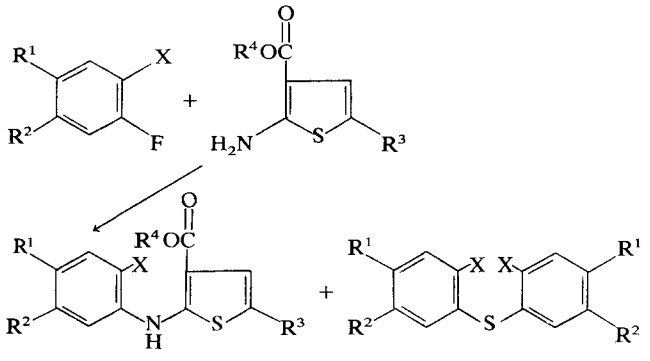
# Electron Impact Induced Fragmentations of 2-(2-Nitroanilino)thiophens and Di(2-nitrophenyl)sulphides

**David N. B. Mallen and Julie M. Smith**
Physical Organic Research, Lilly Research Centre, Erl Wood Manor, Windlesham, Surrey, UK

**A prominent *ortho* interaction occurs during the mass spectral fragmentation of di(2-nitrophenyl)sulphides. No such effects are observed for the corresponding ethers or 2-(2-nitroanilino)thiophens. Variation of aromatic substituents can dramatically alter the effect. Examination of analogous sulphone, sulphoxide, and disulphide molecules, implicates the involvement of the *ortho* nitro substituent and the sulphur atom in this rearrangement.**

## INTRODUCTION

2-(2-Nitroanilino)thiophens (**1–6**) are intermediates in the synthesis of thienobenzodiazepinones[1] and can be formed by the reaction of an aminothiophene with a fluoronitrobenzene. The presence of elemental sulphur



**1–6** **7–9**

| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | X |
|---|---|---|---|---|---|
| **1** | F | H | $CH_3$ | $CH_3$ | $NO_2$ |
| **2** | F | H | $C_2H_5$ | $C_2H_5$ | $NO_2$ |
| **3** | H | H | $CH_3$ | $CH_3$ | $NO_2$ |
| **4** | H | H | $C_2H_5$ | $C_2H_5$ | $NO_2$ |
| **5** | F | F | $CH_3$ | $CH_3$ | $NO_2$ |
| **6** | F | F | $C_2H_5$ | $C_2H_5$ | $NO_2$ |
| **7** | F | H | — | — | $NO_2$ |
| **8** | H | H | — | — | $NO_2$ |
| **9** | F | F | — | — | $NO_2$ |
| **10** | F | H | — | — | H |

in the aminothiophene precursor results in the formation of the corresponding di(2-nitrophenyl)sulphides (**7–9**). The skeletal rearrangements observed in the mass spectra of these latter compounds, a specific example of the general so-called '*ortho* effect,'[2–4] encouraged us to further examine the spectral behaviour of **7–9** and to look for similar effects in analogous compounds.

## RESULTS AND DISCUSSION

The general rationale for the electron impact induced mass spectral fragmentation of compounds **7–9** is shown in Scheme 1. The low resolution mass spectral data are presented in Table 1.

Three competing fragmentation routes are observed. The least favoured route for compounds **7** and **8** involves consecutive losses of nitric oxide and the $[NO_2]$ radical, characteristic of molecules containing a nitro substituent.[5] Alternatively, consecutive losses of the nitro substituent and carbon monoxide are observed to give ion *c*, before elimination of an [SO] radical by a rearrangement process. This type of *ortho* rearrangement is better exemplified in the dominant fragmentation route, for which accurate mass measurements confirm the loss of both [SO] and $[NO_2]$ radicals, the resultant *N*-oxide ion *b* then losing a further oxygen atom to give the fully conjugated ion *d*. Such a rearrangement probably involves the formation of intermediate ion *a*, containing an S–O–N bridgehead, and the transfer of oxygen to the sulphur atom prior to the formation of the cyclic ion product *b*. Although compounds **7** and **8** behave similarly, contrasting mass spectral behaviour is observed for **9** in which both aromatic rings contain two fluorine substituents. These latter substituents increase the relative abundance of the molecular ion and modify the preferred fragmentation of **9** to simple loss of nitric oxide and the nitro substituent rather than the alternative rearrangement discussed for **7** and **8**.

