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Catalytic Reactions of Pyridines. III.[1] γ-Ray-Induced α-Methylation of Pyridine and γ-Picoline with Methanol catalyzed by Nickel Nitrate

Hiroshi Kashiwagi* and Saburo Enomoto

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama-shi, Toyama, 930-01, Japan

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γ-Ray irradiation of a binary solution consisting of pyridine and methanol caused almost no reaction of pyridine. However, the addition of a catalytic amount of nickel nitrate to this binary solution induced the α-methylation of pyridine in good yield upon γ-ray irradiation at room temperature either in air or *in vacuo*. This α-methylation gave α-picoline as a major product. The yield of α-picoline increased with increase in the irradiation time at the initial stage of the reaction, reached a maximum (27.8%) at an irradiation duration of between 8 and 10 h, and then decreased progressively at greater irradiation times. In addition, the yield of α-picoline at a given irradiation time showed a tendency to increase with increasing amount of the nickel nitrate catalyst or with increasing fraction of methanol in the starting solution.

γ-Ray irradiation in the presence of nickel nitrate was also found to induce the catalytic α-methylation of γ-picoline with methanol at room temperature either in air or *in vacuo*, giving 2,4-lutidine as a major product in a maximum yield of 8.3%. Further, the demethylation reaction of α-picoline to pyridine and that of 2,4-lutidine to γ-picoline were also promoted greatly upon γ-ray irradiation at room temperature in air in the presence of both methanol and nickel nitrate.

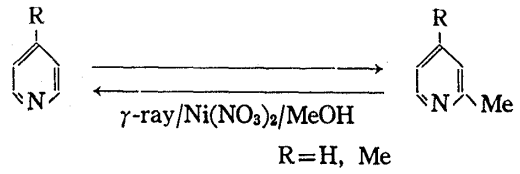
Keywords——pyridine; α-picoline; γ-picoline; 2,4-lutidine; methanol; nickel nitrate; catalyst; methylation; γ-ray

γ-Ray-induced replacement reactions of aromatic compounds have been studied quite extensively, especially as regards the hydroxylation reactions of aromatic compounds in aqueous solutions. However, the yields of hydroxylated derivatives were very low due to the great stability of aromatic rings to γ-rays.[2] On the other hand, the γ-ray-induced alkylation of an aromatic compound has not been reported, although alkylation reactions would be expected to occur (though the yields might be low) upon γ-ray irradiation of an aromatic compound dissolved in a hydrocarbon or an alcohol. Next, attempts were made to activate γ-ray-induced reactions by the use of catalysts. For example, the γ-ray-induced oxidation of hydroxycyclohexadienyl radical, which is the rate-determining step in the hydroxylation of benzene to phenol, was activated by ferricyanide,[3] and the γ-ray-induced activation of oxygen was accelerated in the presence of the oxides of metals or some metal-exchanged zeolites.[4] However, the yields of substituted aromatic compounds still seemed to be low even in the presence of catalysts.

The authors reported previously the thermal amination of pyridine over supported cobalt oxide or supported nickel oxide catalysts[5] and the methylation and ethylation of pyridines

over Ni^{2+}- or Co^{2+}-exchanged zeolites[1] in the vapor phase. The active sites of these reactions were considered to be Ni^{2+} or Co^{2+} and the reactions seemed to proceed by way of complex formation between pyridine and Ni^{2+} or Co^{2+}.

The presence of a catalytic amount of nickel nitrate was found to result in an unexpectedly large increase in the yield of α-picoline when a homogeneous solution containing pyridine and methanol was irradiated with ^{60}Co γ-rays at room temperature either in air or *in vacuo*. The presence of nickel nitrate also greatly increased the formation of 2,4-lutidine from γ-picoline with methanol, as well as the demethylation of α-picoline to pyridine and that of 2,4-lutidine to γ-picoline, as summarized in Chart 1. This is a unique type of γ-ray-induced reaction in the



R=H, Me

Chart 1

following respects. In the first place, the yield of α-methylpyridine produced is exceptionally high as compared with other γ-ray-induced replacement reactions so far investigated. Secondly, γ-ray irradiation was used merely to supply energy for the reaction in the same way that heat is applied in usual thermal catalytic reactions, and no characteristic effect of γ-rays was involved in this reaction.

Experimental

Materials——Pyridine, α-picoline, β-picoline, γ-picoline, and 2,4-lutidine, each having a purity of over 99%, were obtained from a commercial source, and were used after being distilled once. Methanol, nickel nitrate [$Ni(NO_3)_2 \cdot 6H_2O$], and other chemical reagents were of commercial GR grade and were used without further purification. In particular, nickel nitrate was used as a catalyst in the form of the hexahydrate without the removal of any water of crystallization.

