{X}^+ \quad (1)$$

$$\rightarrow \text{R-C}_3\text{H}_5^+ + \text{HX} \quad (2)$$

$$\rightarrow \text{CH}_2^+\text{X}^+ + \text{R-CH}_2\text{CH}_2 \quad (3)$$

$$\text{O} \quad \text{H} \quad \text{C} \quad \text{H}_2 \quad \text{R}_1 \quad \text{H} \quad \text{C} \quad \text{H}_2 \quad \text{CH}_2 \quad \text{CH}_2 \quad \rightarrow \text{CH}_2^+\text{CR}_1\text{OH} + \text{R-CH}_2\text{CH}_2 \quad (4)$$

As can be seen in Fig. 1 fission $\alpha$ to the isothiocyanate group is not favoured except in the case of the lower members of the series. Ions of the type $\text{C}_n\text{H}_{2n+1}^+$ (M$-$58) are not found where $n$ is greater than 5. It is noticeable that in the higher members of the series there is no appreciable increase in the hydrocarbon character of the mass spectra as was found in the case of the aliphatic nitriles. $\alpha$-Fission with rearrangement and with ionization of either the isothiocyanate-containing fragment, or the moiety nominally corresponding to the olefin ions, is found only with the smaller molecules. This process can be formulated as taking place via a six-membered-ring transition state similar

* There exists also the possibility of a four-membered (i) rather than six-membered (ii) intermediate. The two possible products, $\text{HNCS}^+$ and $\text{HSCN}^+$, have similar $\Delta H_f$ values, so a decision between the two could not be made in ethyl isothiocyanate by measuring the appearance potential of the m/e 59 ion (R. C. Shenkel, B. G. Hobrock and R. W. Kiser J. Phys. Chem. 66 (1962) 2074).

$$\begin{align*}
\text{H}_2\text{C} & \quad \text{H} \\
\text{H}_2\text{C} & \quad \text{N=C=S} \\
& \rightarrow \text{H-N=C=S}^+ \quad (59^+) \\
& \quad \text{(i)}
\end{align*}$$

$$\begin{align*}
\text{H}_2\text{C} & \quad \text{S} \\
\text{H}_2\text{C} & \quad \text{N} \\
& \rightarrow \text{H-S-C≡N}^+ \quad (59^+) \\
& \quad \text{(ii)}
\end{align*}$$

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to the cleavage predominant in carbonyl compounds. The resultant ion, $a$, of $m/e$ 59, constitutes the base peak in the mass spectrum (Fig. 1) of ethyl isothiocyanate, but appears with decreasing abundance in the spectra of higher homologues, disappearing in the spectra of C₉ and higher compounds (see Fig. 1).

One peak which can be found in the spectra of all members of this series is at $m/e$ 72 ($b$) and corresponds to the ion CH₂NCS⁺. This appears to be analogous to the ion CH₃NH₂⁺ found in the spectra of primary amines. In the case of the isothiocyanates stabilisation of the positive charge can take place by participation of non-bonding electrons both from the sulfur and from the nitrogen atom.

$$\text{CH}_2\text{N}+\text{C}+\text{S} \rightarrow \text{CH}_2\text{N}+\text{C}+\text{S}^+$$

The other ions of significance in the mass spectra of this series of compounds are found only when the alkyl group is pentyl or higher. This fact supports our suggestion that these are formed by means of a cyclic intermediate and have themselves cyclic structures in some cases.

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In the mass spectrum (Fig. 1) of pentyl isothiocyanate there is a peak at \( m/e \) 96 which cannot be described as being analogous to any peak in the spectra of its lower homologues. In a molecule of this formula this peak can only correspond to the loss of \( \text{SH} \) from the molecular ion. Analogous \( M-33 \) peaks are found in the spectra of the higher compounds; the intensity of these increases with the molecular weight of the parent compound. It is impossible to decide definitely the origin of the hydrogen atom which is lost with the sulfur atom, without examining the spectra of deuterated analogues. However, the fact that this cleavage requires a carbon chain of five atoms suggests that a hydrogen on C-5 is involved. The following scheme appears plausible.

