REACTIONS OF \(\alpha\)-KETOSULFENES WITH 1-AZIRINES\(^1\)

Otobiko Tsuge* and Michibiko Neguchi
Research Institute of Industrial Science, Kyushu University 86,
Hakozaki, Higashi-ku, Fukuoka 812, Japan

The reactions of benzoylsulfene 1 and two cyclic \(\alpha\)-keto-
sulfenes 2 and 3, generated in situ from the corresponding sulfonyl
chlorides and triethylamine, with 3-substituted 2-phenyl-1-azirines
(4a-4c) proceeded through a concerted \([\pi 4s + \pi 2s]\) process. How-
ever, 2-phenyl-1-azirine (4d) showed a different behavior toward
2 and 3 from 4a-4c.

Much of the importance of sulfenes lies in their usefulness in synthe-
sis.\(^2\) Simple sulfenes \((RCH=S\text{O}_2)\) do not react with the C=N bond,\(^3\) although it
has recently been demonstrated that the reaction of phenylsulfene with benz-
ylidenemethylamines proceeded through a concerted \([\pi 2s + \pi 2a]\) process.\(^4\) In
previous papers, we reported that benzoylsulfene 1 reacts with the C=N bonds
of anils,\(^5\) carbodiimides,\(^6\) and ketene imines\(^7\) to give the \([2 + 2]\) and/or \([4 + 2]\) cycloadducts. In addition, cyclic \(\alpha\)-ketosulfenes 2 and 3 added to the C=N
bonds of anils to yield the corresponding cycloadducts.\(^8\) Theses results indi-
cate that the electron-attracting acyl group makes the \(\alpha\)-ketosulfene more re-
active than simple sulfenes, and \(\alpha\)-ketosulfenes 1-3 offer the possibility of
entry into complex heterocyclic systems through thermal symmetry-allowed
We now report the reactions of \( \alpha \)-ketosulfenes 1-2 with 1-azirines which may participate as components in these cycloadditions.

Reaction of Benzoylsulfene 1. Benzoylsulfene 1, generated in situ from benzoylmethanesulfonyl chloride and triethylamine in tetrahydrofuran, was treated with 2,3-diphenyl-1-azirine (I) at room temperature for 20 h, giving a [4 + 2] cycloadduct 5. Structural elucidation of 5 was accomplished on the basis of spectral evidence (Table 1). Further substantiation of structure was provided by the acid-catalyzed hydrolysis of 5 to the sulfonamide 6. The stereochemistry of 5 will be described below.

\[
\begin{align*}
\text{PhCOCH}=\text{SO}_2 & \quad \text{Ph} = \text{SO}_2 \\
1 & \quad 2 \\
\text{PhCON}=\text{SO}_2 & \quad \text{Ph} = \text{SO}_2 \\
3 &
\end{align*}
\]

[\( \pi 4s + \pi 2s \) or [\( \pi 2s + \pi 2a \) pericyclic reactions.

Similarly, ketosulfene 1 reacted with 3-methyl-2-phenyl-1-azirine (4a) and 3,3-dimethyl-2-phenyl-1-azirine (4c) to afford the corresponding [4 + 2] cycloadducts, 5b and 5c (Scheme 1). The yields, physical and spectral data of all 5 are given in Table 1. In the reaction of 1 with 2-phenyl-1-azirine (4d),
Table 1

<table>
<thead>
<tr>
<th>Adduct</th>
<th>Yield %</th>
<th>Mp., °C</th>
<th>Ir(KBr), cm⁻¹</th>
<th>¹H-Nmr(CDCl₃) δ(J, Hz)</th>
<th>M⁺ m/e</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a</td>
<td>65</td>
<td>174-175 (dec)</td>
<td>1615(C=C), 1340, 1150(SO₂)</td>
<td>4.55(1H, s, 3CH), 6.46 (1H, s, =CH), 7.1-7.9 (15H, m, ArH)</td>
<td>375</td>
</tr>
<tr>
<td>5b</td>
<td>65</td>
<td>126-127</td>
<td>1595(C=C), 1340, 1325, 1150(SO₂)</td>
<td>1.15(3H, d, CH₃, J=6) 3.59(1H, q, =CH₂, J=6) 6.42(1H, s, =CH), 7.0-8.0(10H, m, ArH)</td>
<td>313</td>
</tr>
<tr>
<td>5c</td>
<td>59</td>
<td>143-144</td>
<td>1610(C=C), 1325, 1150(SO₂)</td>
<td>1.21(3H, s, CH₃(exo)), 1.71(3H, s, CH₃(endo)), 6.39(1H, s, =CH), 7.2-7.9(10H, m, ArH)</td>
<td>327</td>
</tr>
</tbody>
</table>

1) 5a and 5c, colorless prisms; 5b, colorless spears.
2) ¹³C-Nmr (CDCl₃) δ 47.3, 84.8, 96.9, 126.1, 128.3, 129.1, 129.9, 131.3, 132.2, 132.3, 156.6.

