UDC 547.829.07

117. **Bunsuke Umezawa**: Studies on Tertiary Amine Oxides. IV. Some Reaction of N-(*p*-Dimethylaminophenyl)-*α*-(1-oxido-2-pyridyl)nitrone. (1).

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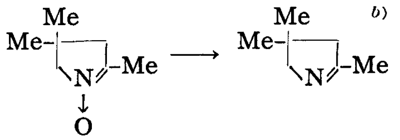
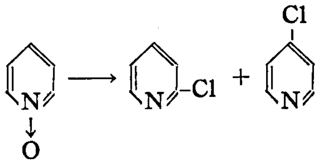
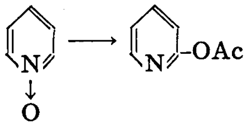
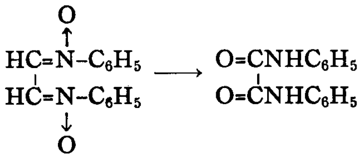
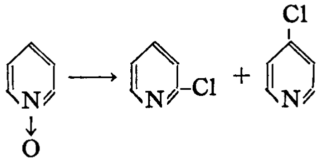
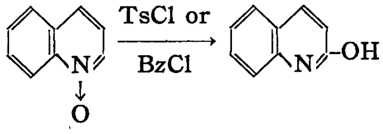
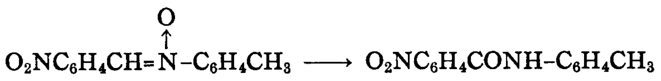
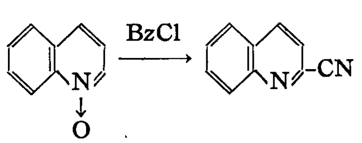
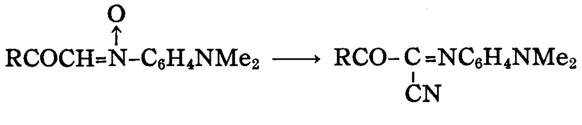
It was reported in the preceding paper[1] that N-(*p*-dimethylaminophenyl)-*α*-(1-oxido-2-pyridyl)nitrone (I) was obtained by the reaction of 1-(1-oxido-2-pyridylmethyl)pyridinium iodide, *p*-nitroso-N,N-dimethylaniline, and potassium hydroxide. (I) has two apparently equal functions, -CH=N(O)-, one of which is aromatic N-oxide and the other aldonitrone. The chemical behavior of these two is similar in some respects, which is obvious from the equality of the arrangement of atoms but should differ from each other in other respects, which is also apparent from the fact that one does not constitute a part of

Table I. Comparison of Reactions of Some Reagents with Aromatic N-Oxides or Aldonitrones[a]

Reagent	Aromatic N-Oxide	Aldonitrone
SO_2	no reaction	 [b]
PCl_3	deoxygenation	——
$POCl_3$		——
Ac_2O		 $\begin{array}{l}\mathrm{HC{=}\overset{\overset{O}{\uparrow}}{N}{-}C_6H_5}\\ \mathrm{HC{=}\underset{\underset{O}{\downarrow}}{N}{-}C_6H_5}\end{array} \longrightarrow \begin{array}{l}\mathrm{O{=}CNHC_6H_5}\\ \mathrm{O{=}CNHC_6H_5}\end{array}$
SO_2Cl_2		——
OH^-		 $\mathrm{O_2NC_6H_4CH{=}\overset{\overset{O}{\uparrow}}{N}{-}C_6H_4CH_3 \longrightarrow O_2NC_6H_4CONH{-}C_6H_4CH_3}$
KCN		 $\mathrm{RCOCH{=}\overset{\overset{O}{\uparrow}}{N}{-}C_6H_4NMe_2 \longrightarrow RCO{-}\underset{\underset{CN}{\vert}}{C}{=}NC_6H_4NMe_2}$

a) Examples were chosen arbitarily; cf. E. Ochiai: J. Org. Chem., **18**, 534(1953); F. Kröhnke: Ann., **604**, 203(1957); A.A. Morton: "The Chemistry of Heterocyclic Compounds," 198(1946); F. Montanari, *et al.*: C.A., **47**, 12387(1953); M. Colonna: *Ibid.*, **48**, 2065(1954).

b) A. Todd, *et al.*: Proc. Roy. Soc. (London), **1957**, 97.

[*1] Katakasu, Fukuoka (梅沢文輔).

[1] Part III. M. Hamana, B. Umezawa, Y. Gotoh, K. Noda: This Bulletin, 8, 692(1960).

aromatic ring while the other does. It seemed of interest to compare chemical properties of these two and this paper describes some reactions of (I) carried out from this point of view. Similarity and difference between these two reported in the literature are summarized in Table I.