![Diagram of molecular structure](image)

In the spectrum of hexyl isothiocyanate and its higher homologues there is a peak at \( m/e \) 115, whose intensity increases with increasing molecular weight. In the case of the hexyl compound this corresponds to the loss of ethylene (the only plausible interpretation of 28 mass units in such a compound). The mechanism shown gives an explanation of striking difference in this mass region between the spectra of pentyl and hexyl isothiocyanates. It is also rather similar to that suggested for the formation of the ion of \( m/e \) 97 in nitrile spectra. In both cases it might be expected that the linear geometry of the functional group might prevent formation of such an intermediate, but linearity may not be retained in the excited molecular ion which is the precursor of this intermediate.

![Diagram of molecular structure](image)

The lower homologue of the \( m/e \) 115 fragment ion is found at \( m/e \) 101. It is present in the spectrum of pentyl isothiocyanate, where it is impossible to form the \( m/e \) 115 ion (\( d \)), and must be formulated as having a five-membered ring (\( e \)). The greater deviation from linearity required to form the intermediate (\( e' \)) is probably responsible for the much lower abundance of \( e \) as compared to \( d \).

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One other peak of interest is found at m/e 96 and appears only when the aliphatic chain is eight or more carbon atoms long. Although the elemental constitution of this ion has not been determined, from simple considerations of mass number it seems probable that it does not contain sulphur. We hope to settle the nature of this fragment by the synthesis of suitably deuterated analogues.

**BRANCHED ALKYL ISOTHIOCYANATES**

In the branched-chain alkyl isothiocyanates there are few exceptions to the patterns of behaviour found among the normal chain compounds. In the spectra (Fig. 2) of the two α-branched compounds, isopropyl and sec-butyl isothiocyanates, the ion b now appears at m/e 86 as would be expected for the ion CH₂CH=NC⁺ obtained by β-fission. There is, however, a peak at m/e 72 in both cases. This must be due to CH₃NC⁺ which can only be formed by a rather involved rearrangement process. There is an analogy in the formation of the C₂H₅⁺ ion in the mass spectrum of isobutane,⁸ which has been studied with the use of labelled compounds.⁹ This involves a rearrangement

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**Fig. 2.** Mass spectra of branched alkyl isothiocyanates.
in which all the carbon atoms of isobutane become equivalent, but a more specific process is probable in the case of the isothiocyanates, e.g. transfer of an α-methyl group to the nitrogen as shown. This hypothesis could be tested by labelling in the α-position.

\[
\text{CH}_3\text{CH} = \text{N} \rightarrow \text{CH}_3\text{CH} = \text{N}^+ \rightarrow \text{CH}_3\text{CH}_2^+ + \text{CH}_2\text{N}^+ \text{C}^+ \text{S}^-
\]

In the spectra of the four β-branched compounds, there occurs along with the peak at \( m/e \) 72 another one at \( m/e \) 73. This must be produced by the other possible six-membered ring transition state of type (4). In these four compounds there are a larger number of hydrogen atoms available for transfer than in the straight-chain analogues. Another possibility involving methyl migration could be excluded, because there exists no peak at \( m/e \) 87 (corresponding to \( \text{C}_6\text{H}_5\text{NCS}^+ \)) in the spectrum (Fig. 2) of 2-ethylbutyl isothiocyanate, which was synthesized for this specific purpose.

\[
\begin{align*}
\text{[H}_{2}\text{C} & \text{(H) C} \text{N} \text{H}_2 \text{CH}_2 \text{CH}_2 \text{CH}_2 \text{N}_{\text{S}} \text{H}^+} \\
\rightarrow & \text{R-CH}_2 \text{C}^\text{CH}_{\text{S}} \text{H}_2 \text{CH}_2 \text{CH}_2 \text{N}_{\text{S}} \text{H}^+ \\
\text{CH}_2 = \text{N} & \text{S} \text{C} \text{H}_2 \text{CH}_2 \text{CH}_2 \text{N}_{\text{S}} \text{H}^+ \\
\end{align*}
\]