However, the sulfonamide 6δ was obtained instead of the expected cycloadduct 5δ. It is evident that 6δ is arisen from the hydrolysis of 5δ, and the reactivity toward hydrolytic cleavage of 5δ seems to be comparable to that of the cycloadduct of thiobenzoyl isocyanate to 4δ.¹⁰ Hydrolysis of cycloadduct 5c gave also the sulfonamide 6c. Structural elucidation of sulfonamides 6 was accomplished on the basis of spectral data.

6a: mp 121-122⁰, colorless prisms, yield 73%; ir (KBr) 3300 (NH), 1705, 1685 (C=O), 1360, 1155 cm⁻¹ (SO₂); ¹H-nmr (CDCl₃) δ 3.91, 4.54 (each 1H, d, CH₂, J=16 Hz), 6.24 (1H, d, =CH, J=7.5 Hz), 6.60 (1H, d, NH, J=7.5 Hz, exchanged with D₂O), 6.9-8.1 (15H, m, ArH).

6c: mp 144-145⁰, colorless needles, yield 93%; ir (KBr) 3340 (NH), 1685,
1675 (C=O), 1330, 1145 cm⁻¹ (SO₂); ¹H-nmr (CDCl₃) δ 7.77 (6H, s, C(CH₃)₂), 4.53 (2H, s, CH₂), 5.9 (1H, broad, NH, exchanged with D₂O), 7.2-8.1 (10H, m, ArH).

6d: mp 132.5-134⁰, colorless prisms, yield 41%; ir (KBr) 3280 (NH), 1705, 1685 (C=O), 1340, 1140 cm⁻¹ (SO₂); ¹H-nmr (CDCl₃) δ 4.77 (2H, d, NHCH₂, J=5.5 Hz), 4.79 (2H, s, CH₂), 5.9 (1H, broad, NH, exchanged with D₂O), 7.2-8.1 (10H, m, ArH).

Now, two stereoisomers, exo-R¹ A and endo-R¹ structure B (R¹=Ph or Me), are possible for cycloadducts 5a and 5b. The signals at δ 1.21 and 1.71 in the ¹H-nmr spectrum of 5c (Table 1) are assignable to those of the exo and endo methyl protons respectively, from analogy with the nmr chemical shifts of the methyl groups in 2,2-dimethyl-3-phenylaziridine.¹¹ By comparison of the nmr chemical shift of the methyl group in 5b with those in 5c, it may be deduced that the methyl group (δ 1.15) in 5b is situated exo. From consideration of the chemical shift of methine proton in 5a,¹² 5a as well as 5b is concluded to be the exo structure A.

As will be described below, the reactions of cyclic α-ketosulfenes 2 and 3 with 1-azirines 4a and 4b afforded also the corresponding exo isomers. The exclusive formation of the exo isomers in these cycloadditions suggests that the reaction would proceed through a concerted [π4s + π2s] process (depicted as 5) rather than a stepwise process.

As mentioned above, phenylsulfene reacted with benzylidenemethyamines
to give the \([2 + 2]\) cycloadducts. However, phenylsulfene did not add to \(4a\), but instead trans-stilbene was formed as a sole product along with recovery of \(4a\).

**Reaction of Cyclic \(\alpha\)-Ketosulfenes.** Next our attention was directed toward the reaction of cyclic \(\alpha\)-ketosulfenes \(2\) and \(3\) with 1-azirines \(4\). The reaction of cyclic \(\alpha\)-ketosulfene \(2\), generated in situ from 2-chlorosulfonyl-indanone and triethylamine in tetrahydrofuran, with 3-substituted 2-phenyl-1-azirines, \(4a-4c\), at room temperature for 20 h afforded the corresponding \([4 + 2]\) cycloadducts, \(7a-7c\). The yields, physical and spectral data are given in Table 2. On the basis of the nmr chemical shifts of the methine and methyl protons, it is reasonable to conclude that both \(7a\) and \(7b\) are \(\text{exo}\) structures.

