Reaction of Aromatic *N*-Oxides with Dipolarophiles. Part 18.† Formation Mechanism and X-Ray Structure of the Cycloadduct from Sequential Pericyclic Reaction of Pyridine *N*-Oxides with Phenylsulfonylallene

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Sequential pericyclic reactions of pyridine *N*-oxides (**1**) with phenylsulfonylpropadiene (**2**) and 1-phenylsulfonylpropyne (**3**) were investigated. 3,5-Dimethylpyridine *N*-oxide (**1a**) was allowed to react with **2** in $CHCl_3$ at room temperature to give a mixture of the [1,5]-sigmatropic rearrangement product (**4a**) of the 1:1 cycloadduct and the 1:2 azetidine-type cycloadduct (**5a**). The structure of **5a** was established by single crystal X-ray analysis. The reaction rate of **1a** with **2** was about 50 000 times that of **1a** with *N*-phenylmaleimide. The reaction of **1a** with **3** did not give **5a** but **4a** as the sole product. The reactivity, regio- and peri-selectivity and formation mechanism of **4** and **5** are discussed in terms of the frontier molecular orbital consideration based on kinetic and molecular orbital calculation data.

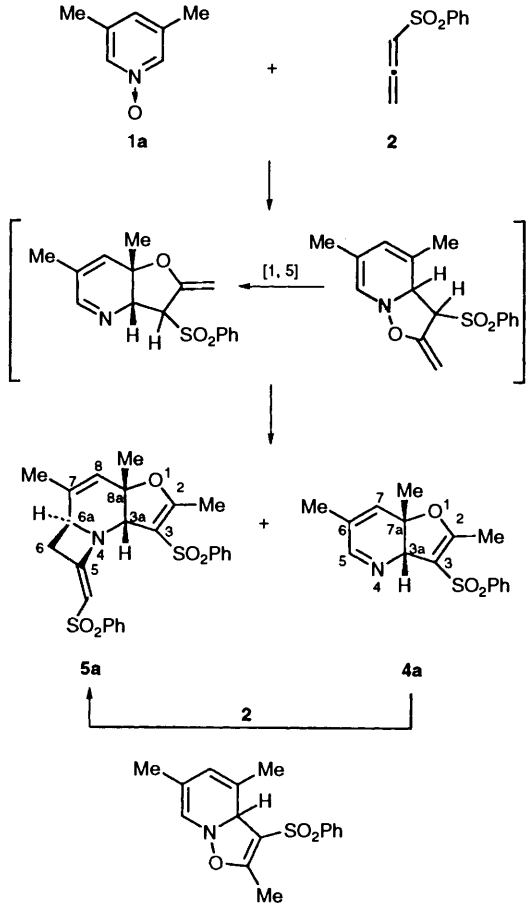
The 1,3-dipolar cycloadditions of pyridine *N*-oxides with unsaturated compounds have been scarcely known except for acetylenes[1] and heterocumulenes[2] as they are unreactive due to a high degree of aromaticity.[2] In the past several years, we have examined the pericyclic reactions of pyridine *N*-oxides with various dipolarophiles such as phenyl isocyanates, *N*-substituted maleimides and 1,4-epoxy-1,4-dihydronaphthalene and elucidated mechanistic aspects of the reaction based on its kinetics and frontier molecular orbital (FMO)[3] calculations. To our knowledge, 1,3-dipolar cycloaddition of pyridine *N*-oxides with allenes has not been reported except for our report on dimethylpenta-2,3-dienedioate toward pyridine *N*-oxides.[4]

In connection with this, we have communicated that phenylsulfonylallene was highly reactive in cycloadditions with pyridine *N*-oxides.[5] The reactions are discussed here with newly obtained data to clarify the overall character of the reactions.

Results

Cycloaddition of 3,5-*Dimethylpyridine* N-*Oxide* (**1a**) *with Phenylsulfonylpropadiene* (**2**).—As reported in our previous paper,[5] the reaction of 3,5-dimethylpyridine *N*-oxide (**1a**) with phenylsulfonylpropadiene (**2**) in $CHCl_3$ at room temp. gave the [1,5]-sigmatropic rearrangement product (**4a**) of the primary cycloadduct and 1:2 azetidine-type product (**5a**) (Scheme 1). The structures of **4a** and **5a** were determined by their ^1H NMR, ^{13}C NMR and mass spectra.[5] The MS of **4a** showed a mass ion (M^+, 303) and a fragment peak ($M^+ - PhSO_2$, 162), suggesting the formation of a 1:1 cycloadduct of **1a** and **2**. The ^1H NMR spectrum of **4a** exhibited three methyl signals [δ 1.39, 1.85 (showing allylic coupling) and 2.18]. Assignments were confirmed by 2D-COSY spectrum. The ^{13}C NMR of **4a** showed two additional sp^3 carbons, suggesting that **4a** is not an endocyclic primary adduct but one derived from endocyclic [1,5]-sigmatropic rearrangement.

The MS of **5a** showed a mass ion (M^+, 483), corresponding to a 1:2 adduct of **1a** and **2**. Isolated **4a** was allowed to react with the allene **2** to give the adduct **5a**. In the ^1H NMR spectrum of **5a**, signals similar to those for **4a** were observed, except for the signal at δ 7.50 (5-H). Therefore, we proposed that the second molecule of **2** formally cycloadded to the C=N of **4a** to give an azetidine ring. Furthermore, two methylene protons were observed at δ 2.91 and 2.98, (J 15.75 Hz) suggesting that the 2,3-double bond of **2** had cycloadded to **4a**. Assignments were confirmed by 2D-COSY and 2D-^1H-^{13}C-COSY spectra. However, as the stereochemistry of the azetidine moiety and configuration of the exocyclic $PhSO_2HC{=}C$ group were not evident we performed a single crystal X-ray analysis of **5a**.



Scheme 1

† For Part 17, see ref. 5.

