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Studies on 1,3-Benzoxazines. II.[1] New Rearrangement Modes in the Reaction of 4-Chloro-2,2-dimethyl-2H-1,3-benzoxazine with Substituted Pyridine N-Oxides

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New rearrangement modes in the reaction of 4-chloro-2,2-dimethyl-2H-1,3-benzoxazine (1) with various α- and/or γ-substituted pyridine N-oxides are described. The benzoxazine moiety was introduced into the side chain and/or β-position of the pyridine ring, in addition to the α-position. possible mechanism of the reactions are discussed.

Keywords——1,3-benzoxazine; picoline N-oxide; lutidine N-oxide; imidoyl chloride; rearrangement

In the preceding paper,[1] we reported a new synthetic method for primary 2-aminopyridine derivatives which involved hydrolysis of the rearrangement products obtained from the reaction of pyridine N-oxides with imidoyl chlorides of 1,3-benzoxazine derivatives, as outlined in Chart 1. This reaction resulted in the introduction of the oxazine moiety into the α-position of the pyridine ring through rearrangement of the initially formed cycloadducts and was quite general for most pyridine N-oxides except those with alkyl or alkoxy substituents at either the α- or γ-position.

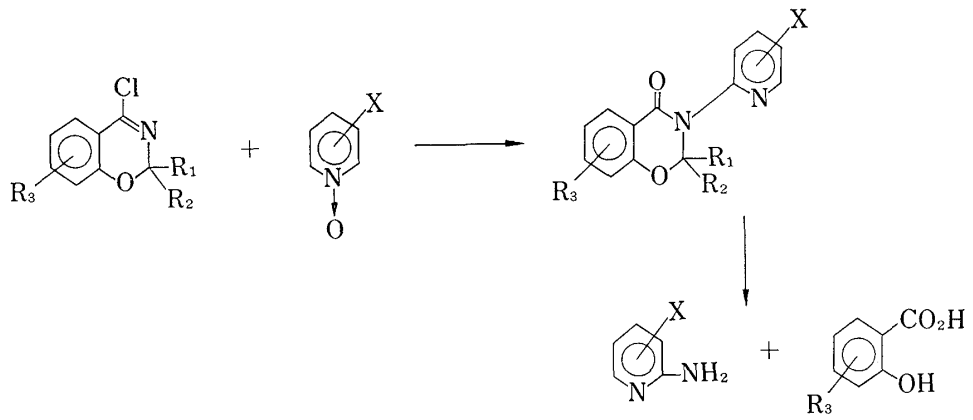

Chart 1

In this paper, we report other new rearrangement modes in the reaction of 4-chloro-2,2-dimethyl-2H-1,3-benzoxazine (**1**) with pyridine N-oxides possessing alkyl or aralkyl substituents at their α- and/or γ-positions. In this reaction, the oxazine moiety is introduced into the side chain of the pyridine ring, in addition to its α- and/or β-positions.

A number of similar rearrangement reactions of various alkyl-substituted pyridine N-

1) Part I of this series: K. Wachi and A. Terada, *Chem. Pharm. Bull.*, **28**, 465 (1980).

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oxides have been reported using acid anhydrides,[3] acid chlorides and sulfonyl chlorides.[4] The various mechanisms for the formation of the β-position and/or the side chain rearrangement products of the pyridine ring by the reaction of α- or γ-picoline N-oxides with acid anhydrides have been reviewed in recent reports by Traynelis[5] and Oae.[6] On the other hand, Abramovitch and co-workers reported the reaction of picoline N-oxides with N-phenylbenzimidoyl chloride in the presence of a strong base to yield side chain acylaminated products.[7]