Hydrolysis of \(7c\) under mild conditions gave the sulfonamide \(8c\) in 80\% yield. \(8c\): mp 183-185\(^\circ\), colorless needles; ir (KBr) 3260 (NH), 1710, 1685 (C=O), 1330, 1150, 1145 cm\(^{-1}\) (SO\(_2\)); \(^1\)H-nmr (CDCl\(_3\)) \(\delta\) 1.82 (6H, s, C(CH\(_3\))\(_2\)), 3.5 (2H, m, CH\(_2\)), 4.11 (1H, dd, \(\text{J}=4.5, 7.5\) Hz), 5.95 (1H, broad, NH, exchanged with D\(_2\)O), 7.1-8.2 (9H, m, ArH).

On the other hand, cyclic \(\alpha\)-ketosulfene \(2\) reacted with 2-phenyl-1-azirine \((4d)\) to give the sulfonamide \(8a\), 1:1 adduct \(9\), 1:2 adduct \(10\), and/or 2,5-di-phenylpyrazine \((11)\)\(^{13}\) whose yields depended on the amounts of \(4d\) employed (Scheme 2). Structural elucidation of \(8a\), mp 161-162\(^\circ\), was accomplished on the following spectral data. ir (KBr) 3310 (NH), 1715, 1685 (C=O), 1330, 1150, 1130 cm\(^{-1}\) (SO\(_2\)); \(^1\)H-nmr (CDCl\(_3\)) \(\delta\) 3.6 (2H, m, CH\(_2\)), 4.43 (1H, dd, \(\text{J}=4.5\)),
Table 2

<table>
<thead>
<tr>
<th>Adduct</th>
<th>Yield (%)</th>
<th>Mp., °C</th>
<th>( \text{Ir(KBr), cm}^{-1} )</th>
<th>( ^1H\text{-nmr(CDC13)} )</th>
<th>( M^+ )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>( \delta(J, \text{Hz}) )</td>
<td>m/e</td>
</tr>
<tr>
<td>( \text{7a} )</td>
<td>42</td>
<td>183-185 (dec)</td>
<td>1620(C=C), 1380, 1335, 1170, 1150 (SO2)</td>
<td>3.89(2H, s, CH₂), 4.49 (1H, s, =CH₂), 7.2-7.8</td>
<td>387</td>
</tr>
<tr>
<td>( \text{7b} )</td>
<td>52</td>
<td>132-133</td>
<td>1595(C=C), 1325, 1170, 1155(SO₂)</td>
<td>1.18(3H, d, CH₃, J=6), 3.49(1H, q, =CH, J=6)</td>
<td>325</td>
</tr>
<tr>
<td>( \text{7c} )</td>
<td>51</td>
<td>164-165</td>
<td>1620(C=C), 1370, 1170, 1150(SO₂)</td>
<td>1.22(3H, s, CH₃(exo)), 1.65(3H, s, CH₃(endo))</td>
<td>339</td>
</tr>
</tbody>
</table>

1) \( \text{7a} \), colorless prisms; \( \text{7b} \), colorless spears; \( \text{7c} \), colorless needles.
2) \( ^13\text{C-nmr} \) (CDCl₃) \( \delta \) 32.7, 48.4, 87.3, 106.3, 120.8, 124.8, 127.2, 127.4, 127.9, 128.3, 129.8, 130.8, 131.1, 134.7, 136.7, 137.3, 138.1, 139.0; MS \( m/e \) 311 (\( M^+ \)).

The assigned epoxy structure for 1:1 adduct \( \text{9} \) was based on the spectral data. \( \text{9} \): mp 219-224°C (dec); ir (KBr) 3340 (NH), 1320, 1160, 1150 cm\(^{-1}\) (SO₂); \( ^1H\text{-nmr} \) (CDCl₃) at 100 MHz \( \delta \) 3.68 (1H, dd, CH₂, J=16.0, 3.8 Hz), 4.03 (1H, dd, CH₂, J=16.0, 11.5 Hz), 5.08 (1H, broad dd, NH, exchanged with D₂O), 6.2-7.5 (9H, m, ArH), 7.58 (1H, pseudo s, =CH); \( ^13\text{C-nmr} \) (CDCl₃) \( \delta \) 47.8, 66.0, 69.1, 123.6, 125.0, 126.8, 128.3, 128.9, 129.4, 129.8, 133.5, 136.7, 137.3, 138.1, 139.0; MS \( m/e \) 311 (\( M^+ \)).