Table 1 Bond distances (Å) for non-hydrogen atoms

C(10)–C(11)	1.355(5)	C(15)–C(17)	1.312(6)
C(11)–C(12)	1.496(5)	C(17)–C(18)	1.490(5)
C(11)–N(13)	1.365(4)	C(18)–O(20)	1.482(4)
C(12)–C(14)	1.547(6)	C(18)–C(24)	1.554(4)
N(13)–C(14)	1.468(4)	O(20)–C(21)	1.347(4)
N(13)–C(24)	1.429(5)	C(21)–C(23)	1.336(5)
C(14)–C(15)	1.498(5)	C(23)–C(24)	1.507(4)

Table 2 Bond angles (°) for non-hydrogen atoms

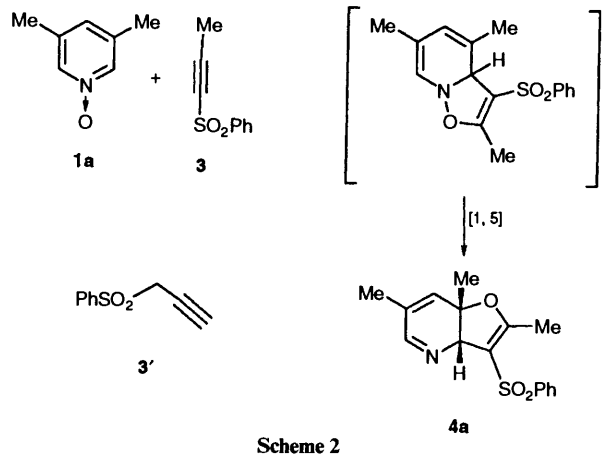
C(12)–C(11)–N(13)	93.1(3)	C(15)–C(17)–C(18)	127.5(3)
C(11)–C(12)–C(14)	85.4(3)	C(17)–C(18)–O(20)	104.7(2)
C(11)–N(13)–C(14)	93.5(3)	C(17)–C(18)–C(24)	113.8(3)
C(11)–N(13)–C(24)	129.2(3)	C(18)–O(20)–C(21)	109.0(2)
C(14)–N(13)–C(24)	124.6(2)	O(20)–C(21)–C(23)	112.7(3)
C(12)–C(14)–N(13)	87.1(2)	C(21)–C(23)–C(24)	111.1(3)
C(12)–C(14)–C(15)	116.8(3)	N(13)–C(24)–C(18)	111.7(2)
N(13)–C(14)–C(15)	111.9(3)	N(13)–C(24)–C(23)	113.4(3)
C(14)–C(15)–C(17)	120.4(3)	C(18)–C(24)–C(23)	100.6(2)

X-Ray Crystallographic Analysis of the Azetidine-type Cycloadduct (**5a**) *from the Reaction of* **1a** *with* **2**.—The single crystals suitable for X-ray analysis were obtained by slow evaporation of a C_6H_6–AcOEt solution. The structure was solved by the direct method using the MULTAN78[6] programs and refined by the block-diagonal least-square method. The final *R* value obtained was 0.038. The computer-generated drawing of **5a** with the numbering sequence used in this paper is depicted in Fig. 1. As shown **5a** is considered to be a formal [2 + 2] cycloadduct of **4a** and **2**, in which the azetidine ring was formed *via* stereospecific attack of the terminal double bond of **2** on the C=N bond of **4a** from the sterically less hindered face.

Bond distances and angles are summarized in Tables 1 and 2. The sum of the angles around N(13) is *ca.* 347.7°, indicating that N(13) has considerable sp^2 character. C(12) deviates by 0.2 Å from the plane of C(14)–N(13)–C(11), indicating that the azetidine ring is slightly distorted. Selected torsion angles are listed in Table 3. O(26) is approximately co-planar with the adjacent phenyl group. O(27) is likewise approximately co-planar with the C(21)–C(23) double bond. Similar conformation is observed in another phenylsulfonyl group attached to C(10). The S(7)–C(10)–C(11)–N(13) fragment adopts an *anti* configuration, which is almost planar. The dihydrofuran ring is virtually planar. The distances for the endocyclic double bond between C(21) and C(23) and exocyclic double bond between C(10) and C(11) are both unremarkable. Angles between six- and four-membered rings and between six- and five-membered rings from the best plane calculation are 106.9° and 120.1°, respectively.

Cycloaddition of **1a** *with* 1-*Phenylsulfonylpropyne* (**3**) *and* 3-*Phenylsulfonylpropyne* (**3'**).—The reaction of **1a** with alkyne **3** gave **4a** as a sole product in 41% yield. In this case, the formation of **5a** was not observed. In contrast, terminal acetylene **3'** did not show any reactivity in cycloadditions with **1a** and **4a**.

Cycloaddition of 3-*Methylpyridine*-N-*oxide* (**1b**) *with* **2**.—Next, we studied the periselectivity of the reaction using **1b**. A solution of **1b** and **2** (1 : 1) in $CHCl_3$ was stirred at room temp. for 19 h giving rise to a mixture of **4b** and **5b**. The products were separated by chromatography on silica gel. The MS of **4b** showed a mass ion (M^+, 289) and a fragment peak ($M^+ - PhSO_2$, 148), suggesting the formation of a 1 : 1 cycloadduct of **1b** and **2**. The ^1H NMR spectrum of **4b** exhibited two methyl signals [δ 1.42 (no allylic coupling), and 2.20], and three olefinic



Scheme 2

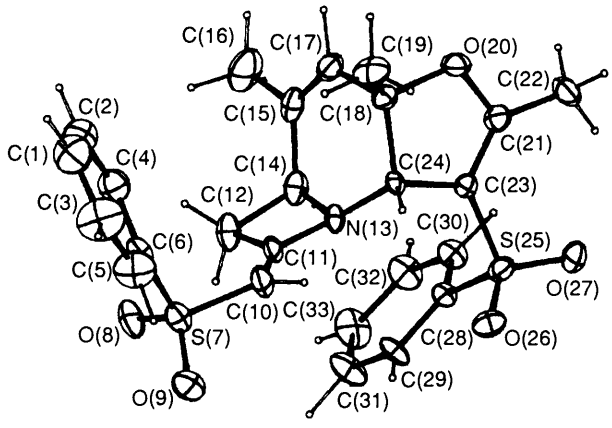


Fig. 1 ORTEP Drawing of **5a**

protons in the range δ 5.94–7.71. The ^{13}C NMR spectrum of **4b** showed two additional sp^3 carbons, suggesting that **4b** is not the primary adduct but the [1,5]-sigmatropic rearrangement product arising from the cycloaddition of **2** at the 2-position of **1b**.