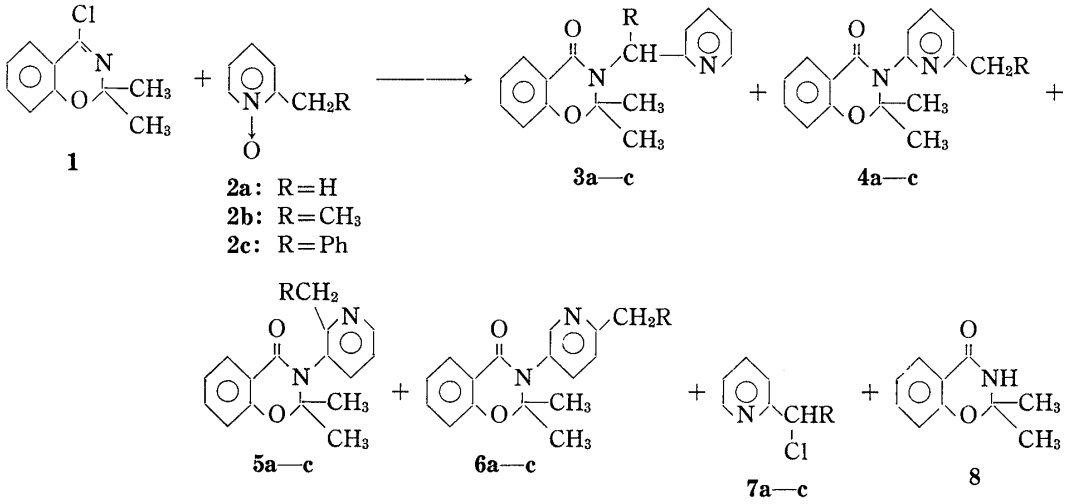


Chart 2

Treatment of α-picoline N-oxide (**2a**) with **1** in 1,2-dichloroethane under reflux for 2 hr afforded 2,2-dimethyl-3-(2-pyridylmethyl)-4-oxo-4H-1,3-benzoxazine (**3a**), 2,2-dimethyl-3-(6-methylpyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**4a**), 2,2-dimethyl-3-(2-methylpyrid-3-yl)-4-oxo-4H-1,3-benzoxazine (**5a**), 2,2-dimethyl-3-(2-methylpyrid-5-yl)-4-oxo-4H-1,3-benzoxazine (**6a**), 2-chloromethylpyridine (**7a**) and 2,2-dimethyl-4-oxo-4H-1,3-benzoxazine (**8**) in 49, 22, 2, 3, 8 and 18% yields, respectively (Chart 2). The structure of the first reaction product, **3a**, was assigned on the basis of spectroscopic and elemental analysis data ($C_{16}H_{16}N_2O_2$). The mass (MS) spectrum exhibited a molecular ion peak at *m/e* 268 which was consistent with loss of hydrogen chloride from the adduct of **1** and **2a**. The infrared (IR) spectrum of **3a** exhibited a new absorption band due to an amide band at 1660 cm^{-1}. The nuclear magnetic resonance (NMR) spectrum of **3a** showed no methyl group on the pyridine ring but showed a new singlet at 4.93 ppm (2H) due to the methylene protons, a doublet of doublets at 8.00 ppm (1H, J=2 and 8 Hz) due to the proton at the 5-position on the benzoxazine ring and another doublet of doublets at 8.55 ppm (1H, J=2 and 5 Hz) assigned to the α-proton on the pyridine ring. The structure of **3a** was further confirmed by its conversion to the known compound, 2-aminomethylpyridine (**9**),[8] and salicylic acid (**10**) by saponification. The elemental analysis and

3) *a*) V. Boekelheide and W.J. Linn, *J. Am. Chem. Soc.*, **76**, 1286 (1954); *b*) O.H. Bullitt, Jr., and M.T. Maynard, *ibid.*, **76**, 1370 (1954); *c*) S. Oae, T. Kitao, and Y. Kitaoka, *ibid.*, **84**, 3362 (1962); *d*) T. Cohen and J.H. Fager, *ibid.*, **87**, 5701 (1965); *e*) V.J. Traynelis and A.I. Gallagher, *ibid.*, **87**, 5710 (1965); *f*) T. Cohen and G.L. Deets *ibid.*, **94**, 932 (1972).

4) J.F. Vozza, *J. Org. Chem.*, **27**, 3856 (1962); T. Koenig and J.S. Wieczocek, *ibid.*, **33**, 1530 (1962).

5) V.J. Traynelis, "Rearrangement of O-Acylated Heterocyclic N-Oxides" in "Mechnisms of Molecular Migrations," ed. by B.S. Thyagarajan, Vol. 2, 1, Interscience Pub., New York, 1969.

6) S. Oae, *Heterocycles*, **6**, 583 (1977).

7) R.A. Abramovitch and T.D. Bailey, *J. Heterocyclic Chem.*, **12**, 1079 (1975); R.A. Abramovitch and I. Shinkai, *Accounts Chem. Res.*, **9**, 192 (1976); R.A. Abramovitch and D.A. Abramovitch, *Chem. Commun.*, **1979**, 956.

