# REACTIONS OF α-KETOSULFENES WITH 1-AZIRINES[1]

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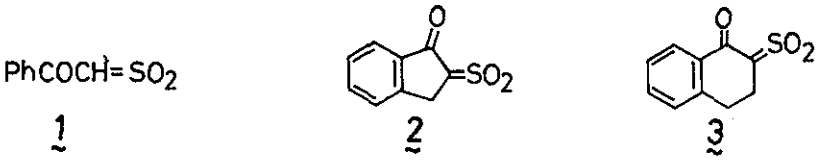
The reactions of benzoylsulfene 1 and two cyclic α-ketosulfenes 2 and 3, generated in situ from the corresponding sulfonyl chlorides and triethylamine, with 3-substituted 2-phenyl-1-azirines (4a-4c) proceeded through a concerted [π4s + π2s] process. However, 2-phenyl-1-azirine (4d) showed a different behavior toward 2 and 3 from 4a-4c.

Much of the importance of sulfenes lies in their usefulness in synthesis.[2] Simple sulfenes ($RCH{=}SO_2$) do not react with the C=N bond,[3] although it has recently been demonstrated that the reaction of phenylsulfene with benzylidenemethylamines proceeded through a concerted [π2s + π2a] 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 α-ketosulfenes 2 and 3 added to the C=N bonds of anils to yield the corresponding cycloadducts.[8] Theses results indicate that the electron-attracting acyl group makes the α-ketosulfene more reactive than simple sulfenes, and α-ketosulfenes 1-3 offer the possibility of entry into complex heterocyclic systems through thermal symmetry-allowed

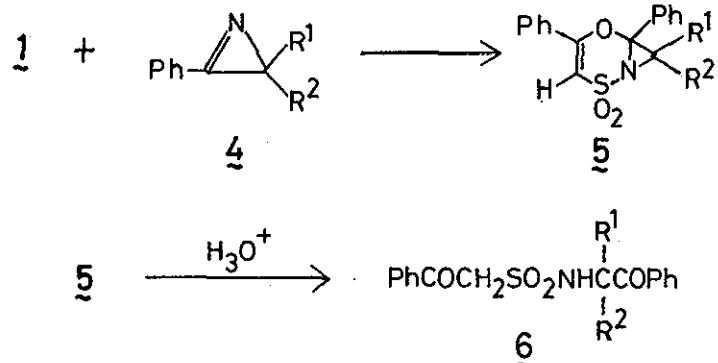



1 2 3

[π4s + π2s] or [π2s + π2a] pericyclic reactions.

We now report the reactions of α-ketosulfenes 1-3 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 (4a) at room temperature for 20 h, giving a [4 + 2] cycloadduct 5a.[9] Structural elucidation of 5a was accomplished on the basis of spectral evidence (Table 1). Further substantiation of structure was provided by the acid-catalyzed hydrolysis of 5a to the sulfonamide 6a. The stereochemistry of 5a will be described below.




a: $R^1$=Ph, $R^2$=H; b: $R^1$=Me, $R^2$=H; c: $R^1$=$R^2$=Me; d: $R^1$=$R^2$=H

Scheme 1

Similarly, ketosulfene 1 reacted with 3-methyl-2-phenyl- (4b) 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

| Adduct[1] | Yield % | Mp., °C | Ir(KBr), $cm^{-1}$ | $^1$H-Nmr($CDCl_3$) δ(J, Hz) | $M^+$ m/e |
|---|---|---|---|---|---|
| 5a[2] | 65 | 174-175 (dec) | 1615(C=C), 1340, 1150($SO_2$) | 4.55(1H, s, ≥CH), 6.46 (1H, s, =CH), 7.1-7.9 (15H, m, ArH) | 375 |
| 5b | 65 | 126-127 | 1595(C=C), 1340, 1325, 1150($SO_2$) | 1.15(3H, d, $CH_3$, J=6) 3.59(1H, q, ≥CH, J=6) 6.42(1H, s, =CH), 7.0-8.0(10H, m, ArH) | 313 |
| 5c | 59 | 143-144 | 1610(C=C), 1325, 1320, 1150($SO_2$) | 1.21(3H, s, $CH_3$(*exo*)), 1.71(3H, s, $CH_3$(*endo*)), 6.39(1H, s, =CH), 7.2-7.9(10H, m, ArH) | 327 |