For the corresponding diphenyl ethers **11–14** the above rearrangement was not observed, although diphenyl ethers are known to undergo *ortho* rearrangements.[6,7] Hence the presence of a sulphur atom in compounds **7–9** exerts a controlling influence on their fragmentation.

The ethers **11–14** fragment as expected by simple scission of the C–O bond and extrusion of carbon monoxide. However, a low relative abundance ion resulting from a rearrangement process is observed following the loss of oxygen as an [OH] radical. The

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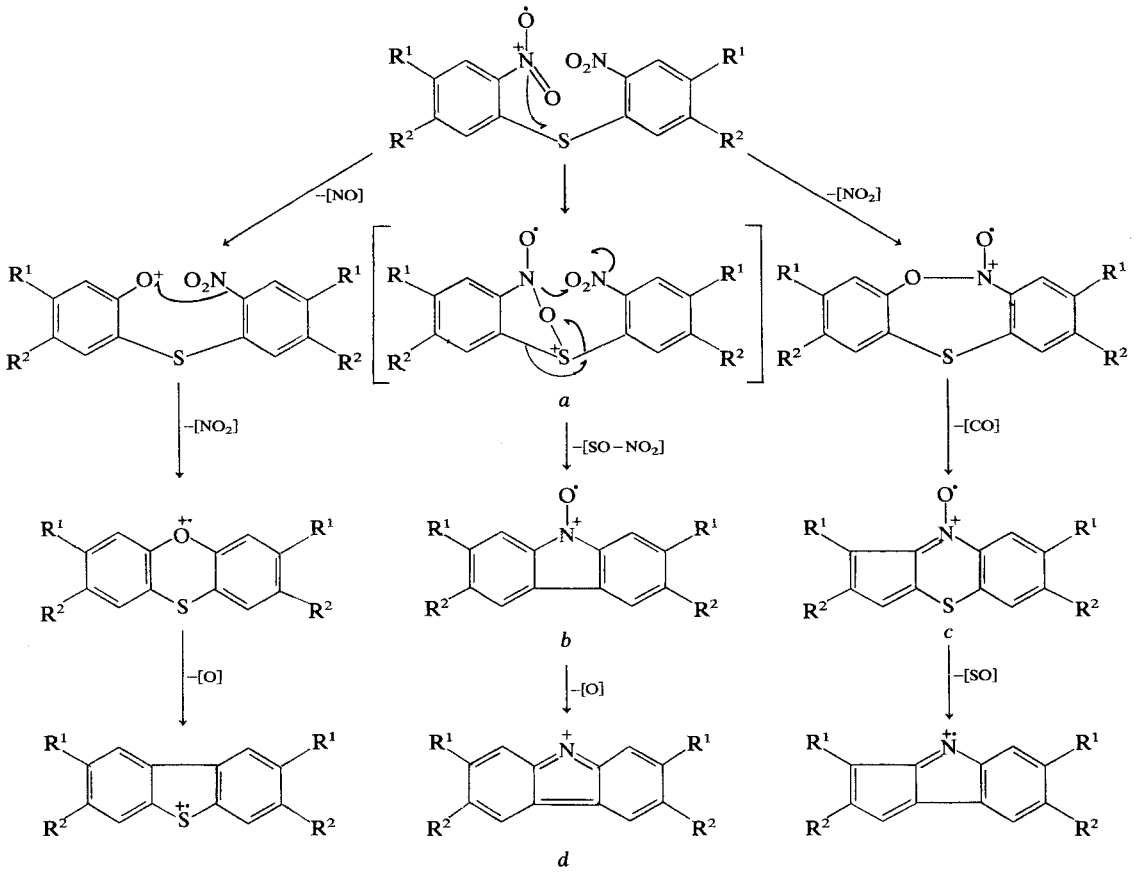
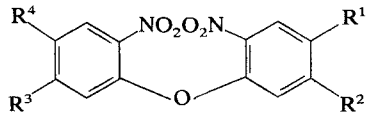


