Studies on Ring-opening of Heterocyclic Compounds. II\(^1\)
Alternative Preparation of Pyridine N-Oxide and N-Aminopyridinium Chloride

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Preparations of pyridine N-oxide (7a) and N-amino- pyridinium chloride (10a) by ring opening of a quaternary pyridinium salt and successive recyclication were investigated, and the following methods established. Treatment of N-(2,4-dinitrophenyl)pyridinium chloride (5a) with hydroxylamine, followed by refluxing the resulting 5-(2,4-dinitroanilino)-2,4-pentadienial 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-amino- pyridinium chloride (10a) in 50% yield from pyridine. The methods were proved to be applicable to conversions of \(\beta\)-, \(\gamma\)-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-pentadienial oxime (6a) and the cyclization reaction of 6a to 7a. The method for N-amino- pyridinium 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 resulting 5-(2,4-dinitroanilino)-2,4-pentadienial hydrazone (9a) gave 10a. These methods were also successfully applied to \(\beta\)-, \(\gamma\)-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 1939\(^5\) the cyclizations of gluconaldehyde sodium salt (1), gluconaldehyde dioxime (2) and gluconaldehyde 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 gluconaldehyde derivatives, (1–3), 5-acetoxy-2,4-pentadienial (4),\(^6\) 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-pentadienial oxime (6a) shown in Chart 2 was found to be best in yield and also in ease of operation. This route provides a preparative method without oxidizing reagent for pyridine N-oxides.

The gluconaldehyde 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

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(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 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 the NMR spectrum of trans-trans 1,3-butadienes and assigned $J$ 13.1—17.7 cps for the trans double bonds and

<table>
<thead>
<tr>
<th>Glut. deriv.</th>
<th>Yield of Glut. deriv. from py. (%)</th>
<th>Solvent</th>
<th>Yield of py. N-oxide (7a) (as picrate) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a, b)</td>
<td>71</td>
<td>methanol</td>
<td>34</td>
</tr>
<tr>
<td>2b)</td>
<td>22b)</td>
<td>methanol</td>
<td>5b)</td>
</tr>
<tr>
<td>3b)</td>
<td>82</td>
<td>nitrobenzene</td>
<td>67</td>
</tr>
<tr>
<td>4b)</td>
<td>67</td>
<td>dioxane-water</td>
<td>50</td>
</tr>
<tr>
<td>5a a, c)</td>
<td>98</td>
<td>dioxane-water (4:1)</td>
<td>50</td>
</tr>
<tr>
<td>6a</td>
<td>94</td>
<td>dioxane-water (4:1)</td>
<td>82</td>
</tr>
</tbody>
</table>

<ref>a) A solution of the glutaraldehyde derivative and hydroxylamine hydrochloride (1 equiv. mole) was refluxed.

b) lit. 5
c) lit. 5</ref>
TABLE II. Ring-opening Reaction of N-(2,4-Dinitrophenyl)pyridinium Chloride (5a) to 5-(2,4-Dinitroanilino)-2,4-pentadienal Oxime (6a)

<table>
<thead>
<tr>
<th>5a (mole)</th>
<th>NH$_2$OH-HCl (mole)</th>
<th>Et$_2$N (mole)</th>
<th>Solvent (ml)</th>
<th>Yield of 6a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.015</td>
<td>0.02</td>
<td>0.035</td>
<td>MeOH(30)</td>
<td>96</td>
</tr>
<tr>
<td>0.015</td>
<td>0.03</td>
<td>0.045</td>
<td>MeOH(30)</td>
<td>97</td>
</tr>
<tr>
<td>0.015</td>
<td>0.03</td>
<td>0.045</td>
<td>EtOH(160)</td>
<td>95</td>
</tr>
</tbody>
</table>

Fig. 1

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), γ-picoline N-oxide (7c) and 3,5-lutidine N-oxide.

