[Chem. Pharm. Bull. 19(1) 130—138 (1971)]

UDC 547.833.1.07

Studies on Ring-opening of Heterocyclic Compounds. II[1]. Alternative Preparation of Pyridine N-Oxide and N-Aminopyridinium Chloride

YASUMITSU TAMURA, NOBUKO TSUJIMOTO and MITSUHIKO MANO

Faculty of Pharmaceutical Sciences, Osaka University[2]

(Received July 23, 1970)

Preparations of pyridine N-oxide (**7a**) and N-aminopyridinium chloride (**10a**) by ring opening of a quaternary pyridinium salt and successive recyclization were investigated, and the following methods established. Treatment of N-(2,4-dinitrophenyl)pyridinium chloride (**5a**) with hydroxylamine, followed by refluxing the resulted 5-(2,4-dinitroanilino)-2,4-pentadienal oxime (**6a**) in dioxane–water (4:1) gave pyridine N-oxide (**7a**) in 87% yield from pyridine. Refluxing a mixture of N-(2,4-dinitrophenyl)pyridinium chloride (**5a**) and hydrazine hydrate in dioxane–water (4:1) after being kept overnight at room temperature, gave N-aminopyridinium chloride (**10a**) in 50% yield from pyridine. The methods were proved to be applicable to conversions of β-, γ-picoline and 3,5-lutidine into the corresponding N-oxides and N-amino derivatives.

Recently, we reported the preparative methods for pyridine N-oxides (**7a—d**) and N-aminopyridinium chlorides (**10a,b,d**).[1] The method for pyridine N-oxide (**7a**) consists of the ring-opening reaction of N-(2,4-dinitrophenyl) pyridinium chloride (5a)[3] with hydroxylamine to 5-(2,4-dinitroanilino)-2,4-pentadienal oxime (**6a**) and the cyclization reaction of **6a** to **7a**. The method for N-aminopyridinium chloride (**10a**) is essentially the same as the above method for **7a**, except in using hydrazine instead of hydroxylamine. The ring-opening of **5a** with hydrazine followed by the cyclization of the resulted 5-(2,4-dinitroanilino)-2,4-pentadienal hydrazone (**9a**) gave **10a**. These methods were also successfully applied to β-, γ-picoline and 3,5-lutidine. The present paper describes a full account of these experiments.

Syntheses of Pyridine N-Oxides (7a—d)

Direct oxidation[4] of pyridines by the action of hydrogen peroxide or peracid is most widely used as a general method for pyridine N-oxides. Baumgarten and co-workers reported in 1933[5] the cyclizations of glutaconaldehyde sodium salt (**1**), glutaconaldehyde dioxime (**2**) and glutaconaldehyde monoanil monoxime (**3**), obtained by ring opening of pyridine, to pyridine N-oxide (**7a**). However the over-all yields of **7a** from pyridine are not satisfactory. In order to explore a novel method for **7a** by such a route, we investigated cyclizations of several glutaconaldehyde derivatives, (**1—3**), 5-acetoxy-2,4-pentadienal (**4**),[5] N-(2,4-dinitrophenyl) pyridinium chloride (**5a**)[3] and **6a** (Chart 1) into **7a** by refluxing in various solvents. The results are described in experimental part and Table I. Among these, the route *via* 5-(2,4-dinitroanilino)-2,4-pentadienal oxime (**6a**) shown in Chart 2 was found to be best in yield and also in easiness of operation. This route provides a preparative method without oxidizing reagent for pyridine N-oxides.

The glutaconaldehyde anil-oxime(**6a**) was prepared by two methods. In the first method, a solution of **5a** (0.015 mole), hydroxylamine hydrochloride (0.03 mole) and triethylamine

1) Part I: Y. Tamura and N. Tsujimoto, *Chem. & Ind.*, in press.
2) Location: *Toneyama, Toyonaka, Osaka.*
3) *a*) Th. Zincke, G. Heuser and W. Möller, *Ann.*, **333**, 296 (1904); *b*) A.F. Vompe and N.F. Turitsyna, *Z. Obshch. Khim.*, **27**, 3282 (1957) [*C.A.*, **52**, 9112d (1958)].
4) J. Meisenheimer, *Ber.*, **59**, 1848 (1926); E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).
5) P. Baumgarten, R. Merlander and J. Olshausen, *Ber.*, **66**, 1802 (1933).

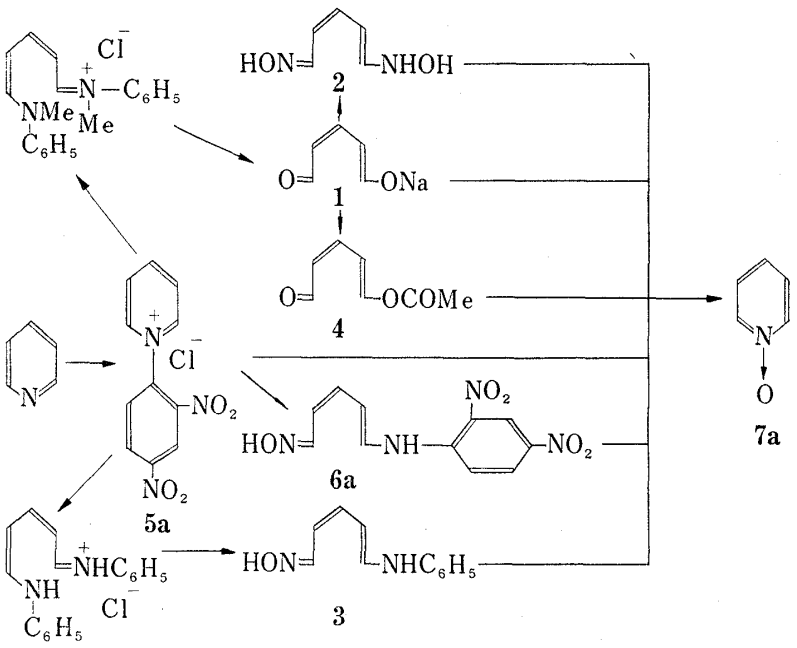

Chart 1

Table I. Yield of Pyridine N-Oxide (**7a**) by Cyclization of Glutaconaldehyde Derivatives