Isolated **4b** was allowed to react with **2** to give **5b**, which was shown by its spectral data to be the azetidine-type product.

In this reaction, beside **4b** and **5b**, we obtained a trace amount of crude **4'b**, whose structure was established by ^1H NMR (see Experimental). Furthermore, we detected another spot by TLC, assumed to be the product **5'b** (Scheme 3) arising from the cycloaddition of **2** at the 6-position of **1b**. However, the compound was present in quantities too minute to isolate under the conditions used.

Rate Study

Next, the kinetic study of the reaction was performed. Strictly speaking, it is difficult to measure precisely the concentration of **2** throughout the reaction period with **1a**, because the reaction involves successive processes. However, the concentration of **4a**, the species that can react with a second molecule of **2**, is very low in an early stage of the reaction. Therefore, we assumed that the rate of the primary cycloaddition of **1a** with **2** can be evaluated at least in the early stages of the reaction. On this assumption, the second-order rate constants in $CHCl_3$ within 0.5 h at 40 °C were obtained by following the decrease of the concentration of **1a** by HPLC. In the same manner, the reaction of **1a** with **3** was also examined. The results are shown in Fig. 3.

To examine the formation mechanism of **5a**, we measured solvent effect on the rate of addition of **4a** and **2** and the results are summarized in Table 4. The E_T values of Reichardt *et al.*,[7] based on the bands of solvatochromism of pyridinium *N*-

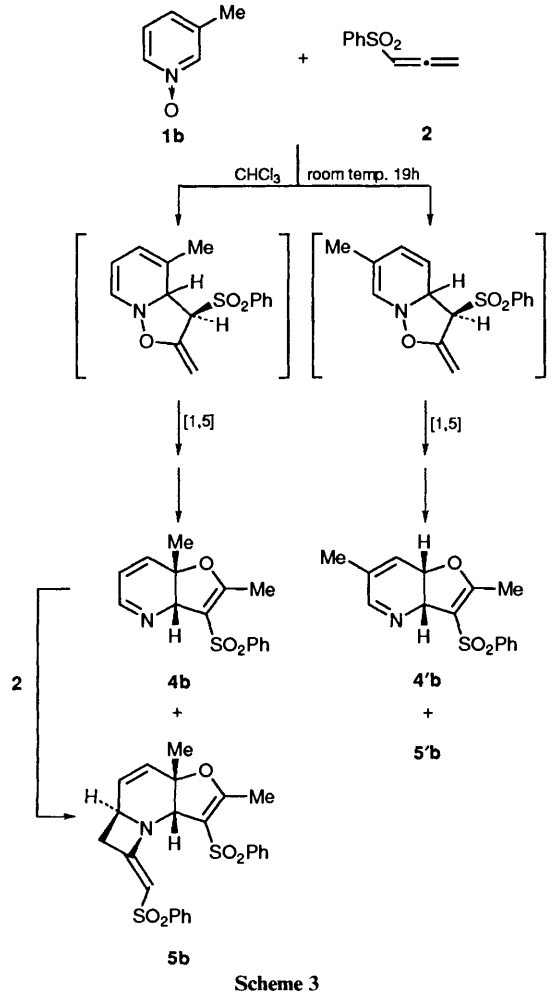
Table 3 Selected torsion angles (°)

C(11)–C(12)–C(14)–N(13)	6.82	C(11)–N(13)–C(14)–C(12)	−7.46
C(12)–C(11)–N(13)–C(14)	7.72	N(13)–C(11)–C(12)–C(14)	−7.33
C(14)–C(15)–C(17)–C(18)	5.19	O(20)–C(21)–C(33)–C(24)	−2.49
C(26)–C(25)–C(28)–C(29)	8.08	C(21)–C(23)–C(25)–C(27)	6.50
C(8)–C(7)–C(10)–C(11)	9.93	C(5)–C(6)–C(7)–C(9)	8.30

Table 4 Sensitivity of various reactions to solvent ionizing power (E_T value)

Reaction	Solvent sensitivity parameter, $a^a \times 10^2$
2-Oxyallyl Fe^{II} cation with dimethylaminofulvene	44.1[b]
Cycloaddition of tetracyanoethylene with ethyl isobutenyl ether	27.8[c]
endo [4 + 2]π Cycloadduct of phencyclone and *N*-(ethoxycarbonyl)azepine[d]	6.62[b]
Cycloaddition of **4a** with **2**	3.71
1,3-Dipolar cycloaddition of pyridine *N*-oxide with phenyl isocyanate	0.09[e]

[a] $\log k_2 = aE_T + b$. [b] See ref. 13. [c] See ref. 14. [d] [3,3]-Sigmatropic rearrangement. [e] See ref. 2.



Scheme 3

phenolbetaines, were used as a scale of solvent ionizing power in studying the effect of solvent polarity on the rate of reaction.

Discussion

In order to elucidate the mechanistic features of the reaction, MNDO-PM3 calculations[8a] of **1a**, **b**, **2** and **3** were performed. The PM3 calculations of **1a**, **b** and **2** suggest that the FMO interaction between the HOMO of **1a**, **b** and LUMO of **2** is greater than that between the LUMO of **1a**, **b** and HOMO of **2**, and is responsible for 'normal-type reaction' in Sustmann's classification in cycloaddition.[3a] The regiochemistry prediction based on the 'large–large and small–small rule'[3d] is in fair agreement with the synthetic results.