$J$ 10.4—11.3 cps for the 2,3-single bond. Later, Katritzky, et al. showed 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), γ-picoline N-oxide (7c) and 3,5-lutidine N-oxide.

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

<table>
<thead>
<tr>
<th>Solvent (a)</th>
<th>Temperature</th>
<th>Yield of py. N-oxide (7a) (as picrate) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dioxane-water (4:1)</td>
<td>reflux</td>
<td>92</td>
</tr>
<tr>
<td>Dioxane</td>
<td>reflux</td>
<td>82</td>
</tr>
<tr>
<td>Nitrobenzene</td>
<td>105—110°</td>
<td>5</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>105—110°</td>
<td>7</td>
</tr>
<tr>
<td>Dioxane-methanol</td>
<td>reflux</td>
<td>52</td>
</tr>
<tr>
<td>Ethanol-HCl</td>
<td>80—85°</td>
<td>33</td>
</tr>
<tr>
<td>Water-HCl</td>
<td>90—95°</td>
<td>72</td>
</tr>
</tbody>
</table>

(a) Compound (7a) is almost insoluble in H₂O, MeOH and benzene. Cyclization of 7a by refluxing in these solvents failed.

![Chemical structures](image)

Chart 3

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

<table>
<thead>
<tr>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>Yield of 7 (as picrate) (%) by route of 5→6→7</th>
<th>Yield of 7 (as picrate) (%) by route of 5→8→6→7</th>
<th>mp of 7 (as picrate) (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>H</td>
<td>H</td>
<td>88.3</td>
<td>88.3</td>
<td>180.5—182 (lit.(a) 179.5)</td>
</tr>
<tr>
<td>b</td>
<td>Me</td>
<td>H</td>
<td>53.5</td>
<td>—</td>
<td>125—126.5 (lit.(b) 125—126.5)</td>
</tr>
<tr>
<td>c</td>
<td>H</td>
<td>Me</td>
<td>65.5</td>
<td>—</td>
<td>158—159 (lit.(b) 158.7—159.7)</td>
</tr>
<tr>
<td>d</td>
<td>Me</td>
<td>H</td>
<td>32.5</td>
<td>45.8</td>
<td>134—135</td>
</tr>
</tbody>
</table>

(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 glutaraldehyde anil oxime (6a). Heating of 6a in dioxane-water

(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\textsuperscript{10} have been reported on the synthesis of N-aminopyridinium chloride (10a). Among them, the Gösl’s method\textsuperscript{10e} 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-pentadienyl 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\textsuperscript{11} as shown in Chart 5.


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.10) Colorless needles, mp 190° (lit.12) mp 190°—191°.

N-(2,4-Dinitrophenyl)-β-β′-picolinium Chloride (5b) — Prepared from β-β′-picoline in quantitative yield according to the procedure of Vompe, et al.10) Colorless needles, mp 208°—209° (lit.12) 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.15) Colorless needles, mp 163°—164° (lit.13) mp 163°—164°.

N-(2,4-Dinitrophenyl)-3,5-lutidinium Chloride (5d) — A solution of 3,5-lutidine (10.5 g) and 2,4-di- nitrochlorobenzene (20.3 g) in dry-CH₂COCH₃ (160 ml) was refluxed for 5 hr. After cooling, precipitates were collected and recrystallized from EtOH to give 5d (28.4 g, 92%), mp 205°—204° (decomp.). Anal. Caled. for C₁₅H₁₂O₃NCl: 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-pentadial (8a) — Prepared in quantitative yield according to the procedure of Zincke, et al.15) Red crystals, mp 175° (lit.15) mp 180°. NMR (in DMSO) ν: 0.49 (1H, doublet, Jₙₙ = 7.8 cps, H₃), 3.94 (1H, quartet, Jₙₙ = 7.8, Jₙₙ = 15.3 cps, H₃), 2.54 (1H, quartet, Jₙₙ = 15.3, Jₙₙ = 12.7 cps, H₃), 3.40 (1H, triplet, Jₙₙ = 12.7, Jₙₙ = 12.7 cps, H₃), 2.05 (1H, doublet, Jₙₙ = 12.7 cps, H₃), 1.15 (1H, doublet, Jₙₙ = 3 cps, H₃), 1.55 (1H, quartet, Jₙₙ = 3, Jₙₙ = 10 cps, H₃), 2.22 (1H, doublet, Jₙₙ = 10 cps, H₃), —0.48 (2H, singlet, NH₂) (Fig. 1).

