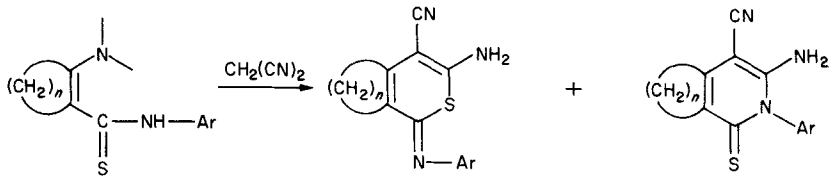
Decomposition of Thiopyrans to Thiophenes Under Electron Impact

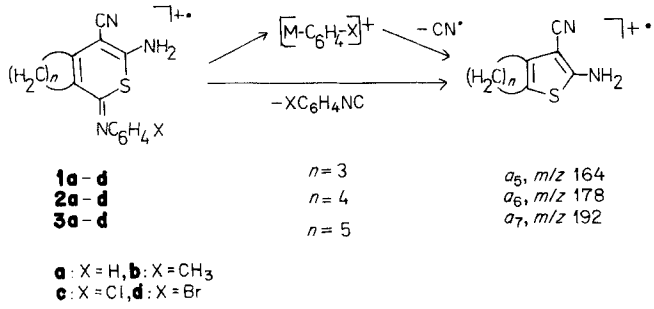
The electron impact induced fragmentation of some new derivatives of thiopyran has been examined. The main fragmentation pathways have been determined with the help of the appropriate metastables and precursor ion measurements. The proposed structures and the composition of the ions have been confirmed by deuterium labelling and by high resolution measurements.

In the continuation of our study on the reactivity of cyclic β-ketocarboxylic acid anilides,[1–3] we directed our attention to the reaction of enamines of cyclic β-ketocarbothionic acid anilides with malononitrile. This reaction was found to be a new and efficient method for the synthesis of a wide range of *o*-aminonitrile derivatives of cycloalkenothiopyran and cycloalkenopyridine (Scheme 1).



Scheme 1

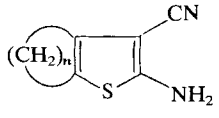
Since the chemical, IR and ^{1}H NMR spectral properties of both series of isomers were very similar, distinction between the corresponding isomeric pairs was made on the basis of mass spectrometry. In this paper, the fragmentation patterns of recently described 1-arylimino-3-amino-4-cyano-1*H*-thiopyrans fused to five- (**1**), six- (**2**) and seven-membered (**3**) cycloalkeno rings are discussed. The substituents (X) in the *para* position in the aryl moiety were H, CH_3, Cl or Br (Scheme 2).



Scheme 2

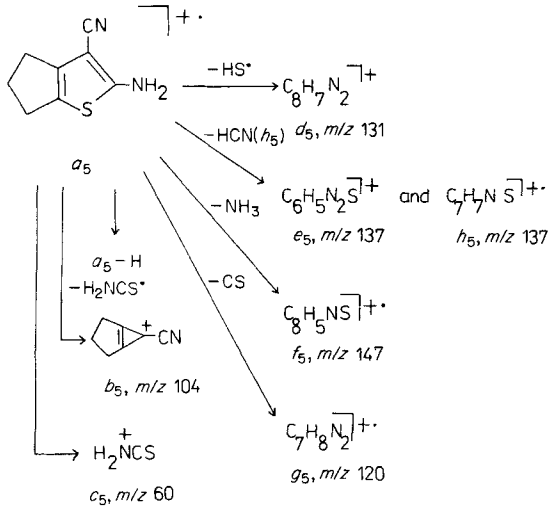
The mass spectra of the compounds revealed peaks of high intensity in the molecular ion region, their relative abundances varying from 20 to 60% of the base peak. The fragmentation of the molecular radical ion occurred as a one-step process with ejection of the XC_6H_4NC (m^*) molecule as well as by a two-step process involving loss of $XC_6H_4^{\cdot}$ and $CN^{\cdot}$ radicals. Ions $[M-XC_6H_4NC]^{+\cdot}$ resulting in these reactions, designated in Scheme 2 as a_5, a_6, and a_7, which structurally correspond to 2-amino-3-cyano-4,5-cycloalkenothiophenes, appeared as the base peaks.