Aromatic N-oxide group is indifferent towards sulfur dioxide[2] and can be deoxygenated with phosphorus trichloride.[3] Conversely, nitrone is thought, in general, to be reduced by sulfur dioxide[4] and no reports on the reaction of nitrone with phosphorus trichloride are available. The treatment of a solution of (I) with sulfur dioxide in chloroform gave a substance (II) of m.p. 218~219° in a considerable yield. (II), having the same empirical formula, $C_{14}H_{15}O_2N_3$, as (I), was by no means an anil, which would be expected to be formed by the deoxygenation of nitrone function, but an acid anilide was suggested from its infrared spectrum. The rearrangement of N-oxide by this reagent being improbable, it was assumed that only the rearrangement of nitrone had taken place, which was verified by its deoxygenative conversion to (III) as shown in Chart 1.

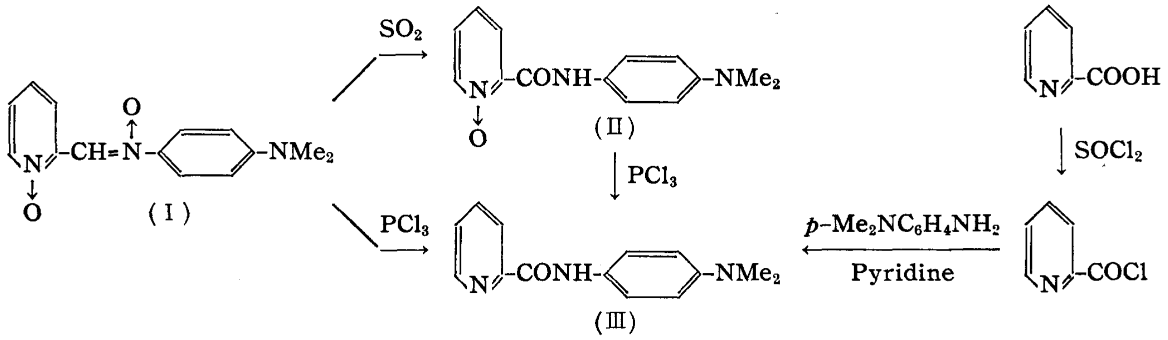


Chart 1. Synthesis of (III) and Deoxygenation of (II)

On the contrary, treatment of (I) with phosphorus trichloride gave in a good yield a substance (III) of m.p. 130~131°, which had an empirical formula, $C_{14}H_{15}ON_3$, showing that one oxygen atom had been lost. However, even in this case, not only a simple deoxygenation of the N-oxide but also rearrangement of the nitrone occurred. This was confirmed finally by the synthesis of (III) as shown in Chart 1. Moreover, (II) was converted to (III) by deoxygenation with phosphorus trichloride (see Chart 1). In this case, it would be assumed that the reagent might have first attacked the N-oxide and phosphoryl chloride*[2] thus formed might have caused rearrangement of the nitrone. Indeed, (I) was shown to yield (II) together with a small amount of (III) by treatment with phos-

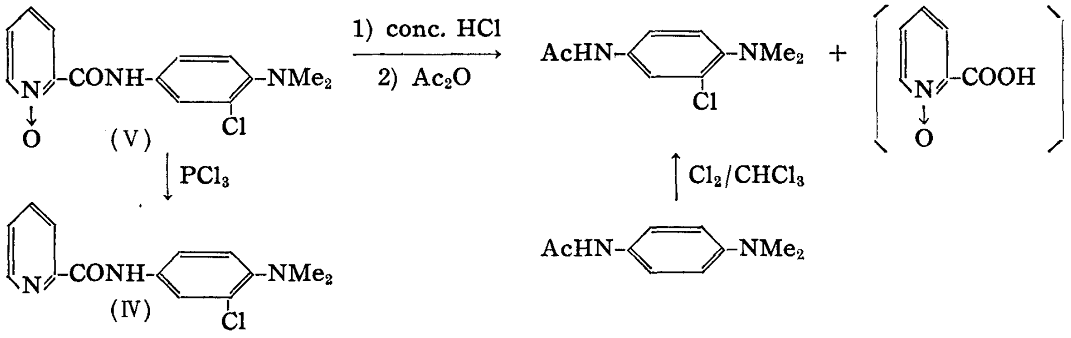


Chart 2. Saponification and Deoxygenation of (V)

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*[2] Phosphoryl chloride has been known as a reagent of rearrangement of ketonitrone. cf. O. Exner: Collection Czechoslov. Chem. Communs., **16**, 258; Chem. Listy, **45**, 388(1951) (C. A., **47**, 5884(1953)).

