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Reaction of Aromatic *N*-Oxides with Dipolarophiles. XI.[1a] 1,3-Dipolar Cycloaddition Reaction of Pyridine *N*-Oxides with Tosyl Isocyanate and One-Pot Synthesis of 2-Oxooxazolo-[4,5-*b*]pyridine Derivatives[1b]

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The cycloaddition reactivity of tosyl isocyanate toward pyridine *N*-oxides was calculated by the CNDO/2 method using a perturbation equation, and the results indicated that the initial stage of the reaction might be controlled by the coulombic attraction. The 1,3-dipolar cycloaddition reaction of tosyl isocyanate with two equivalents of 3,5-dibromopyridine *N*-oxide in refluxing benzene gave 6-bromo-2-oxooxazolo[4,5-*b*]pyridine, while the use of one equivalent of 3,5-dichloropyridine *N*-oxide gave 6,7a-dichloro-2-oxo-3-tosyl-3a,7a-dihydrooxazolo[4,5-*b*]pyridine, formed from the 1,5-sigmatropic rearrangement of the corresponding primary cycloadduct. When the reaction was carried out in the presence of triethylamine in benzene, 6-halogeno-2-oxo-3-tosyloxazolo[4,5-*b*]pyridine was isolated.

The observed activation parameters, as well as the small solvent effects, may be interpreted in terms of a concerted pathway.

The reaction should be very valuable as a one-pot synthesis of 2-oxooxazolo[4,5-*b*]pyridines, which are pyridine analogues of 5-chloro-2-benzoxazolinone.

Keywords——3,5-dihalogenopyridine *N*-oxide; tosyl isocyanate; 6-halogeno-2-oxooxazolo-[4,5-*b*]pyridine; kinetics; frontier molecular orbital; solvent effect; 1,3-dipolar cycloaddition; detosylation

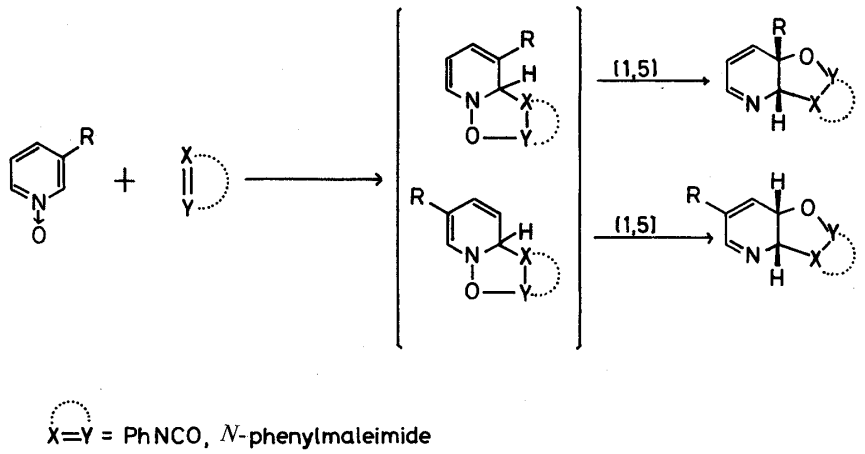
Interest in the chemistry of 1,3-dipolar cycloaddition of aromatic *N*-oxides has led to a continuing search for new reactive dipolarophiles that can be used in the synthesis of condensed heterocycles. Previously, we have studied pericyclic reactions of pyridine *N*-oxides with phenyl isocyanates and maleimides[2] and we recently found that the aromaticity of pyridine *N*-oxides (I), or the ability to form charge-transfer complexes, plays a leading role in determining their cycloaddition reactivities toward dipolarophiles.[1a,2b,c]

On the basis of the previous studies, we concluded that the ideal dipolarophile for cycloaddition with aromatic *N*-oxides would have a highly polarized structure with a low-lying lowest unoccupied molecular orbital (LUMO) energy level. The preliminary CNDO/2[3] calculation revealed that toluenesulfonyl (tosyl) isocyanate (IIa) was suitable for our purpose.

We report here on some cycloadditions of tosyl isocyanate to pyridine *N*-oxides (I). The results are discussed in terms of frontier molecular orbital (FMO) theory,[4] kinetics, and spectral data.