Glut. deriv.	Yield of Glut. deriv. from py. (%)	Solvent	Yield of py. N-oxide (**7a**) (as picrate) (%)
1[a,b]	71	methanol	34
2[b]	22[b]	methanol	5[b]
3[b]	82	nitrobenzene	67
		dioxane–water	50
4[b]	67	methanol	29
5a[a,c]	98	dioxane–water (4:1)	50
6a	94	dioxane–water (4:1)	92
		dioxane	82
		nitrobenzene	5

a) A solution of the glutaconaldehyde derivative and hydroxylamine hydrochloride (1 equiv. mole) was refluxed.
b) lit. 5) *c*) lit. 3)

(0.045 mole) in methanol was stirred at room temperature, giving **6a** in 97% yield. The reaction proceeded similarly in aqueous or ethanol medium, but in the former medium, formation of a considerable amount of resinous material was observed and in the latter medium, a large quantity of the solvent was required due to poor solubility of **5a** (Table II). The second method is the following two-step route. Treatment of **5a** with sodium hydroxide[3] or triethylamine in water or ethanol afforded a high yield of 5-(2,4-dinitroanilino)-2,4-pentadienal (**8a**), which was converted into **6a** with hydroxylamine in methanol in quantitative yield (Chart 2). The second method gave in almost the same over-all yield as that of the first method. However, the first method, one-step synthesis of **6a** from **5a**, is more practical as a preparative method because of a simplicity of operations.

The conformation of **6a** is assumed to be all *trans* conformer from nuclear magnetic resonance (NMR) spectral analysis. Bothner-By and Harris examined[6] the NMR spectrum of *trans-trans* 1,3-butadienes and assigned J 13.1—17.7 cps for the *trans* double bonds and

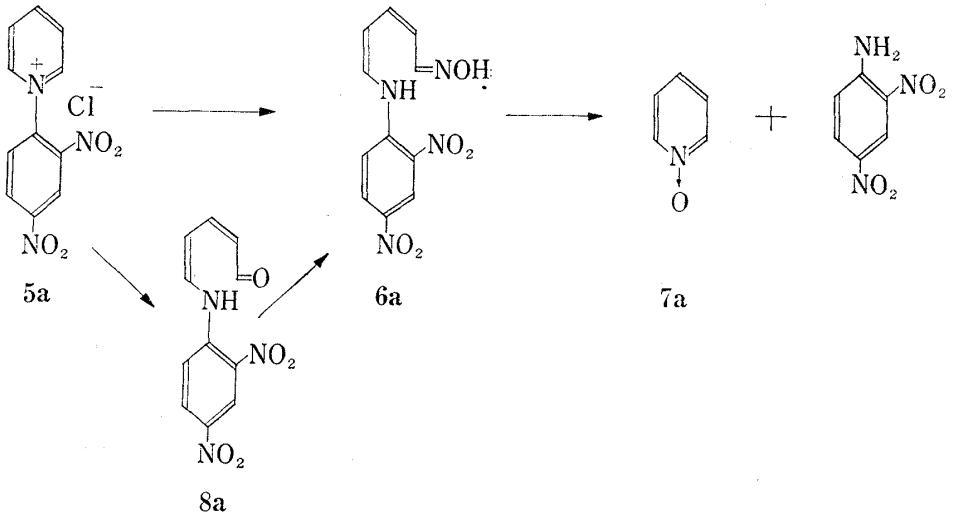

Chart 2

Table II. Ring-opening Reaction of N-(2,4-Dinitrophenyl)pyridinium Chloride(**5a**) to 5-(2,4-Dinitroanilino)-2,4-pentadienal Oxime(**6a**)

5a(mole)	$NH_2OH \cdot HCl$ (mole)	Et_3N(mole)	Solvent(ml)	Yield of **6a** (%)
0.015	0.02	0.035	MeOH(30)	96
0.015	0.03	0.045	MeOH(30)	97
0.015	0.03	0.045	EtOH(160)	95

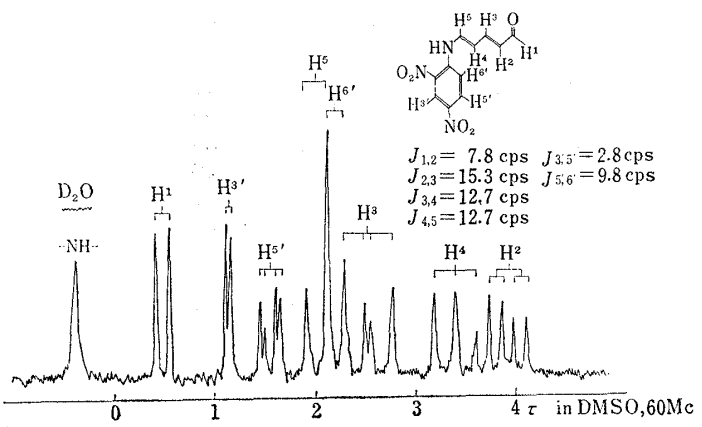

Fig. 1

J 10.4—11.3 cps for the 2,3-single bond. Later, Katritzky, *et al.* showed[7] that the values for the vinyl proton coupling constants of 1,4-disubstituted-1,3-butadienes are in good accord with the results of Bothner-By and Harris. The NMR spectrum of **8a** exhibits the coupling constants of $J_{2,3}$ 15.3, $J_{3,4}$ 12.7 and $J_{4,5}$ 12.7 cps, whose values support strongly that the structure of **8a** is all *trans* form. Accordingly **6a** is guessed to be all *trans* form, because **6a** was prepared from **8a** in quantitative yield. The cyclization of **6a** to **7a** was carried out by heating in the various solvents shown in Table III. Refluxing in dioxane–water (4:1) gave the highest yield (92%).