Further substantiation of structure was provided by reduction of \( \text{9} \) with
\[ \text{Scheme 2} \]

LiAlH\(_4\) to indeno[3,2-e]-3,4-dihydro-2H-1,2-thiazine 1,1-dioxide (12) in 79% yield. 12: mp 202-203.5° (dec); ir (KBr) 3430 (OH), 3240 (NH), 1305, 1160, 1150 cm\(^{-1}\) (SO\(_2\)); \(^1\)H-nmr (CD\(_3\)CN) at 100 MHz \(\delta\) 3.61 (1H, dd, CH\(_2\), \(J=15.5, 6.5\) Hz), 3.81 (1H, dd, CH\(_2\), \(J=15.5, 9.5\) Hz), 3.92 (2H, pseudo s, CH\(_2\)), 4.41 (1H, broad, OH, exchanged with D\(_2\)O), 5.8 (1H, pseudo t, NH, exchanged with D\(_2\)O), 6.7-7.8 (9H, m, ArH); \(^{13}\)C-nmr (CD\(_3\)CN) \(\delta\) 36.5, 57.9, 71.2, 124.9, 125.4, 126.6, 127.5, 128.6, 128.9, 129.5, 139.7, 140.5, 142.6, 143.1; MS m/e 313 (M\(^+\)).

On the basis of spectral data, the 1:2 adduct was deduced to be either eight-membered ring compound 10-1 or 10-2. 10: mp 263-265° (dec); ir (KBr)
3340 (NH), 1325, 1170, 1150 cm⁻¹ (SO₂); ¹H-nmr (CDCl₃) at 100 MHz δ 1.92, 2.62 (each 1H, s, aziridine ring CH₂), 3.54 (1H, dd, CH₂, J=15.5, 3.8 Hz), 3.88 (1H, dd, CH₂, J=15.5, 10.5 Hz), 5.41 (1H, broad dd, NH, J=3.8, 10.5 Hz, exchanged with D₂O), 6.9-7.7 (15H, m, =CH + ArH); ¹³C-nmr (DMSO-d₆) δ 32.7, 52.6, 58.6, 92.7, 104.4, 123.7, 124.3, 125.8, 126.3, 127.8, 128.4, 128.8, 130.3, 134.6, 134.8, 140.1, 142.2, 153.8; MS m/e 428 (M⁺).

However, the pathway for the formation of 9 and 10 is not clear at present.

Cyclic α-ketosulfene 3, generated in situ from 2-chlorosulfonyl-1-tetralone and triethylamine, reacted with 3-substituted 2-phenyl-1-azirines, 4a-4c, under similar conditions, yielding the corresponding [4 + 2] cycloadducts, 13a-13c. The yields, physical and spectral data of 13 are given in Table 3. On the basis of the nmr chemical shifts of the methine and methyl protons, it is evident that both 13a and 13b are exo structures.

![Scheme 3](image-url)
Table 3

<table>
<thead>
<tr>
<th>Adduct&lt;sup&gt;1)&lt;/sup&gt;</th>
<th>Yield</th>
<th>Mp., °C</th>
<th>IR(KBr), cm&lt;sup&gt;-1&lt;/sup&gt;</th>
<th>&lt;sup&gt;1&lt;/sup&gt;H-Nmr(CDC&lt;sub&gt;13&lt;/sub&gt;)</th>
<th>M&lt;sup&gt;+&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td></td>
<td></td>
<td>δ(J, Hz)</td>
<td>m/e</td>
</tr>
<tr>
<td>13a&lt;sup&gt;2)&lt;/sup&gt;</td>
<td>72</td>
<td>184-186</td>
<td>1625(C=C), 1325, 1310, 1170, 1150</td>
<td>2.1-3.8(4H, m, CH&lt;sub&gt;2&lt;/sub&gt;), 4.54(1H, s, ≡CH), 6.9-7.8(14H, m, ArH)</td>
<td>401</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(dec)</td>
<td>1150(SO&lt;sub&gt;2&lt;/sub&gt;)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13b</td>
<td>70</td>
<td>138-139</td>
<td>1625(C=C), 1320, 1160, 1150(SO&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>2.4-3.3(4H, m, CH&lt;sub&gt;2&lt;/sub&gt;), 3.57(1H, q, ≡CH, J=6)</td>
<td>339</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7.0-8.1(9H, m, ArH)</td>
<td></td>
</tr>
<tr>
<td>13c&lt;sup&gt;3)&lt;/sup&gt;</td>
<td>75</td>
<td>175-176</td>
<td>1630(C=C), 1375, 1350, 1310, 1160</td>
<td>1.18(3H, s, CH&lt;sub&gt;3&lt;/sub&gt;(exo)), 1.70(3H, s, CH&lt;sub&gt;3&lt;/sub&gt;(endo)),</td>
<td>353</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(SO&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>2.8(4H, m, CH&lt;sub&gt;2&lt;/sub&gt;), 7.0-7.9(9H, m, ArH)</td>
<td></td>
</tr>
</tbody>
</table>

