[Chem. Pharm. Bull. 28(2) 465—472 (1980)]

Studies on 1,3-Benzoxazines. I. Synthesis of Primary 2-Aminopyridines *via* the Reaction of Imidoyl Chlorides of 1,3-Benzoxazines with Pyridine N-Oxides

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(Received June 20, 1979)

A new synthetic method for primary 2-aminopyridine derivatives is described. Treatment of the imidoyl chlorides of 1,3-benzoxazines (**1a**—**i**) with pyridine N-oxides resulted in the introduction of an oxazine moiety into the α-position of the pyridine ring through rearrangement of the initially formed reaction adduct. Acid hydrolysis of the rearrangement products afforded 2-aminopyridine derivatives in excellent yields. When methoxypyridine N-oxides were used, products of a different type (**10** and **14**) were obtained.

Keywords——1,3-benzoxazine; imidoyl chloride; pyridine N-oxide; rearrangement; 2-aminopyridine derivative

Amino-substituted pyridines are important intermediates for the synthesis of various drugs, such as tripelennamine and pyrilamine (antihistaminics), phenyramidol and propiram (analgesics) and niflumic acid (antiinflammatory). Primary 2-aminopyridines are usually prepared from the parent pyridines by means of the Tschitschibabin reaction, which requires extremely drastic reaction conditions. Abramovitch and co-workers[2] reported that the reaction of pyridine N-oxide with N-phenylbenzimidoyl chloride gave the secondary 2-aminopyridine through rearrangement of the initially formed cycloadduct. Parham and co-workers,[3] however, have reported that the reaction of N-phenylbenzimidoyl chloride with some quinoline N-oxides afforded chlorinated quinoline derivatives rather than 2-aminoquinolines. During the course of our studies on 1,3-benzoxazine derivatives, we have found that primary 2-aminopyridines can be easily obtained by hydrolysis of the rearrangement products obtained from the reaction of pyridine N-oxides and imidoyl chlorides of 1,3-benzoxazines.

In initial studies, 4-chloro-2,2-dimethyl-2H-1,3-benzoxazine (**1a**) was prepared by the reaction of salicyl amide with acetone in the presence of sulfuric acid, followed by chlorination with phosphorus pentachloride in phosphorus oxychloride.

Treatment of **1a** with two molar equivalents of pyridine N-oxide in methylene chloride under reflux for 5 hr afforded 2,2-dimethyl-3-(2-pyridyl)-4-oxo-4H-1,3-benzoxazine (**3a**) in 82% yield. One equivalent of pyridine N-oxide served as an acid scavenger and was recovered in 94% yield as its hydrochloride. The structure of **3a** was assigned on the basis of spectroscopic and elemental analysis data. The mass (MS) spectrum exhibited a molecular ion peak at *m/e* 254 which was consistent with the molecular weight with loss of hydrogen chloride from the adduct of **1a** and pyridine N-oxide. The infrared (IR) spectrum showed a new absorption band due to an amide band at 1670 cm^{-1}. The nuclear magnetic resonance (NMR) spectrum of **3a** showed a doublet of doublets at 8.55 ppm (J=2 Hz, J=5 Hz, 1H) due to the α-proton on the pyridine ring, another doublet of doublets at 8.00 ppm (J=2 Hz, J=8 Hz, 1H) assigned to the proton at the 5 position on the benzene ring, and a singlet at 1.72 ppm (6H)

1) Location: *1-2-58, Hiromachi, Shinagawa-ku, Tokyo.*
2) *a*) R.A. Abramovitch and G.M. Singers, *J. Am. Chem. Soc.*, **91**, 5672 (1969); *b*) R.A. Abramovitch and R.B. Rogers, *Tetrahedron Lett.*, **1971**, 1951; *c*) R.A. Abramovitch and G.M. Singers, *J. Org. Chem.*, **39**, 1795 (1974); *d*) R.A. Abramovitch and R.B. Rogers, *ibid.*, **39**, 1802 (1974); *e*) R.A. Abramovitch, R.B. Rogers and G.M. Singers, *ibid.*, **40**, 41 (1975).
3) W.E. Parham and K.B. Sloan, *Tetrahedron Lett.*, **1971**, 1947.

due to the dimethyl groups. The structure was confirmed by conversion of the compound into 2-aminopyridine (**5a**) and salicylic acid (**6**) under acid conditions, as expected in view of the presence of the acid-labile amidoacetal moiety in **3a**. A possible mechanism for the formation of **3** is illustrated in Chart 1.