Scheme 1

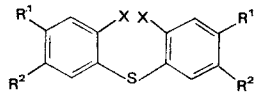
principal spectral features of these compounds are summarized in Table 2.



| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **11** | F | H | H | F |
| **12** | H | H | H | H |
| **13** | F | F | F | F |
| **14** | F | F | H | H |

The 2-(2-nitroanilino)thiophens (**1–6**) also contain no bridging sulphur atom, and consequently show no propensity to undergo *ortho* rearrangements with elimination of S–O species. They fragment as shown in Scheme 2 by loss of alcohol and the formation of ketene ions *g*, *h*, and *j* rather than by the formation of a completely fused cyclic ion. The low resolution mass spectral data of compounds **1–6** are shown in Table 3. As these compounds contain two aromatic rings, the molecular ion becomes the most abundant for **1–4**. Characteristic $[M-NO]^+$ and $[M-NO_2]^+$ ions are observed, but are more apparent when eliminated from the lactam ion *g*. Deuterium exchange of the replaceable hydrogen atom confirms that elimination of alcohol occurs with cyclization onto the bridgehead nitrogen atom. Although formation of an $[M-CO-NO]^+$ ion is often observed for aromatic compounds,[8] for **1–6** the $[M-R^4OH-NO_2-CO]^+$ ion *k* must involve elimination of carbon monoxide from the lactam ring rather than incorporation of carbon from the

**Table 1. Significant ions in the mass spectra (20 eV) of di(2-nitrophenyl)sulphides**

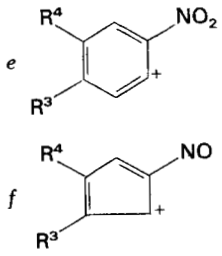


| Compound | $R^1$ | $R^2$ | X | Ion[a] Assignments | m/z (relative abundance) $[M]^{+\cdot}$ | $[b]^{+\cdot}$ | $[d]^+$ | $[M-NO]^+$ | $[M-NO-NO_2]^{+\cdot}$ | $[M-NO_2]^+$ | $[M-NO_2-CO]^+$ | $[M-NO_2-NO_2]^{+\cdot}$ | $[M-NO_2-CO-SO]^{+\cdot}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **7** | F | H | $NO_2$ | | 312 (62) | 218 (89)[b] | 202 (100)[b] | 282 (1) | 236 (<1) | 266 (10)[b] | 238 (24)[b] | 220 (<1) | 190 (25)[b] |
| **8** | H | H | $NO_2$ | | 276 (100) | 182 (77) | 166 (100) | 246 (3) | 200 (<1) | 230 (38) | 202 (22) | 284 (<1) | 154 (26) |
| **9** | F | F | $NO_2$ | | 348 (100) | 254 (<1) | 238 (<1) | 318 (28) | 272 (19) | 302 (8) | 274 (1) | 256 (19) | 226 (<1) |

[a] Ion assignments as shown in Scheme 1.
[b] Formulae confirmed by accurate mass measurement.

**Table 2. Significant ions in the mass spectra (20 eV) of di(2-nitrophenyl) ethers**

| Compound | $R^1$ | $R^2$ | $R^3$ | $R^4$ | m/z (relative abundance) $[M]^{+\cdot}$ | $[M-OH]^+$ | e | f |
|---|---|---|---|---|---|---|---|---|
| **11** | F | H | H | F | 296 (54) | 279 (3) | 140 (100) | 112 (30) |
| **12** | H | H | H | H | 260(21) | 243(4) | 122(100) | 94(6) |
| **13** | F | F | F | F | 332 (17) | 315 (2) | 158 (100) | 130 (<1) |
| **14** | F | F | H | H | 296 (27) | 279 (<1) | 122 (100) | 94 (10) |
| | | | | | | | 158 (4)[a] | 130 (<1)[a] |





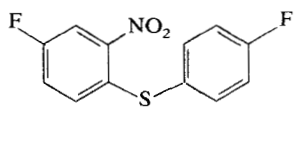


[a] Ions containing substituents $R^1$ and $R^2$.