Results and Discussion

The CNDO/2 orbital energies and coefficients for pyridine *N*-oxide (Iz), 3,5-dichloropy-



X=Y = PhNCO, *N*-phenylmaleimide

Fig. 1. Schematic Representation of the Pericyclic Reaction of Pyridine *N*-Oxides with Dipolarophiles

TABLE I. FMO Energy Levels of 3,5-Dichloropyridine *N*-Oxide (Ia), Tosyl Isocyanate (IIa), Pyridine *N*-Oxide (Iz), Phenyl Isocyanate (IIz) and Methanesulfonyl Isocyanate (IIb) Calculated by the CNDO/2 Method

	Ia	IIa	Iz	IIz	IIb
NLUMO[a]		2.65[d]			2.64
LUMO[a]	1.32[b]	1.58[e]	2.25	2.88	2.20
HOMO[a]	−11.21[c]	−13.49[f]	−10.55	−11.90	−13.74

a) In eV. *b*) Coefficients: O, −0.329; C_2, −0.270. *c*) Coefficients: O, 0.737; C_2, −0.348. *d*) Coefficients: N, 0.042; C, −0.462. *e*) Coefficients: N, 0.008; C, 0.155. *f*) Coefficients: N, 0.556; C, −0.099.

ridine *N*-oxide (Ia), phenyl isocyanate (IIz), tosyl isocyanate (IIa) and methanesulfonyl isocyanate (IIb) are shown in Table I.

As can be seen in Table I, the FMO energies of tosyl isocyanate (IIa) are appreciably lower than those of phenyl isocyanate (IIz) and methanesulfonyl isocyanate (IIb). The lowest unoccupied molecular orbital (LUMO) of IIa is not π-LUMO but is an orbital mainly localized on the sulfur and oxygen atoms. The LUMO and second LUMO (NLUMO) of tosyl isocyanate (IIa) are lowered markedly by the introduction of the SO_2 group, indicating that the reaction behavior of tosyl isocyanate (IIa) toward pyridine *N*-oxides (I) can be explained in terms of a "normal"-type reaction in Sustmann's classification[5] for 1,3-dipolar cycloadditions, wherein the dominant interaction is the one between the highest occupied molecular orbital (HOMO) of I and the LUMO of the tosyl isocyanate (IIa).

The perturbation calculations[6] based on the CNDO/2 orbital energies and coefficients indicate that the coulombic energy term is operative at the early stages of the reaction, as shown in Table II.

The cycloadditions were carried out under various reaction conditions. The results are summarized in Table III.

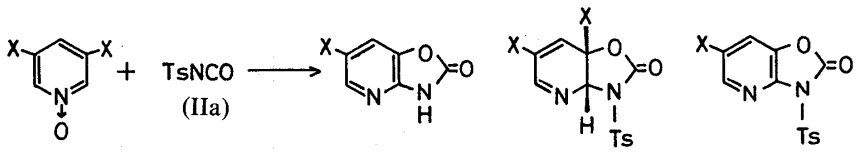
Tosyl isocyanate (IIa) (1 eq) and 3,5-dibromopyridine *N*-oxide (Ib) (2 eq) reacted to give 6-bromo-2-oxooxazolo[4,5-*b*]pyridine (IIIb) in 57% yield (exp. No. 2). The use of excess IIa caused a decrease of the yield of IIIb (exp. No. 1). This trend was not affected by change of the solvent polarity or the reaction temperature. The corresponding 2-aminopyridine derivative (VI) formed by the decarboxylation of the 2,3-dihydropyridine-type compound (IV) could not

TABLE II. Calculated Reactivity of 3,5-Dichloropyridine *N*-Oxide (Ia) toward Phenyl Isocyanate (IIz) and Tosyl Isocyanate (IIa) Based on the Perturbation Equation Derived by Klopman and Salem[a]

Isocyanate	Distance (Å)	Energy changes (eV)		
		E_2[b]	E_3[c]	ΔE[d]
Ph-N=C=O (IIz)	1.75	−0.6149	−0.6780	−1.2929
	3.00	−0.3587	−0.0080	−0.3667
Tol-SO_2–N=C=O (IIa)	1.75	−0.7097	−0.5924	−1.3021
	3.00	−0.4140	−0.0070	−0.4210

a) See ref. 19. *b*) The coulombic repulsion and attraction term (the 2nd term). *c*) The FMO interactions in the 3rd term. *d*) $\Delta E = E_2 + E_3$.

