

# Photochemistry and Thermochemistry of Picolyl Chlorides

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Thermochemistry and photochemistry of picolyl chlorides were studied. The thermal reaction of 2-picolyl chloride in benzene afforded intermolecular condensation product. In the case of 3-picolyl chloride, this type of the reaction did not occur, but polymers were obtained. A cyclic hexamer, suggested by a molecular model, was not formed because of the steric strain and low reactivity. The thermal reaction of 4-picolyl chloride gave a cyclic hexamer as well as a polymer. The cyclic hexamer, identified by NMR spectrum, showed  $\lambda_{\max}$  at 460 nm. The cyclic hexamer was cloven to the linear structure. Photolysis of 2-picolyl chloride at 253.7 nm gave a *para*-isomer followed by polymerization. When a methyl hydrogen of 2-methyl pyridine is substituted by  $\text{CH}_3\text{O}$ , *iso*-PrO, and EtO group, the photoisomerization to the corresponding anilines or *para*-substituted pyridines did not occur within the range of the time used for 2-picolyl chloride. Thermolysis of picolyl chlorides in an acidic methanol solution did not afford any product.

## Introduction

It has been shown by Berlin that 4-picolyl chloride is polymerized by a stepwise mechanism.<sup>1</sup> The polymerization of 2- and 3-picolyl chloride is difficult because of the steric hindrance and the low reactivity, respectively. In this paper, the possibility for the formation of cyclic hexamer, postulated by a molecular model, is studied. Haszeldine isolated the first stable valence bond isomer of a six-membered ring heterocycle.<sup>2</sup> During the course of investigations of the photochemistry of  $\alpha$ -alkylpyridines substituted at the side chain, Ogata and other workers found the photoisomerization of alkyl 2-pyridylacetate and 2-pyridylacetonitrile to alkyl anthranilate and anthranilonitrile, respectively.<sup>3-9</sup> In this paper, the thermolysis of picolyl chlorides in benzene solution and photolysis of 2-picolyl chloride are studied.

## Experimental

**Materials.** Purification of picolyl chlorides; 2-Picolyl chloride·HCl (Aldrich Chemicals Co.) was recrystallized from methanol-diethyl ether (mp 125 °C), 3-picolyl chloride·HCl was sublimed (mp 148 °C), and 4-picolyl chloride·HCl was recrystallized from methanol-diethyl ether (mp 169 °C).

Purified picolyl chloride·HCl was dissolved in distilled water and neutralized with 10 % sodium bicarbonate solution. Free base was extracted three times each with chloroform or dichloromethane and dried over sodium sulfate. Evaporation of the solution under reduced pressure immediately prior to use yielded pure picolyl chloride. Sodium (Wako Pure Chemicals) was used as received. Benzene, acetone, chloroform, diethyl ether, *n*-hexane (Wako Pure Chemicals), dichloromethane (Kanto Chemicals), and methanol (Merck and Wako Chemicals) were used as received or after purification. 2-Py  $\text{CH}_2\text{OCH}_3$  and 2-Py  $\text{CH}_2\text{OPr}^i$  were obtained by photolysis of 2-picolyl chloride in methoxide solution and *i*-propanolic *i*-propoxide solution, respectively (chemical yield; more than 95 %). Kiesel gel GF 254 was used for silica gel thin layer chromatography. TLC pre-coated plates Silica gel 60 with a concentrating zone (Merck) was also used.

Wakogel C-200 was used for column chromatography.

**Irradiation.** The irradiation was carried out in a Rayonet Photochemical Reactor equipped with lamps (RUL 3500 Å D4, RUL 2537 Å B9V) or with a 450 W Hanovia Medium-Pressure Mercury Arc Lamp (CAT. NO. 34245-1).

**Spectra.** <sup>1</sup>H NMR spectra were recorded with a Varian T-60 A spectrometer; chemical shifts were reported in  $\delta$  units. All chemical shifts were reported by using  $\text{Me}_4\text{Si}$  as an internal standard. Perkin-Elmer 267 grating spectrophotometer and Perkin-Elmer 283 B infrared spectrophotometer were used to record ir spectra and Cary 17 Ultraviolet-Visible spectrophotometer was used for absorption spectra.