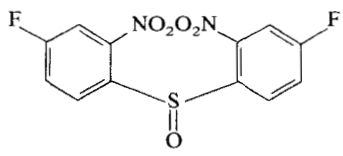
aromatic nucleus. Oxygen is lost from the nitro group to give an $[M-OH]^+$ rather than $[M-O]^+$ ion,[9] the hydrogen atom associated with the *ortho* amino substituent being eliminated via a 6-membered transition state.[10] The effect of the introduction of two electron withdrawing fluorine groups into the phenyl nucleus of these 2-(2-nitroanilino)thiophens is to modify their spectra considerably, encouraging fragmentation of the molecular ion rather than its stabilization, as observed for **7–9**. For **5** and **6** the $[M-CH_3OH]^{+\cdot}$ or $[M-NO_2-C_2H_5OH]^+$ ions *g* and *h* become the most abundant. Whereas for **5** methanol is lost as a primary fragment, for **6** the bulkier ethyl ester only loses ethanol following elimination of the nitro substituent.

Formation of the less significant $[M-2]^{+\cdot}$ ion is partly thermal.

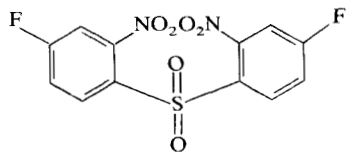
Mass spectral analysis of the sulphides (**10** and **15**), the sulphoxide (**16**) and the sulphone (**17**) further clarifies the involvement of the nitro substituent and