When two series of the reactions **5a**→**6a**→**7a** and **5a**→**8a**→**6a**→**7a** described above were applied to β- and γ-picoline and 3,5-lutidine, the reactions proceeded similarly to give the corresponding β-picoline N-oxide (**7b**),[8] γ-picoline N-oxide (**7c**)[8] and 3,5-lutidine N-oxide

6) A.A. Bothner-By and R.K. Harris, *J. Am. Chem. Soc.*, **87**, 3445 (1965).
7) R. Eisenthal, A.R. Katrizky and E. Lunt, *Tetrahedron*, **23**, 2775 (1967).
8) E.N. Shaw, "Heterocyclic Compounds," Pyridine and Its Derivatives, Part Two, ed. by E. Klingsberg, Intercience Publishers, Inc., New York, 1961, p. 116.

Table III. Cyclization of 5-(2,4-Dinitroanilino)-2,4-pentadienal Oxime(**6a**) to Pyridine N-Oxide(**7a**) in Various Solvents

Solvent[a]	Temperature	Yield of py. N-oxide (**7a**) (as picrate) (%)
Dioxane–water (4:1)	reflux	92
Dioxane	reflux	82
Nitrobenzene	105—110°	5
Acetic acid	105—110°	7
Dioxane–methanol	reflux	52
Ethanol–HCl	80—85°	33
Water–HCl	90—95°	72

a) Compound(**7a**) is almost insoluble in H_2O, MeOH and benzene. Cyclization of **7a** by refluxing in these solvent failed.

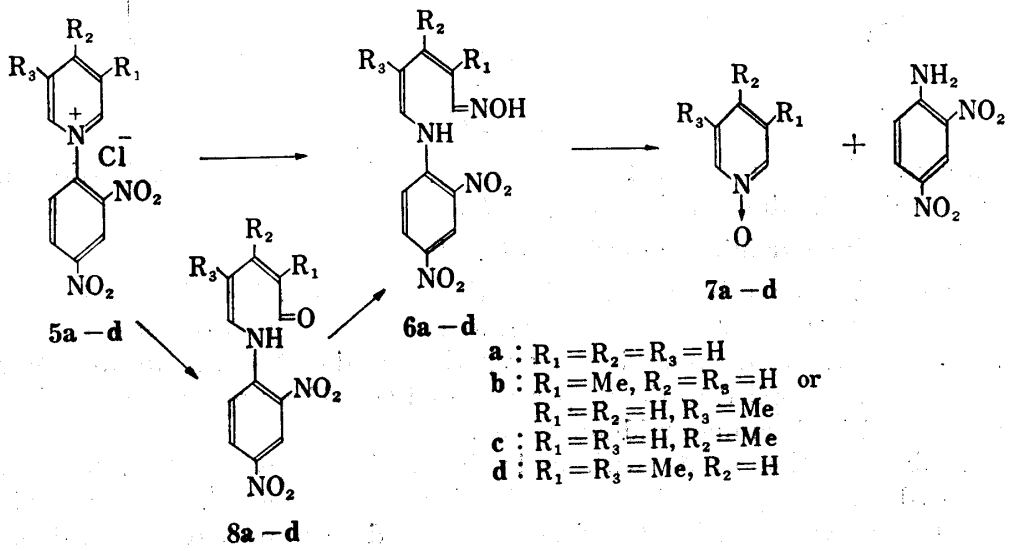

Chart 3

Table IV. Yield of Pyridine N-Oxide Derivatives (**7a—d**)

	R_1	R_2	R_3	Yield of **7** (as picrate) (%) by route of **5**→**6**→**7**	Yield of **7** (as picrate) (%) by route of **5**→**8**→**6**→**7**	mp of **7** (as picrate) (°C)
a	H	H	H	88.3	88.3	180.5—182 (lit.[a] 179.5)
b	Me	H	H	53.5	54	125—126.5 (lit.[b] 125—126.5)
c	H	Me	H	65.5	—	158—159 (lit.[b] 158.7—159.7)
d	Me	H	H	32.5	45.8	134—135

a) lit. 5) b) lit. 8)

(**7d**) (Chart 3). In cases of β- and γ-picoline, the former route gave better yield, but in case of 3,5-lutidine, the latter route was favorable (Table IV).

As to the reaction mechanism[9] for the conversion from **5a** to **7a**, we propose a sequence of reactions shown in Chart 4. The ring-opening of **5a** would proceed through an intermediate i to give the all-*trans* glutaconaldehyde anil-oxime (**6a**). Heating of **6a** in dioxane–water

9) E.N. Marvell, G. Caple and I. Shahidi, *Tetrahedron Letters*, 1967, 277.