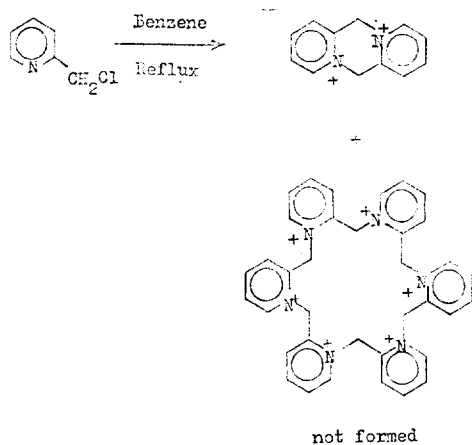
**Thermal Condensation of Picolyl Chlorides.** A benzene solution (500 ml) of 2-picolyl chloride (150 mg) was refluxed in an oil bath for 125 h. On refluxing a benzene solution of 2-picolyl chloride for 125 h, a condensation product was obtained. The singlet [ $\delta(\text{D}_2\text{O})$  4.7 ppm] of methylene protons in NMR spectrum of starting material disappeared and a strong band [ $\text{IR}(\text{KBr})$  760-650  $\text{cm}^{-1}$ ] of C-Cl was very weakened. After the addition of aluminum chloride to a ethylene dichloride solution of 2-picolyl chloride, the mixture was refluxed for 12 h with stirring. Ethylene dichloride was removed under reduced pressure. Acetone was added to the residue and the solution was filtered. Impurities were removed by boiling the ethanol solution with a decolorising charcoal for 2 h, and then filtered. The ethanol was removed under reduced pressure. The product was checked by pre-coated Silica gel 60 TLC plates (solvent;  $\text{MeOH}:\text{Et}_2\text{O}:\text{n-C}_6\text{H}_{14}$  1:1:5 v/v, rf value; ca. 0). Reflux of 3-picolyl chloride (170 mg) in benzene solution (500 ml) under air gave high molecular weight polymers as precipitates. Similarly, 4-picolyl chloride ( $3 \times 10^{-3} M$ ) gave high molecular weight polymers but a cyclic hexamer was obtained in addition to the polymers. The cyclic hexamer was identified by NMR spectral analysis;  $\delta(\text{D}_2\text{O})$  9.1 (12H, *d* of *d*), 8.5 (12H, *d* of *d*), and 8.2 (12H, *d* of *d*). On standing under air at room temperature, the cyclic hexamer was cloven to the linear structure. It was identified by NMR, UV-Visible, and IR spectra;  $\delta(\text{D}_2\text{O})$  9.0 (12H, *d*, broad), 8.0 (12H, *d*, broad), and 6.2

(12H, s, broad).  $\lambda_{\max}(\text{MeOH})$  460, and 260 nm. IR(KBr) 3400, 3030–2920, 1645, 1470, 1365, 1165, and 700  $\text{cm}^{-1}$ . 2-Picolyl chloride in methanolic hydrochloric acid solution was refluxed for 24 h, but there was no reaction product as monitored by TLC and NMR spectrum.

**Photoisomerization of 2-Picolyl Chloride.** A solution of 2-picolyl chloride (150 mg) in methanol (280 ml) was irradiated under nitrogen for 17 h (450 W Hanovia Medium-Pressure Mercury Arc Lamp in ice water-cooled immersion well). UV spectra vs. irradiation time were checked every 1 or 2 h. The solution was evaporated to dryness and the residue was chromatographed on a preparative thin layer chromatography plate in methanol–diethyl ether–*n*-hexane (1:1:5 v/v). The isolated product polymerized under the experimental conditions. When Cl of the 2-methyl pyridine was substituted by  $\text{CH}_3\text{O}$ , *i*-PrO, and EtO group, it was not photoisomerized to the corresponding anilines or *para*-substituted pyridines. It was identified by TLC and NMR spectrum.