TABLE III. Reaction of 3,5-Dihalogenopyridine *N*-Oxides (Ia, b) with Tosyl Isocyanate (IIa)



Ia, b IIIa, b IVa, b Va, b

Exp. No.	X	Molar ratio		Solvent (Reflux)	Duration (h)	Product (%)		
		I	IIa			III	IV	V
1	Br	1	2	Benzene	3	18[a]		
2	Br	2	1	Benzene	3	57[b]		
3	Cl	1	2	Toluene	24	14[a]		
4	Cl	2	1	Benzene	3		10[b]	
5	Br	1	2	Benzene (Et_3N)	3.5			45[a]
6	Cl	1	2	Benzene (Et_3N)	3.5			45[a]

a) Calcd on the basis of I. *b*) Calcd on the basis of II.

be detected in any run.

The reaction of IIa (2 eq) with 3,5-dichloropyridine *N*-oxide (Ia) (1 eq) in benzene gave the corresponding 2-oxooxazolo[4,5-*b*]pyridine derivative (IIIa) in 6—14% yield (exp. No. 3).

On the other hand, the use of two equivalents of Ia in boiling benzene gave the 2,3-dihydropyridine derivative (IVa) derived from 1,5-sigmatropic rearrangement of the primary cycloadduct (exp. No. 4). This result is in sharp contrast to the previous observation[2c]; in the 1,3-dipolar reaction of halogenopyridine *N*-oxides with phenyl isocyanate in dimethylformamide at 110 °C (Chart 1), we could not isolate the 2,3-dihydropyridine-type compound because the pyrolytic *cis*-elimination[7] of hydrogen halide from 2,3-dihydropyridine-type compounds appeared to be very facile at the reaction temperature used (110 °C), leading to restoration of the aromaticity of the pyridine nucleus. The present results indicate that the 2,3-dihydropyridine-type compound (IVa) is still stable in boiling benzene.

The structure of the 2,3-dihydropyridine-type compound (IVa) was determined by comparison of its spectral data with those of the product obtained from the reaction of 3,5-dimethylpyridine *N*-oxide (Ic) with phenyl isocyanate. The infrared (IR) spectrum showed a characteristic band at 1800 cm^{-1} due to a five-membered ring carbonyl group. In the nuclear

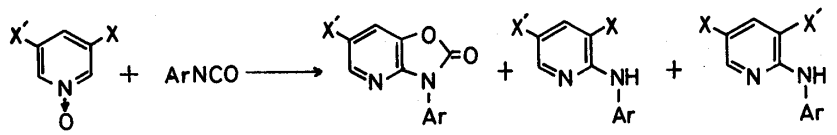


Chart 1

magnetic resonance (NMR) spectrum, the C_{3a} methine proton appeared at 6.15 ppm and the olefinic protons of the dihydropyridine moiety exhibited high field shifts due to loss of the aromaticity of the pyridine nucleus.

In the presence of triethylamine, the reaction of 3,5-dihalogenopyridine *N*-oxide (Ia, b) with IIa in boiling benzene gave the tosylated 2-oxooxazolo[4,5-*b*]pyridine derivative (Va, b) (exp. Nos. 6 and 7). This result indicates that the tosyl group of V was cleaved by the action of hydrogen bromide liberated from the 2,3-dihydropyridine-type compounds (IVa, b) to give III.

Pyridine *N*-oxide and 3-methylpyridine *N*-oxide showed low cycloaddition reactivities toward tosyl isocyanate (IIa), in contrast to the case of halogenopyridine *N*-oxides (Ia, b). The reaction of 3,5-dimethylpyridine *N*-oxide (Ic) (2 eq) with IIa (1 eq) in boiling benzene gave the 2,3-dihydropyridine-type compound (IVc) in 26% yield, whereas treatment of Ic (1 eq) with IIa (2 eq) in refluxing toluene produced the decarboxylation products, *i.e.*, 2-aminopyridine derivatives (VIc and VIIc), in a total yield of 49%. 3-Methyl-2-phenylpyridine *N*-oxide (Id) was much more reactive than other pyridine *N*-oxides examined, and reacted with IIa (2 eq) even at room temperature in chloroform, affording the 2,3-dihydropyridine-type compound (IVd) in 65% yield.