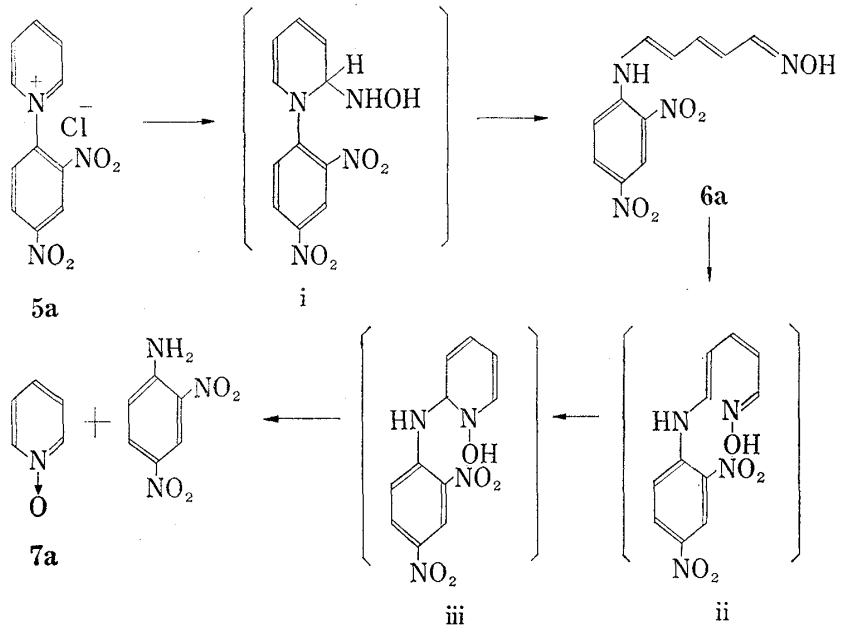

Chart 4

(4:1) causes conversion to the coiled conformer (ii), which undergoes cyclization to iii, followed by removal of 2,4-dinitroaniline to give **7a**.

Syntheses of N-Aminopyridinium Chlorides (10a,b,d)

Several methods[10] have been reported on the synthesis of N-aminopyridinium chloride (**10a**). Among them, the Gösl's method[10c] seems to be superior to the others, especially, in generality. We found that the procedure of preparing pyridine N-oxide (**7a**) from **5a** described above was successfully applied to the preparation of **10a**. This preparation provides a facile and general method for N-aminopyridinium salts.

Ring-opening reaction of **5a** with hydrazine hydrate gave 5-(2,4-dinitroanilino)-2,4-pentadienal hydrazone (**9a**), which was cyclized to N-aminopyridinium chloride (10a) by refluxing in dioxane-water (4:1). The following procedure improved the yield of **10a**; an equimolar mixture of **5a** and hydrazine hydrate in water was kept overnight at room temperature. Then dioxane added to the mixture and the mixture was heated under reflux to give **10a** in 50% yield (Chart 5). The method was successfully applied to β-picoline and 3,5-lutidine, giving N-amino derivatives[11] as shown in Chart 5.

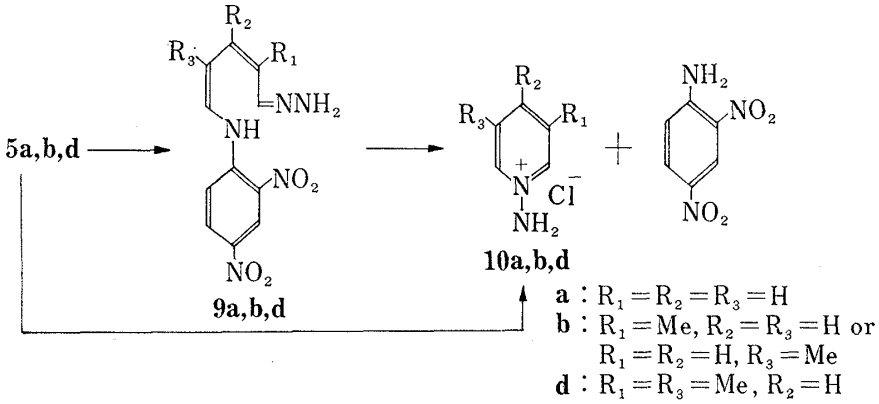

Chart 5

10) *a*) J.A. Moore, *J. Am. Chem. Soc.*, **77**, 3417 (1955); *b*) J.N. Ashley and G.L. Buchanan, *J. Chem. Soc.*, **1947**, 60; *c*) R. Gösl, and A. Meuwsen, *Ber.*, **92**, 2521 (1959); *d*) H. Beyer, K. Leverenz and H. Schilling, *Angew. Chem.*, **73**, 272 (1961).

11) T. Okamoto, M. Hirobe and A. Ohsawa, *Chem. Pharm. Bull.* (Tokyo), **14**, 518 (1966).

Experimental

The NMR spectrum was measured with a Hitachi Perkin-Elmer H-60 type (60 Mc). All melting points and boiling points are uncorrected.

N-(2,4-Dinitrophenyl)pyridinium Chloride (5a)——Prepared from pyridine in 98.5% yield according to the procedure of Vompe, *et al.*[3b] Colorless needles, mp 190° (lit.[3b] mp 190—191°).

N-(2,4-Dinitrophenyl)-β-picolinium Chloride (5b)——Prepared from β-picoline in quantitative yield according to the procedure of Vompe, *et al.*[3b] Colorless needles, mp 208—209° (lit.[3b] mp 208—209°).

N-(2,4-Dinitrophenyl)-γ-picolinium Chloride (5c)——Prepared from γ-picoline in 78% yield according to the procedure of Grochowski, *et al.*[12] Colorless needles, mp 163—164°(lit.[12] mp 163—164°).