**15**



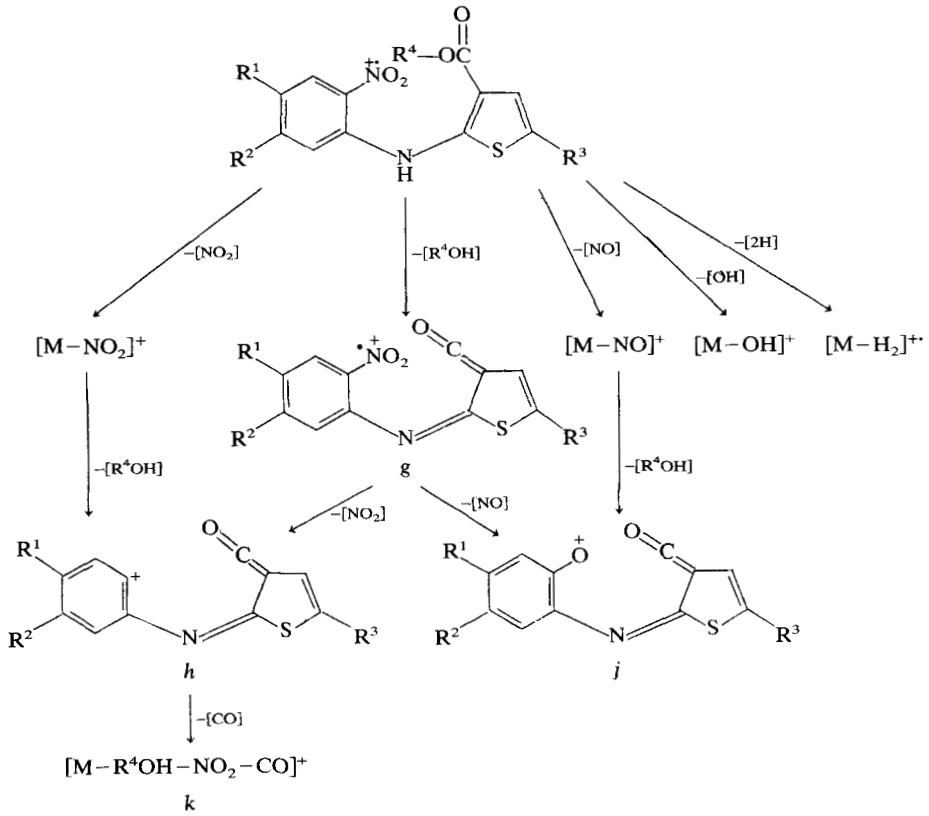

**16**




**17**

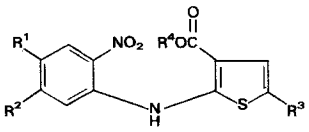
bridgehead sulphur atom in the *ortho* effects. Compound **15** containing only one nitro substituent still shows this rearrangement. Scheme 3 shows the primary fragmentation paths for **15**. Both the tricyclic ions *l* and *m* are formed following loss of $SO_2$ and the formation of an S–O–N intermediate bridging ion. Alternatively, the molecular ion can fragment to give the fused structure ion *a* by simple loss of the nitro moiety. Further primary fragmentations involve the loss of nitric oxide or scission of the S–C bond.

No similar rearrangement fragmentations are observed for compound **10** which has both nitro substituents removed. Its mass spectral behaviour is typical of a diarylsulphide,[11] as it fragments by scission of




**Scheme 2**

**Table 3. Mass spectral data (20 eV) for the analysis of 2-(2-nitroanilino)thiophens**

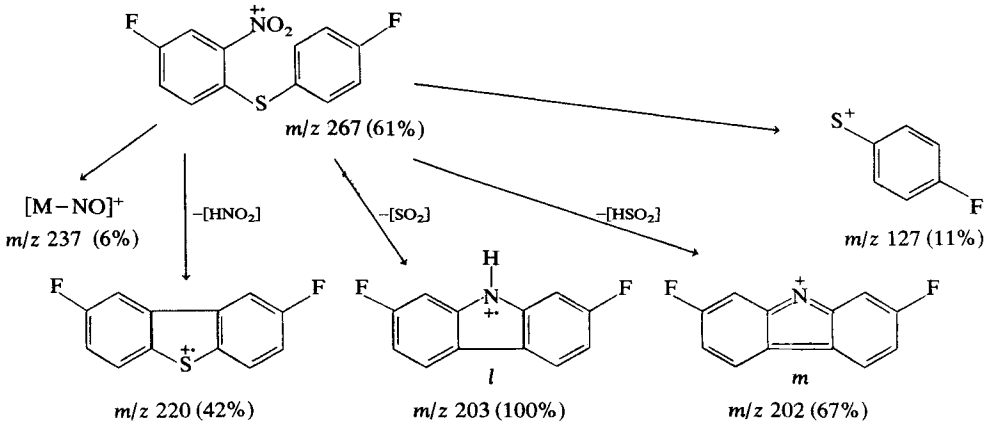


| Compound | $R^1$ | $R^2$ | $R^3$ | $R^4$ | m/z (relative intensity) $[M]^{+\cdot}$ | $[M-2]^{+\cdot}$ | $[M-OH]^+$ | $[M-NO]^+$ | $[M-NO_2]^+$ | $[M-R^4OH]^{+\cdot}$ | $[M-NO-R^4OH]^+$ | $[M-NO_2-R^4OH]^+$ | $[M-NO_2-R^4OH-CO]^+$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | H | $CH_3$ | $CH_3$ | 310 (100) | 308 (8) | 293 (4) | 280 (6) | 264 (<1) | 278 (3) | 248 (16) | 232 (78) | 204 (12) |
| 2 | F | H | $C_2H_5$ | $C_2H_5$ | 338 (100) | 336 (8) | 321 (6) | 308 (3) | 292 (4)[a] | 292 (4)[a] | 262 (10) | 246 (77) | 218 (12) |
| 3 | H | H | $CH_3$ | $CH_3$ | 292(100) | 290(1) | 275(3) | 262(3) | 246(1) | 260(1) | 230(8) | 214(79) | 186(14) |
| 4 | H | H | $C_2H_5$ | $C_2H_5$ | 320 (100) | 318 (11) | 303 (5) | 290 (18) | 274 (5)[a] | 274 (5)[a] | 244 (21) | 228 (76) | 200 (17) |
| 5 | F | F | $CH_3$ | $CH_3$ | 328 (81) | 326 (24) | 311 (1) | 298 (11) | 282 (2) | 296 (100) | 266 (9) | 250 (15) | 222 (20) |
| 6 | F | F | $C_2H_5$ | $C_2H_5$ | 356 (70) | 354 (10) | 339 (<1) | 326 (11) | 308 (<1)[a] | 308 (<1)[a] | 280 (18) | 264 (100) | 236 (7) |