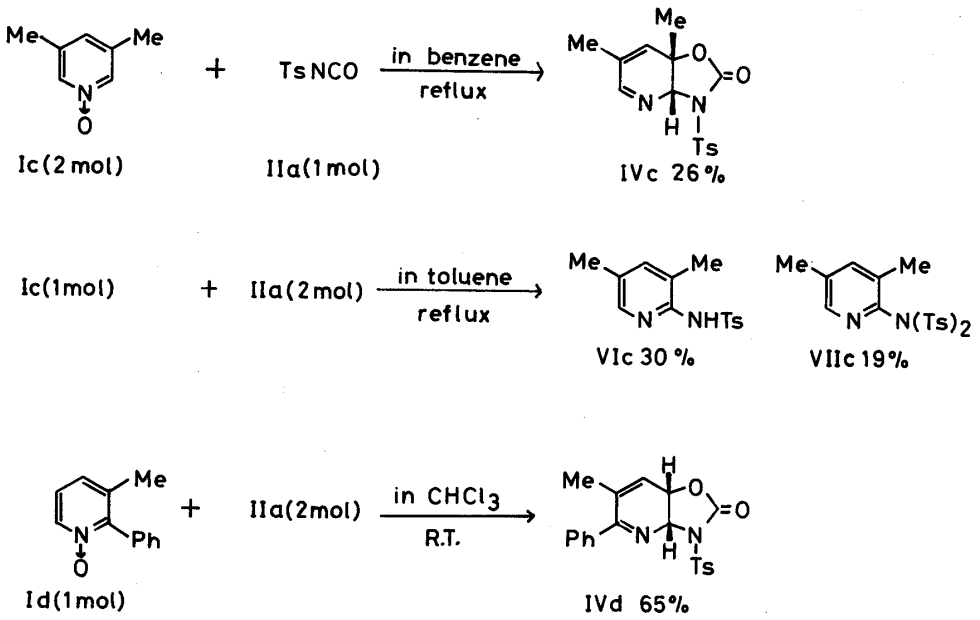


Chart 2

In general, cycloadditions of aromatic *N*-oxide require relatively severe reaction conditions because of the high degree of the ground-state stabilization arising from the aromaticity. However, contrary to expectation, the reaction of Ib with IIa proceeds in refluxing benzene. The second-order rate constants of the reaction of Ib with IIa in several solvents were obtained by following the disappearance of the peak of 3,5-dibromopyridine *N*-oxide (Ib) by high-pressure liquid chromatography (HPLC). The second-order rate constants

TABLE IV. Second-Order Rate Constants for 1,3-Dipolar Cycloaddition of Ib and IIa

Solvent	E_T (kcal·mol^{-1})	Temp (°C)	$k_2 \times 10^5$ (mol^{-1}·s^{-1})[a]
Sulfolane	44.0	90.0	10.2
Nitrobenzene	42.0	90.0	2.95
Anisole	37.2	90.0	3.32
Toluene	33.9	80.0	1.29[b]
		85.0	1.63[b]
		90.0	2.32[b]
		95.0	3.08[b]

a) Average error, *ca.* ±5%. *b*) $E_a = 15.1$ kcal·mol^{-1}, $\Delta S = -43$ e.u.

(k_2) are summarized in Table IV. From the data, the activation parameters were calculated, and are recorded in Table IV. The activation energy for the reaction of Ia with IIa was calculated to be 15 kcal/mol, lying within the range reported for typical 1,3-dipolar cycloadditions, while the entropy of activation is −43 e.u., considerably lower than that for the average 1,3-dipolar reaction.[8]

In the light of successful applications[9] of the E_T values of Dimroth as a scale of solvent ionizing power for evaluation of the degree of charge-separation in the transition state, we studied the effect of solvent on the rate of the reaction and calculated a solvent-sensitivity parameter. Plots of $\log k_2$ against E_T values show a roughly linear relationship. The magnitude of the slope ($a \times 10^2$) is 4.792, the sensitivity of a reaction being rather high as compared with those of typical concerted reactions; the slope for 1,3-dipolar cycloaddition of phenyl isocyanate with pyridine *N*-oxide is 0.092.[2b] The observed response to variation of the polarity of the solvent may indicate that the reaction proceeds through an intermediate involving some degree of charge separation.

