Mass Spectrometric Study of Some 2,3-Diaryl-1,3-thiazolidin-4-ones Under Electron Impact

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The mass spectral fragmentations of some 2,3-diaryl-1,3-thiazolidin-4-ones were established by comparing spectra and by using exact mass measurements. The major fragment ions were identified and their relative importances related to substituent effects and bond strengths. Good correlations were observed between the relative abundances of some of the breakdown products and the Hammett σ constants of substituents in the aromatic rings.

INTRODUCTION

Despite the interest which has been shown in the wide range of biological activity exhibited by the thiazolidinones,¹⁻⁷ little has been reported on their mass spectrometric properties.⁸ Recent studies by ourselves into the mass spectral properties of 2,3-diaryl-1,3thiazolidin-4-ones (1) have widened our understanding of the role of substituents in determining the fragmentation of these compounds under electron impact.

Two series of compounds were examined, viz. the 2-aryl-3-phenyl-1,3-thiazolidin-4-ones (1a-m) and the 3-aryl-2-phenyl-1,3-thiazolidin-4-ones (1n-u) (Scheme 1). The mass spectra of compounds in both of these series are discussed here.

The identities of the fragment ions were established

by exact mass measurement and by comparing the spectra of different compounds within the two series. Comparison of these spectra with that of 5-methyl-2,3-diphenyl-1,3-thiazolidin-4-one (2) also aided the analysis.

EXPERIMENTAL

Compounds **1a–u** were prepared by a modification of Surrey's method⁹ (Scheme 1). Equimolar portions of the amine and aldehyde were dissolved in toluene and heated under reflux for 30 min and allowed to cool. An equimolar portion of mercaptoethanoic acid was added and the heating continued for a further 5 h. The progress of both steps was monitored by azeotropic dis-



Scheme 1. Ar = C_6H_4X , Ar' = C_6H_4Y .

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lon	1a	1Ь	1c	1d	1e	1f	1g
M+•	255 (76)°	285 (44)°	269 (93)	269 (73)°	285 (78)°	289 (29)	333 (20)
а	181 (34)°	211 (17)	195 (27)	195 (30)	211 (26)	215 (23)	259 (11)
- b	180 (47)°	210 (56)°	194 (62)	194 (53)	210 (59)	214 (27)	258 (13)
c	182 (28)°	212 (8)	196 (18)	196 (25)	212 (29)	216 (16)	260 (7)
d	104 (21)	104 (16)°	104 (21)	104 (24)	104 (34)	104 (16)	104 (13)
e	78 (8)	108 (2)	92 (7)	92 (4)	108 (0)	112 (1)	156 (0)
f	77 (76) ^b	107 (1)	91 (29) ^b	91 (22) ^b	107 (0)	111 (2)	155 (0)
a	91 (20) ^b	91 (4)	91 (29) ^b	91 (22) ^b	91 (8)	91 (4)	91 (4)
ĥ	91 (20) ^b	121 (25)°	105 (11)	105 (8)	121 (3)	125 (9)	169 (3)
i	178 (9)	178 (2)	178 (6)	178 (10)	178 (15)	178 (4)	178 (3)
i	136 (26)	166 (46)°	150 (14)	150 (15)	166 (13)	170 (3)	214 (0)
, k	135 (73)°	165 (40)	149 (14)	149 (29)	165 (24)	169 (6)	213 (0)
1		135 (47)°	135 (100) ^b	135 (70) ^b	135 (42)	135 (66)	135 (35)
m	132 (10)	162 (100)°	146 (84)	146 (31)	162 (33)	166 (3)	210 (0)
п	123 (100)°	123 (5)	123 (63)	123 (100)	123 (100)	123 (100)	123 (100)
0	121 (5)	151 (16)°	135 (100) ^b	135 (70) ^b	151 (18)	155 (2)	199 (0)
p	77 (76) ^b	77 (53)	77 (78)	77 (74)	77 (82)	77 (66)	77 (43)
	1h	1i	1j	1k	11	1m	
M+•	273 (58)°	289 (29)	333 (14)°	280 (78)°	300 (46)°	300 (64)°	
а	199 (32)	215 (19)	259 (10)	206 (61)	226 (50)°	226 (54)	
b	198 (39)	214 (21)	258 (11)	205 (37)	225 (19)	225 (18)	
с	200 (34)	216 (21)	260 (9)	207 (62)	227 (46)°	227 (42)°	
d	104 (27)	104 (20)	104 (18)	104 (25)	104 (30)	104 (30)	
е	96 (5)	112 (2)	156 (0)	103 (5)	See n	See n	
f	95 (4)	111 (2)	155 (0)	102 (4)	122 (0)	122 (0)	
g	91 (1)	91 (4)	91 (5)	91 (2)	91 (5)	91 (0)	
h	109 (14)	125 (0)	169 (1)	116 (8)	136 (1)	136 (0)	
i	178 (9)	178 (13)	178 (10)	178 (11)°	178 (11)	178 (10)	
j	154 (16)	170 (2)	214 (1)	161 (25)	181 (18)	181 (17)	
k	153 (51)	169 (4)	213 (1)	160 (55)	180 (13)	180 (6)	
1	135 (6)	135 (44)	135 (3)°	135 (5)	135 (7)	135 (11)	
m	150 (1)	166 (1)	210 (0)	157 (0)	177 (1)	177 (0)	
n	123 (100)	123 (100)	123 (100)°	123 (100)	123 (100)°	123 (100)°	
0	139 (4)	155 (2)	199 (1)	146 (5)	166 (1)	166 (0)	
p	77 (82)	77 (63)	77 (61)	77 (97)	77 (70)	77 (80)	
[C ₆ H₄C=NPh]⁺'					179 (10)	179 (23)°	
[C,H,NOS]+					164 (16)	164 (15)°	
[C_H_S]+					134 (19)	134 (29)9	