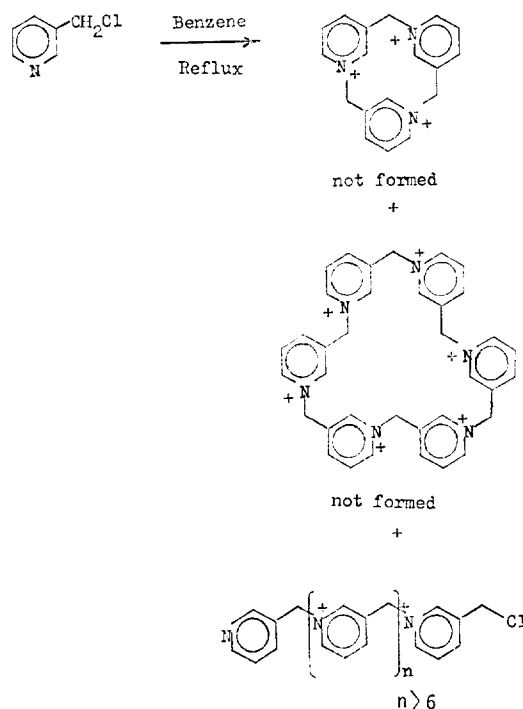
## Results and Discussion

**Thermal Condensation of Picolyl Chlorides.** 2-Picolyl chloride is known to give a self-condensation product and a bimolecular combination was reported to result in the formation of tricyclic *bis*-quaternary salt.<sup>10–11</sup> On refluxing a benzene solution of 2-picolyl chloride for 125 h, the self-condensation product was formed. It was accelerated when aluminum chloride was added as a catalyst. In benzene solution containing aluminum chloride, 2-benzyl pyridine was obtained. But, in ethylene dichloride solution containing aluminum chloride, self-condensation product was obtained. A polymer was not formed because of the steric strain and no cyclic hexamer was formed. The probability of formation of cyclic hexamer was very low because of the steric hindrance between the six  $\text{CH}_2$  groups.

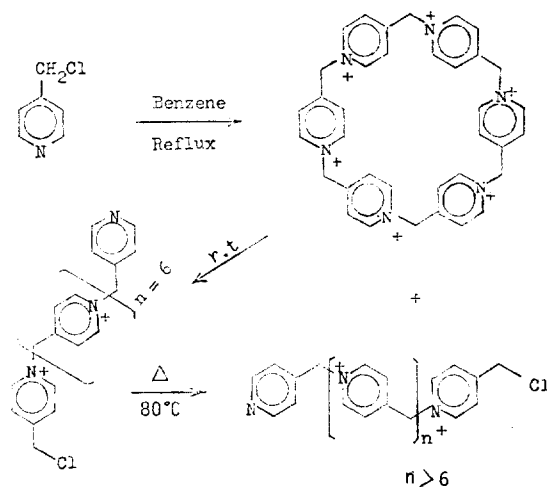


In the case of the thermal reaction of 3-picolyl chloride, a polymer was obtained. The high molecular weight polymer was not soluble in water, methanol, dichloromethane, etc. It was not even soluble in  $\text{CF}_3\text{COOH}$ . Since the steric strain for the cyclic hexamer of 3-picolyl chloride is about half that for the cyclic hexamer of 2-picolyl chloride, the formation of cyclic hexamer of 3-picolyl chloride is more probable.

But none was found. Maybe it is too unstable to be formed at room temperature.

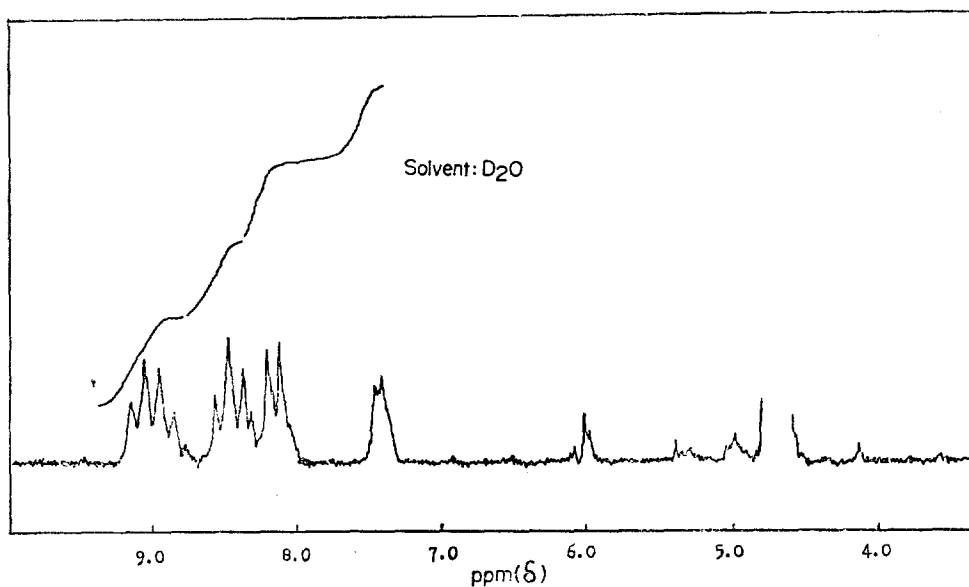


A benzene solution of 4-picolyl chloride was refluxed for 125 h and the solution was filtered to remove the high molecular weight polymers. The solution which is devoid of the polymers was confirmed to be a cyclic hexamer, which was speculated by a molecular model, and characterized by means of NMR spectrum.