(73*)

It is interesting to note that in the spectrum (Fig. 2) of 2-methyloctyl isothiocyanate, there are found strong peaks at \( m/e \) 152 (c: M—33) and \( m/e \) 129 (d*). These are consistent with the earlier discussed fragmentation of long-chain alkyl isothiocyanates (Fig. 1), while only a weak \( m/e \) 73 peak — associated with β-branching — is noted. Clearly, the former type of fragmentation is preferred when both paths are available.

\[
\begin{align*}
\text{[CH}_2\text{CH}_2\text{CH}_2 & \text{CH}_2 \text{C} \text{(S) H}_2 \text{C} \text{C} \text{N} \text{H}_2 \text{CH}_2 \text{CH}_2 \text{N}_{\text{S}} \text{H}^+} \\
\rightarrow & \text{SH} \text{C} \text{C} \text{N} \text{H}_2 \text{CH}_2 \text{CH}_2 \text{N}_{\text{S}} \text{H}^+ \\
\end{align*}
\]

d*(129*)

So far it has not been possible to predict the direction of cleavage at the branched carbon atom. Loss of an alkyl branch is found in all cases except in isobutyl isothiocyanate, where the predominant peak is \( m/e \) 43 (\( \text{C}_3\text{H}_7^+ \)). The difference is probably determined by the stability of the latter ion with respect to the other products of branch cleavage.

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METHYLTHIOALKYL ISOTHIOCYANATES

In Fig. 3 are shown the mass spectra of some straight-chain methylthioalkyl isothiocyanates. In all cases except one (3-methylthiopropyl isothiocyanate)

<table>
<thead>
<tr>
<th>Isothiocyanates</th>
<th>Formula</th>
<th>40</th>
<th>60</th>
<th>80</th>
<th>100</th>
<th>120</th>
<th>140</th>
<th>160</th>
<th>180</th>
<th>200</th>
<th>220</th>
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</thead>
<tbody>
<tr>
<td>Methylthiomethyl</td>
<td>CH₂SCH₂NCS</td>
<td>45</td>
<td>61</td>
<td>72</td>
<td>119</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2-Methylthioethyl</td>
<td>CH₂S(CH₃)₂NCS</td>
<td>119</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3-Methylthiopropyl</td>
<td>CH₂SCH₃NCS</td>
<td>41</td>
<td>69</td>
<td>72</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>4-Methylthiobutyl</td>
<td>CH₂S(CH₂)₂NCS</td>
<td>55</td>
<td>69</td>
<td>72</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-Methylthiopentyl</td>
<td>CH₂SCH₂NCS</td>
<td>69</td>
<td>69</td>
<td>72</td>
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<td></td>
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<td></td>
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<tr>
<td>6-Methylthiophenyl</td>
<td>CH₂S(CH₂)₆NCS</td>
<td>89</td>
<td>100</td>
<td>69</td>
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<tr>
<td>7-Methylthioheptyl</td>
<td>CH₂SCH₂NCS</td>
<td>100</td>
<td>69</td>
<td>72</td>
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</tr>
<tr>
<td>8-Methylthiooctyl</td>
<td>CH₂SCH₂NCS</td>
<td>100</td>
<td>69</td>
<td>72</td>
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</table>

Fig. 3. Mass spectra of ω-methylthioalkyl isothiocyanates.

the base peak occurs at m/e 61 which is also the base peak of all simple alkyl methyl sulphides. This is a typical example of type (3) β-fission with stabilisation of the resultant ion as CH₂S⁺=CH₂. Many of the peaks at m/e 41, 55 and 69 (C₃H₇⁺, C₄H₇⁺ and C₅H₈⁺) are present in the thioether spectra but not those (see Fig. 1) at m/e 43 and 57 (C₃H₇⁺ and C₄H₈⁺). This is to be expected since formation of one of the latter ions from a methylthioalkyl isothiocyanate would involve transfer of a hydrogen from a fragment containing an electronegative atom to one containing only carbon and hydrogen. In all cases the CH₂=NCS ion is present at m/e 72.