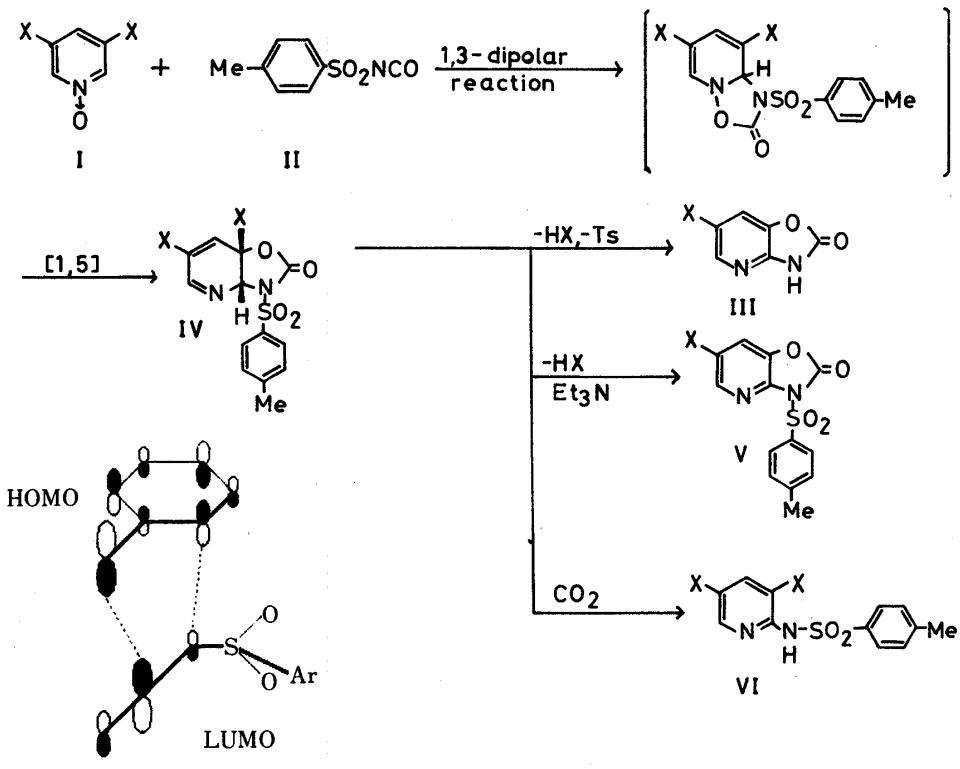


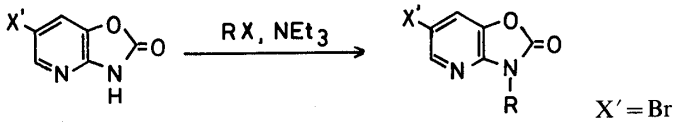
Chart 3

In connection with the previous study on the role of charge-transfer complexes in cycloaddition,[1a] we have spectroscopically investigated the cycloaddition of 3,5-dibromopyridine *N*-oxide (Ib). However, we could not observe any spectroscopic evidence of charge-transfer complexation.

The results hitherto mentioned are fully in accordance with a concerted reaction pathway. The reaction mechanism is depicted in Chart 3.

Finally, from a synthetic standpoint, the reaction provides a basis for a one-pot synthesis of 2-oxooxazolo[4,5-*b*]pyridine derivatives, pyridine analogues of Chlorzoxazone, a centrally acting muscle relaxant.[10] The products were easily converted into *N*-alkyl, *N*-arylsulfonyl or *N*-acyl derivatives (Chart 4). In the reactions of 2-oxooxazolo[4,5-*b*]pyridines with electrophiles, three reaction sites are possible. However, experimental results indicate that electrophiles were exclusively introduced at the 3-position (N_3), in harmony with the deduction based on the HOMO coefficients[11] of the MINDO/3[12] optimized structure of the unsubstituted molecule.

Studies on the structure and activity relationship are in progress.



X′ = Br

RX = $PhCH_2Cl$, PhCOCl, MeOCOCl, EtOCOCl, MeI, TsCl *etc.*

Chart 4

Experimental

All melting points are uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were taken with Hitachi R-600 and JEOL JNM-C-60H spectrometers in *ca.* 5% (w/v) solution with tetramethylsilane as an internal standard; chemical shifts are expressed in δ values. IR spectra were recorded on a JASCO DS-301 infrared spectrophotometer equipped with a grating. Mass spectra (MS) were taken with a JEOL JMS-01SG double-focusing spectrometer operating at an ionization potential of 75 eV. Ultraviolet (UV) spectra were determined with a JASCO UVIDEC-220B digital spectrophotometer.