N-(2,4-Dinitrophenyl)-3,5-lutidinium Chloride (5d)——A solution of 3,5-lutidine (10.5 g) and 2,4-dinitrochlorobenzene (20.3 g) in dry-CH_3COCH_3 (160 ml) was refluxed for 5 hr. After cooling, precipitates were collected and recrystallized from EtOH to give **5d** (28.4 g, 92%), mp 203—204° (decomp.). *Anal.* Calcd. for $C_{13}H_{12}O_4N_3Cl$: C, 50.48; H, 3.92; N, 13.57. Found: C, 50.48; H, 3.96; N, 13.41.

5-(2,4-Dinitroanilino)-2,4-pentadienal (8a)——i) Prepared in quantitative yield according to the procedure of Zincke, *et al.*[3a] Red crystals, mp 175° (lit.[3a] mp 180°). NMR (in DMSO) τ: 0.49 (1H, doublet, $J_{1,2}=7.8$ cps, H^1), 3.94 (1H, quartet, $J_{1,2}=7.8$, $J_{2,3}=15.3$ cps, H^2), 2.54 (1H, qualtet, $J_{2,3}=15.3$, $J_{3,4}=12.7$ cps, H^3), 3.40 (1H, triplet, $J_{3,4}=12.7$, $J_{4,5}=12.7$ cps, H^4), 2.05 (1H, doublet, $J_{1,5}=12.7$ cps, H^5), 1.15 (1H, doublet, $J_{3',5'}=3$ cps, $H^{3'}$), 1.55 (1H, quartet, $J_{3',5'}=3$, $J_{5',6'}=10$ cps, $H^{5'}$), 2.22 (1H, doublet, $J_{5',6'}=10$ cps, $H^{6'}$), −0.48 (2H, singlet, NH_2) (Fig. 1).

ii) To an ice-cooled solution of **5a** (2.8 g) in EtOH (100 ml) was added dropwise a solution of Et_3N (1.0 g) with stirring. The reaction mixture was stirred at room temperature overnight, during which time the colorless mixture gradually changed to red, giving orange precipitates. The precipitates were collected and recrystallized from acetone to give **8a** (1.2 g, 45%), mp 175° (lit.[3a] mp 180°).

5-(2,4-Dinitroanilino)-2(or 4)-methyl-2,4-pentadienal (8b)——Prepared in 92% yield according to the procedure of Grigor'eva, *et al.*[13] Red needles, mp 161° (lit.[13] mp 161°).

5-(2,4-Dinitroanilino)-2,4-dimethyl-2,4-pentadienal (8d)——To a solution of **5d** (5.0 g) in H_2O (50 ml) was added dropwise a solution of 10% NaOH (20 ml). The mixture was heated slowly up to 80° and kept at 80° for 30 min, during which time the reaction mixture separated a blue-violet oil, which solidified as orange crystals. The orange crystals were washed thoroughly with H_2O, and recrystallized from CH_3COCH_3 to give red needles of **8d** (3.2 g, 69%), mp 135—136°. *Anal.* Calcd. for $C_{13}H_{13}O_5N_3$: C 53.61; H, 4.50; N, 14.43. Found: C, 53.53; H, 4.37; N, 14.16.

Cyclization of Glutaconaldehyde Sodium Salt (1) to Pyridine N-Oxide (7a)——i) Preparation of Glutaconaldehyde Sodium Salt (1): Treatment of N-(2,4-dinitrophenyl)pyridinium chloride (**5a**) with N-methylaniline according to the procedure of Zincke, *et al.*[14] gave glutaconaldehyde di-N-methylanil hydrogen chloride in 78% yield (lit.[14] 70—75%), red needles, mp 118—120° (lit.[14] mp 116—118°). Treatment of glutaconaldehyde di-N-methylanil hydrogen chloride with NaOH solution according to the procedure of Malhotra, *et al.*[15] gave **1** in 90% yield, yellow crystals.

ii) Cyclization of **1** to pyridine N-oxide (**7a**) was carried out according to the procedure of Baumgarten, *et al.*[5] The resulted crude **7a** was treated with an ethanolic solution of picric acid to give a picrate of **7a** in 34% yield (lit.[5] 42%), yellow needles, mp 180.5—182° (lit.[5] mp 179.5°).

Cyclization of Glutaconaldehyde Monoanil Monoxime (3) to Pyridine N-Oxide (7a)——i) Preparation of Glutaconaldehyde Monoanil Monoxime (**3**): Treatment of N-(2,4-dinitrophenyl)-pyridinium chloride (**5a**) with aniline according to the procedure of Zincke, *et al.*[3a] gave a glutaconaldehyde dianil hydrogen chloride in 89% yield, red needles, mp 140° (lit.[3a] mp 141—142°). A solution of the glutaconaldehyde dianil hydrogen chloride (2.0 g) in MeOH–H_2O (3:1) (40 ml) was neutralized with 20% NaOH slowly at room temperature to separate yellow precipitates. The yellow precipitates were collected and washed with H_2O and recrystallized from 60% EtOH to give yellow needles of **3** in 92% yield (1.2 g), mp 146° (lit.[14] 146°).

ii) Cyclization of **3** to **7a**: a) In nitrobenzene: Carried out according to the precedure of Baumgarten, *et al.*[5] The resulted crude **7a** was treated with an ethanolic solution of picric acid to give a picrate of **7a** in 67% yield (lit.[5] 76%), yellow needles, mp 180.5—182° (lit.[5] mp 179.5°).

b) In Dioxane–H_2O (4:1): A solution of **3** (1.88 g) in dioxane–H_2O (4:1) (40 ml) was heated under reflux for 3 hr. The solvent was removed at reduced pressure to give an oil. The oil was treated with an ethanolic solution of picric acid to give a picrate of **7a** (1.62 g, 50% yield), yellow needles, mp 180.5—182° (lit.[5] mp 179.5°).