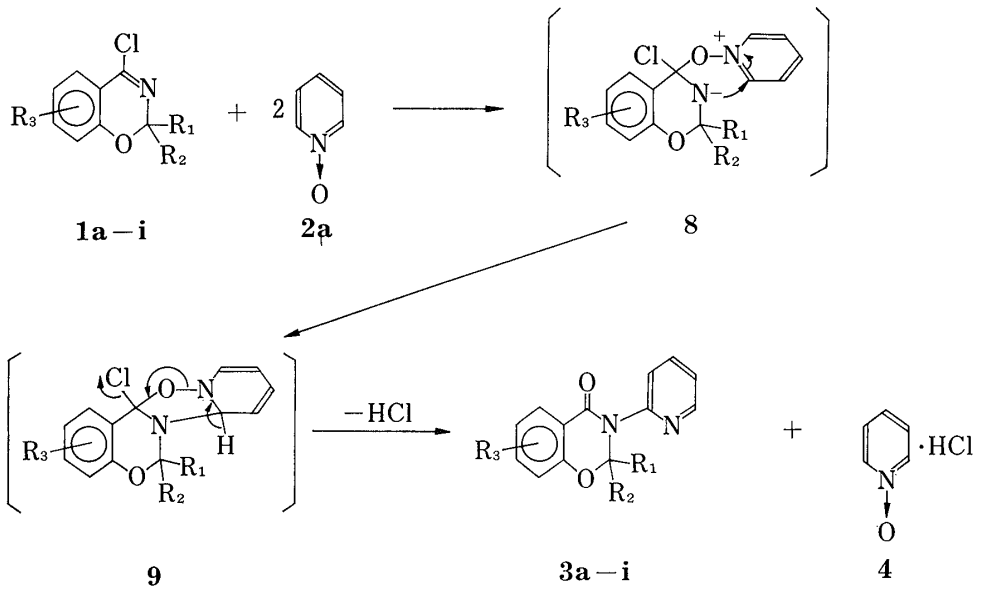


Chart 1

Hydrolysis of **3a** with boiling concentrated hydrochloric acid gave 2-aminopyridine (**5a**) in 95% yield; this was identical with an authentic sample.[4] On the other hand, treatment of **3a** with dilute hydrochloric acid at room temperature afforded N-2-pyridylsalicylamide (**7**)[5] (Chart 2).

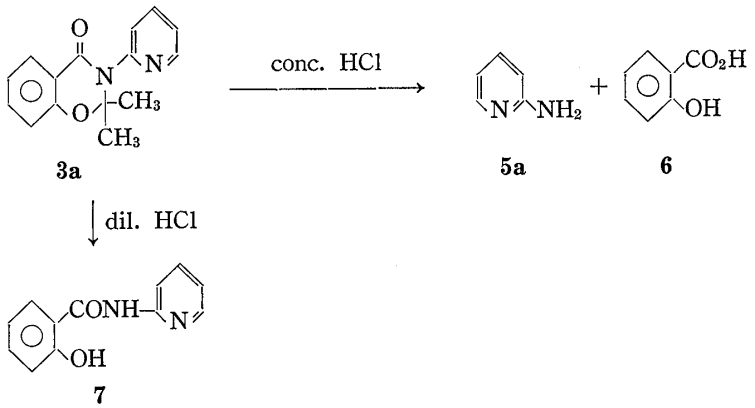


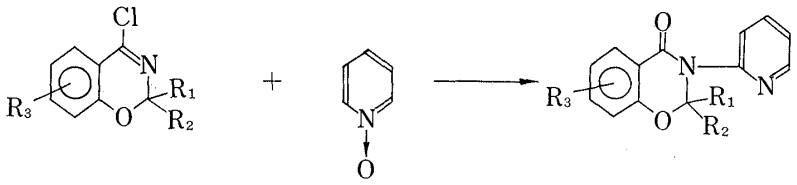
Chart 2

Similar reactions were undertaken with some derivatives of **1a**, and the results are summarized in Table I. Rearrangement products bearing various substituents on the pyridine ring were also prepared by this method, and the results are summarized in Table II.

In the case of the reaction of 3-substituted pyridine N-oxides with **1a**, there is a possibility of substituent rearrangement to the 2 or 6 position of the pyridine ring. However, 3-sub-

4) C.R. Hauser and M.J. Weiss, *J. Org. Chem.*, **14**, 310 (1949).
5) M. Samejima, *Yakugaku Zasshi*, **80**, 1719 (1960) [*C.A.*, **54**, 11648*g* (1960)].