8) J.D. Bower and G.R. Ramage, *J. Chem. Soc.*, **1955**, 2834.

the mass spectrum (M^+: *m/e* 268) of the second product, **4a**, indicated that the molecular formula was $C_{16}H_{16}N_2O_2$, the same as that of **3a**. The IR spectrum showed an absorption band at 1670 cm^{-1} which is typical amide band of 3-(2-pyridyl)-4-oxo-4H-1,3-benzoxazine derivatives.[1] The NMR spectrum of **4a** showed a singlet at 1.77 ppm (6H) due to the dimethyl acetal groups, and another singlet at 2.55 ppm (3H) due to the methyl group on the pyridine ring. No signal corresponding to a pyridine ring α-proton was seen. The structure of **4a** was confirmed by converting it to the known compound, 6-amino-2-picoline (**11**),[9] and **10** by acid hydrolysis. Elemental analysis ($C_{16}H_{16}N_2O_2$), MS (M^+: 268) and NMR spectra for third (**5a**) and fourth (**6a**) reaction products were in agreement for the proposed structures. The NMR spectrum of **5a** showed two singlets at 1.47 (3H) and 1.73 ppm (3H) due to the dimethyl groups of an acetal moiety, another singlet at 2.50 ppm (3H) due to the methyl protons on the pyridine ring and a doublet of doublets at 8.57 ppm (1H, J=2 and 5 Hz) assigned to the α-proton on the pyridine ring. Compound **6a** showed a singlet at 1.60 ppm (6H) due to the dimethyl acetal groups, another singlet at 2.60 ppm (3H) due to the methyl protons on the pyridine ring and a doublet at 8.43 ppm (1H, J=2 Hz) due to the α-proton on the pyridine ring in the NMR spectrum. Integration revealed three pyridine ring protons in the NMR spectra of both **5a** and **6a**, indicating that the benzoxazine moiety was introduced onto the pyridine nucleus. The structures of **5a** and **6a** were determined by their conversion to the known compounds 3-amino-2-picoline (**12**)[10] and 5-amino-2-picoline (**13**),[9] respectively, by saponification. The structure of the fifth reaction product, **7a** (characterized as its hydrochloride), was assigned on the basis of elemental analysis and the NMR spectrum, and by comparison with an authentic sample.[11] The final product, **8**, is a precursor of imidoyl chloride (**1**).

Likewise, 2-ethylpyridine N-oxide (**2b**) was allowed to react with **1** under similar conditions to afford reaction products [**3b** (48%), **4b** (26%), **5b** (3%), **6b** (3%), **7b** (13%) and **8** (16%)] similar to those seen in the reaction of **2a** with **1**. Furthermore, 2-benzylpyridine N-oxide (**2c**) was treated with **1** to give the products **3c**, **5c**, **6c**, **7c** and **8**, but no α-position rearrangement product was isolated in this case.

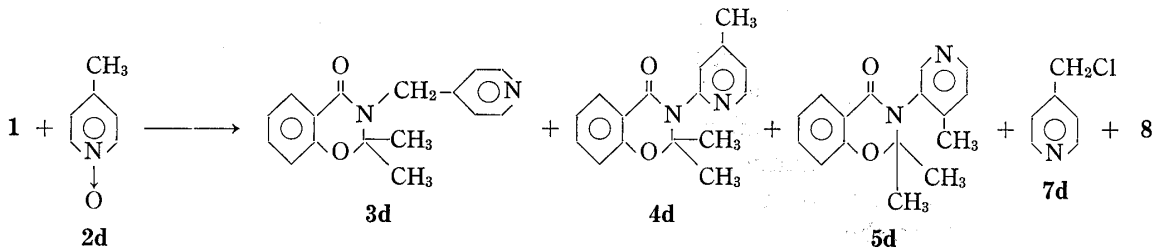


Chart 3

When γ-picoline N-oxide (**2d**) was treated with **1** under similar reaction conditions, 2,2-dimethyl-3-(4-pyridylmethyl)-4-oxo-4H-1,3-benzoxazine (**3d**), 2,2-dimethyl-3-(4-methylpyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**4d**), 2,2-dimethyl-3-(4-methylpyrid-3-yl)-4-oxo-4H-1-3, benzoxazine (**5d**), 4-chloromethylpyridine (**7d**) and **8** were obtained in 33, 12, 4, 23 and 32% yields, respectively (Chart 3). Elemental analysis and MS spectra (M^+: 268) of **3d**, **4d**, and **5d** were consistent with the empirical formula $C_{16}H_{16}N_2O_2$. In the NMR spectrum of **3d**, the signal of the methyl group on the pyridine ring disappeared and a new singlet at 4.80 ppm (2H) due to the methylene group appeared. This spectrum also showed a two proton doublet of doublets at 8.58 ppm (J=1 and 5 Hz) due to the two α-protons on the pyridine ring. The NMR spectrum of **4d** showed a singlet at 1.73 ppm (6H) due to the dimethyl acetal groups,

9) E.D. Parker and W. Shive, *J. Am. Chem. Soc.*, **69**, 63 (1947).
10) F.C. Schmelkes and R.R. Joiner, *J. Am. Chem. Soc.*, **61**, 2562 (1939).
11) W. Baker and K.M. Buggle, J.F.W. McOmie, and D.A.M. Watkins, *J. Chem. Soc.*, **1958**, 3594.