---

12) J.W. Grochowski and K. Okom, *Biul. Wojskowej Akad. Tech.*, **10**, No. 111—112, 68 (1961) [*C.A.*, **57**, 11156e (1962)].
13) N.E. Grigor'eva and I.K. Gintse, *Z. Obshchei Khim.*, **26**, 3455 (1956) [*C.A.*, **51**, 9611 (1957)].
14) Th. Zincke and W. Würker, *Ann.*, **338**, 107 (1904).
15) S.S. Malhotra and M.C. Whiting, *J. Chem. Soc.*, **1962**, 3812.

Cyclization 5-Acetoxy-2,4-pentadienal (4) to Pyridine N-Oxide (7a)——To an ice-cooled solution of **4** (1.40 g, mp 85°; lit.[5] mp 75.5°), prepared from pyridine in 67% yield according to the procedure of Baumgarten, *et al.*[5], in MeOH (20 ml) was added a solution of NH_2OH HCl (1.39 g) and NaOH (0.80 g) in H_2O (8 ml). The mixture was allowed to stand at room temperature for 6 hr. The solvent was removed at reduced pressure. The residue was taken up in $CHCl_3$ (10 ml), the $CHCl_3$ solution was dried (K_2CO_3) and evaporated at atomospheric pressure to give light yellow needles. The needles were treated with an ethanolic solution of picric acid to give a picrate of **7a** (0.94 g, 29% yield), yellow neeedles, mp 180.5—182° (lit.[5] mp 179.5°).

Cleavage and Simultaneous Cyclization of N-(2,4-Dinitrophenyl)pyridinium Chloride (5a) to Pyridine N-Oxide (7a)——An ice-cooled solution of $NH_2OH \cdot HCl$ (1.39 g) and NaOH (0.80 g) in H_2O (8 ml) was added dropwise to **5a** (2.82 g), and then dioxane (32 ml) was added to the mixture. The mixture was heated under reflux for 5 hr. The solvent was removed at reduced pressure and H_2O (40 ml) was added to the residue. The precipitated 2,4-dinitroaniline (1.70 g) was filtered off. The filtrate was concentrated. The residue was taken up in $CHCl_3$ (20 ml) and the $CHCl_3$ solution was dried (K_2CO_3). After removal of $CHCl_3$ at atomospheric pressure, the residue was distilled at reduced pressure to give **7a** (0.45 g, 50% yield), bp_{15} 136—140° (lit.[8] bp_{15} 138—140°), which solidified as colorless crystals. The crystals were treated with an ethanolic solution of picric acid to give a picrate of **7a** (1.6 g, quantitative yield), yellow needles, mp 180.5—182° (lit.[5] mp 179.5°).

General Procedure for the Preparation of Pyridine N-Oxides (7a—d)——i) Preparation of 5-(2,4-Dinitroanilino)-2,4-pentadienal Oxime (**6a—d**): a) From N-(2,4-Dinitrophenyl)pyridinium Chloride Derivative (5a—d): To an ice-cooled solution of N-(2,4-dinitrophenyl)pyridinium chloride derivative (5a—d) (0.015 mole) in MeOH (10 ml) was added dropwise a solution of $NH_2OH \cdot HCl$ (0.03 mole) and Et_3N (0.03 mole) in MeOH (20 ml) with stirring. Triethylamine (0.015 mole) was added to the mixture and the mixture was allowed to stand at room temperature overnight. The precipitates were collected and washed thoroughly with MeOH, H_2O, MeOH and ether to give a crude **6a—d**, which was used to the next cyclization.

b) From 5-(2,4-Dinitroanilino)-2,4-pentadienal Derivative (**8a,b,d**): To a suspension of **8a,b,d** (0.015 mole) in MeOH (10 ml) was added a solution of NH_2OH HCl (0.03 mole) and Et_3N (0.03 mole) in MeOH (20 ml). After the mixture was stirred at room temperature for several hours, the precipitates were collected and washed thoroughly with MeOH, H_2O, MeOH and ether to give a crude **6a,b,d**, which were used to the next cyclization.

ii) Cyclization of **6a—d** to **7a—d**: A suspension of the crude (**6a—d**) in dioxane-H_2O (4:1) (60 ml) was heated under reflux until the suspension changed to a clear solution. The solvent was removed at reduced pressure and H_2O (50 ml) was added to the residue. The precipitated 2,4-dinitroaniline was filtered off and the filtrate was concentrated. The residue was treated with $CHCl_3$ (20 ml) and the $CHCl_3$ solution was dried (K_2CO_3). After removal of $CHCl_3$ at atomospheric pressure, the residue was distilled at reduced pressure or recrystallized to give **7a—d**. Pyridine N-oxide derivative (**7a—d**) was treated with an ethanolic solution of picric acid to give a picrate of **7a—d**.

Pyridine N-Oxide (7a)——i) Preparation of 5-(2,4-Dinitroanilino)-2,4-pentadienal Oxime (**8a**): a) From N-(2,4-Dinitrophenyl)pyridinium Chloride (**5a**): To an ice-cooled solution of **5a** (4.23 g) in MeOH (10 ml) was added dropwise a solution of NH_2OH HCl (2.08 g) and Et_3N (3.00 g) in MeOH (20 ml) with stirring. Triethylamine (1.50 g) was added to the mixture and the mixture was allowed to stand at room temperature overnight, during which time color of the mixture gradually changed from colorless to red-black. The red-black precipitates were collected, washed thoroughly with MeOH, H_2O, MeOH and then ether to give **6a** (4.04 g, 97% yield), mp 168—169° (decomp.), which was used to the next cyclization. Recrystallization from pyridine gave an analytical sample of **6a**, reddish-violet needles, mp 168—169° (decomp.). *Anal.* Calcd. for $C_{11}H_{10}O_5N_4$: C, 47.48; H, 3.62; N, 20.14. Found: C, 47.79; H, 3.82; N, 20.10.