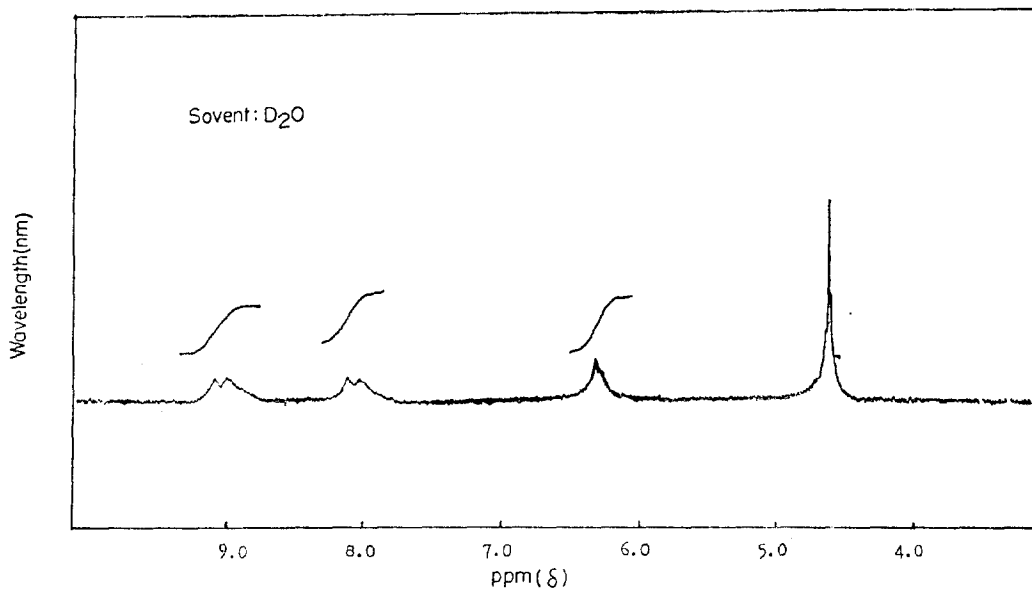


The polymer is likely to be terraced in structure. The steric strain of the cyclic hexamer was much smaller than that of 2- or 3-picolyl chloride. The change in the spatial orientation of the  $\text{CH}_2$  group enable the hexamer to be formed as a cycle. According to the molecular model, the cyclic hexamer is embodied in the form of a cap with a hole at the top to minimize the steric strain.

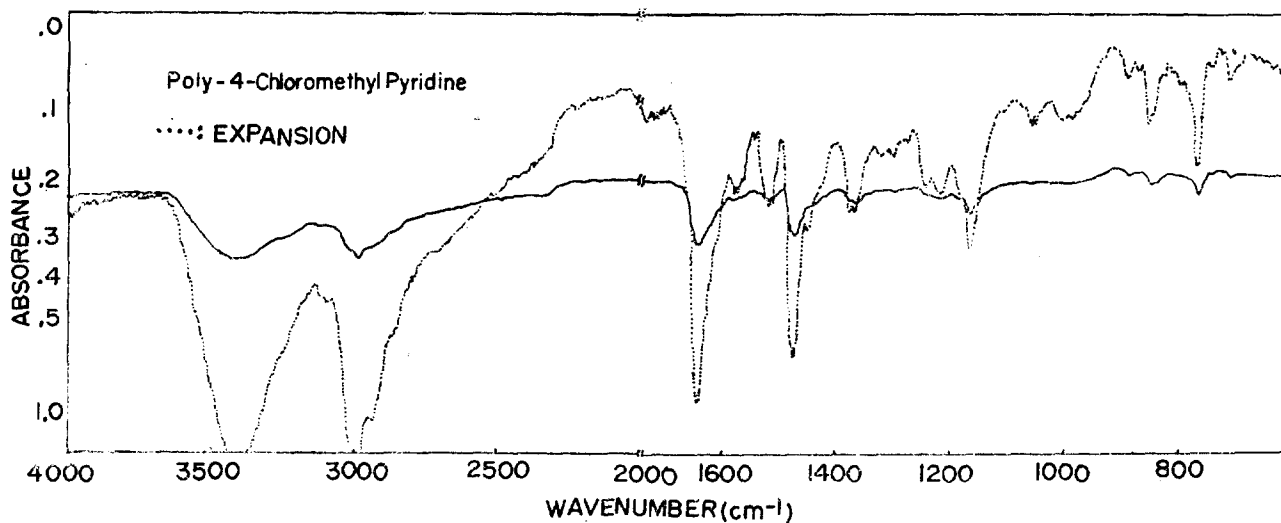
Pure 4-picolyl chloride is a colorless liquid with a pyridine like odor and is a lacrimatory agent. 2- and 4-picolyl chlorides have a nematocidal activity. Meta isomer is known to be a cancer suspect agent. 4-Picolyl chloride as a free base takes on a pink color at room temperature in an hour or