In the spectrum (Fig. 3) of methylthiopropyl isothiocyanate the base peak is at m/e 101 rather than m/e 61. In the next higher (butyl) homologue there is an intense peak at m/e 115. Both peaks represent the loss of 46 mass units (equivalent to thioformaldehyde) from the molecular ion, and they could be produced by a mechanism similar to that invoked for the formation of ions d and e in the alkyl isothiocyanate series. The next homologous peak occurs at m/e 129 in the spectrum of methylthiopentyl isothiocyanate. Its low intensity is a consequence of the lower probability of formation of the necessary seven-membered ring (f).

It is noticeable that when the thioether function becomes further removed from the isothiocyanate group the m/e 101 and 115 peaks reappear as does the M—33 peak. Again the requirements of carbon chain length for forma-

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tion of these ions are the same, as are found (Fig. 1) for the higher alkyl isothiocyanates: C₅ for M−33 and m/e 101, C₆ for m/e 115. In the spectra of the higher homologues there is a peak at M−47 which must be due to the loss of SCH₃.

**UNSATURATED ISO THIOCYANATES**

In the spectra of the unsaturated isothiocyanates (Fig. 4) allylic fission dominates. Where the allylic bond is α to the nitrogen atom (first four examples

<table>
<thead>
<tr>
<th>Isothiocyanates</th>
<th>Formula</th>
<th>40</th>
<th>60</th>
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<th>100</th>
<th>120</th>
<th>140</th>
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</thead>
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<tr>
<td>Allyl</td>
<td>CH₂=CHCH₂NCS</td>
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<td>M⁺</td>
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<tr>
<td>trans-Crotonyl</td>
<td>CH₃CH=CHCH₂NCS</td>
<td>55</td>
<td>M⁺</td>
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<tr>
<td>2-Methylallyl</td>
<td>CH₂=CHCH₂NCS</td>
<td>72</td>
<td>M⁺</td>
<td>113</td>
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<tr>
<td>1-Methylallyl</td>
<td>CH₂=CHCH₃NCS</td>
<td>72</td>
<td>M⁺</td>
<td>113</td>
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<td></td>
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<tr>
<td>3-Butenyl</td>
<td>CH₂CH(CH₂)NCS</td>
<td>72</td>
<td>M⁺</td>
<td>127</td>
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<td></td>
</tr>
<tr>
<td>4-Pentenyl</td>
<td>CH₂CH(CH₃)NCS</td>
<td>72</td>
<td>M⁺</td>
<td>127</td>
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</tr>
</tbody>
</table>

*Fig. 4. Mass spectra of alkenyl isothiocyanates.*

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in Fig. 4), the most abundant ion will be the allyl ion at $m/e$ 41 or 55. When the allylic bond is $\beta$ to the nitrogen atom, as in the case of 3-butenyl isothiocyanate, the predominant ionized fragment is $\text{CH}_3=\text{NCS}^+$ at $m/e$ 72. Finally, where a $\gamma$-relationship exists as in 4-pentenyl isothiocyanate, the most abundant ion is the allyl ion $\text{C}_2\text{H}_5^+$. This behaviour is consistent with our knowledge of the behaviour of the saturated compounds, i.e. that $\text{CH}_3\text{NCS}^+$ is a much more stable ion than NCS$^+$ or $\text{CH}_2\text{CH}_2\text{NCS}^+$. In the spectrum of the last-mentioned compound, the peak at $m/e$ 85 can be explained by postulation of a process similar to that invoked for the formation of the ion of $m/e$ 42 in the spectrum of pent-1-ene.