All the calculations were performed on the FACOM M-382 computer at the computer center of Kyushu University.

Preparation of Materials——The starting materials, 3,5-dibromopyridine *N*-oxide (Ib),[13] 3,5-dichloropyridine *N*-oxide (Ia),[14] 3,5-dimethylpyridine *N*-oxide (Ic),[15] and 3-methyl-2-phenylpyridine *N*-oxide (Id),[16] were prepared according to the previously established methods. Tosyl isocyanate (IIa) was obtained from a commercial supplier and used without further purification.

Reaction of 3,5-Dibromopyridine *N*-Oxide (Ib) with Tosyl Isocyanate (IIa) (General Procedure)——Compound IIa (0.01 mol) was added slowly to a solution of Ib (0.02 mol) in 9 ml of dry benzene at room temperature and the mixture was refluxed for 3 h. When the reaction was over, the solvent was evaporated off under reduced pressure, and 20 ml of acetone–benzene was added to the residue. The mixture was allowed to stand overnight in a refrigerator. The resulting precipitates were collected by suction and then washed with a small amount of cold benzene. The crystalline mass was recrystallized from acetone–*n*-hexane to give a pure sample of IIIb, mp 227—228 °C as colorless crystals in 57% yield. IR (KBr): 3000 (NH), 1780 (C=O) cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 7.95 (1H, d, J=2 Hz, C_7-H), 8.15 (1H, d, J=2 Hz, C_5-H). MS *m/z*: 214 and 216 (relative intensity 1 : 1) (M^+). *Anal.* Calcd for $C_6H_3BrN_2O_2$: C, 33.52, H, 1.41: N, 13.03. Found: C, 33.81; H, 1.55; N, 12.87.

The effects of the reaction temperature, solvent and molar ratio of both addends on the yield of IIIb are summarized in Table III. All the reactions were conducted under anhydrous conditions because IIa is extremely unstable to moisture. The work-up was essentially the same as in the general method.

Reaction of 3,5-Dichloropyridine *N*-Oxides (Ia) with Tosyl Isocyanates (IIa)——Compound IIa (0.02 mol) was added to a solution of Ia (0.01 mol) in 9 ml of dry toluene, and the mixture was refluxed for 24 h. The solvent was evaporated off under reduced pressure, 20 ml of acetone–benzene was added to the residue, and the mixture was allowed to stand at room temperature to give colorless crystals. Recrystallization from benzene gave an analytical sample of IIIa, mp 183—186 °C, in 14% yield. IR (KBr): 3000 (NH), 1790 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.90

(1H, d, J=2 Hz, C_7-H), 8.13 (1H, d, J=2 Hz, C_5-H). MS m/z: 171 and 173 (relative intensity 3:1) (M^+).

The above filtrate was concentrated under reduced pressure and the residue was purified on a column of silica gel. From the benzene eluent, a small amount of 2-tosylamino-3,5-dichloropyridine was obtained as colorless needles, mp 149.5—151 °C (*n*-hexane–benzene). MS m/z: 317 (M^+). *Anal.* Calcd for $C_{12}H_{10}Cl_2N_2O_2S$: C, 45.44; H, 3.18; N, 8.83. Found: C, 45.30; H, 3.10; N, 8.72.

The use of two equivalents of 3,5-dichloropyridine *N*-oxide (Ia) and lowering the reaction temperature to 80 °C in the above reaction gave the corresponding 2,3-dihydropyridine-type compound (IVa) formed from 1,5-sigmatropic rearrangement of the primary cycloadduct. This compound (IVa) was purified by chromatography on silica gel using chloroform–ethyl acetate (2:1) as an eluent. Recrystallization from benzene gave colorless crystals, mp 156—157 °C in 10% yield. IR (KBr): 1800 (C=O) cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 2.48 (3H, s, Me), 6.15 (1H, d, J=4 Hz, C_{3a}-H), 6.55 (1H, d, J=2 Hz, C_7-H), 7.44 (2H, d, J=8 Hz, $-C_6H_4-$), 7.75 (1H, t, J=2 Hz, C_5-H), 8.03 (2H, d, J=8 Hz, $-C_6H_4-$). MS m/z: 325 ($M^+ - Cl$). *Anal.* Calcd for $C_{13}H_{10}Cl_2N_2O_4S$: C, 43.23; H, 2.79; N, 7.76. Found: C, 43.60; H, 2.67; N, 7.71.