another singlet at 2.37 ppm (3H) due to the methyl group on the pyridine ring and a doublet at 8.40 ppm (1H, $J=5$ Hz) assigned to the α-proton on the pyridine ring. Compound **5d** showed two singlets at 1.45 (3H) and 1.78 ppm (3H) assigned to the dimethyl acetal groups, another singlet at 2.67 ppm (3H) assigned to the methyl group on the pyridine ring and signals due to the α-protons on the pyridine ring at 8.47 ppm (singlet) and 8.48 ppm (doublet, $J=5$ Hz) in the NMR spectrum. Integration revealed three pyridine ring protons in the NMR spectrum of **5d**. Accordingly, it is suggested that the benzoxazine moiety was introduced at the β-position on the pyridine ring. The structures (**3d**, **4d** and **5d**) were confirmed by converting them to the corresponding known aminopyridine derivatives (**14**,[12] **15**[13] and **16**[14]) by acid hydrolysis. Similarly, the lutidine N-oxides (**2e** and **2f**) reacted with **1** as summarized in Chart 4. In the case of the reaction of **2e** with **1**, **3e** and **5e** were obtained in 38 and 17% yields, respectively, in addition to the side chain-chlorinated product (**7e**)[15] and **8**. On the other hand, in the case of the reaction of **2f** with **1**, **3f-1**, **3f-2**, **5f** and **6f** were obtained in 11, 8, 3 and 3% yields, respectively, together with **7f-1**, **7f-2** and **8**.

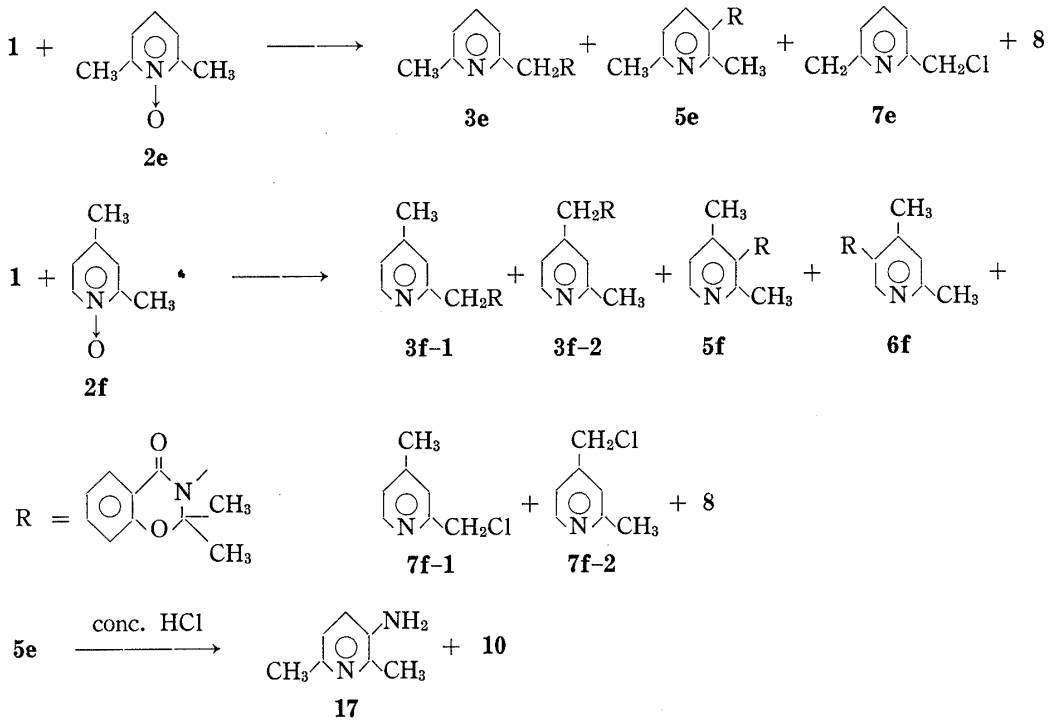


Chart 4

In order to confirm the structure of **5e**, we subjected it to acid hydrolysis. The hydrolysis product, 3-amino-2,6-lutidine (**17**), was identical with an authentic sample prepared by the method of Kröhnke.[16] The structural assignments for other rearrangement products were based on elemental analysis, NMR, IR and MS spectral data. These reaction products are similar to those obtained in the reactions of **1** with **2a** or **2d**.