**Figure 1.** NMR spectrum of 'Cyclic Hexamer', the thermal product of 4-picolyl chloride in benzene.



**Figure 2.** NMR spectrum of 'Linear Hexamer', the cleavage product of 'Cyclic Hexamer'.



**Figure 3.** IR spectrum of a Hexamer ( $n=6$ ), i.e., the one of the thermal product of 4-picolyl chloride.

two and polymerize to give a precipitate after several hours. The cyclic hexamer and linear hexamer are both brick-red in color. The molecular weight of the polymer is related to

the reaction temperature. The polymer with low molecular weight is produced at room temperature. It is soluble in water. The high molecular weight polymers prepared by refluxing at 80 °C for 125 h are not soluble in almost any solvent. According to Berlin,<sup>1</sup> the molecular weight of the polymers as determined by concentration of terminal halide is 700 for the polymer prepared at 25 °C, *i.e.*, there are 5–6 monomer units in the chain. The polymers prepared at 100 °C had 8–9 monomer units. The formation of a cyclic hexamer needs a sufficient number of collisions between monomers and a proper temperature. The cyclic structure was postulated through a molecular model and identified by NMR spectrum. Berlin did not make any comment on the cyclic hexamer. Unfortunately the cyclic hexamer was colven to the linear structure at room temperature in about three days. The absorption maximum of this compound in the visible region is at 460 nm. Aqueous

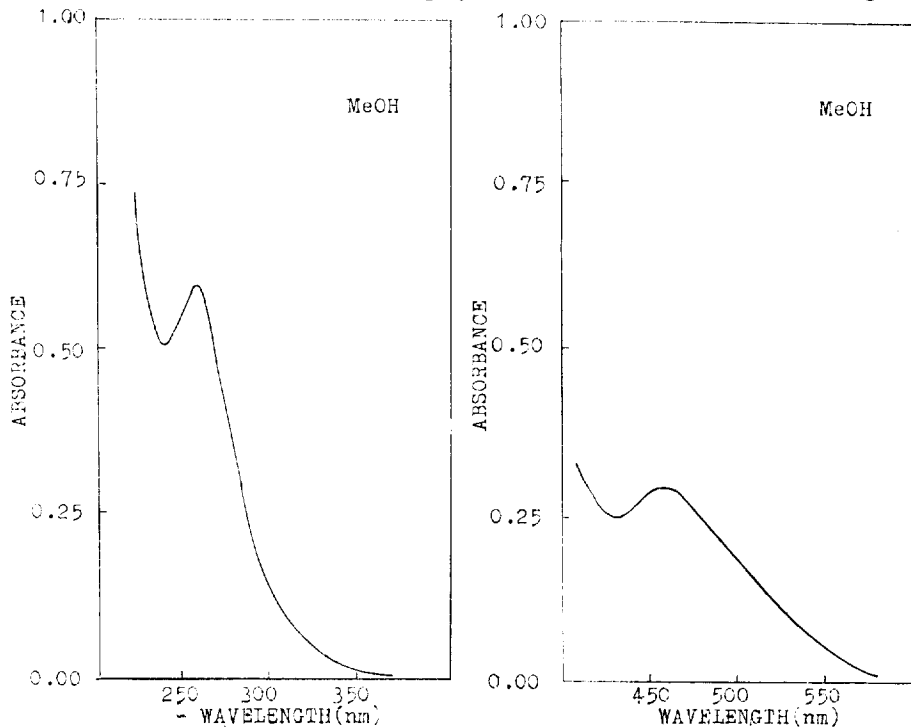


Figure 4. Absorption spectra of a hexamer, *i.e.*, poly-4-chloromethyl pyridine (6 monomer units).