ii) To an ice-cooled solution of 5a (2.8 g) in EtOH (100 ml) was added dropwise a solution of Et₂N (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 ace tone to give 8a (1.2 g, 45%), mp 175° (lit.15) mp 180°.

5-(2,4-Dinitroanilino)-2(or 4)-methyl-2,4-pentadial (8b) — Prepared in 92% yield and according to the procedure of Grigor’eva, et al.15) Red needles, mp 161° (lit.16) mp 161°.

5-(2,4-Dinitroanilino)-2(or 4)-dimethyl-2,4-pentadial (8d) — To a solution of 5d (5.0 g) in H₂O (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 H₂O, and recrystallized from CH₂COCH₃ to give red needles of 8d (3.2 g, 69%), mp 135°—136°. Anal. Caled. for C₁₇H₁₄O₃N₂: 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-methyl-aniline according to the procedure of Zincke, et al.14) gave glutaconaldehyde di-N-methyl-anilin hydrogen chloride in 78% yield (lit.13) 70—75%, red needles, mp 118°—120° (lit.13) mp 116—118°. Treatment of glutaconaldehyde di-N-methyl-anilin hydrogen chloride with NaOH solution according to the procedure of Malhotra, et al.10) 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 reacted 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 Monoxide (3) to Pyridine N-Oxide (7a) — i) Preparation of Glutaconaldehyde Mono anil Monoxide (3): Treatment of N-(2,4-dinitrophenyl)-pyridinium chloride (5a) with aniline according to the procedure of Zincke, et al.14) gave a glutaconaldehyde dianil hydrogen chloride in 89% yield, red needles, mp 140° (lit.13) mp 141—142°. A solution of the glutaconaldehyde dianil hydrogen chloride (2.0 g) in MeOH–H₂O (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 H₂O 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 procedure of Baumgarten, et al.5) The reacted 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 Dioxiane–H₂O (4:1): A solution of 3 (1.88 g) in dioxane–H₂O (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°.

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.9 mp 75.5°), prepared from pyridine in 67% yield according to the procedure of Baumgarten, et al,19, in MeOH (20 ml) was added a solution of NH$_2$OH HCl (1.39 g) and NaOH (0.80 g) in H$_2$O (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$_2$CO$_3$) and evaporated at atmospheric pressure to give light yellow needles. The needles were treated with an ethanolic solution of picric acid to give a precipitate of 7a (0.94 g, 29% yield), yellow needles, mp 180.5—182° (lit.9 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$_2$OH HCl (1.39 g) and NaOH (0.80 g) in H$_2$O (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$_2$O (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$_2$CO$_3$). After removal of CHCl$_3$ at atmospheric pressure, the residue was distilled at reduced pressure to give 7a (0.45 g, 50% yield), bp$_{15}$ 136—140° (lit.6 bp$_{15}$ 138—140°), which solidified as colorless crystals. The crystals were treated with an ethanolic solution of picric acid to give a precipitate 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):  
\[ \text{a) From } N\text{-}(2,4\text{-Dinitrophenyl})\text{pyridinium Chloride Derivative (5a—d): } \]  
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$_2$OH HCl (0.03 mole) and Et$_2$N (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$_2$O, MeOH and ether to give a crude 6a—d, which was used to the next cyclization.

\[ \text{b) From } 5\text{-}(2,4\text{-Dinitroanilino})\text{-2,4-pentadienal Derivative (8a,b,d): } \]  
A suspension of 8a,b,d (0.015 mole) in MeOH (10 ml) was added a solution of NH$_2$OH HCl (0.03 mole) and Et$_2$N (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$_2$O, 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$_2$O (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$_2$O (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$_2$CO$_3$). After removal of CHCl$_3$ at atmospheric 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 precipitate of 7a—d.