[2] E. Ochiai: J. Org. Chem., **18**, 534(1953).

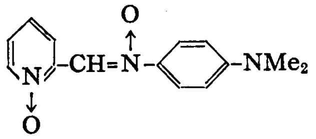
[3] M. Hamana: Yakugaku Zasshi, **71**, 263(1951), *et seq.*

[4] J. Thesing, *et al.*: Chem. Ber., **89**, 2159(1956); A. Todd, *et al.*: J. Chem. Soc., **1959**, 2094.

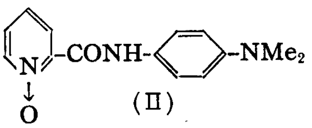
phoryl chloride. As for the formation of the deoxygenated product (III) with this reagent, several similar cases have been reported.[5]

As shown in Chart 2, the nitrone function of (I) was found to undergo facile rearrangement to yield an acid anilide. Furthermore, both N-oxide and nitrone are known to undergo rearrangement with a variety of acylating agents (see Table I), and reaction of (I) with some acylating agents was next investigated in order to compare the reactivity of these two functions (see Table II). First, the treatment of (I) with acetic anhydride gave (II) and 4′-dimethylaminoacetanilide. (I) also underwent rearrangement by means of tosyl, acetyl, or benzoyl chloride to afford (II), the first being the best as such a reagent.[6] When treated with thionyl chloride, (I) gave apparently two new products, (IV), m.p. 76~77°, and (V), m.p. 161~162°, together with a small amount of (III) and a trace of (II). The treatment of (I) with sulfuryl chloride gave only (V). Empirical formulae of (IV) and (V) respectively agreed well with $C_{14}H_{14}ON_3Cl$ and $C_{14}H_{14}O_2N_3Cl$. Moreover, it was assumed from their infrared spectra that both (IV) and (V) might be an acid anilide, the only difference being that (IV) has one and (V) has two oxygen atoms. Thus, it could be assumed that the relationship between (IV) and (V) might be similar to that between (III) and (II), and the chlorine atom might have entered the phenyl ring. Deoxygenation of (V) with phosphorus trichloride, in fact, yielded (IV). The position of the chlorine atom was determined by saponification followed by acetylation. Thus acetanilide, m.p. 117~118°,

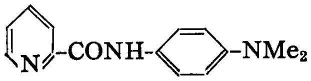
Table II. Rearrangement of (I)



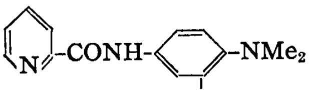
Raegent	Condition	Product (%)			
		(II)	(III)	(IV)	(V)
SO_2	ice-cooling, 2 hr.	50	—	—	—
PCl_3	reflux, 1 hr.	—	82	—	—
$POCl_3$[a)]	reflux, 2 hr.	13.8	4.6	—	—
Ac_2O[c)]	room temp., 2 days, or reflux, 2.5 hr.	36	—	—	—
TsCl	reflux, 2 hr.	24	—	—	—
AcCl	〃	14	—	—	—
BzCl	〃	4	—	—	—
$SOCl_2$ (2.2)[b)]	reflux, 1 hr.	trace	6	17.7	16
SO_2Cl_2 (0.8)	ice-cooling	—	—	—	25.8
SO_2Cl_2 (1.6)	〃	—	—	—	6.8



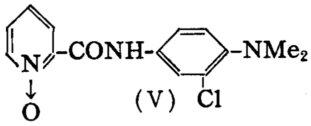
(II)



(III)



(IV)



(V)

Throughout these reaction, $CHCl_3$ was used as a solvent, except for Ac_2O.

a) PCl_5 was shown to be ineffective as a reagent for this rearrangement.

b) Equivalent weight of reagent is shown in parenthese.

c) 4′-Dimethylaminoacetanilide was obtained as a by-product.

d) KOH or MeONa merely caused decomposition of (I).

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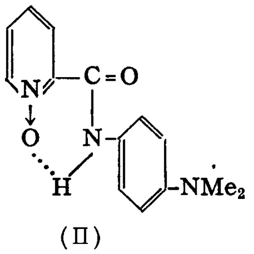
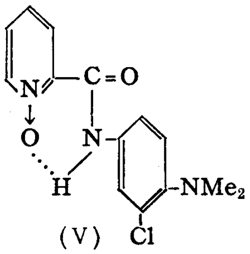
5) M. Ishikawa: Yakugaku Zasshi, **65**, 6(1945); H. J. den Hertog, *et al.*: Rec. trav. chim., **71**, 745 (1952), **74**, 1160(1955), **75**, 1259(1956); E. Ochiai, C. Kaneko: This Bulletin, **7**, 191(1959).