Table I. Reaction of Imidoyl Chlorides of 1,3-Benzoxazine Derivatives with Pyridine N-Oxide



1a—i **2a** **3a—i**

Compd. No.	R_1	R_2	R_3	mp °C (bp °C/mmHg)	Yield (%)	Formula	Analysis (%) Calcd (Found) C	H	N
3a	CH_3	CH_3	H	94—95	82	$C_{15}H_{14}N_2O_2$	70.85 (70.87	5.55 5.67	11.02 10.98)
3b	CH_3	C_2H_5	H	81—83	86	$C_{16}H_{16}N_2O_2$	71.62 (71.51	6.01 5.95	10.44 10.50)
3c	CH_3	C_3H_7	H	(160—170/1.5)	88	$C_{17}H_{18}N_2O_2$	72.32 (72.05	6.43 6.62	9.92 9.81)
3d	CH_3	Ph	H	141—142	78	$C_{20}H_{16}N_2O_2$	75.93 (75.74	5.10 5.07	8.86 8.81)
3e	C_2H_5	C_2H_5	H	104—105	85	$C_{17}H_{18}N_2O_2$	72.32 (72.54	6.43 6.50	9.92 9.87)
3f	H		H	148—150	83	$C_{18}H_{18}N_2O_2$	73.45 (73.35	6.16 5.98	9.52 9.48)
3g	CH_3	CH_3	6-Cl	103—104	92	$C_{15}H_{13}ClN_2O_2$	62.40 (62.54	4.54 4.54	9.70 9.63)
3h	CH_3	CH_3	6-OCH_3	110—111	88	$C_{16}H_{16}N_2O_3$	67.59 (67.86	5.67 5.67	9.85 9.70)
3i	CH_3	CH_3	7-CH_3	114—115	90	$C_{16}H_{16}N_2O_2$	71.62 (71.79	6.01 5.98	10.44 10.28)

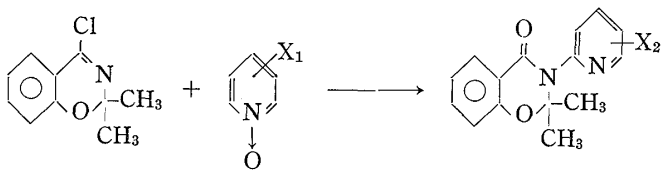
stituted pyridine N-oxides afforded 6-substituted compounds predominantly, as shown in Table II. These results can be explained in terms of the steric hindrance at the 2 position of the pyridine ring. Acid hydrolysis of these rearrangement products afforded 2-aminopyridine derivatives in excellent yields (Table III).

The reaction of **1a** with substituted pyridine N-oxides seems to be quite general, except for 2-methoxy- and 4-methoxypyridine N-oxides. When 2-methoxypyridine N-oxide (**2b**) was treated with **1a** in chloroform under reflux for 5 hr, a new reaction product, 2,2-dimethyl-4-(2-oxo-2H-pyrid-1-yl)oxy-2H-1,3-benzoxazine (**10**), was obtained in 94% yield, and the usual rearrangement product was not obtained. The structure of **10** was deduced from its spectral properties. The elemental analysis and the mass spectrum (M^+: *m/e* 270) indicated that the molecular formula is $C_{15}H_{14}N_2O_3$ which apparently lacks one methyl group from the one-to-one adduct. In the NMR spectrum of **10**, the signal of the methoxy group on the pyridine ring was absent, but a singlet at 1.50 ppm due to the dimethyl groups and a multiplet at around 6.00—7.80 ppm due to eight aromatic protons were present. The IR spectrum showed an amide absorption band at 1700 cm^{-1} and a >C=N– band at 1670 cm^{-1}. The reaction product, **10**, was hydrolyzed with concentrated hydrochloric acid at room temperature to give 2-hydroxypyridine N-oxide (**11**) and salicyl amide (**12**). The properties of **11** and **12** were identical with those of authentic samples.[6]

On the other hand, the reaction of 4-methoxypyridine N-oxide with **1a** under similar conditions, followed by careful silica gel chromatography, afforded the expected product,

6) J.N. Gardner and A.R. Katritzky, *J. Chem. Soc.*, **1957**, 4375.