AROMATIC ISOTHIOCYANATES

In the spectra (Fig. 5) of the aromatic isothiocyanates similarities can be found to the behaviour of other aromatic compounds. The most intense peak

<table>
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<th>Isothiocyanates</th>
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<td>Phenyl</td>
<td>$\text{C}_6\text{H}_5\text{NCS}$</td>
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<td>51</td>
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<tr>
<td>Benzyl</td>
<td>$\text{C}_6\text{H}_5\text{CH}_2\text{NCS}$</td>
<td>91</td>
<td></td>
<td></td>
<td>91</td>
<td>149</td>
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<tr>
<td>a-Methoxybenzyl</td>
<td>$\text{C}_6\text{H}_4\text{CH}_2\text{NCS}$</td>
<td>121</td>
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<td></td>
<td></td>
<td>179</td>
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</tr>
<tr>
<td>m-Methoxybenzyl</td>
<td>$\text{C}_6\text{H}_4\text{CH}_2\text{NCS}$</td>
<td>121</td>
<td></td>
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<td></td>
<td>179</td>
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<tr>
<td>p-Methoxybenzyl</td>
<td>$\text{C}_6\text{H}_4\text{CH}_2\text{NCS}$</td>
<td>106</td>
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</tr>
<tr>
<td>1-Phenylethyl</td>
<td>$\text{C}_6\text{H}_4\text{CH}_2\text{NCS}$</td>
<td>91</td>
<td>19</td>
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<td>145</td>
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<tr>
<td>2-Phenylethyl</td>
<td>$\text{C}_6\text{H}_4\text{CH}_2\text{NCS}$</td>
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<td>145</td>
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<tr>
<td>1-Phenylpropyl</td>
<td>$\text{C}_6\text{H}_4\text{CH}_2\text{NCS}$</td>
<td>91</td>
<td>19</td>
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<td></td>
<td>145</td>
<td></td>
<td>177</td>
<td></td>
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</tr>
</tbody>
</table>

Fig. 5. Mass spectra of aromatic isothiocyanates.

in the spectrum of phenyl isothiocyanate is $\text{C}_6\text{H}_5^+ (m/e 77)$ which is formed by fission of the only single bond in the molecule. As was found with the allyl isothiocyanates, the fragment NCS$^+$ does not appear as an ion to any great extent. The behaviour of the benzyl homologue is similar except that the increased lability of a benzylic over a phenyllic bond is reflected in the lower

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abundance of the molecular ion. The next higher homologue, \( \beta \)-phenylethyl isothiocyanate, exhibits a very intense \( m/e 91 \) peak as does the benzyl compound. This is similar to the behaviour of alkyl benzenes where the very stable ion of \( m/e 91 \) has been shown to be the tropyl ion.\(^{12}\) Although the spectra of \( \beta \)-phenylethyl esters\(^{13}\) exhibit an abundant styrene ion \( (m/e \ 104) \), this is not the case (see Fig. 5) in \( \beta \)-phenylethyl isothiocyanate where the tropyl ion \( (m/e \ 91) \) represents the base peak and no corresponding peak at \( m/e \ 104 \) is observed.

This benzylic fission is also noted in the spectra (Fig. 5) of \( \alpha \)-phenylethyl and \( \alpha \)-phenylpropyl isothiocyanates, where this process is accompanied by a hydrogen migration. No analogous spectra of pairs of \( \alpha \) - and \( \beta \)-phenylpropyl isomers have been reported, but the highest peak at \( m/e \ 91 \) in the spectrum (Fig. 5) of 1-phenylpropyl isothiocyanate shows clearly the operation of the following fragmentation through the detection of a metastable peak at \( m/e \ 70 \) (caled. 69.6 for transition \( m/e \ 119 \rightarrow m/e \ 91 \)):

\[
\text{[CH-CH-NCS]}^+ \rightarrow \text{[CH}^+ \text{CHCH}_2\text{H]} \rightarrow \text{[CH}^+ \text{CH}_2\text{]} \ (119^+) \rightarrow \text{[CH}^+ \text{]} \ (91^+)
\]

It is noticeable that in the spectra of the isothiocyanates all rearrangements of type (4) are much more prevalent when the hydrogen to be transferred is primary, rather than secondary or tertiary. This is contrary to our experience with amides\(^ {14} \) or steroid ketones.\(^ {15} \)

The three isomeric methoxybenzyl isothiocyanates have significantly different mass spectra (Fig. 5), the greatest difference being in the intensity of the \( m/e \ 91 \) peak, which is much stronger in the ortho isomer than in the other two substances. In all three isomers, benzylic fission gives rise to the peak at \( m/e \ 121 \), which will be the methoxybenzyl \(^ {16} \) (or methoxytropyl \(^ {12} \)) ion.