6) M. Kuhara, *et al.*: Mem. Coll. Sci. Kyoto Imperial Univ., **1**, 349(1916).

so obtained, was proved to be identical with 3′-chloro-4′-dimethylaminoacetanilide,7) m.p. 119~120°(see Chart 2). It would be quite reasonable that, owing to the great +M effect of dimethylamino group, chlorinium cation could have entered the position *ortho* to the directing group. Examination of infrared spectra of (II), (III), (IV), and (V) clearly indicates the fact that the characteristic NH (secondary acid amide) bands of (II) and (V) are shifted towards longer wave length to overlap with Nujol absorption bands, probably owing to the formation of intramolecular hydrogen bond (see Experimental).



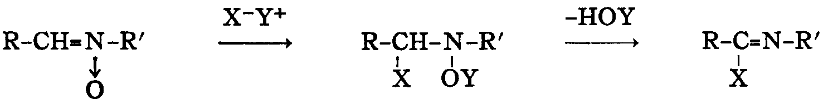
(II)



(V)

Above results make it clear that the nitrone is more susceptible to rearrangement than the N-oxide function.

In 1957, Kröhnke8) summarized the results of rearrangement of nitrone published up to that time and postulated a general mechanism[*3] which was quite analogous to that of N-oxide.9)



$$R\text{-}CH{=}\underset{\underset{O}{\downarrow}}{N}\text{-}R' \xrightarrow{X^-Y^+} R\text{-}\underset{X}{\underset{|}{CH}}\text{-}\underset{OY}{\underset{|}{N}}\text{-}R' \xrightarrow{-HOY} R\text{-}\underset{X}{\underset{|}{C}}{=}N\text{-}R'$$

X : OH^-, CN^-, OAc^- Y : H^+, K^+, Ac^+

This rearrangement is initiated by 1,3-addition of ionisable reagent, X^-Y^+, to aldonitrone grouping, followed by elimination of HOY and by hydrolysis of X.

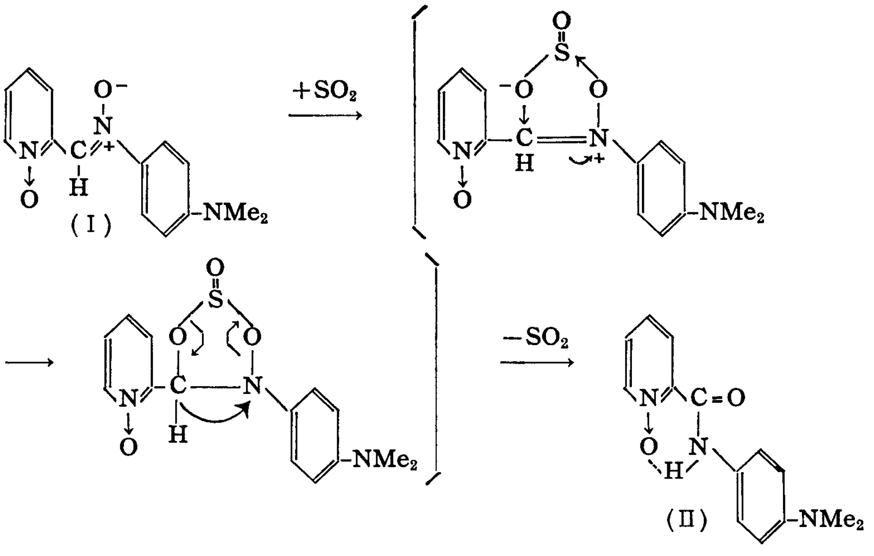


Chart 3. Rearrangement Mechanism of (I) with Sulfur Dioxide

[*3] Kröhnke's postulation seems to be deduced from both the presence of nitrone hydrate and the success of Bellavita reaction, but E. Schmitz (Chem. Ber., **91**, 1488(1958)) stated a doubt about acetic anhydride.

7) E. E. Ayling, J. H. Gorvin, *et al.* : J. Chem. Soc., **1942**, 755.

8) F. Kröhnke : Ann., **604**, 203(1957).

9) M. Katada : Yakugaku Zasshi, **67**, 51(1947); E. Ochiai, T. Okamoto : *Ibid.*, **68**, 88(1948).