TABLE II. Reaction of Pyridine N-Oxide Derivatives with **1a**

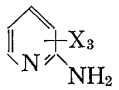


1a **2** **13**

Starting material (2) X_1	Product (13) Compd. No.	X_2	mp °C	Yield (%)	Formula	Analysis (%) Calcd (Found) C	H	N
4-OCH_3	**a**	4-OCH_3	83— 85	23	$C_{16}H_{16}N_2O_3$	67.59 (67.56	5.67 5.60	9.85 9.93)
4-NO_2	**b**	4-NO_2	125—127	4	$C_{15}H_{13}N_3O_4$	60.19 (60.14	4.38 4.34	14.04 13.89)
4-Cl	**c**	4-Cl	77— 79	90	$C_{15}H_{13}ClN_2O_2$	62.40 (62.50	4.54 4.50	9.70 9.84)
4-Ph	**d**	4-Ph	175—178[a]	88	$C_{21}H_{18}N_2O_2 \cdot HCl$	68.75 (68.53	5.22 5.13	7.63 7.33)
3-CH_3	**e**	5-CH_3	111—113	84	$C_{16}H_{16}N_2O_2$	71.62 (71.81	6.01 5.92	10.44 10.50)
3-Cl	**f**	5-Cl	115—116	68[b]	$C_{15}H_{13}ClN_2O_2$	62.40 (62.52	4.54 4.51	9.70 9.70)
3-CN	**g**	5-CN	152—153	23[c]	$C_{16}H_{13}N_3O_2$	68.80 (68.85	4.69 4.54	15.05 15.06)
3-$CH_2CO_2C_2H_5$	**h**	5-$CH_2CO_2C_2H_5$	102—104	47	$C_{19}H_{20}N_2O_4$	67.04 (66.97	5.92 5.83	8.23 8.31)
2-Cl	**i**	6-Cl	173—175	84	$C_{15}H_{13}ClN_2O_2$	62.40 (62.32	4.54 4.36	9.70 9.78)

a) As the hydrochloride.
b) The 2-substituted compound (**13j**) was isolated in 8% yield.
c) **1a** was recovered in 40% yield.

TABLE III. 2-Aminopyridine Derivatives (**5**)



Compd. No.	X_3	mp °C	Yield (%)
5a	H	58[a]	95[b]
5b	4-OCH_3	117—118[c]	89
5c	4-Cl	130—131[d]	95
5d	4-Ph	162—163[e]	91
5e	5-CH_3	76—77[f]	98
5f	5-Cl	129—131[g]	95
5g	5-CO_2H	317 (dec.)[h]	88
5h	5-CH_2CO_2H	164—166[i,j]	92
5i	6-Cl	70—72[k]	93

a) See ref. 5.
b) From **3a**.
c) G.B. Barlin and W. Pfleiderer, *J. Chem. Soc.*, **1971**, 1425.
d) C.W.N. Cumper and A. Singleton, *J. Chem. Soc.*, **1968**, 645.
e) F.H. Case and T.J. Kasper, *J. Am. Chem. Soc.*, **78**, 5842 (1956).
f) N.J. Leonard and B.L. Ryder, *J. Org. Chem.*, **18**, 598 (1953).
g) P.A. van Zwieten, J.A. van Velthujujsen and H.O. Huismann, *Rec. Trav. Chim.*, **80**, 1066 (1961).
h) C. Rath and F. Schiffmann, *Ann.*, **487**, 127 (1931).
i) As the hydrochloride.
j) F. Ostermayer, Ger. Patent 2222791 (1972) [*C.A.*, **78**, 71915*y* (1973)].
k) J.P. Wibaut and J.R. Nicolai, *Rec. Trav. Chim.*, **58**, 709 (1939).

2,2-dimethyl-3-(4-methoxypyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**13a**), with 2,2-dimethyl-4-(4-oxo-4H-pyrid-1-yl)oxy-2H-1,3-benzoxazine (**14**) in 23 and 52% yields, respectively. The elemental analysis of 14 indicated the empirical formula $C_{15}H_{14}N_2O_2$. The mass spectrum exhibited a molecular ion peak at *m/e* 270. The NMR spectrum of **14** showed a new AB-type quartet at 6.33 (J=8 Hz, 2H) and 7.47 ppm (J=8 Hz, 2H) due to the 4-pyridone ring and a singlet at 1.50 ppm due to the dimethyl groups, while the signal of the methoxy group on the pyridine ring was absent. The IR spectrum showed a carbonyl absorption band at 1690 cm^{-1}. The structure of **14** was confirmed by the conversion of **14** into 4-hydroxypyridine N-oxide hydrochloride (**15**)[7] and **12**.