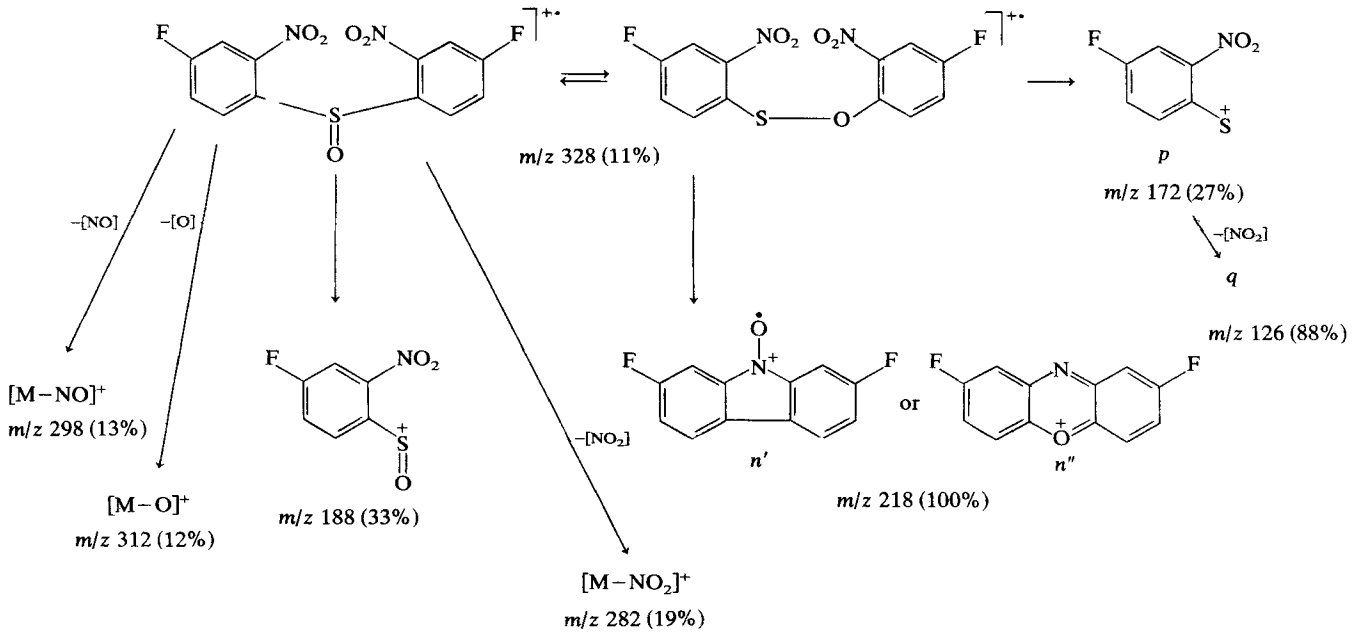
[a] Doublet peaks.

the C—S bond or by extrusion of sulphur. Di(4-nitrophenyl)sulphide only shows fragmentation of the nitro substituents.