The unexpected rearrangement of (I) with sulfur dioxide, however, is inexplicable by Kröhnke's mechanism. Furthermore, the fact that less than one equivalent weight of sulfuryl chloride (0.8 mole) is needed seems to suggest another possibility, i.e. a cyclic mechanism. The oxygen atom of nitrone would preferentially attack the sulfur atom of sulfur dioxide. The anionic center formed would be present in the oxygen atom of the reagent. The cationic center at nitrogen atom would be neutralized by the π-electron pair of C=N double bond to leave a carbonium cation, which would be attacked by the anionic oxygen. The whole course of rearrangement of (I) would be possible as shown in Chart 3. As a result, the oxygen atom of nitrone seems to be highly negatively charged as compared to that of N-oxide. The *trans* configuration[10] of nitrone (in respect to C-H and N-O bonds) and the presence of *p*-dimethylamino group (+M effect) would be favorable to this facile rearrangement of (I).

If this assumption is true, one equivalent of a reagent would not be neccessary owing to catalytic nature of a reagent. In exploring the scope of this cyclic mechanism, the following experiments were undertaken. (1) Treatment of (I) with varying amounts of acetic anhydride in acetonitrile or of phosphoryl chloride at room temperature (see Table III or IV). (2) Employment of triphenyl phosphate as a reagent. In the case of acetic anhydride, it would be difficult to decide whether the cyclic mechanism is correct or not. In the case of phosphoryl chloride, the total yield of (II) and (V)[*4] in two experiments was the same, irrespective of its amount used. Triphenyl phosphate was also proved to be effective as a rearrangement reagent (15.6% yield of (II)).

Table III. Reaction Product of (I) with Acetic Anhydride in Acetonitrile

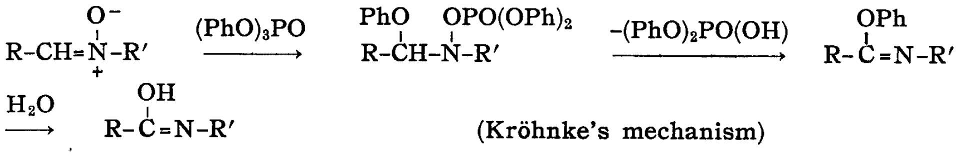
Weight of Ac_2O g.	Anilide (II) Isolated mg. (%)
1	140 (27)
0.2	70 (13.7)
0.05	50 (10)

Table IV. Reaction Products of (I) with Phosphoryl Chloride at Room Temperature

Wt. of (I) mg.	Wt. of $POCl_3$ mg. (eq. weight)	Products Isolated*		
		(II) mg. (%)	(V) mg. (%)	Total (%)
530	300 (1)	80 (15.6)	50 (8.6)	24.2
530	150 (0.5)	60 (10.3)	70 (13.7)	24.0

* Separation was effected by chromatography over alumina (elution with $CHCl_3$).

The course of rearrangement of Kröhnke's mechanism applied to triphenyl phosphate would be illustrated as shown in Chart 4. However, there remain some doubts about the ionization of triphenyl phosphate and the hydrolysis of phenoxyl group in one of the plausible intermediates.



$$\text{R-CH=}\overset{\text{O}^-}{\underset{+}{\text{N}}}\text{-R}' \xrightarrow{(\text{PhO})_3\text{PO}} \text{R-}\overset{\text{PhO}}{\text{C}}\text{H-}\overset{\text{OPO(OPh)}_2}{\text{N}}\text{-R}' \xrightarrow{-(\text{PhO})_2\text{PO(OH)}} \text{R-}\overset{\text{OPh}}{\text{C}}\text{=N-R}' \xrightarrow{\text{H}_2\text{O}} \text{R-}\overset{\text{OH}}{\text{C}}\text{=N-R}'$$

(Kröhnke's mechanism)

[*4] The reaction of (I) with phosphoryl chloride in chloroform under reflux affords (II) and (III), while similar treatment at room temperature gives (II) and (V).

10) J. Thesing, *et al.*: Chem. Ber., **91**, 1978(1958).

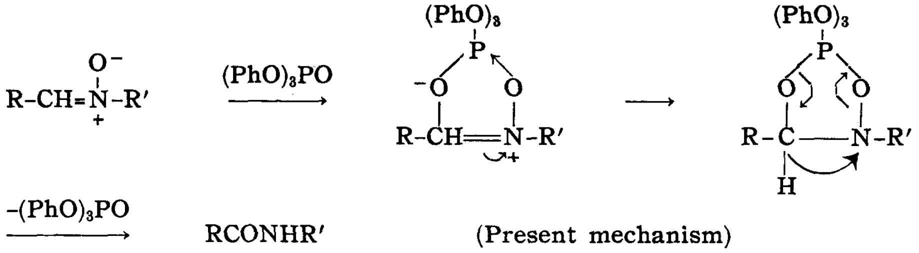


Chart 4.