To confirm the structures proposed for ions a_5, a_6 and a_7, we compared the mass spectra of **1**, **2** and **3** with those of 2-amino-3-cyanothiophene fused to the five- (**4**), six- (**5**) and seven-membered (**6**) rings. Compounds **4**, **5** and **6** were prepared for this purpose as model compounds.[4]



4; $n = 3$
5; $n = 4$
6; $n = 5$

As expected, the mass spectrum of compound **1** below m/z 164 was identical with the spectrum of the model compound **4**. Similarly, for compounds **2** and **3**, the mass spectra below m/z 178 and m/z 192 were identical with the spectra of the model compounds **5** and **6**, respectively. The metastable peaks generated by ejection reaction of ethylene from the $[M-XC_6H_4NC]^{+\cdot}$ ion of compound **2a** and from the molecular ion of the model compound **5**, recorded at HV (high voltage) scan, have the same width at half-height. Measurements were recorded at increased energy resolution of the system by decreasing the β-slit-width. Since the measurements were performed under the same conditions, they seemed to be sufficient evidence for the assumption of identical structures for the ions in question.[5]



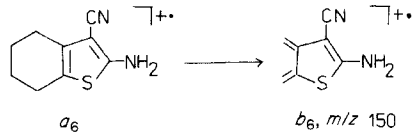
Scheme 3

Further fragmentation of the radical ions $[M-XC_6H_4NC]^{+\cdot}$ originating from compounds **1**, **2** and **3** (and thus also the model compounds **4**, **5** and **6**) differed substantially from each other and therefore will be considered separately.

The most favoured fragmentations of the radical ion a_5 involved elimination of the H$^{\cdot}$ radical, ammonia, hydrogen cyanide molecules, the HS$^{\cdot}$ radical, the CS molecule and the $H_2NCS^{\cdot}$ radical, respectively (Scheme 3).

The mass spectra of the deuteriated compounds with two deuterium atoms in the amino group did not exhibit any shift of m/z peaks for the ions b_5 and f_5. The peaks corresponding to the ions d_5 were shifted upwards by one mass unit and peaks corresponding to the c_5, e_5, g_5 and h_5 ions, were displaced upwards by two mass units. Thus, one can assume that rearrangement of the radical ion a_5 occurred without participation of the amino group.

The mass spectra recorded with decreasing electron energy (90, 70, 20 eV) exhibited lack of, or low intensity of, the peaks corresponding to the ions which might be produced by detachment without rearrangement, i.e. a_5-H, b_5 and c_5.[6] The others, i.e. d_5, e_5, f_5, g_5 and h_5 arise as the result of specific rearrangements.



Scheme 4

In summary, we can assume that the fragmentation of the radical ion a_5 proceeds either with or without rearrangement, as is possible in the thiophene itself.[7]

The mass spectra of cyclohexenothiopyrans (**2**) were less complicated than the spectra of the above-described cyclopentenothiopyrans (**1**). As in the case of compounds **1**, the fragmentation of **2** started with the cleavage of the heterocyclic ring inducing loss of the phenyl isocyanide molecule XC_6H_4NC (Scheme 2) producing the radical ion a_6 responsible for the peak at m/z 178 (base peak). Further fragmentation of this ion gave the second prominent peak at m/z 150. It was undoubtedly formed by elimination of ethylene in the retro-Diels–Alder (RDA) reaction (Scheme 4).

Apart from the above two peaks (m/z 178 and m/z 150) and molecular peak (20–40% of the base peak), the intensities of the other peaks were less than 6%. The RDA elimination is fairly common and has been observed by other authors for various 4,5,6,7-tetrahydrobenzothiophene derivatives.[8]

According to expectations the first step of the fragmentation of compounds **3** was analogous to the fragmentation of compounds **1** and **2**. The elimination of the XC_6H_4NC molecule yielded the radical ion a_7 at m/z 192 (Scheme 2), which appeared as the base peak. Further fragmentation of a_7 was different from that of a_5 but to some extent was similar to that of a_6, since the main fragmentation pathways involved the carbocyclic ring. The fragmentation of the radical ion a_7 produced five intense ions (Scheme 5). Four of them, b_7 (m/z 177), c_7 (m/z 163) (formed by loss of $CH_3^{\cdot}$ and $C_2H_5^{\cdot}$), d_7 (m/z 164) and e_7 (m/z 150) (produced by ejection of C_2H_4 and C_3H_6), were created directly from a_7. The detachment of the $C_3H_3^{\cdot}$ radical from b_7 yielded the fifth intense ion, f_7. Other fragmentation pathways gave ions of intensities lower than 7%.