The anil-oxime (**6a**) was also prepared using EtOH or H_2O in place of MeOH as solvent in the above procedure. A reaction of **5a** (4.23 g) in EtOH (60 ml) with NH_2OH HCl (2.08 g) and Et_3N (3.00 g) in EtOH (100 ml) gave (97% yield) of **6a**, mp 168—169° (decomp.).

A reaction of **5a** (4.23 g) in H_2O (10 ml) with NH_2OH HCl (2.08 g) and Et_3N (3.00 g) in H_2O (20 ml) gave reddish-violet crystals of a crude **6a**, mp 140—141° (decomp.). Recrystallization from pyridine gave **6a** (1.41 g, 34%), mp 168—169° (decomp.).

b) From 5-(2,4-Dinitroanilino)-2,4-pentadienal (**8a**): To a suspension of **8a** (3.93 g) in MeOH (10 ml) was added a solution of NH_2OH HCl (2.08 g) and Et_3N (3.00 g) in MeOH (20 ml). The mixture was stirred at room temperature for 5 hr, during which time the orange crystals of **8a** gradually changed to reddish-violet crystals. The crystals were collected and washed thoroughly with MeOH, H_2O, MeOH and ether to give reddish-violet crystals of **6a** [4.00 g, quantitative yield, mp 168—169° (decomp.)], which were identical with the product (**6a**) in all respects.

ii) Cyclization of **6a** to **7a**: a) In Dioxane-H_2O (4:1): A suspension of **6a** (4.04 g, mp 168—169° decomp.) in dioxane-H_2O (4:1) (60 ml) was heated under reflux for 6 hr. The solvent was removed at reduced pressure and H_2O (40 ml) was added to the residue. The insoluble 2,4-dinitroaniline (2.7 g) was filtered off and the filtrate was concentrated. The residue was treated with $CHCl_3$ (20 ml) and the $CHCl_3$ solution was dried (K_2CO_3). After removal of $CHCl_3$ at atomospheric pressure, the residue was distilled at

reduced pressure to give **7a** [1.26 g, 88% yield from **5a**], bp_{15} 136—140° (lit.[8] bp_{15} 138—140°), which solidified as colorless crystals. The crystals were treated with an ethanolic solution of picric acid to give a picrate of **7a** (4.3 g quantitative yield), yellow needles, mp 180.5—182° (lit.[5] mp 179.5°).

b) In Dioxane: A suspension of **6a** [4.04 g, mp 168—169° (decomp.)], in dioxane (60 ml) was heated under reflux for 9 hr. The reaction mixture was treated in a similar manner to that described above in a) to give 1.15 g (82% yield) of **7a**, which gave 3.83 g (quantitative yield) of a **7a** picrate.

c) In Nitrobenzene: A suspension of **6a** [4.04 g, mp 168—169° (decomp.)], in nitrobenzene (60 ml) was heated at 105—110° for 10 hr. Water (40 ml) was added to the cooled reaction mixture and the precipitates were filtered off. The pale yellow filtrate was washed with C_6H_6 (30 ml × 2). The aqueous solution was concentrated under reduced pressure. The residue was treated with an ethanolic solution of picric acid to give a picrate of **7a** (0.24 g, 5% yield).

d) In AcOH: A suspension of **6a** [4.04 g, mp 168—169° (decomp.)], in AcOH (60 ml) was heated at 105—110° for 10 hr. The solvent was removed at reduced pressure and H_2O (40 ml) was added to the residue. The black precipitates were filtered off and the filtrate was concentrated. The residue was treated with an ethanolic solution of picric acid to give a picrate of **7a** (0.34 g, 7% yield).

e) In MeOH–Dioxane: A suspension of **6a** [4.04 g, mp 168—169° (decomp.)], in MeOH–dioxane (4:1) (60 ml) was heated under reflux for 10 hr. Treatment of the reaction mixture in a similar manner to that described in a) gave **7a** (0.72 g, 52% yield), which gave 2.43 g (quantitative yield) of a **7a** picrate in quantitative yield.

f) In EtOH–conc. HCl: A suspension of **6a** [4.04 g, mp 168—169° (decomp.)], in EtOH–conc. HCl (40:3) (60 ml) was heated at 80—85° for 10 hr. Treatment of the reaction mixture in a similar manner to that described in d) gave a picrate of **7a** (1.75 g, 33% yield).

g) In H_2O–conc. HCl: A suspention of **6a** [4.04 g, mp 168—169° (decomp.)], in H_2O–conc. HCl (40:3) (60 ml) was heated at 90—95° for 10 hr. Treatment of the reaction mixture in a similar manner to that described in d) gave a picrate of **7a** (3.39 g, 72% yield).