PM3 calculation of **1b** shows that the coefficient at C6 is larger than that at C2, predicting that the cycloaddition tends to occur at O and C6 (Fig. 2). Furthermore, inspection of steric interference suggests that the cyclization towards C2 is less favourable than the other. However, as mentioned above, cycloaddition occurred predominantly towards the 2-position of **1b**, which is opposite to the prediction. Similar results were observed in the reaction of **1b** with phenylisocyanates, cyclizing towards C2.[2] As the simple FMO treatment did not give a satisfactory prediction, the transition states for model reactions of unsubstituted allene with **1b** were located using SADDLE and TS routines implemented in MOPAC-V6.0.[8] Inspection of the calculated data revealed that the transition state cyclizing toward C2 is 0.27 kcal mol^{-1} * more stable than the other in heat of formation, supporting the experimental results.†

Though the heats of formation of intermediary structure cannot directly embody the activation barrier, Fleming[3d] mentioned that the high energy transition state generally gives high energy product. Therefore, the comparison of the PM3 calculation data for the ground-state structures is considered to provide a clue to the reaction pathway. The calculations on the intermediary structures (**A**, **A'**, **B** and **B'**) and **4a** were started from geometries based on the conventional molecular models and fully optimized. The results were shown in Scheme 4.

The calculated heat of formation of primary adduct (**A**) arising from the *exo*-addition is 7.4 kcal mol^{-1} smaller than that of the primary adduct (**A'**) arising from the *endo*-addition, suggesting that the primary cycloaddition occurred by *exo*-approach. Similar consideration allows us to conclude that **A** exclusively undergoes [1,5]-sigmatropic rearrangement to give **4a** *via* **B**, ruling out the alternative pathway. These results suggest that the reaction proceeds along the solid line in Scheme 4 to give **4a**.

In cycloaddition in which secondary orbital interaction can be expected, *endo*-cycloadduct is predominantly formed, because the *endo*-transition state is more stabilized than the *exo*-transition state.[3] However, inspection of the FMO and geometries of **1a** and **2** indicates that secondary orbital interactions between the N and phenylsulfonyl groups can be neglected in this case. This suggests that steric factors operate in the transition state to form the *exo*-primary adduct (**A**). The synthetic results are in fair agreement with the FMO consideration. Bond order at N–O of **A** is 0.902 (1.538 Å),

* 1 cal = 4.184 J.

† Calculated heat of formation for cyclization toward C2 was 104.34 kcal mol^{-1} and that for C6 was 104.61 kcal mol^{-1}. Detailed results will be published in separate paper.

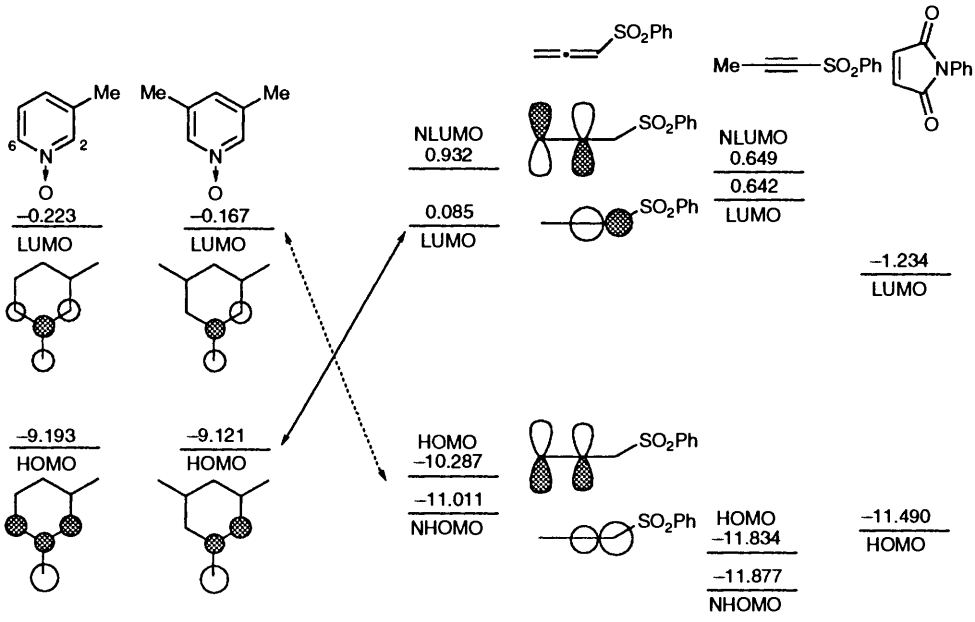
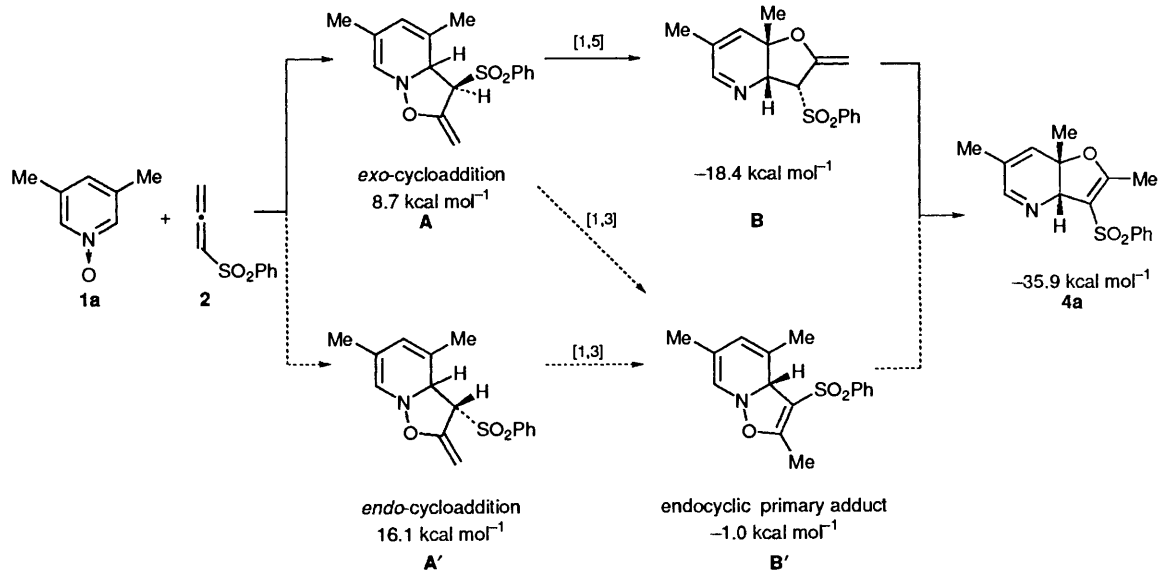