Pyridine N-Oxide (7a) — i) Preparation of 5-(2,4-Dinitroanilino)-2,4-pentadienal Oxime (8a):  
\[ \text{a) From } N\text{-}(2,4\text{-Dinitrophenyl})\text{pyridinium Chloride (5a): } \]  
An ice-cooled solution of 5a (4.23 g) in MeOH (10 ml) was added dropwise a solution of NH$_2$OH HCl (2.08 g) and Et$_2$N (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$_2$O, MeOH and 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$_9$O$_2$N$_4$: C, 47.48; H, 3.62; N, 20.14. Found: C, 47.79; H, 3.82; N, 20.10.

The aniloxime (6a) was also prepared using EtOH or H$_2$O in place of MeOH as solvent in the above procedure. A reaction of 5a (4.23 g) in EtOH (60 ml) with NH$_2$OH HCl (2.08 g) and Et$_2$N (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$_2$O (10 ml) with NH$_2$OH HCl (2.08 g) and Et$_2$N (3.00 g) in H$_2$O (20 ml) was reacted with red—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):  
A suspension of 8a (3.93 g) in MeOH (10 ml) was added a solution of NH$_2$OH HCl (2.08 g) and Et$_2$N (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 red—violet crystals. The crystals were collected and washed thoroughly with MeOH, H$_2$O, MeOH and ether to give red—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$_2$O (4:1): A suspension of 6a (4.04 g, mp 168—169° decomp.) in dioxane—H$_2$O (4:1) (60 ml) was heated under reflux for 6 hr. The solvent was removed at reduced pressure and H$_2$O (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$_2$CO$_3$). After removal of CHCl$_3$ at atmospheric pressure, the residue was distilled at
reduced pressure to give 7a [1.26 g, 88% yield from 5a], bp_H 136—140° (lit. b bp_H 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. b 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 3.85 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_5 (30 ml x 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 a) gave a picrate of 7a (1.75 g, 33% yield).

g) In H_2O—conc. HCl: A suspension 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-cold 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_4OH 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 125—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. Calc. for C_19H_15O_8N_2: 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-dinitroaniline)-2,4-dimethyl-2,4-pentadienial (8d) (4.37 g) in MeOH (10 ml) was added a solution of NH_4OH 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 125—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 (1.07 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 acidified 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_2NH_2·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·H_2O (1.5 ml)
Table V. Yield of N-Aminopyridinium Chloride Derivatives (10a,b,d)

<table>
<thead>
<tr>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>Yield (%) of 10 (as picrate) by the route of 5 → 10</th>
<th>mp (°C) of 10 (as picrate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>H</td>
<td>H</td>
<td>50</td>
<td>147—152 (lit.a) 154</td>
</tr>
<tr>
<td>b</td>
<td>Me</td>
<td>H</td>
<td>34</td>
<td>147—149 (lit.b) 149</td>
</tr>
<tr>
<td>d</td>
<td>Me</td>
<td>Me</td>
<td>47</td>
<td>163—165 (lit.b) 164.5</td>
</tr>
</tbody>
</table>

a) lit. 10c)  
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, H₂O, 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-H₂O (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 H₂O (50 ml) was added to the residue. The precipitates were filtered off. The filtrate was decolorized 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 H₂O (8 ml) was added dropwise a solution of NH₄H₂SO₄, H₂O (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 1 hr. The solvent was removed at reduced pressure and H₂O (50 ml) was added to the residue. The precipitates were filtered off. The filtrate was decolorized 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, 56% yield), yellow needles, mp 147—152° (lit.10a) 154°).