1) 5a and 5c, colorless prisms; 5c, colorless spears.
2) $^{13}$C-Nmr ($CDCl_3$) 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 6d was obtained instead of the expected cycloadduct 5d. It is evident that 6d is arisen from the hydrolysis of 5d, and the reactivity toward hydrolytic cleavage of 5d seems to be comparable to that of the cycloadduct of thiobenzoyl isocyanate to 4d.[10] Hydrolysis of cycloadduct 5c gave also the sulfonamide 6c. Structural elucidation of sulfonamides 6 was accomplished on the basis of spectral data.

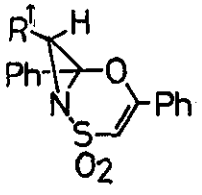
6a: mp 121-122°, colorless prisms, yield 73%; ir (KBr) 3300 (NH), 1705, 1685 (C=O), 1360, 1155 $cm^{-1}$ ($SO_2$); $^1$H-nmr ($CDCl_3$) δ 3.91, 4.54 (each 1H, d, $CH_2$, J=16 Hz), 6.24 (1H, d, ≥CH, J=7.5 Hz), 6.60 (1H, d, NH, J=7.5 Hz, exchanged with $D_2O$), 6.9-8.1 (15H, m, ArH).

6c: mp 144-145°, colorless needles, yield 93%; ir (KBr) 3340 (NH), 1685,

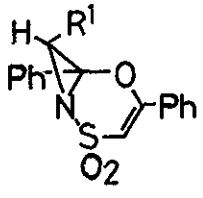
1675 (C=O), 1330, 1145 $cm^{-1}$ ($SO_2$); $^1$H-nmr ($CDCl_3$) δ 1.77 (6H, s, $C(\underline{CH_3})_2$), 4.53 (2H, s, $\underline{CH_2}$), 5.9 (1H, broad, $\underline{NH}$, exchanged with $D_2O$), 7.2-8.1 (10H, m, Ar$\underline{H}$).

6d: mp 132.5-134°, colorless prisms, yield 41%; ir (KBr) 3280 (NH), 1705, 1685 (C=O), 1340, 1140 $cm^{-1}$ ($SO_2$); $^1$H-nmr ($CDCl_3$) δ 4.77 (2H, d, $NHC\underline{H_2}$, J=5.5 Hz), 4.79 (2H, s, $\underline{CH_2}$), 5.9 (1H, broad, $\underline{NH}$, exchanged with $D_2O$), 7.2-8.1 (10H, m, Ar$\underline{H}$).

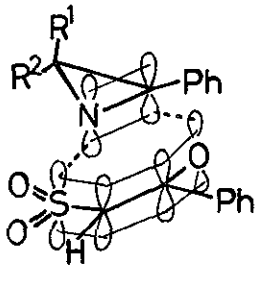
Now, two stereoisomers, *exo*-$R^1$ A and *endo*-$R^1$ structure B ($R^1$=Ph or Me), are possible for cycloadducts 5a and 5b. The signals at δ 1.21 and 1.71 in the $^1$H-nmr spectrum of 5c (Table 1) are assignable to those of the *exo* and *endo* methyl protons respectively, from analogy with the nmr 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.




A




B



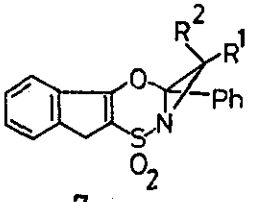

C ($R^1 > R^2$)

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 C) rather than a stepwise process.

As mentioned above, phenylsulfene reacted with benzylidenemethylamines

to give the [2 + 2] cycloadducts.[4] 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 α-Ketosulfenes. Next our attention was directed toward the reaction of cyclic α-ketosulfenes 2 and 3 with 1-azirines 4. The reaction of cyclic α-ketosulfene 2, generated in situ from 2-chlorosulfonylindanone 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



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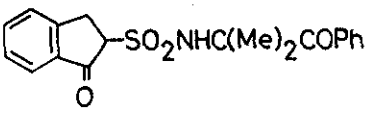
a: $R^1$=Ph, $R^2$=H
b: $R^1$=Me, $R^2$=H
c: $R^1$=$R^2$=Me



8c

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 *exo* structures.