Fig. 2 FMO energy levels and coefficients by PM3



Scheme 4

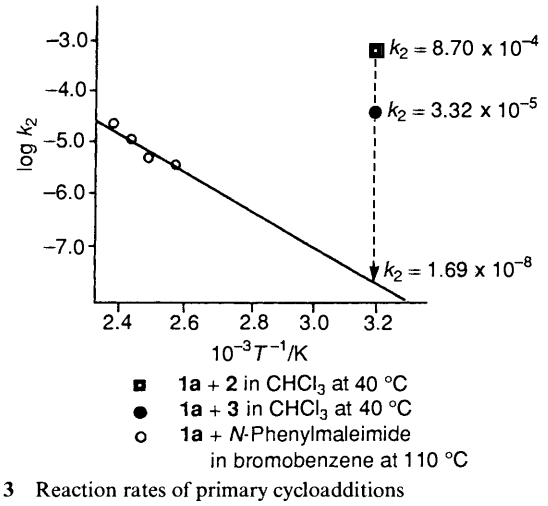


Fig. 3 Reaction rates of primary cycloadditions

suggesting that [1,5]-sigmatropic rearrangement of **A** readily proceeds to give **B**.

Previously, we reported a kinetic study[2] of the reaction of **1a** with *N*-phenylmaleimide, which proceeds only over 100 °C. In order to compare the relative rate, the rate constant at 40 °C was estimated by extrapolation of the Arrehenius plot. As can be seen in Fig. 3, the reaction of **1a** with **2** proceeds about 50,000 times faster than the reaction of **1a** with *N*-phenylmaleimide.

The previous study of this series revealed that the reactivity of pyridine *N*-oxides toward olefins is considerably lower than the case of aliphatic *N*-oxides because of the high degree of aromaticity.[2] The remarkably enhanced cycloaddition reactivity of electron-deficient allenes toward pyridine *N*-oxides may arise from an additional stabilizing overlap of the p_y orbitals of both addends (Fig. 4).[4]

On the formation mechanism of **5a** from **4a** and **2**, three reaction pathways are formally possible: (1) stepwise, ionic cycloaddition *via* ylide formation; (2) [2 + 2] cycloaddition of terminal double bond of **2** with C=N; (3) sequential pericyclic reaction [hetero-Diels–Alder (DA) reaction → aza-Cope rearrangement].

If the formation of **5a** proceeds through path 1, the rate of this step is affected by solvent polarity. The rate data indicate that

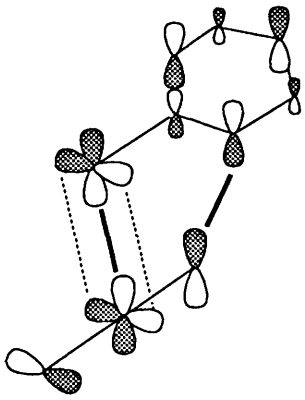


Fig. 4 Secondary interactions in primary cycloaddition

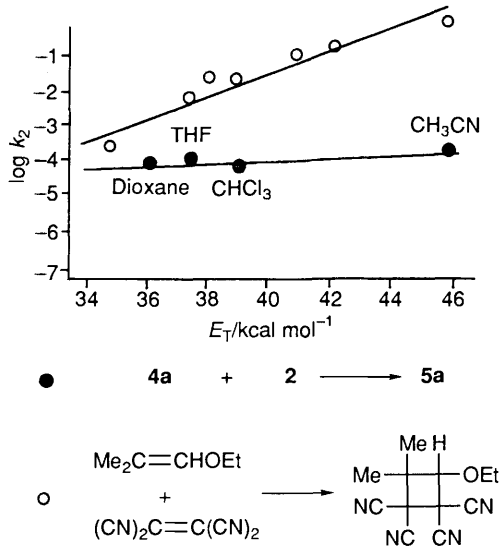


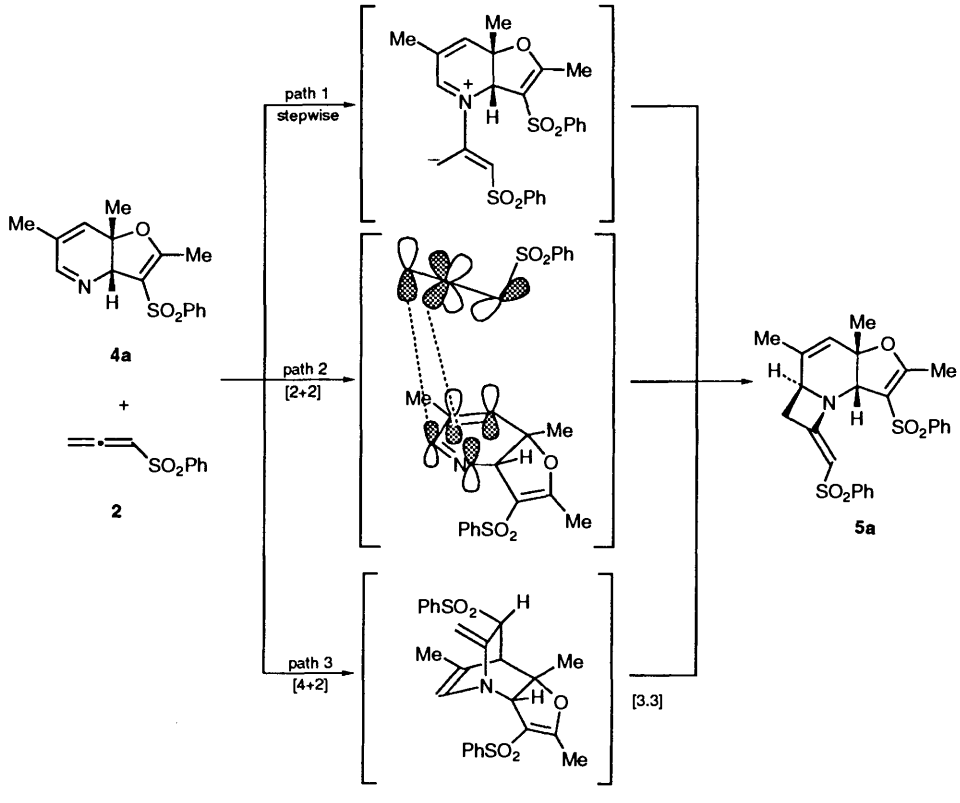
Fig. 5 Solvent effect on the reaction between **4a** and **2**