1) 13a-13c, colorless prisms.
2) <sup>13</sup>C-Nmr (CDC<sub>13</sub>) δ 19.1, 26.9, 47.2, 84.0, 106.6, 123.8, 127.0, 127.1, 127.8, 128.2, 128.3, 129.7, 131.1, 137.4, 148.7.
3) <sup>13</sup>C-Nmr (CDC<sub>13</sub>) δ 14.6, 18.6, 23.0, 26.9, 51.8, 85.2, 107.2, 123.8, 126.8, 127.1, 127.2, 127.8, 128.2, 128.5, 129.5, 130.7, 133.4, 137.2, 151.0.

On the other hand, the reaction of 3 with 2-phenyl-1-azirine (4d) did not give the corresponding [4+2] cycloadduct, but instead the sulfonamide and 2:2 adduct 15 were formed. The yields of 14 and 15 depended on the amounts of 4d employed (Scheme 3).<sup>14</sup>

14: mp 116-117°; ir (KBr) 3290 (NH), 1705, 1690, 1670 (C=O), 1310, 1300, 1140, 1130 cm<sup>-1</sup> (SO<sub>2</sub>); <sup>1</sup>H-nmr (CDC<sub>13</sub>) δ 2.4-3.4 (4H, m, CH<sub>2</sub>), 4.29 (1H, dd, ≡CH, J=5, 7 Hz), 4.78 (2H, d, CH<sub>2</sub>, J=5.5 Hz), 6.13 (1H, broad t, NH, J=5.5 Hz, exchanged with D<sub>2</sub>O), 7.1-8.2 (9H, m, ArH); MS m/e 279 (M<sup>+</sup> - SO<sub>2</sub>).
It is obvious that 13 contains two convertible moieties to 14 in the molecule, because the hydrolysis of 13 (1 mol as C₃₆H₇₀N₂₀S₂) with hydrochloric acid in refluxing ethanol afforded 1.5 mol of 14. On the basis of the above fact as well as of spectral data, ten-membered cyclic compound was tentatively assigned for the structure of 15.

15: mp 179-181° (dec); ir (KBr) 3300 (NH), 1620 (C=O), 1320, 1170, 1160, 1150 cm⁻¹ (SO₂); H-nmr (CDCl₃) δ 2.5-3.2 (8H, m, CH₂), 3.96 (1H, dd, CH₂, J=16, 9 Hz), 4.54 (1H, dd, CH₂, J=16, 5 Hz), 5.55 (1H, broad, NH, exchanged with D₂O), 5.78 (1H, s, =CH), 6.5-8.2 (18H, m, ArH); C-nmr (CDCl₃) δ 22.6, 23.9, 27.5, 31.7, 98.7, 111.1, 117.4, 124.3, 125.6, 126.2, 126.5, 127.1, 127.7, 128.0, 128.9, 129.2, 129.4, 129.8, 130.7, 131.2, 131.5, 136.9, 137.4, 137.7, 147.3, 150.6, 155.8.
REFERENCES AND NOTES


9. All new compounds gave satisfactory elementary analyses. Nmr spectra were recorded on a Hitachi R-20 and JEOL FX-100 nmr spectrometers with tetramethylsilane as internal standard. Mass spectra were obtained on a Hitachi RMS-4 mass spectrometer, using a direct inlet and an ionization energy of 70 eV.


14. When two moles of 94 was employed, dimer of 3, mp 174-175°, was obtained in 6% yield.

Received, 13th December, 1977