We next investigated the reaction of **1** with a bicyclic N-oxide, 2-methylquinoline N-oxide (**2g**) (Chart 5). This reaction gave ratios of reaction products similar to those obtained with the monocyclic systems. The results of the reaction of N-oxide derivatives with **1** are shown in Table I.

12) B. Prijs, A.H. Lutz, and H. Erlenmeyer, *Helv. Chim. Acta.*, **31**, 571 (1948).
13) O. Seide, *Chem. Ber.*, **57**, 791 (1924).
14) S. Sugasawa, S. Akahori, S. Toda, and H. Tomisawa, *J. Pharm. Soc. Jap.*, **72**, 192 (1952).
15) R.A. Abramovitch, R.B. Rogers, and G.M. Singer, *J. Org. Chem.*, **40**, 41 (1975).
16) J. Curtze, P. Wild, and F. Kröhnke, *Ann. Chem.*, **1975**, 864.

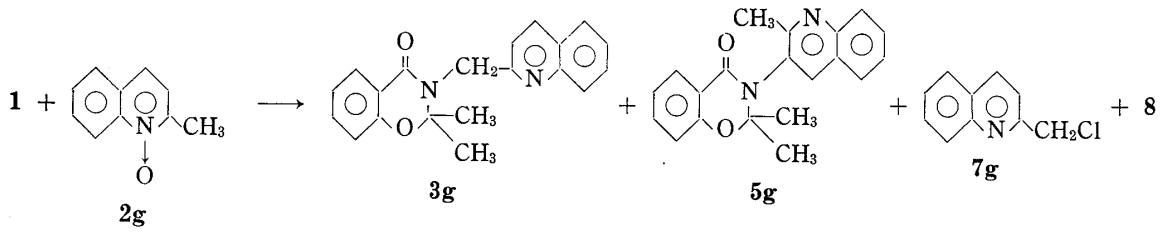
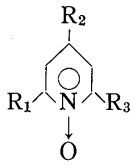
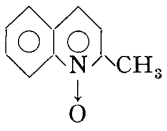


Chart 5

TABLE I. Reactions of Imidoly Chloride (**1**) with Pyridine N–Oxides (**2**)



	R_1	R_2	R_3	Product yield (%) 3	4	5	6	7	8
a	CH_3	H	H	49	22	2	3	8	18
b	C_2H_5	H	H	48	26	3	3	13	16
c	CH_2Ph	H	H	15	—	3	4	51	65
d	H	CH_3	H	33	12	4	—	23	32
e	CH_3	H	CH_3	38	—	17	—	22	34
f	CH_3	CH_3	H	11[a] 8[b]	—	3	3	5[a] 3[b]	32
g				28	—	17	—	25	42

a) α-Position.
b) γ-Position.

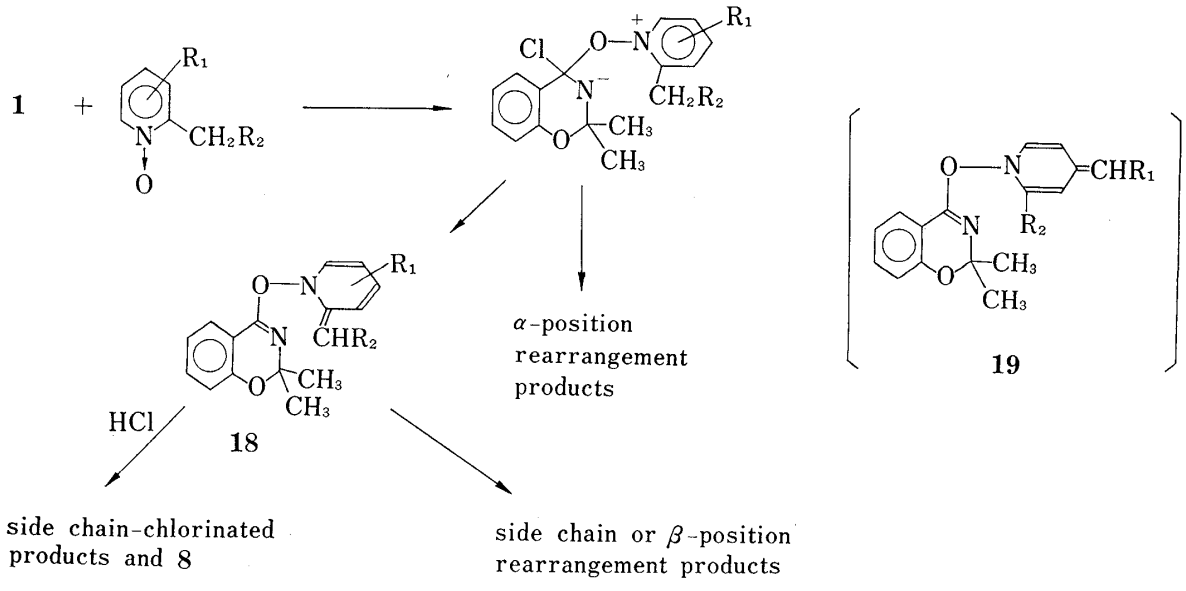
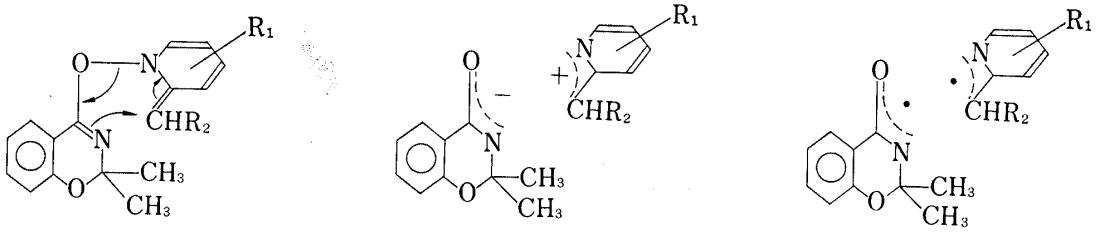