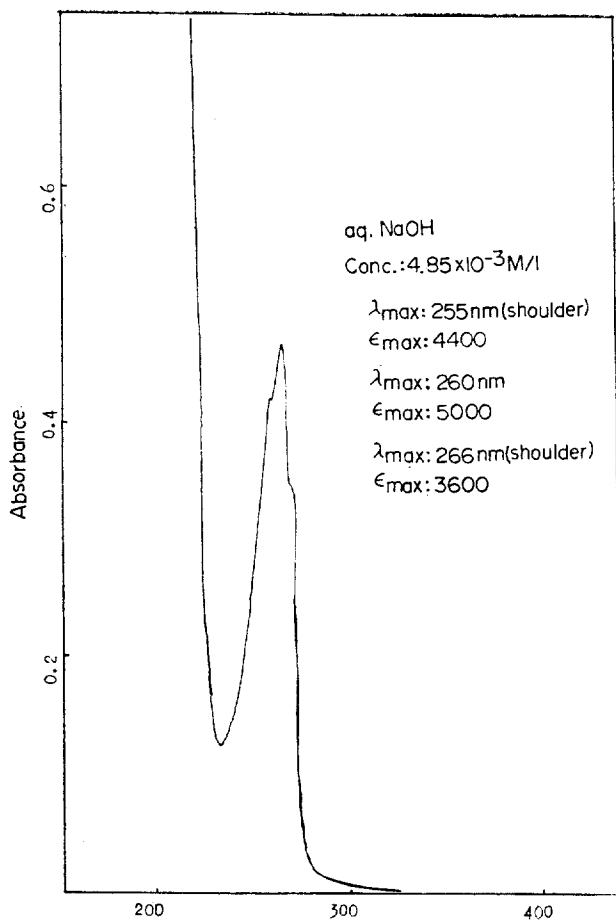


Figure 5. UV spectrum of 2-picolyl chloride in aq. NaOH.

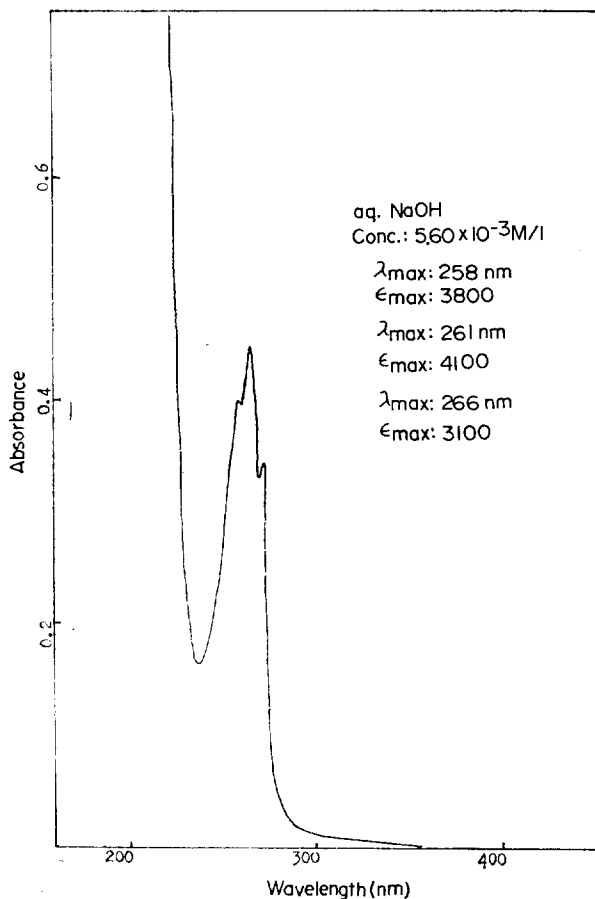
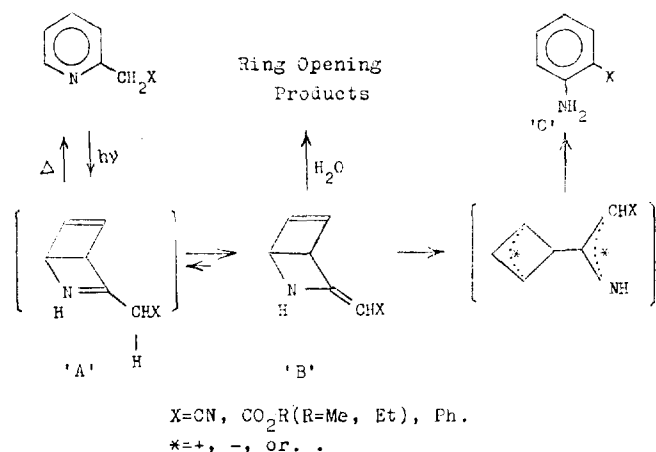


Figure 6. UV spectrum of 3-picolyl chloride in aq. NaOH.

solutions of the hexamer were also red in color. Adding ammoniumhydroxide to the solution of the hexamer turns the brick-red into purple. Under the action of ammonium hydroxide, poly-4-chloromethylpyridine is known to be transformed to the colored polymericyclide.<sup>1</sup>