It seems quite probable that this ion is the benzyl rather than tropyl ion, since the latter should be the same in all three cases. This would be consistent with the behaviour of the methoxybenzyl chlorides, which exhibit in their mass spectra ions at \( m/e \ 121 \), which have been shown\(^ {16} \) to possess the methoxybenzyl structure. The exceptionally intense \( m/e \ 91 \) peak in \( \alpha \)-methoxybenzyl isothiocyanate has also been noted in several other organic compounds possessing the \( \alpha \)-methoxybenzyl fragment and its formation will be discussed elsewhere in detail.

**EXPERIMENTAL**

All mass spectra were obtained with a Consolidated Electrodynamics Corporation 21—103C mass spectrometer fitted with an all-glass heated inlet system, which was maintained at 200\(^ {\circ} \). An ionizing current of 50 \( \mu A \) and an ionizing potential of 70 eV were used.

Most of the isothiocyanates employed in the present investigation were synthesized in the Copenhagen laboratory from the corresponding amines by standard procedures. The long-chain, aliphatic mustard oils \( (C_8, C_{10}, C_{12}, C_{14}, C_{16}) \) were prepared by Dr. D. Willis and kindly placed at our disposal through the good offices of Dr. S. F. Cox, I.C.I.A.N.Z., Ascot Vale, Victoria, Australia.

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Several of the compounds were specifically synthesized in connection with current studies of naturally derived isothiocyanates, including 2-butyl,17 2-methylbutyl,17 methyl-
thiomethyl,18 2-methylthioethyl,19 3-methylthiopropyl,20 4-methylthiobutyl,21 5-methyl-
thyopentyl,2 6-methylthiohexyl,19 7-methylthioheptyl,19 and 8-methylthiooctyl isothio-
cyanate.19 Again, trans-crotol,22 1-methylallyl,23 2-methylallyl,23 3-butenyl,23 and 4-pento-
nyl isothiocyanate 24 were species prepared for similar purposes. Of the aromatic mustard oils, o-methoxybenzyl,25 m-methoxybenzyl,26 and p-methoxybenzyl isothiocyanate 27
were synthesized as reference samples for these studies.

The majority of the products utilized for mass spectrometry were analytical speci-
mens, proved to be homogeneous on vapour phase chromatography.

The following three isothiocyanates were prepared for the first time in connection
with the present studies.

(±)-1-Phenylpropyl isothiocyanate. (±)-1-Phenylpropylamine (5.4 g), prepared from
propiophenone by the Leuckart-reaction, was dissolved in chloroform (50 ml) and added,
in the course of 2 h, to an ice-cooled solution of thiocarbonyl chloride (6.9 g) in chloro-
form (200 ml).

Excess chloroform and thiocarbonyl chloride were distilled through a column, and
the residue was distributed between ether and dilute HCl. From the aqueous phase,
unchanged amine (2.2 g) was recovered. After removal of the solvent, the isothiocyanate
was distilled twice to give a pure specimen (58 % yield, based on unrecovered amine),
as a colourless oil, b.p. 128–129°/9 mm, nD20 1.5717 (Found: C 67.86; H 6.31; N 7.92. Calc.
for C9H11NS: C 67.75; H 6.26; N 7.90).

On reaction with ammonia, the isothiocyanate was converted into 1-(1-phenylpropyl)-
thiourea, m.p.* 135–136° (Found: C 61.71; H 7.40; N 14.29. Calc. for C9H11N2S: C 61.80; H
7.26; N 14.42). The corresponding phenylthiourea was formed on reaction with aniline,

2-Ethylbutyl isothiocyanate. 2-Ethylbutanenitrile, prepared in 70 % yield from 2-
ethylbutyric acid via the acid chloride and amide, essentially as described elsewhere,28
served as a convenient starting material for the synthesis of 2-ethylbutylamine, required
for production of the mustard oil.