Chart 6

A plausible mechanism for the formation of these rearrangement products is shown in Chart 6. The rearrangement to the α-position on the pyridine ring may be explained by the mechanism proposed in the preceding paper.[1] Side chain-chlorinated products and **8** may arise by nucleophilic addition of a chloride ion to the anhydro-base (**18** or **19**). This is mechanistically similar to the reaction of acyl chlorides with picoline N-oxides.[4] The side chain and β-position rearrangement products might be formed from **18** or **19**. It is possible to consider three mechanistic pathways: a concerted sigmatropic reaction mechanism (A), an ion pair mechanism (B) and a radical pair mechanism (C) (Chart 7).



A B C

Chart 7

In the reaction of picoline N-oxides with acid anhydrides, a concerted sigmatropic mechanism was ruled out by the ^{18}O tracer studies of Oae[6,17] and Katritzky.[18] An intimate ion-pair mechanism was proposed in view of their results. An aza-Cope rearrangement (sigmatropic reaction mechanism), however, was proposed as one possible reaction path in the reaction of N-phenylbenzimidoyl chloride with picoline N-oxides by Abramovitch,[7] The radical pair mechanism was not supported by the results of studies with radical scavengers.[3d,17]

In our cases, a radical mechanism (C) could not be involved since the rearrangement products were obtained even in the presence of a radical scavenger such as *m*-dinitrobenzene. A sigmatropic mechanism (A) may be involved in the formation of the side chain and β-position rearrangement products, and the ion-pair mechanism (B) also seems to be reasonable for the reaction pathway. It is very difficult to decide which mechanism actually operates without any kinetic data.

Contrary to our expectaion, the reaction of 2-benzylpyridine N-oxide or 2,4-lutidine N-oxide with **1** gave no α-position rearrangement products. It may be reasonable to consider that the formation of anhydro-base (**18** or **19**) is faster than rearrangement reaction involving the α-position on the pyridine ring in these cases because of stabilization due to conjugation of the benzene ring in 2-benzylpyridine and hyper-conjugation of another methyl group in 2,4-lutidine.

Experimental

All melting points are uncorrected. IR spectra were recorded on a Jasco IRA-2 spectrophotometer. NMR spectra were determined on a Varian A-60 or HA-100 instrument using tetramethylsilane as an internal standard; coupling constants are given in Hz. MS spectra were taken on a JEOL JMS-01SG instrument.

General Procedure for Reaction of Substituted Pyridine N-Oxides (2a—f) or 2-Methylquinoline N-Oxide (2g) with 4-Chloro-2,2-dimethyl-2H-1,3-Benzoxazine (1)——A solution of the imidoyl chloride **1** (0.01 mol) and pyridine N-oxide (0.022 mol) in 1,2-dichloroethane (50 ml) was refluxed vigorously for 2—5 hr with stirring. The reaction mixture was then poured into ether (200 ml), and washed with two 50 ml portions of water. The ether layer was concentrated under reduced pressure and the residue was separated by column chromatography on silica-gel, using ethyl acetate-benzene as a solvent, to give side chain rearrangement products (Table II), α-position rearrangement products (Table III) and β-position rearrangement products

17) S. Oae, Y. Kitaoka, and T. Kitao, *J. Am. Chem. Soc.*, **84**, 3359 (1964); *idem*, *Tetrahedron*, **20**, 2685 (1964); S. Kozuka, S. Tamagaki, T. Negoro, and S. Oae, *Tetrahedron Lett.*, **1968**, 923.