Table 1. 70 eV mass spectra of compounds 1a-m: m/z (% relative intensity of base peak)^a

^a Only ions containing ¹²C, ³²C, ^{as}Cl and ⁷⁹Br are recorded. All intensities have been corrected for other isotopic contributions.

^b Mixed peaks.

° Identities confirmed by exact mass measurements.

tillation using a Dean and Stark apparatus. The solution was evaporated to dryness and the product recrystallized from ethanol.

Compound 2 was prepared similarly using 2mercaptopropanoic acid in place of mercaptoethanoic acid.

Mass spectra were recorded on a VG Micromass 16F spectrometer equipped with a VG2000 data system. Exact mass measurements were made using an AEI MS902 spectrometer. Both instruments were calibrated against perfluorokerosene. Spectra were obtained at 20 and 70 eV using a temperature of ~470 K and a pressure of ~3 × 10⁻⁶ Torr (1 Torr = 133.3 Pa).

RESULTS AND DISCUSSION

Compounds 1a-u were shown to fragment extensively (see below and Tables 1 and 2). All of the important ions observed were identified except that at m/z 164 in the spectra of 11 and 1m. Exact mass measurement showed the formula of this ion to be C_8H_6NOS , although its structure was not resolved.

The formation of all the fragment ions was found to be highly substituent dependent. On the whole, the ions $[ArCH=NAr']^+$ (a), $[ArCHNHAr']^+$ (c), $[M - Ar]^+$ (i), $[ArC_2H_3S]^+$ (j), $[ArCHNCO]^+$ (m), $[CH_2=SAr']^+$ (n) and $[ArC=S]^+$ (o) were found to have low energy requirements, giving peaks of fairly similar abundances at both 20 and 70 eV. The formation of the ion $[Ar']^+$ (p), however, was found to be consistently energy dependent for the compounds for which it occurred, with much greater peak intensities being observed at 70 than at 20 eV.

Ions $[ArCH=NAr']^+$ (a), $[ArC=NAr']^+$ (b) and $[ArCHNHAr']^+$ (c)

The formation of ions of the Schiff bases (a) and their deprotonated and protonated forms (b and c,