The nitrile (13.4 g) was reduced with lithium aluminium hydride (7.8 g) in ether solu-
tion (200 ml) in the usual way to give a 74 % yield of distilled 2-ethylbutylamine, b.p.
124°, nD20 1.4200 (Lit. values: b.p. 121–122°/725 mm,29 74–75°,30 125°). The picrate was
prepared, m.p. 175–177° (Lit. 168–169°).31

The amine (9.1 g), dissolved in chloroform (35 ml), was added, in the course of 15 min,
to a cooled and vigorously stirred mixture of thiocarbonyl chloride (20.7 g), dissolved in
chloroform (100 ml), and sodium hydroxide (20 g) in water (100 ml). The organic phase
was washed with acid and water, and dried. After removal of the solvent over a small
column, 2-ethylbutyl isothiocyanate distilled as a colourless oil (7.1 g). The product
was redistilled before analysis, b.p. 80.5°/9 mm, nD20 1.4967 (Found: C 58.61; H 9.13;
N 9.64. Calc. for C10H17NS: C 58.71; H 9.15; N 9.78). The phenylthiourea, formed upon
reaction with aniline, separated from ether/pentane in colourless prisms, m.p. 57°. (Found:
C 66.00; H 8.58; N 11.72. Calc. for C10H15N2S: C 66.06; H 8.53; N 11.85).

(±)-2-Methylolctyl isothiocyanate. (±)-2-Octanol was converted into 2-chlorooctane,
uncontaminated with the 3-isomer,23 with thionyl chloride by a procedure based on the
extensive studies of this reaction by Gerrard.23

A solution of 2-octanol (69.1 g) in ether (50 ml) was added dropwise in the course of
1 h to another solution of thionyl chloride (70 g) in ether (100 ml). The yellow solution
was kept in the ice-box overnight. Ether and excess thionyl chloride was removed in
vacuo at room temperature. Pyridine hydrochloride (10 g) was now added to the residue,
largely consisting of 2-octyl chlorosulphite, and the mixture was kept at 60° for 1.5 h
and then poured into water. The organic phase was separated and dried. After removal
of the ether, 2-chlorooctane (48.2 g) distilled at 74°/27 mm, following a forerun (13 g),
containing some octene. Redistillation, b.p. 68.5°/24 mm, afforded a pure product, as
estimated from gas chromatography.

2-Chlorooctane was converted into 2-methyloctanenitrile by reaction with sodium
cyanide, essentially as described by Smiley and Arnold.24 The nitrile was distilled, b.p.
79–81°/10 mm, nD20 1.4187. (Lit.24 b.p. 88°/12 mm).

* Melting points are uncorrected and determined in capillary tubes.

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2-Methyloctanenitrile was then reduced with lithium aluminum hydride in other solution in the usual way to 2-methyloctylamine in 74% yield, b.p. 85—88°/9 mm. (Lit.²⁸: b.p. 185—186°). The hydrochloride was prepared, m.p. 130° (Lit.²⁸, m.p. 130°).

On reaction with thiocarbonyl chloride, as described above, the amine was converted into 2-methyloctyl isothiocyanate in 84% yield. A yellow contamination was removed from the distillate by treatment with charcoal and redistillation. The colourless mustard oil had b.p. 119—120°/8 mm, n₂₀° 1.4852 (Found: C 64.65; H 10.35; N 7.42. C₂₁H₄₂N₂S; C 64.80; H 10.33; N 7.56) and was homogeneous on gas chromatography.

Upon reaction with aniline the crystalline phenylthiourea was obtained, m.p. 55—56°. (Found: C 69.07; H 9.34; N 10.24. Calc. for C₁₅H₁₅N₂S: C 69.00; H 9.41; N 10.07).

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