Reaction of 3,5-Dibromopyridine *N*-Oxide (Ib) with Tosyl Isocyanate (IIa) in the Presence of Triethylamine——A solution of Ib (0.01 mol), IIa (0.01 mol) and triethylamine (0.02 mol) in benzene (15 ml) was refluxed for 3 h. After cooling, chloroform was added to the mixture. The solution was washed with water and dried over anhydrous Na_2SO_4. The solvent was evaporated off under reduced pressure. The residue was purified by chromatography on silica gel using chloroform–ethyl acetate (5:1) as an eluent. The crude product was recrystallized from benzene–*n*-hexane to give Vb, colorless needles, mp 196—198 °C, in 45% yield. IR (KBr): 1825 (C=O) cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 2.50 (3H, s, Me), 7.32 (2H,d, J=8 Hz, $-C_6H_4-$), 7.67 (1H, d, J=2 Hz, C_7-H), 7.95 (2H, d, J=8 Hz, $-C_6H_4-$), 8.18 (1H, d, J=2 Hz, C_5-H). MS m/z: 324 and 326 (relative intensity 3:1) (M^+); 323 and 325 (relative intensity 3:1) ($M^+ - 1$). *Anal.* Calcd for $C_{13}H_9BrN_2O_4S$: C, 42.29; H, 2.46; N, 7.59. Found: C, 42.36; H, 2.54; N, 7.65.

Similarly, the reaction of 3,5-dichloropyridine *N*-oxide (Ia) with IIa gave the corresponding product (Va), mp 217.5—219 °C (*n*-hexane–acetone) in 45% yield. IR (KBr): 1820 (C=O) cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 2.50 (3H, s, Me), 7.45 (1H, d, J=8 Hz, $-C_6H_4-$), 7.52 (1H, d, J=2 Hz, C_7-H), 8.18 (1H, d, J=8 Hz, $-C_6H_4-$), 8.30 (1H, d, J=2 Hz, C_5-H).

Reaction of 3,5-Dimethylpyridine *N*-Oxide (Ic) with Tosyl Isocyanate (IIa)——Compound IIa (0.01 mol) was allowed to react with Ic (0.02 mol) for 3.5 h in refluxing benzene (20 ml). After removal of the solvent, the residue was purified by chromatography on silica gel. Recrystallization from ether gave IVc, colorless crystals, mp 152—153 °C, in 26% yield. IR (KBr): 1775 (C=O) cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 1.77 (3H, s, C_6-Me), 2.09 (3H, d, J=1.2 Hz, C_{7a}-Me), 2.59 (3H, s, Me of Ts), 5.84 (1H, d, J=1.2 Hz, C_{3a}-H), 6.00 (1H, d, J=1.2 Hz, C_7-H), 7.56 (2H, d, J=8.4 Hz, $-C_6H_4-$), 7.87 (1H, t, J=2.4 Hz, C_6-H), 8.21 (2H, d, J=8.4 Hz, $-C_6H_4-$). *Anal.* Calcd for $C_{15}H_{16}N_2O_4S$: C, 56.24; H, 5.04; N, 8.74. Found: C, 56.50; H, 5.01; N, 8.41.

Reaction of 3-Methyl-2-phenylpyridine *N*-Oxide (Id) with Tosyl Isocyanate (IIa)——A solution of IIa (0.005 mol) in chloroform (2 ml) was added to Id (0.01 mol) in chloroform (5 ml). The solution was stirred at room temperature for 24 h. After removal of the solvent, the residue was dissolved in ether. The solution was allowed to stand in a refrigerator and filtered to give colorless needles in 65% yield, mp 143—144 °C (acetone–*n*-hexane). IR (KBr): 1780 (C=O) cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 1.90 (3H, s, C_6-Me), 2.33 (3H, s, Me of Ts), 5.04 (1H, t, J=14 Hz, C_{7a}-H), 6.16 (2H, d, J=7 Hz, C_{3a}-H and C_7-H), 7.13 (2H, d, J=8 Hz, $-C_6H_4-$), 7.38 (5H, s, -Ph), 8.00 (2H, d, J=8 Hz, $-C_6H_4-$). *Anal.* Calcd for $C_{20}H_{18}N_2O_4S$: C, 62.81; H, 4.74, N. 7.33. Found: C, 63.03; H, 4.83; N, 7.26.