Judging from these results, it seems better to conclude that although no conclusive view can be deduced in the case of acetic anhydride, the rearrangement of nitrone should proceed through a cyclic intermediate in some cases; namely, sulfur or phosphorus atom, which belongs to Period 3 in the periodic table, is able to expand its original octet and is capable of rearranging nitrone through a cyclic intermediate. It may, therefore, be possible to make the following conclusion.

(1) Nitrone is more reactive than N-oxide towards various reagents, except phosphorus trichloride. This fact is undoubtedly attributable to the inherent differnce of N-O bond orders of N-oxide and nitrone.

(2) Rearrangement mechanism of nitrone is not restricted to that presented by Kröhnke, but a mechanism including a cyclic intermediate should be assumed at least in some cases.

Experimental*[5]

Reaction with Sulfur Dioxide—Dried SO_2 was passed through a solution of 0.53 g. of (I) in 30 cc. of $CHCl_3$ for 2 hr. under ice-cooling. Washing the solution with dil. NaOH and recrystallization of the product from MeOH afforded light yellow fine needles (II), m.p. 218~219°; 0.25 g. (50% yield). *Anal.* Calcd. for $C_{14}H_{15}O_2N_3$: C, 65.35; H, 5.88; N, 16.33. Found : C, 65.03; H, 6.08; N, 16.45. IR cm^{-1} : 1663 (amide I), 1552 (amide II).

Reaction with Phosphorus Trichloride—To a solution of 1.06 g. of (I) in 30 cc. of $CHCl_3$, a solution of 0.7 g. of PCl_3 in 5 cc. of the same solvent was added dropwise under stirring and ice-cooling, and the whole was refluxed on a water bath for 1 hr. Usual treatment, followed by chromatography over alumina (elution with $CHCl_3$), and recrystallization from a mixture of AcOEt and petr. benzine afforded light yellow rods (III), m.p. 130~131°; 0.82 g. (82% yield). *Anal.* Calcd. for $C_{14}H_{15}ON_3$: C, 69.69; H, 6.27; N, 17.42. Found : C, 69.67; H, 6.25; N, 17.33. IR cm^{-1} : 3387 (NH), 1672 (amide I), 1529 (amide II).

Reaction with Acetic Anhydride—a) At room temperature : A solution of 2.5 g. of (I) dissolved in 20 cc. of Ac_2O with warming was allowed to stand for 2 days at room temperature. During this period, orange yellow needles precipitated out. Removal of Ac_2O by distillation *in vacuo* and addition of a small amount of MeOH to this residue afforded orange yellow crystals, melting at 219°; 1.0 g. (36% yield). This was identified with the above-mentioned (II) by mixed fusion. Analytical sample was recrystallized twice from MeOH. *Anal.* Calcd. for $C_{14}H_{15}O_2N_3$: C, 65.35; H, 5.88; N, 16.33. Found : C, 65.23; H, 6.15; N, 16.19.

b) Under reflux : A suspension of 1.5 g. of (I) in 10 cc. of Ac_2O was refluxed for 2.5 hr. Working up as above afforded a small amount of (II). The MeOH mother liquor was evaporated to dryness leaving a dark-brown oil. Chromatography over alumina (elution with $CHCl_3$) afforded an orange oil, distillation of which *in vacuo* gave a distillate of b.p$_{15}$ 210~220° (bath temp.); yield, 200 mg. This solidified on standing. Recrystallization from a mixture of benzene and petr. benzine afforded colorless plates, m.p. 132~133°. *Anal.* Calcd. for $C_{10}H_{14}ON_2$: C, 67.38; H, 7.92; N, 15.72. Found : C, 67.57; H, 7.91, N, 15.60.

This was identified by mixed fusion with an authentic specimen of 4'-dimethylaminoacetanilide, m.p. 13[illegible]°.

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*[5] The starting material was dehydrated over P_2O_5 at 100~110° for 2~3 hr. under a reduced pressure before use. Unless otherwise noted, 1~1.2 equivalent weight of the reagent was used except for Ac_2O and SO_2. Infrared spectra were obtained in Nujol with Koken Model DS 301 spectrophotometer. All melting points are uncorrected.