Hydrolysis of 7c under mild conditions gave the sulfonamide 8c in 80% yield. 8c: mp 183-185°, colorless needles; ir (KBr) 3260 (NH), 1710, 1685 (C=O), 1330, 1150, 1145 $cm^{-1}$ ($SO_2$); $^1$H-nmr ($CDCl_3$) δ 1.82 (6H, s, $C(CH_3)_2$), 3.5 (2H, m, $CH_2$), 4.11 (1H, dd, >CH, J=4.5, 7.5 Hz), 5.95 (1H, broad, NH, exchanged with $D_2O$), 7.1-8.2 (9H, m, ArH).

On the other hand, cyclic α-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-diphenylpyrazine (11)[13] whose yields depended on the amounts of 4d employed (Scheme 2). Structural elucidation of 8a, mp 161-162°, 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 ($CDCl_3$) δ 3.6 (2H, m, $CH_2$), 4.43 (1H, dd, >CH,

Table 2

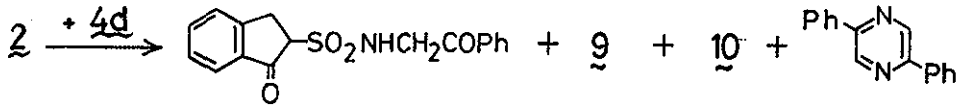
| Adduct[1] | Yield % | Mp., °C | Ir(KBr), $cm^{-1}$ | $^1$H-Nmr($CDCl_3$) δ(J, Hz) | $M^+$ m/e |
|---|---|---|---|---|---|
| 7a[2] | 42 | 183-185 (dec) | 1620(C=C), 1380, 1335, 1170, 1150 ($SO_2$) | 3.89(2H, s, $CH_2$), 4.49 (1H, s, $\geq CH$), 7.2-7.8 (14H, m, ArH) | 387 |
| 7b | 52 | 132-133 | 1595(C=C), 1325, 1170, 1155($SO_2$) | 1.18(3H, d, $CH_3$, J=6), 3.49(1H, q, $\geq CH$, J=6) 3.83(2H, s, $CH_2$), 7.2-8.0(9H, m, ArH) | 325 |
| 7c | 51 | 164-165 | 1620(C=C), 1370, 1170, 1150($SO_2$) | 1.22(3H, s, $CH_3$ *(exo)*), 1.65(3H, s, $CH_3$ *(endo)*), 3.82(2H, s, $CH_2$), 7.2-8.0(9H, m, ArH) | 339 |

1) 7a, colorless prisms; 7b, colorless spears; 7c, colorless needles.
2) $^{13}$C-Nmr ($CDCl_3$) δ 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, 140.3, 155.4.

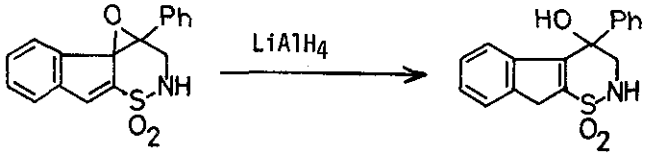
J=5, 7.5 Hz), 4.60, 4.99 (each 1H, dd, $CH_2$, J=5, 18 Hz), 6.02 (1H, pseudo t, NH, exchanged with $D_2O$), 7.3-8.2 (9H, m, ArH).

The assigned epoxy structure for 1:1 adduct 9 was based on the spectral data. 9: mp 219-224° (dec); ir (KBr) 3340 (NH), 1320, 1160, 1150 $cm^{-1}$ ($SO_2$); $^1$H-nmr ($CDCl_3$) at 100 MHz δ 3.68 (1H, dd, $CH_2$, J=16.0, 3.8 Hz), 4.03 (1H, dd, $CH_2$, J=16.0, 11.5 Hz), 5.08 (1H, broad dd, NH, exchanged with $D_2O$), 6.2-7.5 (9H, m, ArH), 7.58 (1H, pseudo s, =CH); $^{13}$C-nmr ($CDCl_3$) δ 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 ($M^+$).