In the case of the deuteriated compounds containing two deuterium atoms in the amino groups, all of these five peaks were shifted upwards by 2 u. This observation confirms an exclusive participation of the hydrogen atoms attached to the cycloheptene ring in the rearrangement necessary to eliminate the alkyl radicals ($CH_3^{\cdot}$, $C_2H_5^{\cdot}$) and the C_2H_4 and C_3H_6 molecules. Further evidence for these fragmentation pathways was provided by the metastables m^* and the precursors of the fragmentation ions. The compositions of these ions were determined by high resolution mass measurements, although it was difficult to determine their structures, because of the ease of rearrangement of thiophene and its alkyl derivatives under electron impact.[7]

Some information concerning the structure of the ions was achieved by comparing the spectra of compounds **3** with those of **1** and **2**. The ions responsible for peaks c_7 and d_7 from **3** have the same composition and relative intensity as the two most intense ions a_5-H and a_5 from **1**. Similarly ion e_7 from **3** has the same composition as the second most intense ion b_6 from **2**. One can assume that the structure of a_5 (Scheme 3) is present to some extent in ion d_7 whereas b_6 (Scheme 4) participates in ion e_7, but the range of this participation is not known.

One may conclude that:

(i) Electron impact induced fragmentation of 1-arylimino-3-amino-4-cyano-1*H*-cycloalkeno[*c*]thiopyrans involves reduction of the thiopyran ring to that of a thiophene, due to the ejection of the aryl isocyanide molecule, and the formation of cycloalkenothiophenes.

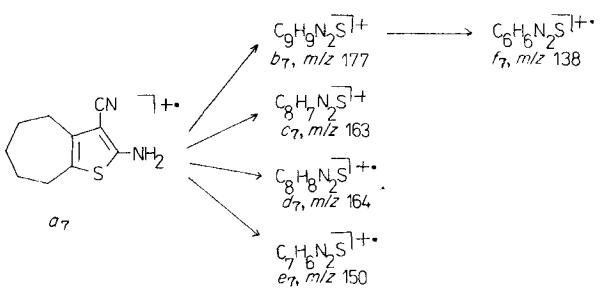
(ii) Further fragmentation of the cycloalkenothiophene $[M-XC_6H_4NC]^{+\cdot}$ radical ions depends mainly upon the size of the carbocyclic ring fused to the thiophene system: (a) In the case of the cyclopentenothiophene ion the fragmentation involves skeletal rearrangement of the thiophene ring and its degradation. (b) The cyclohexenothiophene ion eliminates ethylene in the retro-Diels–Alder reaction. (c) The cycloheptenothiophene ion undergoes cleavage of the carbocyclic ring with ejection of alkyl radicals and hydrocarbon molecules.

The 1-arylimino-3-amino-4-cyano-1*H*-cycloalkeno[*c*]thiopyrans were prepared by the method described previously,[2] based on the reaction of the appropriate enamines of cyclic β-ketocarbothionic acid anilides and malononitrile.

2-Amino-3-cyano-4,5,6,7-tetrahydrobenzothiophene (**5**) was synthesized according to the method described in Ref. 4. Compounds **4** and **6** were unknown, and were prepared in the same manner, starting from cyclopentanone or cycloheptanone, malononitrile, and sulphur in the presence of triethylamine. 2-Amino-3-cyano-5,6-dihydro-4*H*-cyclopenta[*b*]thiophene (**4**): Pale yellow prisms from methanol, m.p. 158–160 °C. IR: 1625 C=C, 2200 CN, 3220, 3340, 3450 NH cm^{-1}. $C_8H_8N_2S$ mol. wt = 164. Calc. %C 58.5, %H 4.8, %N 17.1, %S 19.5; found %C 58.3, %H 4.8, %N 17.0, %S 19.8. 2-Amino-3-cyano-5,6,7,8-tetrahydro-4*H*-cycloheptal[*b*]thiophene (**6**): Pale yellow prisms from methanol, m.p. 125–126 °C. IR: 1620 C=C, 2210 CN, 3220, 3310, 3450 NH cm^{-1}. $C_{10}H_{12}N_2S$ mol. wt = 192. Calc. %C 62.5, %H 6.3, %N 14.6, %S 16.7; found %C 62.2, %H 6.2, %N 14.5, %S 16.4.