Reaction Rate——A toluene solution (5 ml) containing Ib (0.5 mmol), IIa (0.5 mmol) and 2,3-dichloro-1,4-naphthoquinone (35 mg) as an internal standard was prepared. The flask was sealed with a ground-glass stopper and immersed in a constant-temperature oil bath controlled to 90.0±0.05 °C. At appropriate intervals, samples were withdrawn and quenched in *ca.* 1 ml of ether saturated with water. The rate was followed by measuring the decrease of Ib using HPLC (JASCO FAMILIC-100N). The rate constants in other solvents or at other temperatures were measured in the same manner. The second-order rate constants were obtained in the usual manner. The data were treated by means of a nonweighted least-squares program. The kinetic data are listed in Table IV.

Derivatization of IIIb——A solution of IIIb (0.5 mmol) and acyl halides or arylsulfonylchlorides or alkyl halides in acetone (5 ml) containing triethylamine (0.14 ml) was refluxed for 1 h. After removal of the solvent, the residue was dissolved in chloroform and washed with saturated sodium bicarbonate solution. The chloroform layer was washed with water and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave the crude product. The resulting crystalline mass was recrystallized from ether–*n*-hexane to give the pure sample.

With Tosyl Chloride——mp 196—197.5 °C (acetone–*n*-hexane). Yield 97%. Identical with compound Vb.

With Benzyl Chloride——mp 210—211.5 °C (benzene–*n*-hexane). Yield 26%. IR (KBr): 1740 cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 5.50 (2H, s, $-CH_2-$), 7.45 (5H, s, Ph), 7.75 (1H, d, J=2 Hz, C_7-H), 8.33 (1H, d, J=2H, C_5-H). *Anal.* Calcd for $C_{13}H_9BrN_2O_2$: C, 51.17; H, 2.97; N, 9.18. Found: C, 51.23; H, 3.03; N, 8.77.

With Benzoyl Chloride——mp 146.5—148 °C (benzene–*n*-hexane). Yield 31%. IR (KBr): 1800, 1740 cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 7.51—8.01 (6H, m), 8.28 (11H, d, C_5-H). *Anal.* Calcd for $C_{13}H_7BrN_2O_3$: C, 48.93; H, 2.21; N, 8.78. Found: C, 48.93; H, 2.30; N, 8.84.

With Methyl Chloroformate——mp 184—186 °C (benzene–*n*-hexane). Yield 60%. IR (KBr): 1825, 1750 (C=O) cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 4.14 (3H, s, -Me), 7.71 (1H, d, J=2 Hz, C_7-H), 8.39 (1H, d, J=2 Hz, C_5-H). *Anal.* Calcd for $C_8H_5BrN_2O_4$: C, 35.19; H, 1.85; N, 10.26. Found: C, 35.09; H, 1.81; N, 10.01.

With Ethyl Chloroformate——mp 135—137 °C (benzene–*n*-hexane). Yield 63%. IR (KBr): 1820, 1755 cm^{-1}. ^{1}H-NMR (in $CDCl_3$) δ: 1.49 (3H, t, -Me), 4.53 (2H, q, $-CH_2-$), 7.69 (1H, d, J=2 Hz, C_7-H), 8.36 (1H, d, J=2 Hz, C_5-H). *Anal.* Calcd for $C_9H_7BrN_2O_4$: C, 37.66; H, 2.46; N, 9.76. Found: C, 37.55; H, 2.37; N, 9.51.

MO Calculation——The FMO energies and coefficients were obtained by means of semiempirical SCF MO calculations based on the CNDO/2 approximation.[3] Atomic distances and bond angles of the important functional groups (>N–O, –NCO, $-SO_2-$) of Ia and IIa were taken from the X-ray results of compounds[17,18] having the same partial structure and from the MINDO/3[12] optimized structures[2b] of pyridine *N*-oxide and phenyl isocyanate.

Computer programs (CNDO/2 and MINDO/3) were locally modified for use on a FACOM M-382 computer.

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