the attack of the first molecule of **2** on **1a** in $CHCl_3$ is 12.6 times faster than that of the second molecule of **2** on **4a**. As illustrated in Fig. 5, plots of log k_2 *vs.* E_T values show a linear relationship. The magnitude of the slope has been used as a measure of the sensitivity of a reaction to the ionizing power of the medium. The value is only 3.71×10^{-2}, the sensitivity to ionizing power being very low as compared with those of stepwise reactions (Table 4). The small response to the solvent polarity rules out path 1 involving any significant degree of charge separation such as a zwitterionic intermediate.

Inspection of the PM3 calculation data of **4a** implies that the attack of **2** toward the C=N moiety is not plausible because the C=N coefficients are relatively small (Fig. 6). Additionally, Gompper *et al.*[9] reported that **2** reacts with aminoisobutenes to give methylene cyclobutanes, which are formed by reaction with the 1,2-double bond of **2**. As far as we know, there is no report concerning cycloaddition of **2** at 2,3-double bond. More recently, Bernardi *et al.*[10] reported that the [2 + 2] cycloaddition of ketene with ethene involves zwitterionic character. These facts rule out the path 2.

Path 3 is considered to be most plausible at present. The PM3 results on path 3 suggest that both FMO interaction energies are almost identical ('neutral-type reaction').[3a] Simple FMO consideration based on the FMOs gave opposite predictions on regiochemistry, whereas the perturbation calculation[3e] on both FMO interactions between **4a** and **2** can explicate the experimental result.

Thus, formed hetero-DA adduct would give the final product (**5a**) through aza-Cope rearrangement. The orbital interactions in aza-Cope rearrangement of the [4 + 2] adduct can be interpreted in terms of the three-system interaction theory.[3c] As shown in Fig. 7, the severing bond (1–1′, LUMO) is considered to be significantly weakened by phenylsulfonyl group, which is favourable to the rearrangement. Steric effects between phenylsulfonyl group and methyl group might also operate in this step.



Scheme 5

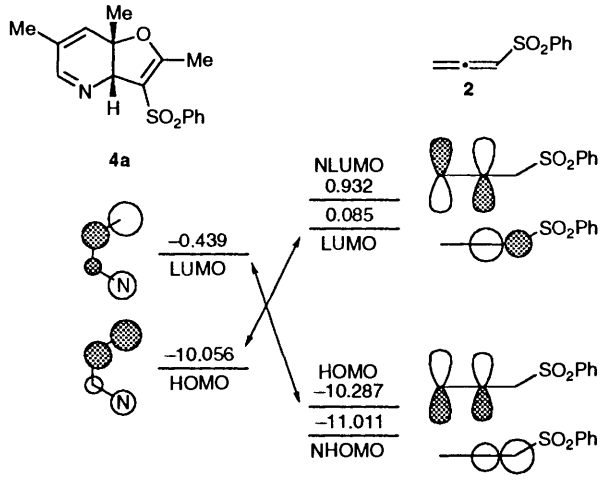


Fig. 6 FMO Interaction between **4a** and **2**

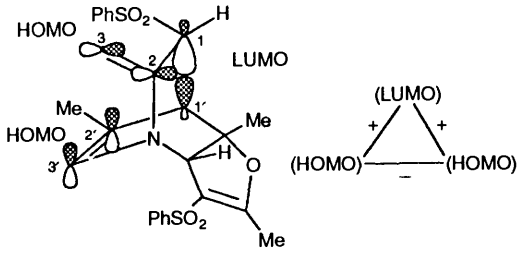


Fig. 7 Three system interaction in hetero-DA adduct

Path 3 can well explain the stereochemistry of the azetidine structure of **5a**.

To clarify the reaction mechanism, high level molecular mechanics (MM) calculations involving electronic interactions are necessary.

Experimental

All melting points are uncorrected. ^{1}H NMR spectra were taken with Hitachi R-600 (60 MHz) and JEOL GX-400 (400 MHz) spectrometers for *ca.* 10% (w/v) solution with tetramethylsilane (TMS) as an internal standard; chemical shifts are expressed in δ values and coupling constants (J) are expressed in Hz. IR spectra were recorded on a Hitachi 270-30 infrared spectrophotometer equipped with a double-blade grating. MS were taken with a JEOL JMS-DX303HF double-focussing spectrometer operating at an ionization potential of 75 eV. Molecular orbital calculations were performed on a FACOM M-780 computer at the Kumamoto University Information Processing Centre and on a Fujitsu S4/2 engineering work station (EWS). Graphic analysis of the MO calculation and X-ray data were performed on a Fujitsu S4/2 EWS and a Fujitsu FMR-60HD personal computer. All structure-solving programs were from the Kumamoto University Information Processing Centre with the Universal Crystallographic Computation Program System (UNICS III).[11]

Materials.—3,5-Dimethylpyridine *N*-oxide (**1a**) and 3-methylpyridine *N*-oxide (**1b**) were prepared according to the established methods.[1] Phenylsulfonylpropadiene (**2**), 1-phenylsulfonylpropyne (**3**) and 3-phenylsulfonylpropyne (**3'**) were prepared according to the established method by Stirling[12a] and Sato[12b] from thiophenol and propargyl bromide. Allene **2** was prepared *in situ* from **3'** and triethylamine.[12a]

Cycloaddition of **1a** *with* **2**.—A solution of **3'** (0.8 g, 4.4 mmol) and triethylamine (1.6 cm^3) in 20 cm^3 of $CHCl_3$ was stirred for 15 min at room temp. After the consumption of **3'** (observed by TLC), **1a** (0.27 g, 2.2 mmol) was added and the reaction mixture stirred for a further 11 h. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel using C_6H_6–AcOEt (5:1) as an eluent to give **4a** (0.10 g, 14.9%, m.p. 117–120 °C, colourless prisms from C_6H_6–AcOEt) and **5a** (0.16 g, 15.0%, m.p. 227–229 °C, colourless prisms from C_6H_6–AcOEt).