I ADIC 4. / U C V IIIASS SOCULA UI CUMDUUNUS III U AIRU 4. III/2 V /0 I CIALIVE IIICHSILV UI DASC DEAT	Table 2.	70 eV	' mass spectra of	f compounds	In-u and 2:	mlz (%	relative	intensity	of base	peak
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lon	1n	10	1p	1q	1r	1s	1t	1u	2
M+-	271 (63)°	285 (67)°	269 (59)	289 (50)	333 (48)	333 (49)°	299 (74)	300 (33)°	269 (30)°
8	197 (26)°	211 (20)°	195 (37)	215 (24)	259 (21)	259 (25)	225 (86)	226 (26)	181 (45)°
b	196 (30)°	210 (6)	194 (40)	214 (37)	258 (24)	258 (34)	224 (92)	225 (21)	180 (45)°
c	198 (11)	212 (8)	196 (20)	216 (15)	260 (17)	260 (10)	226 (25)	227 (35)	182 (14)
d	120 (14)°	134 (6)	118 (13)	138 (17)	182 (11)	182 (12)	148 (16)	149 (12)	104 (19)
8	78 (2)	78 (1)	78 (6)	78 (8)	78 (11)	78 (12)	78 (12)	78 (5)	78 (8)
f	77 (10)	77 (13)	77 (13)	77 (27)	77 (23)	77 (22)	77 (27)	77 (14)	77 (59) ^b
g	107 (0)	121 (7)	105 (2)	125 (0)	169 (0)	169 (0)	135 (51) ^b	136 (29) ^b	91 (6) ^b
h	91 (19)	91 (18)	91 (73) ^b	91 (21)	91 (23)	91 (29)	91 (13)	91 (16)	91 (6) ⁵
i	194 (4)	208 (0)	192 (0)	212 (3)	256 (4)	256 (6)	222 (8)	223 (9)	192 (7)°
j	136 (21)	136 (28)	136 (27)	136 (26)	136 (33)	136 (37)	136 (23)	136 (29) ^b	150 (13)° [PhC_H_S]+
k	135 (92)°	135 (90)°	135 (79)	135 (100)	135 (100)	135 (100)	135 (51) [»]	135 (53)°	135 (32)°, 149 (19)° [PhC_H_S]*
m	132 (4)	132 (0)	132 (5)	132 (49)	132 (68)	132 (91)	132 (67)	132 (100)°	132 (0)
n	139 (100)°	153 (100)°	137 (100)	157 (83)	201 (71)	201 (49)	167 (44)	168 (3)	137 (100)° [CHMe-SPh]+
0	121 (7)	121 (7) ^b	121 (9)	121 (9)	121 (11)	121 (13)	121 (19) ⁶	121 (10)	121 (7)
p	93 (14)	107 (0)	91 (73) ^b	111 (37)	155 (21)	155 (25)°	121 (19) ^b	122 (4)	77 (59) ^b
[PhCH	-NC _s H₄0]⁺	196 (24)°							
[PhCH	NHC H_]+							181 (11)	
[PhCH	=NC _s H ₄]⁺							180 (14)	
[PhC-	NC ₆ H ₄] ^{+•}							179 (9)	
^{a-c} See	e footnotes to	Table 1.							

respectively) was found to be of major importance. The elimination of thiiranone from the molecular ion followed by the loss of a hydrogen atom accounted for the formation of ions a and b whereas ion c appeared to form directly from the molecular ion.

The identities of all three ions were verified by several exact mass measurements carried out on a selection of the compounds (Tables 1 and 2).

Ions analogous to *a*, *b* or *c* but lacking the substituents in Ar or Ar' were observed in the spectra of 11, 1m, 1o and 1u. The presence of the ion $[C_6H_4C=NPh]^{+*}$ (*m*/*z* 179) in the spectra of 11 and 1m was verified by exact mass measurement on the latter compound. Ions corresponding to *a*, *b* and *c* but lacking the NO₂ group were found in the spectrum of 1u. The ion at *m*/*z* 196 in the spectrum of 1o was shown by exact mass measurement to correspond to $[PhCH=NC_6H_4O]^+$.

Ions $[CH=NAr']^+(d)$, $[ArH]^{+}(e)$, $[Ar]^+(f)$, $[NAr']^{+}(g)$ and $[ArCH_2]^+(h)$

The identity of ion d (Ar' = Ph), m/z 104, in the spectra of **1a-m** was verified by its replacement by ions with the expected increase in mass for **1n-u** and by exact mass measurement of this ion in the spectra of **1b** and **1n** which confirmed the composition and showed the presence of Ar'.

The ion $[ArH]^{+}$ (e) gave low-intensity peaks and was found for compounds with substituents in either aromatic ring. In contrast, the ion $[Ar]^+$ (f) gave moderately intense peaks and was only found for compounds in which Ar = Ph, i.e. **1n-u**. Other aromatic ions corresponding to $[NAr']^{+}$ (g) and $[ArCH_2]^+$ (h) were also observed.