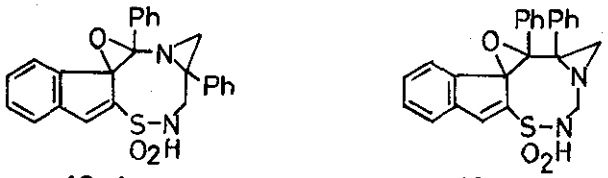
Further substantiation of structure was provided by reduction of 9 with




| | 8a | | | 11 |
|---|---|---|---|---|
| 2/4d(mol/mol) | | | | |
| 1/1 | 16% | trace | 5% | - |
| 1/2 | 7% | 15% | 22% | 6% |




9 12




10-1 10-2

Scheme 2

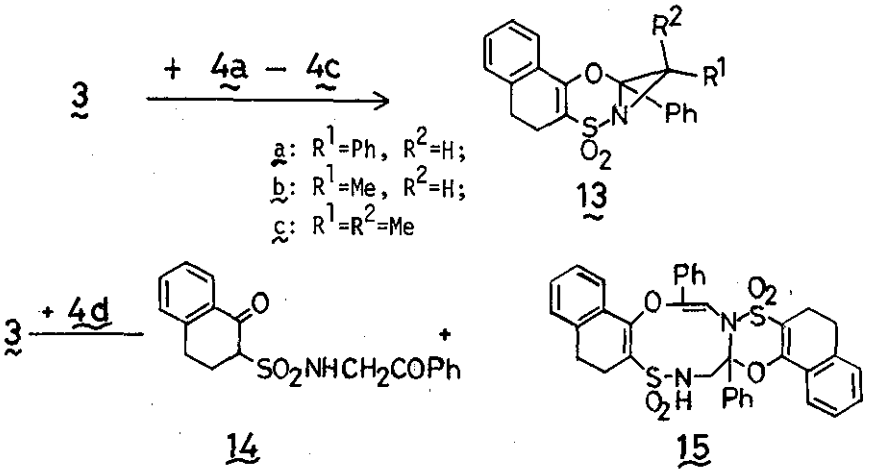
$LiAlH_4$ to indeno[3,2-e]-3,4-dihydro-2H-1,2-thiazine 1,1-dioxide (12) in 79% yield. 12: mp 202-203.5° (dec); ir (KBr) 3430 (OH), 3240 (NH), 1305, 1160, 1150 $cm^{-1}$ ($SO_2$); $^1$H-nmr ($CD_3CN$) at 100 MHz δ 3.61 (1H, dd, $CH_2$, J=15.5, 6.5 Hz), 3.81 (1H, dd, $CH_2$, J=15.5, 9.5 Hz), 3.92 (2H, pseudo s, $CH_2$), 4.41 (1H, broad, OH, exchanged with $D_2O$), 5.8 (1H, pseudo t, NH, exchanged with $D_2O$), 6.7-7.8 (9H, m, ArH); $^{13}$C-nmr ($CD_3CN$) δ 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 $cm^{-1}$ ($SO_2$); $^1$H-nmr ($CDCl_3$) at 100 MHz δ 1.92, 2.62 (each 1H, s, aziridine ring $CH_2$), 3.54 (1H, dd, $CH_2$, J=15.5, 3.8 Hz), 3.88 (1H, dd, $CH_2$, J=15.5, 10.5 Hz), 5.41 (1H, broad dd, NH, J=3.8, 10.5 Hz, exchanged with $D_2O$), 6.9-7.7 (15H, m, =CH + ArH); $^{13}$C-nmr (DMSO-$d_6$) 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.




| 3/4d(mol/mol) | | |
|---|---|---|
| 1/1 | 16% | 6.5% |
| 1/2 | 9% | 34.5% |

Scheme 3

Table 3

| Adduct[1] | Yield % | Mp., °C | Ir(KBr), $cm^{-1}$ | $^1$H-Nmr($CDCl_3$) δ(J, Hz) | $M^+$ m/e |
|---|---|---|---|---|---|
| 13a[2] | 72 | 184-186 (dec) | 1625(C=C), 1325, 1310, 1170, 1150 ($SO_2$) | 2.1-3.8(4H, m, $CH_2$), 4.54(1H, s, ≥CH), 6.9-7.8(14H, m, ArH) | 401 |
| 13b | 70 | 138-139 | 1625(C=C), 1320, 1160, 1150($SO_2$) | 1.16(3H, d, $CH_3$, J=6) 2.4-3.3(4H, m, $CH_2$), 3.57(1H, q, ≥CH, J=6) 7.0-8.1(9H, m, ArH) | 339 |
| 13c[3] | 75 | 175-176 | 1630(C=C), 1375, 1350, 1310, 1160 ($SO_2$) | 1.18(3H, s, $CH_3$(*exo*)), 1.70(3H, s, $CH_3$(*endo*)), 2.8(4H, m, $CH_2$), 7.0-7.9(9H, m, ArH) | 353 |

1) 13a-13c, colorless prisms.