4a (Found: C, 63.59; H, 5.73; N, 4.65. $C_{16}H_{17}NO_3S$ requires C, 63.34; H, 5.65; N, 4.62%); ν_{max}(KBr)/cm^{-1} 1154 (SO_2), 1304 (SO_2) and 1630 (C=C); δ_H 1.39 (3 H, s, 7a-Me), 1.85 (3 H, d, J 1.47, 6-Me), 2.18 (3 H, d, J 1.46, C2-Me), 4.92 (1 H, d, J 1.46, 3a-H), 5.78 (1 H, dd, J 1.46, 1.47, 7-H), 7.50 (1 H, d, J 1.46, 5-H), 7.46–7.60 (3 H, m, aromatic C-H) and 8.00–8.10 (2 H, m, aromatic C-H); δ_C 13.9 (q), 19.2 (q), 27.7 (q), 69.0 (d), 80.9 (s), 112.0 (s), 125.8 (d), 127.4 (d), 128.6 (d), 128.8 (s), 132.5 (d), 143.5 (s), 155.3 (d) and 167.0 (s); m/z 303 (M^+), 288 (M^+ – Me) and 162 (M^+ – $PhSO_2$).

5a (Found: C, 61.83; H, 5.06; N, 2.90; $C_{25}H_{25}NO_5S_2$ requires C, 62.08; H, 5.22; N, 2.90%); ν_{max}(KBr)/cm^{-1} 1136 (SO_2), 1300 (SO_2) and 1626 (C=C); δ_H 1.46 (3 H, s, 8a-Me), 1.61 (3 H, d, J 1.47, 7-Me), 2.25 (3 H, d, J 1.46, 2-Me), 2.91 (1 H, ddd, J 15.75, 2.93, 1.46, 6-H), 2.98 (1 H, ddd, J 15.75, 5.13, 1.47, 6-H), 3.11 (1 H, m, 6a-H), 4.49 (1 H, d, J 1.46, 3a-H), 5.28 (1 H, m, C-5=CH), 5.36 (1 H, dd, J 1.47, 1.46, 8-H) and 7.26–7.90 (10 H, m, aromatic C-H); δ_C 14.2 (q), 18.0 (q), 27.8 (q), 34.3 (t), 55.0 (d), 63.2 (d), 82.2 (s), 92.5 (d), 106.5 (s), 122.9 (d), 126.0 (d), 127.1 (d), 128.7 (d), 129.0 (d), 132.1 (d), 132.9 (d), 138.4 (s), 142.1 (s), 145.2 (s), 163.8 (s) and 167.4 (s); m/z 483 (M^+) and 342 (M^+ – $PhSO_2$).

Cycloaddition of **1a** *with* **3**.—A solution of **3** (0.75 g, 4.17 mmol) and **1a** (0.51 g, 4.17 mmol) in 8 cm^3 of $CHCl_3$ was stirred for 11 h at room temp. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel using C_6H_6–AcOEt (5:1) as eluent to give **4a** (0.52 g, 40.8%, m.p. 117–120 °C, colourless prisms from C_6H_6–AcOEt).

Cycloaddition of **4a** *with* **2**.—A solution of **3'** (0.12 g, 0.67 mmol) and triethylamine (0.25 cm^3) in 5 cm^3 of $CHCl_3$ was stirred for 15 min at room temp. After the consumption of **3'** (observed by TLC), **4a** (0.20 g, 0.67 mmol) was added and stirring continued for a further 48 h. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel using C_6H_6–AcOEt (4:1) as an eluent to give **5a** (0.12 g, 37.5%, m.p. 227–229 °C, colourless prisms from C_6H_6–AcOEt).

X-Ray Crystallography.—Crystal data. $C_{25}H_{25}NO_5S_2$ (**5a**) M = 483.6. Triclinic, a = 12.683(10), b = 11.507(10), c = 8.888(7) Å, α = 107.97(6), β = 76.70(6), γ = 88.39(7)°, V = 1194(2) Å^3, D_m = 1.345 g cm^{-3} (aq. KI), D_c = 1.332 g cm^{-3}, Z = 2, Mo-Kα radiation (40 kV–20 mA), λ = 0.7107 Å. The cell constants were determined by a least-squares procedure using the value of the Bragg angles of 17 reflections measured on a Rigaku AFC-6 four-circle autodiffractometer equipped with a graphite monochromated Mo-Kα source. The apparatus was interfaced to a PANAFACOM U-1200 minicomputer. The space group $P\bar{1}$ (No. 2) was selected from the number of molecules per unit cell (Z = 2) and was later confirmed in the course of the structure refinement. Intensity data were collected in the range of $2\theta < 55°$ using the ω–2θ scan technique. A variable scan rate was adopted. Two reflections were monitored after measurement of every 100 reflections. Of the 2378 independent reflections, 2084 were treated as observed ($F_0 > 3\sigma F$). The intensities were corrected for Lorentz and polarization effects, but no correction was applied for absorption.