Ion $[M - Ar]^+(i)$

Loss of Ar^{\cdot} was found to give rise to ions (i) of low to moderate abundances in the spectra of most of the com-

pounds examined. Exact mass measurement of this ion, m/z 178, in the spectrum of 1k verified its composition as C_9H_8NOS , which corresponds to $[M^{+} - C_6H_4CN]$. The presence of Ar' in ion *i* was also demonstrated by the fact that this ion, at m/z 178 in the spectra of 1a-m (Ar' = Ph), was replaced by ions with the expected increase in mass in the spectra of compounds 1n-u.

Ions $[ArC_2H_3S]^+$ (*j*), $[ArC_2H_2S]^+$ (*k*) and $[C_8H_7S]^+$ (*l*)

Loss of an aryl isocyanate containing Ar' from the molecular ions was found to give rise to $[ArC_2H_3S]^+$ ions (*j*) although for the majority of the compounds examined the ion $[ArC_2H_2S]^+$ (*k*) was found to be more abundant, possibly as a result of rearrangement to a substituted tropylium ion.

The presence of C(5) in ion j was verified by the fact that, in the spectrum of 2 the peak at m/z 136 due to $[PhC_2H_3S]^{+*}$ was found to be absent but was replaced by a peak at m/z 150 corresponding to $[PhC_3H_5S]^{+*}$. The formula of this ion was confirmed by exact mass measurement. Ions analogous to k or to its methylated form were detected at m/z 135 and 149, respectively, and were identified by exact n ass measurements.

The fact that ions at m/2 136 and 135, corresponding to j and k, respectively, were only found in the spectra of 1n-u (Ar = Ph), being replaced by ions with the expected increase in mass for compounds 1a-m, demonstrated the presence of Ar in these ions.

Ions similar to j but lacking the substituent, X, in Ar were observed for a number of compounds and in some cases gave rise to ions (l) of high abundance, possibly due to stabilization by rearrangement to a substituted tropylium ion. For some compounds (e.g. 1f, g and i) the abundance of ion l far exceeded that of j.

Exact mass measurement showed that the ion at m/z134 in the spectrum of 1m had the composition C₈H₆S. Possibly this resulted from the loss of HNO₂ from ion *j*. A similar ion was observed in the spectrum of 1l.



Figure 1. Graph of the relative intensities (%) of the peaks of [ArCHNCO]⁺ ions (m) against Hammett's σ constant for compounds with a substituent in Ar.

Ions $[ArCHNCO]^+$ (m) and $[CH_2=SAr']^+$ (n)

Splitting of the molecular ion into fragments of composition ArCHNCO and CH_2 =SAr' was found to occur, the charge separation depending on the substituents present in the aromatic rings and hence on the stability of the ion formed. A rearrangement in which the Ar' ring was transferred to the sulphur atom was necessary to explain the formation of ions m and n.

Except for those compounds which contained an electron-donating group in Ar or an electronwithdrawing group in Ar', the formation of $[CH_2=SAr']^+$ was generally found to be more favourable than the formation of $[ArCHNCO]^+$. The exceptions are commented on below.

Formation of [ArCHNCO]⁺

The identity of the [ArCHNCO]⁺ ion (m) in the spectra of **1b** and **1u** was confirmed by exact mass measurements and similar ions were found in the spectra of many of the other compounds. (An analogous ion was found in the spectra of 2-methylene-1,3-thiazolidin-4ones by Ceder and Stenhede,⁸ although a cyclic structure was proposed for it.)

The formation of the ion [ArCHNCO]⁺ was found to be favoured by electron-donating substitutents in Ar and inhibited by electron-withdrawing substituents in this ring. Some suggestion of a correlation was observed between ionic relative intensity and Hammett's σ constant for electron-donating and weakly electronwithdrawing substituents ($\sigma \leq 0.23$) in Ar and gave the regression line,

relative intensity =
$$-183.1\sigma + 39.1$$

$$(r = 0.894; n = 7)$$

(Fig. 1). This could have been a result of the stabilizing or destabilizing effects on ion m of electron-donating and -withdrawing groups, respectively. (Correlations between ionic intensities in mass spectrometry and Hammett's σ constants have also been noted by other workers, e.g. Bursey and McLafferty.¹⁰)

In contrast to these effects, the formation of [ArCHNCO]⁺ appeared to be favoured by electron-

withdrawing groups in Ar', a good correlation being observed between relative intensity and σ for the substituent in Ar' and giving the regression line

relative intensity = $104.2\sigma + 29.9$

(r = 0.945; n = 9)

(Fig. 2). It seemed likely that this was not due to changes in the stability of the product radical as this would have been stabilized by both electron donation or withdrawal by the ring substituent. Instead, it might have been because electron-withdrawing substituents reduced the stability of the ion whose fragmentation was thereby encouraged.