Reaction with Phosphoryl Chloride—To a solution of 1.2 g. of (I) in 20 cc. of $CHCl_3$, 0.9 g. of $POCl_3$ was added under ice-cooling and the whole was refluxed on a water bath for 2 hr. After cooling and making alkaline with dil. NaOH, the aqueous layer was extracted repeatedly with the same solvent. This solution was evaporated to dryness leaving a dark-brown viscous oil, which was chromatographed over alumina. Elution first with $CHCl_3$ afforded a yellow oil, which was discarded, and the next with AcOEt gave yellowish crystals. On recrystallization from MeOH, apparently two kinds of substances seemed to be mixed. Therefore, this was again chromatographed over a large amount of alumina. Elution with $CHCl_3$ first afforded light yellow crystals, m.p. 128° (from a mixture of benzene and petr. benzine); 50 mg. (4.6% yield). Next, a mixture of yellow and orange yellow crystals, and finally orange yellow crystals, m.p. 216° (from MeOH), 160 mg. (13.8% yield), were obtained. The yellow and orange crystals were identical with (III) and (II), respectively.

Synthesis of 4′-Dimethylaminopicolinanilide—Picolinic acid was converted to the corresponding acyl chloride by refluxing with excess of $SOCl_2$ for 5 hr. Excess of the reagent was distilled off *in vacuo* and the residue was dissolved in dehyd. benzene. Treatment of this solution with freshly distilled *p*-dimethylaminoaniline in the presence of an equivalent amount of pure pyridine afforded the desired anilide as light yellow crystals (from petr. benzine), m.p. 130~131°. This was identified with the above-mentioned (III) by mixed fusion.

Conversion of (II) to (III)—To a solution of 620 mg. of (II) in 10 cc. of $CHCl_3$, 500 mg. of PCl_3 was added cautiously and the whole was refluxed for 1.5 hr. The reaction mixture was treated as usual, the product was dissolved in benzene, and treated with activated charcoal. On concentration of this solution, yellow crystals, melting at 130° and weighing 170 mg., were obtained. This was identified by mixed fusion with an authentic specimen of 4′-dimethylaminopicolinanilide (III).

Reaction with Tosyl Chloride—A solution of 1.2 g. of (I) and 860 mg. of tosyl chloride in 20 cc. of $CHCl_3$ was refluxed for 2 hr. on a water bath. Usual treatment afforded (II), m.p. 216°; 250 mg. (24% yield).

Reaction with Acetyl Chloride—To a solution of 500 mg. of (I) in 10 cc. of $CHCl_3$, 150 mg. of AcCl was added, when heat evolved. The whole was refluxed for 2 hr. on a water bath. Usual treatment afforded (II), m.p. 215°; 70 mg. (14% yield).

Reaction with Benzoyl Chloride—To a solution of 500 mg. of (I) in 20 cc. of $CHCl_3$, 270 mg. of BzCl was added and the whole was refluxed for 2 hr. on a water bath. (II), m.p. 215°, ca. 20 mg. (4% yield).

Reaction with Thionyl Chloride—To a solution of 1.2 g. of (I) in 20 cc. of $CHCl_3$, 1.2 g. (ca. 2.2 equiv. weight) of freshly distilled $SOCl_2$ was added slowly and the whole was refluxed on a water bath for 1 hr. During this period, color of the solution changed to deep red. This was cooled to room temperature, basified with dil. NaOH, and the product was extracted repeatedly with $CHCl_3$. The product was chromatographed over alumina (elution with $CHCl_3$ and a mixture of $CHCl_3$-MeOH (50:1 by vol.)) and afforded two fractions. The first fraction gave colorless needles (from petr. benzine), m.p. 77°; 220 mg. (17.7% yield). Analytical sample was purified by another chromatography over alumina (elution with benzene and Et_2O). It melted at 76~77° (IV). *Anal.* Calcd. for $C_{14}H_{14}ON_3Cl$: C, 61.0; H, 5.12; N, 15.2. Found: C, 61.3; H, 5.12; N, 15.0. IR cm^{-1}: 3294 (NH), 1688 (amide I), 1520 (amide II).

The second fraction gave yellow crystals. This was again chromatographed over alumina (elution with $CHCl_3$). Recrystallization of the eluted product from a mixture of benzene and petr. benzine afforded yellow crystals, melting up to 155°; 210 mg. (16% yield). From this mother liquor, 70 mg. of (III), m.p. 125° (from a mixture of benzene and petr. benzine) (6% yield), was obtained.

The yellow crystal melting up to 155° was dissolved in benzene and chromatographed over alumina (elution with Et_2O). Easily eluted fraction afforded yellow plates (V), m.p. 161~162° (from MeOH). *Anal.* Calcd. for $C_{14}H_{14}O_2N_3Cl$: C, 57.6; H, 4.84; N, 14.4. Found: C, 57.63; H, 5.11; N, 14.0. IR cm^{-1}: 1684 (amide I), 1508 (amide II).