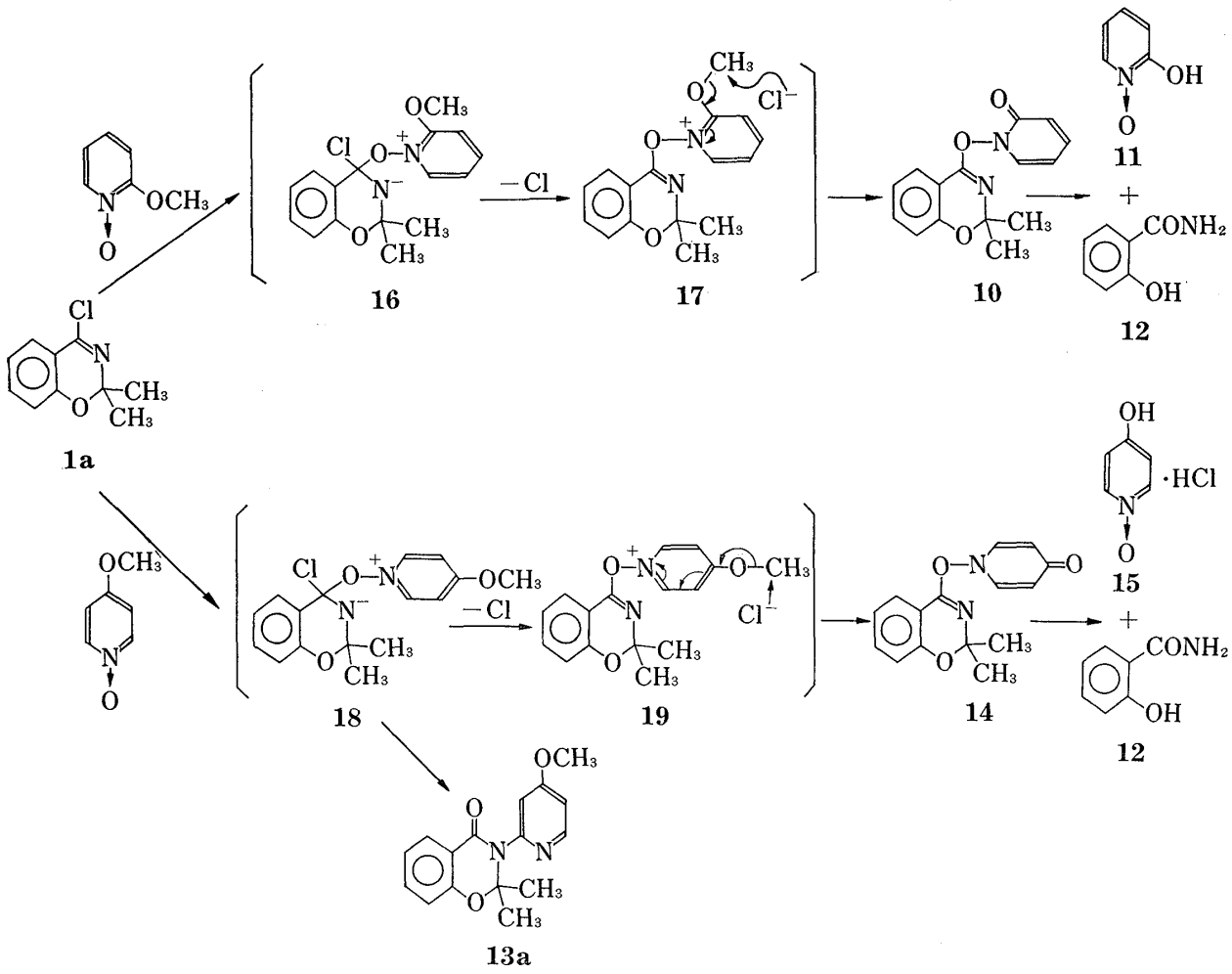


Chart 3

As depicted in Chart 3, the reaction products **10** and **14** may be formed by nucleophilic attack of chloride on the reaction intermediates, **17** and **19**. This mechanism is similar to that proposed for the reaction of 2-ethoxypyridine N-oxide with acetyl chloride, giving N-acetoxy-2-pyridone and ethyl chloride.[8]

When 4-nitropyridine N-oxide was treated with **1a** in 1,2-dichloroethane under reflux for 8 hr, 2,2-dimethyl-3-(4-nitropyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**13b**), which was the desired rearrangement product, 2,2-dimethyl-3-(4-chloropyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**13c**) and 4-chloropyridine N-oxide (**2e**) were isolated in 4, 8 and 20% yields, respectively

7) E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).
8) L.A. Paquette, *J. Am. Chem. Soc.*, **87**, 1407, 5186 (1965).