**Photoisomerization of 2-Picolyl Chloride.** 2-Pyridyl acetonitrile, 2-pyridyl acetate, and 2-benzyl pyridine are photoisomerized to orthosubstituted aniline via a Dewar pyridine tautomer.<sup>3-9</sup> The substituent in the side chain has a double bond character and acts as an electron releasing group. Two hydrogens of the CH<sub>2</sub>X moiety in structure 'A' are activated. Hence 'A' can be converted to 'B' easily as shown below.<sup>9</sup>



However, photolysis of 2-picolyl chloride gave 4-picolyl chloride. UV spectra of picolyl chlorides in aq. NaOH solution were measured (Figures 5-7). UV spectra vs. irradiation time were checked every 1 or 2 h (Figure 8). This photoisomerization is likely to proceed *via* a prismane intermediate.

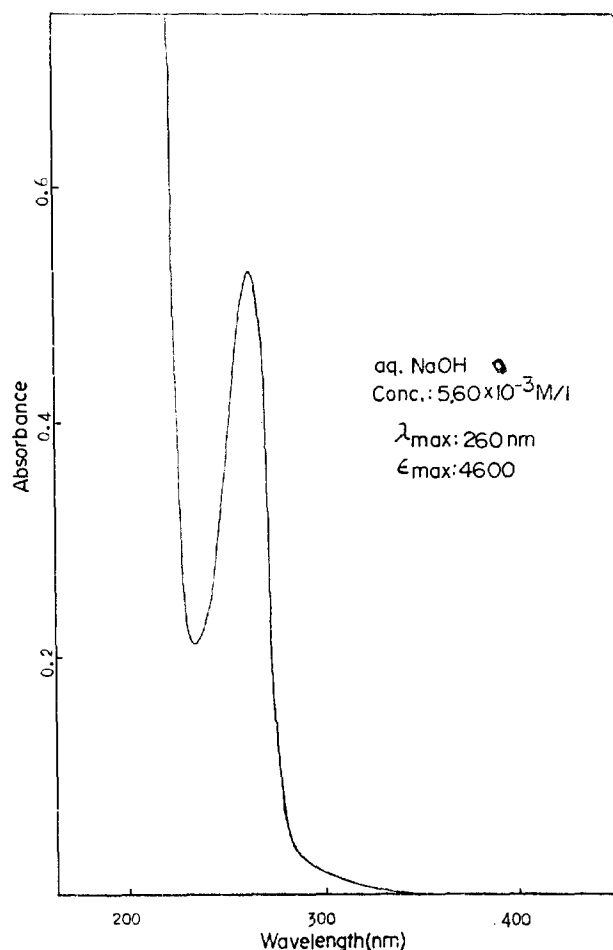
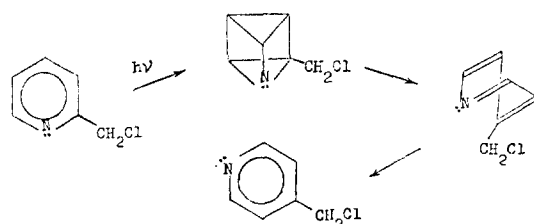


Figure 7. UV spectrum of 4-picolyl chloride in aq. NaOH.