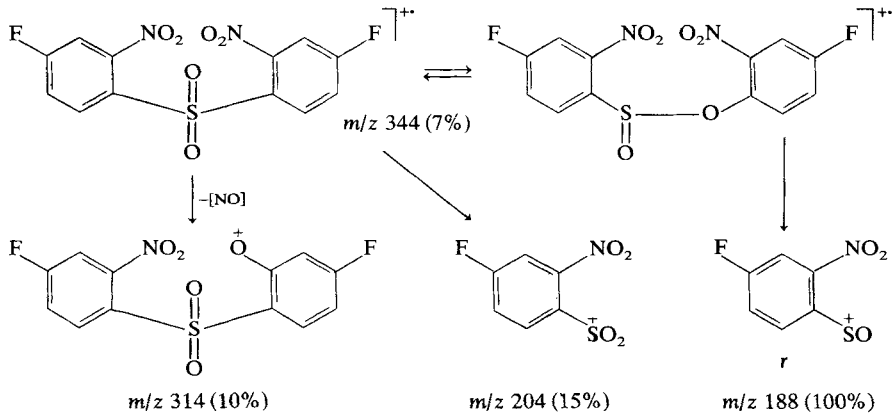
The sulphoxide compound (**16**), corresponding to sulphide **7**, readily undergoes an *ortho* rearrangement (Scheme 4). As aromatic sulphoxides can undergo an electron impact induced aryl migration[12] from sulphur to oxygen to give an ionized sulphenate, a rearrangement fragmentation mechanism analogous to that for sulphides **7–9** can be envisaged. However, as ion *n'* does not lose oxygen, a feature characteristic of *N*-oxides, it may exist as the alternative fused ion structure *n''*. Formation of this latter ion would involve a double rearrangement process involving the transfer of both oxygen atoms. A competitive fragmentation also involves the same aryl migration followed by scission




**Scheme 3**




**Scheme 4**

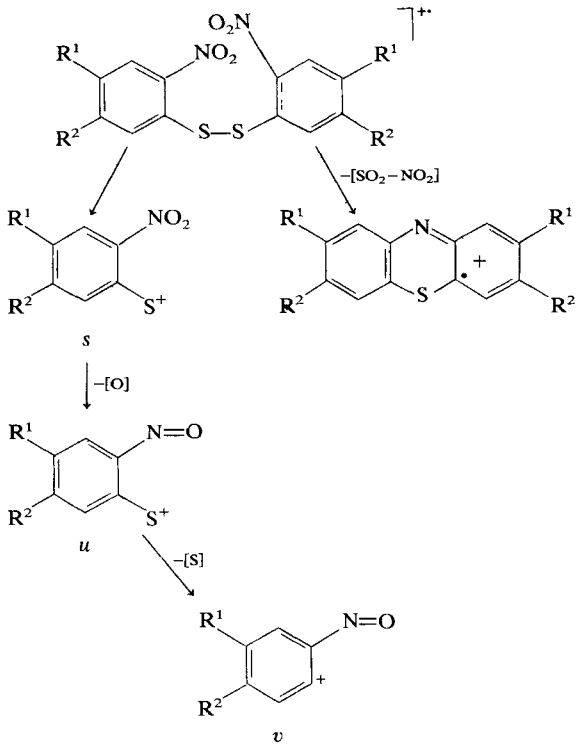



**Scheme 5**

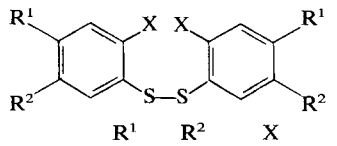
of the S–O bond to give ion *p*. This ion can then fragment further with loss of the nitro group to give ion *q*. Less abundant ions characteristic of the nitro group can also be observed.

The sulphone **17** is again able to undergo an electron impact induced aryl migration[13] prior to formation of base ion *r* (Scheme 5). However, more significantly, **17** does not show an *ortho* rearrangement effect. This is presumably because the sulphur atom is no longer able to form a bridgehead bond due to steric or electronic restrictions.