(Chart 4). The poor yield of the desired product (**13b**) may be due to the decreased reactivity of the α-position on the pyridine ring or the poor nucleophilicity of the N-oxide function in 4-nitropyridine N-oxide. The chlorine substituent of **13c** may be introduced by nucleophilic displacement of the 4-nitro group either in the parent N-oxide or in the reaction intermediate (**20**). Nucleophilic displacement of the nitro group in 2- and 4-nitropyridine N-oxide is well documented.[9] The structural assignment of **13c** was confirmed by its physical data and by comparison of its spectral data with those for the product obtained by the reaction of **1a** with 4-chloropyridine N-oxide.

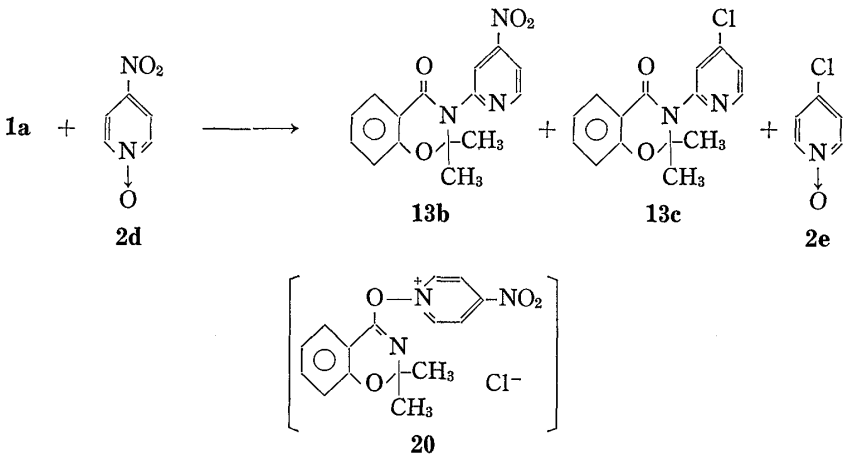


Chart 4

In the reaction of **1a** with various pyridine N-oxides, two molar equivalents of pyridine N-oxide were used; one of them was used as an acid scavenger, as mentioned above. When equimolar amounts of pyridine N-oxides were used in the presence of triethylamine as a scavenger of hydrogen chloride, rearrangement products were not obtained, except in the reaction of **1a** with 2-chloropyridine N-oxide. At present, we have no explanation for the general failure of triethylamine as an acid scavenger.

The reactions of 2- and 4-alkyl substituted pyridine N-oxides with **1a** take a somewhat different course compared with unsubstituted compounds, and will be reported in a subsequent paper.

Experimental

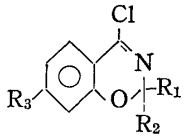
All melting points are uncorrected. IR spectra were recorded on a Jasco IRA-2 spectrophotometer. NMR spectra were determined on a Varian A-60, T-60 or HA-100 instrument using tetramethylsilane as an internal standard; coupling constants are given in Hz. The abbreviations are as follows: s (singlet), d (doublet), dd (doublet of doublets), t (triplet) and m (multiplet). MS spectra were taken on a JEOL JMS-01SG instrument.

General Procedure for the Preparation of the Starting Imidoyl Chlorides of 1,3-Benzoxazines (1a—i)——A solution of 1,3-benzoxazine (0.1 mol) and PCl_5 (0.1 mol) in $POCl_3$ (10 ml) was stirred for 1 hr at room temperature, and then the mixture was heated at 50° for 2 hr. After the removal of $POCl_3$ *in vacuo*, the residue was distilled to give **1**. Yields and boiling points of the products are listed in Table IV.

Reaction of the Imidoyl Chlorides of 1,3-Benzoxazines (1a—i) with Pyridine N-Oxide——General Procedure: A solution of imidoyl chloride (0.01 mol) and pyridine N-oxide (0.022 mol) in methylene chloride (20 ml) was boiled under reflux for 5 hr with stirring. After cooling to room temperature, the precipitate was collected by filtration and recrystallized from isopropanol to give pyridine N-oxide hydrochloride, mp 178—180°.[10] The filtrate was concentrated *in vacuo* and the residue was chrcmatographed on silica gel,

9) A.R. Katritzky and J.M. Lagowski, "Organic Chemistry, A Series of Monographs. Vol. 19: Chemistry of the Heterocyclic N-Oxides," ed. by A.T. Blomquist, Academic Press, New York, 1971, Chapter IV.
10) Y. Namba, T. Oda, H. Ito, and T. Watanabe, *Bull. Chem. Soc. Jpn.*, 33, 1618 (1960).