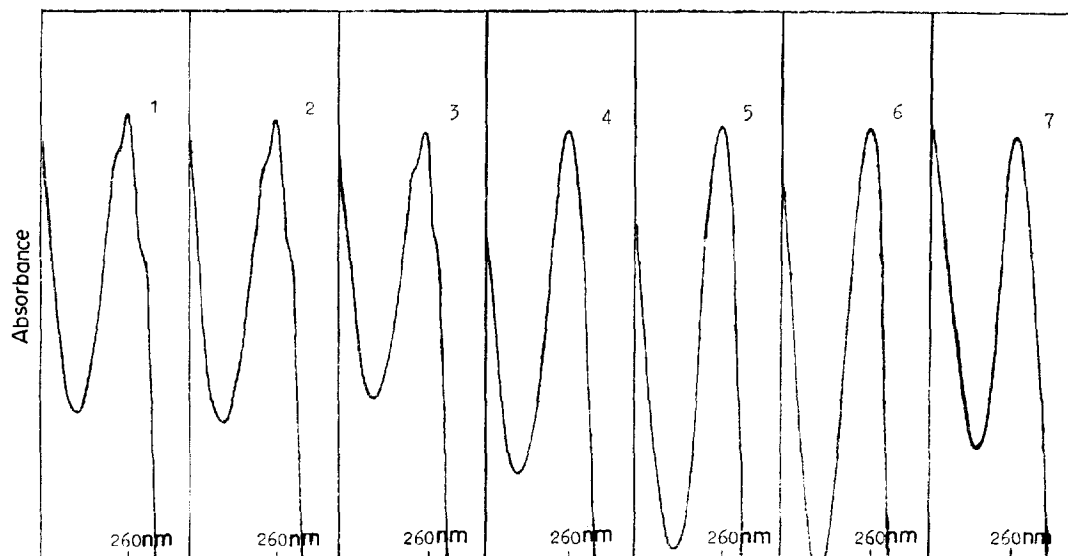
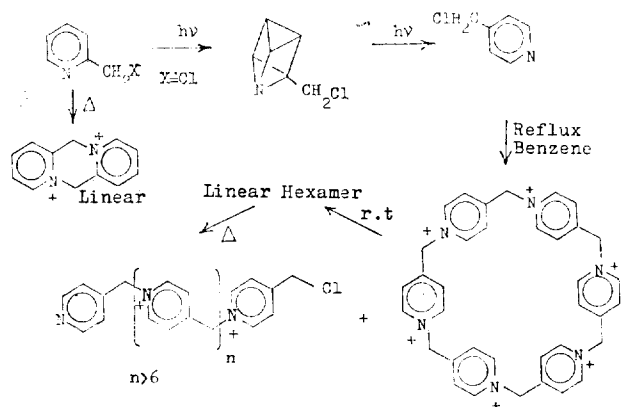


Figure 8. Qualitative description for the change of UV spectrum according to irradiation time in photolysis of 2-Picolyl Chloride in methanol. 1 is absorption spectrum of the reactant. 2, 3, 4, 5, 6, and 7 correspond to the absorption spectrum of the solution irradiated for 1, 3, 5, 9, 11, and 17 h, respectively.



**Scheme 1.** Thermochemical and photochemical profiles of 2-picolyl chloride.

When a hydrogen of 2-methyl pyridine is substituted by  $\text{CH}_3\text{O}$ , *iso*-PrO, and EtO group, it did not undergo photoisomerization to the corresponding aniline or para-substituted pyridines within the range of the time used for 2-picolyl chloride (chemical yield; 0) as checked by TLC and NMR spectrum. When chlorine atom is substituted by CN, COOMe, or Ph, the formation of Dewar pyridines is facilitated because the two methylene hydrogens are activated by the double bonds or the triple bond at the both sides. These hydrogens are at allylic position for two double bonds (or a double bond and a triple bond) at both sides. Since no aniline is obtained

in the case of 2-Py $\text{CH}_3$ <sup>8</sup> and 2-Py $\text{CH}_2\text{Cl}$ , the formation of Dewar pyridines is not likely and the photoisomerization of these compounds to parasubstituted picoline and 4-picolyl chloride occurs probably through prismane intermediates as summarized in scheme 1.

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## Photocyclodimerization of Maleimide

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The photoreaction of maleimide, one of the best model compounds of DNA molecules for psoralen-DNA photoreactions, is studied in order to investigate the photoreactivity and the mechanism of the maleimide-psoralen photoreaction. The (2+2) photocyclodimer of maleimide was obtained in solution state by direct or sensitized irradiation. The rate constant of dimerization is determined by quenching studies and found to be of the order of  $10^9 \text{ M}^{-1}\text{sec}^{-1}$ . The direct dimerization of maleimide is found to undergo through the triplet excited state. The quantum yields of dimerization are dependent on the maleimide concentration.

### Introduction

The (2+2) photocyclodimerization of maleic anhydride and maleimide derivatives has been studied by several groups.<sup>1-8</sup> Maleic anhydride has been reported to photodimerize in the crystalline state.<sup>9,10</sup> Schenck *et al.*<sup>1</sup> reported that the photodimerization of dimethylmaleic anhydride in benzene was photosensitized by benzophenone. Under this condition (which differed mainly in the use of a medium-

rather than a high-pressure mercury arc lamp), the consistent addition of benzophenone slightly reduced the rate of dimerization. The known photodimer of dimethylmaleic anhydride was shown, on chemical and crystallographic evidence, to have *trans* structure.<sup>4</sup> The spectral data of photodimer of N-substituted maleimides are shown in Table 1. However, crystal structure analysis of the monomer indicates neither parallel double bonds nor contacts between two monomer units at distances adequate for photodi-