Structure solution and refinement. An overall temperature factor obtained from a Wilson plot did not give the correct solution. Therefore, the value of 5.0 Å^2 was used to calculate the normalized structure factor. The structure was solved by the direct method using the MULTAN78 series of programs.[6] An *E* map calculated with 390 signed *E*'s ($E > 1.2$), which give a combined figure of merit of 2.255, revealed the positions of all the non-hydrogen atoms. Refinements were carried out by the block-diagonal least-squares method. Six cycles of isotropic refinement and 6 cycles of anisotropic refinement led to an *R* index of 0.094. All the hydrogens were located at calculated positions. After adding the hydrogens but keeping their thermal parameters fixed [$B(H) = B(C) + 1.0$], we obtained a final *R* of 0.038. Thermal parameters of the hydrogens attached to the methyl were fixed for their anisotropic vibration. In final refinements, the following weights were used for the observed reflections: $w = 1.0$ for $F_o < 20.0$, $w = 400/F_o^2$ for $F_o > 20.0$. Atomic positional parameters, anisotropic temperature factors, and bond lengths and angles have been deposited with the Cambridge Crystallographic Data Centre.†

Cycloaddition of **1b** *with* **2**.—A solution of **3'** (4.0 g, 22 mmol) and triethylamine (4.0 cm^3) in 15 cm^3 of $CHCl_3$ was stirred for 15 min at room temp. After the consumption of **3'** (observed by TLC), **1b** (1.2 g, 11 mmol) was added and the reaction mixture stirred for a further 19 h. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel using C_6H_6–AcOEt (5:1) as an eluent to give **4b** (0.26 g, 11.4%, colourless oil), **5b** (0.76 g, 15.0%, m.p. 225–227 °C, colourless prisms from C_6H_6–AcOEt) and trace amount of crude **4'b**.

4b (Found: M^+, 289.0782. $C_{16}H_{17}NO_3S$ requires *M*, 289.0773); ν_{max}(neat)/cm^{-1}; 1156 (SO_2), 1308 (SO_2) and 1624 (C=C); δ_H 1.42 (3 H, s, 7a-Me), 2.20 (3 H, d, *J* 1.46, 2-Me), 5.03 (1 H, d, *J* 1.46, 3a-H), 5.94 (1 H, dd, *J* 10.27, 3.67, 6-H), 6.10 (1 H, d, *J* 10.27, 7-H), 7.71 (1 H, d, *J* 3.67, 5-H), 7.47–7.56 (3 H, m, aromatic C-H) and 8.02–8.04 (2 H, m, aromatic C-H); δ_C 13.9 (q), 27.7 (q), 69.3 (d), 79.9 (s), 120.6 (d), 129.0 (s), 132.5 (d), 151.5 (d) and 166.8 (s); *m/z* 289 (M^+) and 148 ($M^+ - PhSO_2$).

5b (Found: C, 61.50; H, 4.99; N, 2.98. $C_{24}H_{23}NO_5S_2$ requires C, 61.39; H, 4.94; N, 2.98%); ν_{max}(KBr)/cm^{-1}; 1137 (SO_2), 1302 (SO_2) and 1629 (C=C); δ_H 1.48 (3 H, s, 8a-Me), 2.26 (3 H, d, *J* 1.10, 2-Me), 2.89 (1 H, ddd, *J* 15.8, 3.48, 1.84, 6-H), 3.00 (1 H, ddd, *J* 15.8, 4.40, 1.10, 6-H), 3.19 (1 H, m, 6a-H), 4.57 (1 H, d, *J* 1.10, 3a-H), 5.28 (1 H, br s, 5-H), 5.65 (1 H, dd, *J* 9.53, 1.10, 8-H), 5.98 (1 H, dd, *J* 9.53, 1.84, 7-H), 7.30–7.36 (4 H, m, aromatic CH), 7.51–7.60 (4 H, m, aromatic C-H), 7.73–7.75 (2 H, m, aromatic C-H) and 7.86–7.88 (2 H, m, aromatic C-H); δ_C 14.2 (q), 27.3 (q), 35.1 (t), 52.1 (d), 63.6 (d), 80.1 (s), 92.9 (d), 106.6 (s), 127.2 (d), 130.3 (d), 163.6 (s) and 167.4 (s); *m/z* 469 (M^+) and 328 ($M^+ - PhSO_2$).

4'b ν_{max}(neat)/cm^{-1}; 1156 (SO_2), 1308 (SO_2) and 1624 (C=C); δ_H 1.89 (3 H, br s, 6-Me), 2.20 (3 H, d, *J* 1.10, 2-Me), 4.97 (1 H, dd, *J* 1.10, 8.60, 3a-H), 5.21 (1 H, dd, *J* 8.60, 3.2, 7a-H), 6.02 (1 H, m, 7-H), 7.63 (1 H, d, *J* 1.46, 5-H), 7.46–7.60 (3 H, m, aromatic C-H) and 8.00–8.10 (2 H, m, aromatic C-H).

Kinetic Study on the Reaction of **1a** *with* **2**.—A solution of **1a** (0.42 mol dm^{-3}) in $CHCl_3$ and a solution of **3'** (0.84 mmol) plus triethylamine (0.24 cm^3) in $CHCl_3$ were thermostatted at 40 ± 0.05 °C in a ground-glass stoppered tube. The former solution (1 cm^3) was pipetted into the latter solution, and the resultant solution was exactly diluted to 5 cm^3 with $CHCl_3$. The rate was followed by measuring the decrease of **1a** by HPLC. Methyl *p*-nitrobenzoate was used as an internal standard.

Kinetic Study on the Reaction of **1a** *with* **3**.—A solution of **1a** (0.42 mol dm^{-3}) in $CHCl_3$ and a solution of **3** (0.84 mmol) in $CHCl_3$ were thermostatted at 40 ± 0.05 °C in ground-glass stoppered tube and the reaction monitored in an identical procedure to that above.

Solvent Effect on the Reaction of **4a** *with* **2**.—A solution of **4a** (0.42 mol dm^{-3}) in a given solvent and a solution of **3'** (0.42 mmol) plus triethylamine (0.24 cm^3) in the solvent were thermostatted at 40 ± 0.05 °C in ground-glass stoppered tube. The former solution (1 cm^3) was pipetted to the latter solution, and the resultant solution was exactly diluted to 5 cm^3 with the given solvent. The rate was followed by measuring the decrease of **4a** by HPLC. Methyl *p*-nitrobenzoate was used as an internal standard.

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