Table IV. Imidoyl Chlorides of 1,3-Benzoxazines



Compd. No.	R_1	R_2	R_3	bp °C/mmHg	Yield (%)
1a	CH_3	CH_3	H	85—86/2.5	72
1b	CH_3	C_2H_5	H	104—105/3	76
1c	CH_3	C_3H_7	H	107—109/2.5	73
1d	CH_3	Ph	H	138—140/3	24
1e	C_2H_5	C_2H_5	H	101—102/2.5	84
1f	H		H	133—135/4	46
1g	CH_3	CH_3	6-Cl	97—99/3	53
1h	CH_3	CH_3	6-OCH_3	122—125/2.5	55
1i	CH_3	CH_3	7-CH_3	95—97/2.5	67

eluting with benzene–ethyl acetate (5: 1) to give **3**. Melting points and analytical data are summarized in Table I.

Hydrolysis of 2,2-Dimethyl-3-(2-pyridyl)-4-oxo-4H-1,3-benzoxazine (3a): 2-Aminopyridine (5a)——A mixture of 2,2-dimethyl-3-(2-pyridyl)-4-oxo-4H-1,3-benzoxazine (**3a**) (1.3 g) and conc. HCl (5 ml) was boiled under reflux for 8 hr, then the solvent was evaporated off. The residue was washed well with CH_2Cl_2 and then dissolved in H_2O (0.5 ml); this solution was made basic with saturated aq. Na_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ layer was dried, and concentrated. The residue was recrystallized from ether-hexane to give 0.45 g of **5a**, mp 58°. The sample was identical with an authentic sample.[4]

N-2-Pyridylsalicylamide (7)——A mixture of **3a** (0.26 g) and 10% HCl (2 ml) was stirred at room temperature overnight. The solvent was evaporated off and the residue was recrystallized from ethyl acetate–hexane to give 0.20 g of **7**, mp 211—212° (lit.,[5] mp 203°).

5b, c, d, e, f, h and **i** were also prepared by the method described above using conc. HCl; their melting points and yields are listed in Table III.

6-Aminonicotinic Acid (5g)——A mixture of 2,2-dimethyl-3-(5-cyanopyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**13g**) (0.28 g) and conc. HCl (2 ml) was boiled under reflux for 6 hr, then the solvent was evaporated off. The residue was washed with $CHCl_3$ then dissolved in H_2O (0.5 ml), and this solution was neutralized with saturated aq. $NaHCO_3$ and extracted with ethyl acetate. The ethyl acetate layer was dried, and concentrated. The residue was recrystallized from ethyl acetate-hexane to give 0.12 g of **5g**, mp 317° (dec.). The sample was identical with an authentic sample (Table III).

Reaction of 2-Methoxypyridine N-Oxide with 1a——A solution of 2-methoxypyridine N-oxide (5.0 g) and **1a** (4.0 g) in $CHCl_3$ (30 ml) was refluxed for 5 hr with stirring, then cooled and concentrated, and the residue was chromatographed on silica gel, eluting with benzene–ethyl acetate (1: 1) to give 2,2-dimethyl-4-(2-oxo-2H-pyrid-1-yl)oxy-2H-1,3-benzoxazine (**10**) 4.9 g (94%), mp 77—78° (ether-hexane). *Anal.* Calcd for $C_{15}H_{14}N_2O_3$: C, 66.65; H, 5.22; N, 10.37. Found: C, 66.88; H, 5.26; N, 10.37. MS *m/e*: 270 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1700 (C=O). NMR ($CDCl_3$) δ: 1.58 (6H, s), 6.00—7.80 (8H, m).

Hydrolysis of 10——A mixture of **10** (1.3 g) and conc. HCl (5 ml) was stirred at room temperature for 3 hr and the solvent was evaporated off. The residue was washed well with CH_2Cl_2 and then recrystallized from ethanol–hexane to give 2-hydroxypyridine N-oxide (**11**) in a yield of 0.50 g (90%), mp 148—150°.[6] The CH_2Cl_2 was evaporated off and the residue was recrystallized from ethyl acetate–hexane to give 0.59 g of salicyl amide (**12**), mp 138—140°. The NMR ($CDCl_3$) was identical with that of an authentic sample.[11]

Reaction of 4-Methoxypyridine N-Oxide with 1a——A solution of 4-methoxypyridine N-oxide (5.3 g) and **1a** (4.1 g) in $CHCl_3$ (30 ml) was refluxed for 5 hr with stirring, then cooled and concentrated, and the residue was chromatographed on silica gel, eluting with benzene–ethyl acetate (1: 1) to give 2,2-dimethyl-3-(4-methoxypyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**13a**) (1.3 g), mp 83—85° (ether–hexane). *Anal.* Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.56; H, 5.60; N, 9.93. MS *m/e*: 284 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1670 (C=O). NMR ($CDCl_3$) δ: 1.75 (6H, s), 3.87 (3H, s), 8.03 (1H, dd, J=2 and 8), 8.37 (1H, dd, J=2 and 5).