18) R. Bodalski and A.R. Katritzky, *Tetrahedron Lett.*, **1968**, 257; *idem.*, *J. Chem. Soc.*, **1969**, 831.

Table II. Side Chain Rearrangement Products (3)

Compd. No.	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	N	NMR δ ppm; pyridine ring or quinoline ring α-H	α- or γ-CH_2 (or CH)	α- or γ-CH_3
3a	162—163	$C_{16}H_{16}N_2O_2$ ·HCl	63.05 (62.78	5.62 5.56	9.19 9.06)	8.55 (1H, dd, J=2, 5 Hz)	4.93 (2H, s)[a,c]	
3b	126—127	$C_{17}H_{18}N_2O_2$	72.32 (72.55	6.43 6.45	9.92 9.88)	8.55 (1H, dd, J=2, 5 Hz)	5.30 (1H, q, J=8 Hz)[c]	
3c	148—149	$C_{22}H_{20}N_2O_2$	76.72 (77.06	5.85 5.81	8.13 8.10)	8.57 (1H, dd, J=2, 5 Hz)	6.08 (1H, s)[c]	
3d	80— 81	$C_{16}H_{16}N_2O_2$	71.62 (71.78	6.01 6.03	10.44 10.52)	8.58 (2H, dd, J=1, 5 Hz)	4.80 (2H, s)[c]	
3e	99—100	$C_{17}H_{18}N_2O_2$	72.32 (72.37	6.43 6.30	9.92 9.98)		4.90 (2H, s)	2.53 (3H, s)[c]
3f-1	202—204	$C_{17}H_{18}N_2O_2$ ·HCl	64.04 (63.84	6.00 6.21	8.78 8.77)	8.60 (1H, d, J=5 Hz)	5.40 (2H, s)	2.60 (3H, s)[d]
3f-2	180—183	$C_{17}H_{18}N_2O_2$ ·HCl	64.04 (63.87	6.00 6.13	8.78 8.66)	8.62 (1H, d, J=5 Hz)	5.05 (2H, s)	2.90 (3H, s)[b]
3g	99—100	$C_{20}H_{18}N_2O_2$	75.45 (75.36	5.70 5.63	8.80 8.88)		5.13 (2H, s)[c]	

a) free base; b) measured in CD_3OD; c) measured in $CDCl_3$; d) measured in CD_2Cl_2.

Table III. α-Position Rearrangement Products (4)

Compd. No.	mp (°C)	Formual	Analysis (%) Calcd (Found) C	H	N	NMR δ ppm; pyridine ring[a] α or γ-CH_3 (or C_2H_5)	α-H
4a	116—117	$C_{16}H_{16}N_2O_2$	71.62 (71.58	6.01 5.98	10.44 10.52)	2.55 (3H, s)	
4b	100—101	$C_{17}H_{18}N_2O_2$	72.32 (72.58	6.43 6.42	9.92 9.76)	1.30 (3H, t, J=7 Hz) 2.83 (2H, q, J=7 Hz)	
4d	83— 84	$C_{16}H_{16}N_2O_2$	71.62 (71.84	6.01 6.01	10.44 10.61)	2.37 (3H, s)	8.40 (1H, d, J=5 Hz)

a) measured in $CDCl_3$.

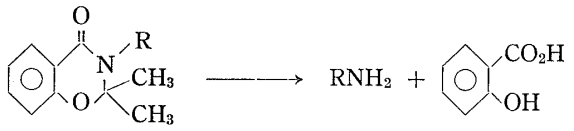
Table IV. β-Position Rearrangement Products (5 and 6)

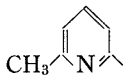
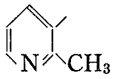
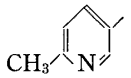
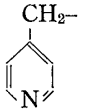
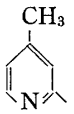
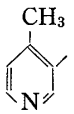
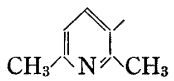
Compd. No.	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	N	NMR δ ppm; pyridine ring or quinoline rine α- or γ-CH_3 (and C_2H_5 or CH_2Ph)	α-H
5a	126—128	$C_{16}H_{16}N_2O_2$	71.62 (71.56	6.01 6.11	10.44 10.26)	2.50 (3H, s)	8.75 (1H, dd, J=2, 5 Hz)[a]
6a	99—100	$C_{16}H_{16}N_2O_2$	71.62 (71.80	6.01 6.07	10.44 10.52)	2.60 (3H, s)	8.43 (1H, d, J=2 Hz)[a]
5b	197—200	$C_{17}H_{18}N_2O_2$ ·HCl	64.04 (63.87	6.00 6.04	8.78 8.68)	1.37 (3H, t, J=8 Hz) 3.10 (2H, q, J=8 Hz)	8.93 (1H, dd, J=2, 5 Hz)[b]