Next eluted fraction afforded impure (I), melting at 207~209° and weighing less than 10 mg.

Reaction with Sulfuryl Chloride—To a sloution of 1.2 g. of (I) in 20 cc. of $CHCl_3$, 0.5 g. (ca. 0.8 equiv. weight) of SO_2Cl_2 was added cautiously under ice-cooling and the whole was allowed to stand over night in a refrigerator. The residual oil obtained was dissolved in a mixture of benzene and a small amount of petr. benzine, and chromatographed over alumina. The columm was eluted successively with benzene, $CHCl_3$, and a mixture of $CHCl_3$ and a small amount of MeOH. From the fraction eluted with a mixture of $CHCl_3$ and MeOH, yellow crystals (from MeOH), m.p. 158~161°; 340 mg. (25.8% yield), were obtained. This was identified with (V) by mixed fusion. When the same amount of (I) was reacted with 1 g. (ca. 1.6 equiv. weight) of SO_2Cl_2 under similar conditions, the yield of the desired product decreased to 90 mg. (6.8% yield).

Saponification of (V)—A solution of 380 mg. of (V) in 5 cc. of conc. HCl was refluxed for 1 hr. The mixture was basified with dil. NaOH and the product was extracted with $CHCl_3$. The $CHCl_3$ layer was worked up as usual to leave an oily residue, which was treated with excess of Ac_2O.

The acetylated product was taken up in $CHCl_3$ and chromatographed over alumina (elution with the same solvent). A substance, m.p. 117~118°. recrystallized from a mixture of benzene and petr. benzine was identified with an authentic specimen of 3′-chloro-4′-dimethylaminoacetanilide, m.p. 119~120°, by mixed fusion. Admixture with an authentic specimen of 2′-chloro-4′-dimethylaminoacetanilide, m.p. 117~118°, showed a sharp depression of m.p.

Conversion of (V) to (IV)—To a solution of 250 mg. of (V) in 20 cc. of $CHCl_3$, 150 mg. of PCl_3 was added cautiously, and the whole was refluxed for 1.5 hr. on a water bath. The product was chromatographed over alumina, eluted with $CHCl_3$ and treatment of the product with activated charcoal afforded a substance (from a mixture of benzene and petr. benzine) of m.p. 76~77°; 150 mg. This was identified with (IV) by mixed fusion.

Reaction with Acetic Anhydride in Acetonitrile—To a solution of 530 mg. of (I) in 20 cc. of acetonitrile, 1 g. (5 equiv. weight), 200 mg. (1 equiv. weight), or 50 mg. (0.25 equiv. weight) of Ac_2O was added. Each solution was refluxed for 1 hr. on a water bath. The yield of corresponding anilide (II) is shown in Table III.

Reaction with Phosphoryl Chloride—a) At room temperature: Reaction of (I) and $POCl_3$ was carried out by standing over night at room temperature. Both (II) and (V) were obtained. These were identified by mixed fusion with authentic specimens. The results are shown in Table IV.

b) Under reflux: To a solution of 530 mg. of (I) in 15 cc. of $CHCl_3$, three drops of $POCl_3$ were added and the whole was refluxed for 1 hr. on a water bath. During this period, the solution turned red. Product, 40 mg. (7.8% yield) of (II).

c) To a solution of 530 mg. of (I) in 20 cc. of $CHCl_3$, a solution of 150 mg. (0.5 equiv. weight) of $POCl_3$ in 10 cc. of the same solvent was added dropwise under reflux for 40 min. The whole was allowed to stand for 30 min. at room temperature. Usual treatment afforded (II), m.p. 217~218°; 50 mg. (9.8% yield).

Reaction with Triphenyl Phosphate—A solution of 530 mg. of (I) and 650 mg. of triphenyl phosphate in 20 cc. of $CHCl_3$ was refluxed for 30 min. on a water bath. Chromatography of the product over alumina (elution with $CHCl_3$) afforded (II), m.p. 216~217°; 80 mg. (15.6% yield).

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Summary

The aldonitirone function of N-(*p*-dimethylaminophenyl)-α-(1-oxido-2-pyridyl)nitrone (I) was shown to undergo facile rearrangement with various reagents, such as sulfur dioxide, thionyl and sulfuryl chloride, phosphorus trichloride, phosphoryl chloride, triphenyl phosphate, and acetic anhydride. To elucidate some of these rearrangement, a cyclic mechanism was postulated.

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