The second fraction, eluted with ethanol, gave 2,2-dimethyl-4-(4-oxo-4H-pyrid-1-yl)oxy-2H-1,3-benzoxazine (**14**) (2.8 g), mp 176—177° ($CHCl_3$-hexane). *Anal.* Calcd for $C_{15}H_{14}N_2O_3$: C, 66.65; H, 5.22; N, 10.37. Found: C, 66.55; H, 5.11; N, 10.33.

11) A. Spilker, *Ber.*, **22**, 2769 (1889).

Reaction of 4-Nitropyridine N-Oxide with 1a——A solution of 4-nitropyridine N-oxide (5.6 g) and **1a** (4.0 g) in 1,2-dichloroethane (50 ml) was boiled under reflux for 12 hr, then the solvent was removed *in vacuo* and the residual oil was chromatographed on silica gel, eluting with benzene–ethyl acetate (20: 1) to give 2,2-dimethyl-3-(4-chloropyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**13c**) (0.46 g), mp 77—79° (ether–hexane). *Anal.* Calcd for $C_{15}H_{13}ClN_2O_2$: C, 62.40; H, 4.54; Cl, 12.28; N, 9.70. Found: C, 62.40; H, 4.54; Cl, 12.23; N, 9.84. MS *m/e*: 288 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1680 (C=O). NMR ($CDCl_3$) δ: 1.77 (6H, s), 8.03 (1H, dd, $J=2$ and 8), 8.43 (1H, d, $J=5$).

The second fraction, eluted with benzene–ethyl acetate (15: 1), afforded 2,2-dimethyl-3-(4-nitropyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**13b**) (0.24 g), mp 125—127° (ether–hexane). *Anal.* Calcd for $C_{15}H_{13}N_3O_4$: C, 60.19; H, 4.38; N, 14.04. Found: C, 60.41; H, 4.34; N, 13.89. MS *m/e*: 299 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1680 (C=O). NMR ($CDCl_3$) δ: 1.83 (6H, s), 6.90—8.20 (6H, m), 8.83 (1H, d, $J=5$).

The last fraction, eluted with ethanol, gave 4-chloropyridine N-oxide (**2e**) (0.52 g), mp 180° (dec.). This was identical with an authentic sample.[12]

Reaction of 3-Chloropyridine N-Oxide with 1a——A solution of 3-chloropyridine N-oxide (1.3 g) and **1a** (1.0 g) in $CHCl_3$ (30 ml) was boiled under reflux for 4 hr with stirring. After cooling to room temperature, the precipitate was removed by filtration and the filtrate was concentrated *in vacuo*. The residue was chromatographed on silica gel, eluting with benzene–ethyl acetate (9: 1), to give 2,2-dimethyl-3-(5-chloropyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**13f**) (0.98 g), mp 115—116° (ether–hexane). *Anal.* Calcd for $C_{15}H_{13}ClN_2O_2$: C, 62.40; H, 4.54; Cl, 12.28; N, 9.70. Found: C, 62.52; H, 4.51; Cl, 12.36; N, 9.70. MS *m/e*: 288 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1680 (C=O). NMR ($CDCl_3$) δ: 1.73 (6H, s), 8.03 (1H, dd, $J=2$ and 8), 8.50 (1H, d, $J=2$).

The second fraction, eluted with benzene–ethyl acetate (6: 1), gave 2,2-dimethyl-3-(3-chloropyrid-2-yl)-4-oxo-4H-1,3-benzoxazine (**13j**, 0.12 g), mp 143° (ether–hexane). *Anal.* Calcd for $C_{15}H_{13}ClN_2O_2$: C, 62.40; H, 4.54; Cl, 12.28; N, 9.70. Found: C, 62.42; H, 4.51; Cl, 12.24; N, 9.68. MS *m/e*: 288 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1680 (C=O). NMR ($CDCl_3$) δ: 1.52 (3H, s), 1.95 (3H, s), 7.90 (1H, dd, $J=2$ and 8), 8.50 (1H, dd, $J=2$ and 5).

13d, e, g, h and **i** were prepared under similar conditions, and their melting points and yields are listed in Table II.

12) A.R. Katritzky and J.M. Lagowski, *J. Chem. Soc.*, **1961**, 43.