Formation of [CH₂=SAr']⁺

Exact mass measurements for seven compounds confirmed the composition of the ion $[CH_2=SAr']^+$ (n) and further confirmation of its identity was provided by the spectrum of 2, in which the peak at m/z 123 corresponding to $[CH_2=SPh]^+$ was replaced by a new base peak at m/z 137 indicating the addition of a methyl group and demonstrating the presence of C(5). The presence of Ar' in ion n was further verified by its occurrence at m/z 123 in the spectra of **1a-m** and by its replacement by peaks with the expected increase in mass in the spectra of **1n-u**. For the majority of the compounds examined, ion n was found to be the base peak.

In contrast to the formation of ion m, the formation of n was found to be inhibited by electron-donating groups (except 3-Me) in Ar and by electronwithdrawing groups in Ar'. A good correlation was observed between the relative intensity of the ion n peak and σ for electron-withdrawing substituents in Ar' and gave the regression line

relative intensity = $-140.1\sigma + 105.3$

(r = -0.988; n = 6)

(Fig. 3). It seemed likely that these effects resulted from a relative favouring of ion m formation as explained above. Additionally, the presence of an electron-withdrawing substituent in Ar' might have tended to



Figure 2. Graph of the relative intensities (%) of the peaks of [ArCHNCO]⁺ ions (m) against Hammett's σ constant for compounds with a substituent in Ar'.

inhibit the formation of the Ar'-S bond as a result of repulsion between Ar' and a positive charge on the sulphur atom.

Ion $[ArC=S]^+(o)$

The presence of an arylthionium ion, $[ArC=S]^+$, (*o*) in the mass spectra of some of the compounds was confirmed by exact mass measurement on the ion at m/z151 ($[4-MeOC_6H_4C=S]^+$) in the spectrum of 1b. The presence of Ar in ion *o* was shown by the replacement of the ion at m/z 121, corresponding to $[PhC=S]^+$, by ions with the expected increase in mass when Ar was substituted. Ion *o* was found to be of moderate abundance (i.e. 7-18%) for compounds with a substituent in Ar', for 1b and 1e and, possibly, for 1c and 1d (although in these two cases the peaks observed were mixed). For all the other compounds examined, the abundance of ion *o* was 5% or less.

It appeared that the nature of the substituent in Ar was critical in determining the stability of ion o, with electron-donating substituents enhancing its stability and electron-withdrawing substituents reducing it.

There seemed to be some indication that the presence of an electron-withdrawing group in Ar' favoured the formation of ion o. This would be expected since electron withdrawal by Ar' would tend to weaken the C-N bond, favouring its cleavage. Possibly there was also reduced competition from other ions whose formation was inhibited by the presence of electron-withdrawing groups in Ar', e.g. ion n (Fig. 3).

Ion [Ar'] + (p)

The formation of $[Ar']^+$ ions (p) was shown by the presence of ions at m/z 77 in the spectra of **1a-m** and by their replacement by ions with the expected increase in mass in the spectra of **1n-u**. Exact mass measurement of the ion at m/z 155 in the spectrum of **1s** also confirmed its composition as C_6H_4Br .

Comparison of the mass spectra obtained at 20 and 70 eV showed that the formation of ion p was of major importance for most of the compounds examined, but only at 70 eV when it generally gave rise to ions of high abundance. Although the formation of ion p almost certainly did not result from a primary cleavage of the N-Ar' bond in the molecular ion, the high energy required for its formation probably indicates that the species from which this ion formed was one in which the N-Ar' bond was strengthened by $p-\pi$ overlap of



Figure 3. Graph of the relative intensities (%) of the peaks of $[CH_2=SAr']^+$ ions (*n*) against Hammett's σ constant for compounds with a substituent in Ar'.

the lone pair on the N atom with the π orbitals of the aromatic ring. This contrasts with the loss of Ar^{*} from the molecular ion to form ion *i*, which was found to be far less energy dependent, as might have been expected from a weaker bond.

In the spectra of 1a-m, abundant $[Ar']^+$ ions were observed irrespective of the substituent. This was not surprising since substituents in Ar are likely to have little effect on the fairly distant N-Ar' bond. A far greater variation of the $[Ar']^+$ abundance was observed with different substituents in Ar'. Possibly this variation was a result of competition with the formation of alternative ions.

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