High resolution mass spectrometry: b_5 for C_7H_6N calc. 104.05002, found 104.04906; d_5 for $C_8H_7N_2$ calc. 131.06091, found 131.06013; e_5 for $C_6H_5N_2S$ calc. 137.01733, found 137.01634; f_5 for C_8H_5NS calc. 147.01426, found 147.01438; h_5 for C_7H_7NS calc. 137.02991, found 137.02813; c_7 for $C_8H_7N_2S$ calc. 163.03295, found 163.03322; d_7 for $C_8H_8N_2S$ calc. 164.04077, found 164.04134; e_7 for $C_7H_6N_2S$ calc. 150.02513, found 150.02615; f_7 for $C_6H_6N_2S$ calc. 138.02513, found 138.02558.

The low resolution mass spectra were recorded on a LKB 9000S spectrometer using direct inlet under the following conditions: electron energy 90, 70 and 20 eV; accelerating voltage 3.5 kV; ion source temperature 250 °C; direct inlet temperature 70–100 °C. The high resolution mass measurements were performed on a Varian MAT instrument. Metastable peaks were measured on the same instrument by the defocusing technique in the Regional Laboratory of the University of Gdańsk, Poland. The IR spectra were recorded on a UR-10 Zeiss Jena spectrophotometer in Nujoll mulls. Elemental analyses were made on a Perkin–Elmer Analyser Type 240.



Scheme 5

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Book Review

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Tandem Mass Spectrometry
Wiley–Interscience, New York, 1983. Price US $46.20.

This reasonably priced book contains a wide range of articles catering for the interests of a broad audience of mass spectroscopists.

There are 26 mini-reviews in this volume, most are concerned with double focusing mass spectrometers ('normal' or 'reversed' geometry) and the scan methods available for investigating fragmentations in different field free regions. Although these are considered as 'tandem' instruments I would have preferred to see that name reserved for instruments having more than one each of magnetic and electric sectors or having multiple quadrupole mass analysers. Thus the bulk of the chapters describe the use of conventional double focusing mass spectrometers. The use of and results from collisionally induced fragmentations of mass-identified ions are considered throughout but surprisingly, unimolecular ion kinetic energy spectra are barely discussed. A few chapters are excellent and help to make up for the unremarkable majority: 'Analytical Applications' (K. L. Busch and R. G. Cooks), 'Tandem Quadrupole Mass Spectrometry' (R. A. Yost and C. G. Enke), 'Collisionally Activated Dissociation of High Kinetic Energy Ions' (P. J. Todd and F. W. McLafferty), and 'Tandem High Resolution Mass Spectrometry' (P. J. Todd, D. C. McGilvery and F. W. McLafferty), live up to the reputations of their authors and should be required reading for anyone studying the mass spectrometric arts; indeed these chapters could have been much longer.

Less noteworthy but, nevertheless, valuable extra reading material, are the sections by P. H. Dawson and D. J. Douglas on 'Collisionally Activated Dissociation of Low Kinetic Energy Ions', by W. J. Richter, W. Blum, U. P. Schlunegger and M. Senn on 'Tandem Mass Spectrometry of Pharmaceuticals', and M. M. Bursey and J. R. Hass on 'Tandem Mass Spectrometry for Environmental Problems'.

For the most part, the remaining material is rather disappointing in so far as it does not live up to expectations. 'Ionic Reaction Mechanisms from Tandem Mass Spectrometry' by J. W. Zwinselman, N. M. M. Nibbering, B. Ciommer and H. Schwarz, is not nearly as critical as it should be for an area of study which is undergoing continuous revision. 'Structural Information from Tandem Mass Spectrometry' by K. Levsen unfortunately repeats much that is found in other chapters and 'Linked Scans' by K. R. Jennings and R. S. Mason inevitably rides again—without examples being presented to show the unique utility of the various scan methods for solving problems.

This typescript-ready book is almost free from error, but the brevity of some of the discussions make a few figures difficult to understand.

What this book most seriously lacks is the authoritative coordination of the subject which comes from a single-author book (so well represented for example, by Levsen's book, *Fundamental Aspects of Organic Mass Spectrometry* (1978)).

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