Structural modification of compounds **7–10** to give the corresponding disulphides (**18–21**), does not markedly inhibit the previously observed *ortho* effect. Accurate mass measurements confirm the loss of [$SO_2$] and [NO] radicals. These observations clearly parallel the thermal and photochemical induced transfer of oxygen from an *o*-nitro group to the adjacent sulphur atom noted for di(2-nitrophenyl)disulphides.[14]




**Scheme 6**

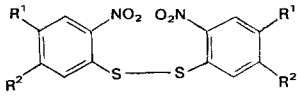


| | R¹ | R² | X |
|---|---|---|---|
| **18** | F | H | $NO_2$ |
| **19** | H | H | $NO_2$ |
| **20** | F | F | $NO_2$ |
| **21** | F | H | H |

The relative abundance of the molecular ion for **18** and **19** is reduced compared with that for compounds **7** and **8**. Characteristic scission of the S–S bond for disulphides to give ion *s* (Scheme 6) competes with the *ortho* effect to give ion *t*. The mass spectral data for compounds **18–20** are shown in Table 4. Ion *s* fragments further by loss of oxygen and sulphur. The presence of four fluorine atoms in **20** reduces the fragmentation of the molecular ion and inhibits the *ortho* rearrangement, an effect previously observed for the tetrafluorosulphide (**9**).

Fragmentation of the disulphide (**21**), which retains neither nitro group, is typical of other diphenyl sulphides.[15] No *ortho* rearrangements are observed and

**Table 4. Significant ions in the mass spectra (20 eV) of di(2-nitrophenyl)disulphides**



| Compound | R¹ | R² | Ion[a] assignments | m/z (relative abundance) [M]⁺· | t | s | u | v |
|---|---|---|---|---|---|---|---|---|
| **18** | F | H | | 344 (51) | 234 (42) | 172 (100) | 156 (49) | 124 (50) |
| **19** | H | H | | 308 (45) | 198 (47) | 154 (100) | 138 (54) | 106 (50) |
| **20** | F | F | | 380 (100) | 270 (<1) | 190 (<1) | 174 (11) | 142 (<1) |

[a] Ion assignments as shown in Scheme 6; formulae confirmed for **18** by accurate mass measurement.

the molecular ion fragments by successive extrusion of sulphur atoms.

## CONCLUSION

The *ortho* effect observed for di(2-nitrophenyl)-sulphides is mimicked by di(2-nitrophenyl)sulphones and di(2-nitrophenyl)disulphides. The effect can be inhibited by modification of one of the following structural features—suitable substitution within the aromatic ring, replacement of both nitro groups, or replacement of the sulphide group.

## EXPERIMENTAL

All low resolution mass spectra were recorded by an LKB 9000S mass spectrometer. Samples were introduced either by direct insertion probe or by GCMS using a 2 m 3% QFI column (temperature programmed from 100–250 °C, 15 °C $min^{-1}$). Operating conditions were: ion accelerating voltage 3.5 kV, electron voltage 20 eV, source temperature 270 °C.

High resolution accurate mass measurements were obtained from a Varian MAT 731 double focusing mass spectrometer.

### Preparation of compounds

**2-(2-Nitroanilino)thiophens (1–6).** The requisite fluoronitrobenzene (12 mg) was reacted with the aminothiophene (15 mg), using anhydrous $K_2CO_3$ as catalyst and dimethylacetamide solvent. The mixture was heated at 95 ± 5 °C for approximately 20 h. Prior to GCMS analyses, samples were poured into water and extracted into dichloromethane.

**Di(2-nitrophenyl)sulphides (7–9), ethers (11–14) and disulphides (18–20).** The above reaction was repeated with the requisite fluoronitrobenzene but with elemental sulphur replacing the aminothiophene. A mixture of the corresponding sulphide, ether and disulphide compounds were formed. The sulphide **10** was prepared by the $AlCl_3$ catalysed reaction of monofluorobenzene and sulphur at room temperature. The mononitrosulphide (**15**) and the disulphide (**21**) were prepared simultaneously by the reaction at 70 °C of difluoronitrobenzene with *p*-fluorothiophenol using $K_2CO_3$ catalyst and dimethylacetamide.

**Di(2-nitrophenyl)sulphoxide (16) and sulphone (17).** Compounds **16** and **17** were prepared simultaneously from the corresponding sulphide (**7**) by the addition of dichloromethane and an excess of *m*-chloroperoxybenzoic acid.

Further structural analysis of reaction products was achieved by NMR or microanalysis.

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