Preparation of Lutidine N-Oxide (7d)——a) To an ice-cooled solution of N-(2,4-dinitrophenyl)-3,5-lutidinium chloride (**5d**) (4.65 g) in MeOH (10 ml) was added dropwise a solution of NH_2OH HCl (2.08 g) and Et_3N (3.00 g) in MeOH (20 ml) with stirring. Triethylamine (1.50 g) was added to the mixture and the mixture was allowed to stand at room temperature overnight, during which time color of the mixture gradually changed from colorless to red-black. The red-black precipitates were collected, washed thoroughly with MeOH, H_2O, MeOH and ether to give a crude **6d** [1.57 g, mp 123—125° (decomp.)]. A suspension of the crude **6d** (1.57 g) in dioxane–H_2O (4:1) (30 ml) was heated under reflux for 6 hr. The solvent was removed at reduced pressure and H_2O (20 ml) was added to the residue. The insoluble stuff was filtered off and the filtrate was concentrated. The residue was treated with an ethanolic solution of picric acid to give a picrate of **7d** [1.39 g, 32.5% yield from **5d**], yellow needles, mp 134—135°. *Anal.* Calcd. for $C_{13}H_{12}O_8N_4$: C, 44.32; H, 3.43; N, 15.91. Found: C, 44.57; H, 3.66; N, 15.72.

b) To a suspension of 5-(2,4-dinitroanilino)-2,4-dimethyl-2,4-pentadienal (**8d**) (4.37 g) in MeOH (10 ml) was added a solution of NH_2OH HCl (2.08 g) and Et_3N (3.00 g) in MeOH (20 ml). The mixture was stirred at room temperature for 5 hr, during which time the orange crystals of **8d** gradually changed to reddish-violet crystals. The crystals were collected and washed thoroughly with MeOH, H_2O, MeOH and ether to give reddish-violet crystals of a crude **6d** (3.20 g), mp 123—125° (decomp.), which was used to the next cyclization. A suspension of the crude **6d** (3.20 g) in dioxane–H_2O (4:1) (60 ml) was treated in a similar manner to that described in a) to give a picrate of **7d** [1.97 g, 45.8% yield from **8d**], yellow needles, mp 134—135°.

General Procedure for the Preparation of N-Aminopyridinium Chlorides (10a,b,d) from N-(2,4-Dinitrophenyl) pyridinium Chloride Derivatives (5a,b,d)——a) To an ice-cooled solution of **5a,b,d** (0.015 mole) in MeOH (30 ml) was added dropwise a solution of NH_2NH_2 H_2O (0.03 mole). Triethylamine (0.015 mole) was added to the mixture and the mixture was allowed to stand at room temperature overnight. The precipitates were collected and washed thoroughly with MeOH, H_2O, MeOH and ether to give a crude **9a,b,d.** A suspension of the crude **9a,b,d** in dioxane–H_2O (4:1) (80 ml) was heated under reflux until the suspension changed to a clear solution. The mixture was acidfied with HCl (0.02 mole). The solvent was removed at reduced pressure and H_2O (50 ml) was added to the residue. The precipitates were filtered off. The filtrate was decolored with animal charcoal. The colorless filtrate was concentrated to yield white hygroscopic needles, which were treated with an ethanolic solution of picric acid to give a picrate of **10a,b,d.**

b) To an ice-cooled solution of **5a,b,d** (0.01 mole) in H_2O (8 ml) was added dropwise a solution of NH_2-$NH_2 \cdot H_2O$ (0.01 mole) with stirring. The mixture was allowed to stand at room temperature for 3 hr. Dioxane (32 ml) was added to the mixture. The mixture was refluxed for several hours. After the solvent was removed at reduced pressure at 40—50° and H_2O (50 ml) was added to the residue. The precipitates were filtered off. The filtrate was decolored with animal charcoal. The colorless filtrate was concentrated to give white hygroscopic needles, which were treated with an ethanolic solution of picric acid to give a picrate of **10a,b,d,** yellow needles. Yield and mp of the picrate of **10a,b,d** are described in Table V.

N-Aminopyridinium Chloride (10a) from N-(2,4-Dinitrophenyl)pyridinium Chloride (5a)——a) To an ice-cooled solution of **5a** (4.23 g) in MeOH (30 ml) was added dropwise a solution of $NH_2NH_2 \cdot H_2O$ (1.5 ml)

Table V. Yield of N-Aminopyridinium Chloride Derivatives (**10a,b,d**)

	R_1	R_2	R_3	Yield (%) of **10** (as picrate) by the route of **5** → **10**	mp (°C) of **10** (as picrate)
a	H	H	H	50	147—152 (lit.[a] 154)
b	Me	H	H	34	147—149 (lit.[b] 149)
d	Me	H	Me	47	163—165 (lit.[b] 164.5)

a) lit. 10*c*) *b*) lit. 11)

with stirring. Triethylamine (1.50 g) was added to the mixture and the mixture was allowed to stand at room temperature for 1 hr. The precipitates were collected and washed thoroughly with MeOH, H_2O, MeOH and ether to give a crude **9a** [4.0 g, mp 143—144° (decomp.)]. A suspension of the crude **9a** (4.0 g) in dioxane–H_2O (4:1) (80 ml) was heated under reflux until the suspension changed to a clear solution. The cooled solution was acidified with conc. HCl (2 ml), the solvent was removed at reduced pressure and H_2O (50 ml) was added to the residue. The precipitates were filtered off. The filtrate was decolored with animal charcoal (1 g). The colorless filtrate was concentrated to give white hygroscopic needles, which were treated with an ethanolic solution of picric acid to give a picrate of **10a** (0.39 g, 8% yield), yellow needles, mp 147—152° (lit.[10c] 154°).

b) To an ice-cooled solution of **5a** (2.82 g) in H_2O (8 ml) was added dropwise a solution of $NH_2NH_2 \cdot H_2O$ (0.5 ml) with stirring. The mixture was allowed to stand at room temperature overnight. Dioxane (32 ml) was added to the mixture. The mixture was heated under reflux for 11 hr. The solvent was removed at reduced pressure and H_2O (50 ml) was added to the residue. The precipitates were filtered off. The filtrate was decolored with animal charcoal (1 g). The colorless filtrate was concentrated to give colorless hygroscopic needles, which were treated with an ethanolic solution of picric acid to give a picrate of **10a** (1.60 g, 50% yield), yellow needles, mp 147—152° (lit.[10c] mp 154°).