2) $^{13}$C-Nmr ($CDCl_3$) 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) $^{13}$C-Nmr ($CDCl_3$) 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 14 and 2:2 adduct 15 were formed. The yields of 14 and 15 depended on the amounts of 4d employed (Scheme 3).[14]

14: mp 116-117°; ir (KBr) 3290 (NH), 1705, 1690, 1670 (C=O), 1310, 1300, 1140, 1130 $cm^{-1}$ ($SO_2$); $^1$H-nmr ($CDCl_3$) δ 2.4-3.4 (4H, m, $CH_2$), 4.29 (1H, dd, ≥CH, J=5, 7 Hz), 4.78 (2H, d, $CH_2$, J=5.5 Hz), 6.13 (1H, broad t, NH, J=5.5 Hz, exchanged with $D_2O$), 7.1-8.2 (9H, m, ArH); MS m/e 279 ($M^+ - SO_2$).

It is obvious that 15 contains two convertible moieties to 14 in the molecule, because the hydrolysis of 15 (1 mol as $C_{36}H_{30}N_2O_6S_2$) 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=C), 1320, 1170, 1160, 1150 $cm^{-1}$ ($SO_2$); $^1$H-nmr ($CDCl_3$) δ 2.5-3.2 (8H, m, $CH_2$), 3.96 (1H, dd, $CH_2$, J= 16, 9 Hz), 4.54 (1H, dd, $CH_2$, J=16, 5 Hz), 5.55 (1H, broad, NH, exchanged with $D_2O$), 5.78 (1H, s, =CH), 6.5-8.2 (18H, m, ArH); $^{13}$C-nmr ($CDCl_3$) δ 22.6, 23.9, 27.5, 51.7, 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

1. Studies of α-Ketosulfenes. XI. Part X of this series: O. Tsuge and M. Noguchi, Chem. Lett., 1977, 749.

2. For a recent summary of work in this area see J. F. King, Acc. Chem. Res., 1975, 8, 10.

3. H. Ulrich, 'Cycloaddition Reactions of Heterocummulenes', Academic Press, New York, N. Y., 1967, p. 286.

4. T. Hiraoka and T. Kobayashi, Bull. Chem. Soc. Jpn., 1975, 48, 480.

5. O. Tsuge and S. Iwanami, ibid., 1970, 43, 3543.

6. O. Tsuge and S. Iwanami, Nippon Kagaku Zasshi, 1971, 92, 448.

7. O. Tsuge and S. Iwanami, Org. Prep. & Proced. Int., 1971, 3, 283.

8. O. Tsuge and M. Noguchi, Chem. Lett., 1974, 113.

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.

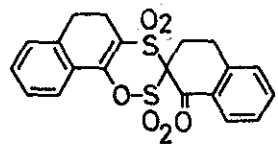
10. V. Nair and K. H. Kim, J. Org. Chem., 1974, 39, 3763.

11. S. J. Brois, ibid., 1962, 27, 3532.

12. In general, signals of methine protons in aziridines appear at δ 3-3.5 (M. Ohtsuru and K. Tori, J. Mol. Spectry., 1968, 27, 296).

13. Structural elucidation of 11, mp 199° (lit.[15] mp 196°), was accomplished on the basis of spectral data. Dimerization of 1-azirines, followed by oxidation to pyrazines is well known (H. Taniguchi and K. Isomura, J. Syn. Org. Chem. Jpn., 1972, 30, 280).

14. When two moles of 4d was employed, dimer of 3, mp 174-175°,[8] was obtained in 6% yield.



Dimer of 3

15. L. Wolff, Ber., 1887, 20, 425.

Received, 13th December, 1977