Compd. No.	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	N	NMR δ ppm; pyridine ring or quinoline ring: α- or γ-CH_3 (and C_2H_5 or CH_2Ph)	α-H
6b	219—222	$C_{17}H_{18}N_2O_2 \cdot HCl$	64.04 (63.80	6.00 6.00	8.78 8.72)	1.48 (3H, t, J=8 Hz) 3.23 (2H, q, J=8 Hz)	8.97 (1H, d, J=2 Hz)[b]
5c	126—128	$C_{22}H_{20}N_2O_2$	76.72 (76.69	5.85 5.96	8.13 8.05)	4.04 (1H, d, J=8 Hz) 4.30 (1H, d, J=8 Hz)	8.64 (1H, dd, J=1, 3 Hz)[a]
6c	128—129	$C_{22}H_{20}N_2O_2$	76.72 (76.71	5.85 5.83	8.13 7.93)	4.22 (2H, s)	8.47 (1H, d, J=2 Hz)[a]
5d	96— 98	$C_{16}H_{16}N_2O_2$	71.62 (71.62	6.01 6.09	10.44 10.42)	2.67 (3H, s)	8.47 (1H, s) 8.48 (1H, d, J=5 Hz)[a]
5e	124—126	$C_{17}H_{18}N_2O_2$	72.32 (72.22	6.43 6.42	9.92 9.98)	2.46 (3H, s)[a] 2.56 (3H, s)	
5f	195—197 (dec.)	$C_{17}H_{18}N_2O_2 \cdot HCl \cdot H_2O$	60.62 (60.49	6.28 6.28	8.31 8.24)	2.50 (3H, s) 2.80 (3H, s)	8.75 (1H, d, J=5 Hz)[b]
6f	213—215	$C_{17}H_{18}N_2O_2 \cdot HCl \cdot H_2O$	60.62 (60.84	6.28 6.12	8.31 8.56)	2.47 (3H, s) 2.97 (3H, s)	8.53 (1H, s)[a,c]
5g	113—114	$C_{20}H_{18}N_2O_2$	75.45 (75.58	5.70 5.65	8.80 8.85)	2.72 (3H, s)[a]	

a) measured in $CDCl_3$; *b*) measured in CD_3OD; *c*) free base.

TABLE V. Hydrolysis of the Rearrangement Products



Compd. No.	Aminopyridines R	Yield (%)	mp °C (bp °C/mmHg)
11		82	40—43[9]
12		93	111—113[10]
13		93	94—96[9]
14		86	(120—125/15)[12]
15		94	96—98[13]
16		90	103—104[14]
17		92	120—122[16]

(Table IV). Chlorinated products (**7a**,[11] **b**,[19] **c**,[20] **d**,[21] **e**,[15] **f-1**,[22] **f-2**[23] ang **g**[22]) and the 1,3-benzoxazine **8** were identical with corresponding authentic specimens as determined by comparison of their melting or boiling points and spectral data.

2-Aminomethylpyridine (**9**)——A mixture of 2,2-dimethyl-3-(2-pyridylmethyl)-4-oxo-4H-1,3-benzoxazine (**3a**) (0.9 g) and conc. HCl (3 ml) was refluxed vigorously for 3 hr, then the solvent was evaporated off. The residue was washed well with ethyl acetate and then dissolved in H_2O (0.5 ml), and this solution was made basic with 30% aq. NaOH and extracted with benzene. The benzene layer was dried and concentrated. The residue was distilled to give **9** (0.24 g), bp 100—105°/20 mmHg (bath temp.) (lit.[8] bp 78—80°/12 mmHg.) This was identical with an authentic sample. The ethyl acetate layer was washed with water, and dried over anhydrous Na_2SO_4. Removal of the solvent gave **10** as colorless needles (0.44 g); mp 158°. This product was identical with an authentic specimen.

Aminopyridines (**11**, **12**, **13**, **14**, **15**, **16** and **17**) were prepared by the method described above using conc. HCl. The samples were idnetical with corresponding authentic samples (Table V).

19) P. Arnall and N.R. Clark, *Mfg. Chemist Aerosol News*, **37**, 39 (1966).
20) D.S. Noyce, J.A. Virgilio, and B. Bartman, *J. Org. Chem.*, **38**, 2657 (1973).
21) H.S. Mosher and J.E. Tessieri, *J. Am. Chem. Soc.*, **73**, 4925 (1951).
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23) S. Furukawa, *Pharm. Bull.* (Japan), **3**, 413 (1955).