Procedure——An ampule of Pyrex glass (20 mm in inside diameter, 2.5 mm in thickness, and about 20 ml in capacity) was usually charged with 2.0 g of either pyridine or γ-picoline, 4.0 g of methanol, and 0.5 g of $Ni(NO_3)_2 \cdot 6H_2O$, and then was sealed in air. If necessary, the solution was degassed by the freeze-and-thaw technique, or was bubbled through with a stream of nitrogen, oxygen, or hydrogen for 30 min before the ampule was sealed. The sealed glass ampule was then exposed to ^{60}Co γ-rays (4.0×10^4 Re/h) at room temperature (23°C) for 2—24 h.

Analysis——The reaction mixture was analyzed by gas chromatography using a 3 mm × 5 m stainless steel column with PEG (400) 15% + Uniport B 85%. The carrier gas was H_2 and the analysis temperature was 110°C. Reaction products were separated by distillation under reduced pressure and each component was identified by comparing its boiling point, UV spectrum, IR spectrum, and relative retention time in gas chromatography with those of an authentic sample. The yield of alkylpyridine was calculated from Eq. (1).

$$\text{Yield} = \frac{\text{mol of alkylpyridine produced}}{\text{mol of pyridine supplied}} \times 100 \text{ (mol \%)} \qquad (1)$$

Results and Discussion

Catalysts Effective for the α-Methylation of Pyridine

When a homogeneous binary solution composed of 2.0 g of pyridine and 4.0 g of methanol was irradiated with ^{60}Co γ-rays for 8 h at room temperature in air, a large portion of pyridine remained unchanged, and only 0.5% α-picoline, 0.1% β-picoline, and 0.2% γ-picoline were formed. Next, the above binary solution was admixed with 0.5 g of either nitrate or chloride of Cr, Mn, Fe, Co, Ni, Cu, Zn, Cd, Ag, Hg, Na, K, Rb, Cs, Mg, Ca, Sr, or Ba, and the mixture was irradiated with γ-rays for 8 h at room temperature in air. There was practically no difference in the yields of picolines between catalyst-containing and catalyst-free solutions for the majority of nitrates and chlorides listed above. When $Co(No_3)_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$,

$Ni(NO_3)_2 \cdot 6H_2O$, or $NiCl_2 \cdot 6H_2O$ was used as a catalyst, however, the yield of α-picoline increased markedly with irradiation time and was maximal (11.3, 9.0, 27.8, or 19.0%, respectively) at the irradiation time of 8 h. In contrast, almost no β-picoline or γ-picoline was formed. Next, the dependence of the yield of α-picoline on the anionic part of the catalyst was examined using a homogeneous solution consisting of 2.0 g of pyridine, 4.0 g of methanol, and 0.5 g of a Ni^{2+}-containing catalyst. Irradiation with γ-rays was carried out for 8 h at room temperature in air. The yield of α-picoline was found to be 24.9% in the case of the nickel acetate catalyst, and to be 17.1 and 18.9%, respectively, for the nickel bromide and the nickel iodide catalysts. However, it was less than 8% when an insoluble or a slightly soluble nickel salt, such as nickel carbonate, nickel sulfate, nickel phosphate, or nickel hydroxide, was used as a catalyst. A similar tendency was observed in the methylation catalyzed by cobalt salts. However, the yield of α-picoline was found to be less than one-half of that obtained using the corresponding nickel salt. For example, α-picoline was produced in 10.1% yield by the γ-ray-induced methylation of pyridine in the presence of cobalt acetate catalyst. Accordingly, the active site in this α-methylation of pyridine appears to be the cationic part of the catalyst, either Ni^{2+} or Co^{2+}, in solution, and the anionic moiety has only a small effect on the catalytic activity.

Moreover, Ni^{2+}- or Co^{2+}-containing catalysts were also found to be effective for the γ-ray-induced α-methylation of γ-picoline. For example, when a binary solution containing 2.0 g of γ-picoline, 4.0 g of methanol, and 0.5 g of $Co(NO_3)_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$, $Ni(NO_3)_2 \cdot 6H_2O$, or $NiCl_2 \cdot 6H_2O$ was irradiated with ^{60}Co γ-rays for 8 h at room temperature in air, the yield of 2,4-lutidine was found to be 3.3, 2.5, 8.3, or 6.7%, respectively.

The γ-ray irradiation of pyridine at room temperature in air was accompanied by the generation of small amounts of gaseous products such as acetylene, ethylene, ethane, and methane. The total yield of gaseous products increased with irradiation time, but was less than 2%, and more than 98% of the pyridine was recovered even after an irradiation period of 24 h, independent of the presence or absence of $Ni(NO_3)_2 \cdot 6H_2O$. In the case of the γ-ray irradiation of picolines and lutidines, the total yield of gaseous products sometimes reached 10% due mainly to decomposition of the substituent groups. However, more than 98% of the pyridine ring remained intact even after an irradiation time of 24 h. Therefore, the pyridine ring was rather stable to γ-ray irradiation.

In the following sections, we will describe in some detail the α-methylations of pyridine and γ-picoline using the nickel nitrate catalyst, the most effective one among the catalysts examined in this section.

α-Methylation of Pyridine with Methanol

Fig. 1 depicts the influence of the duration of γ-ray irradiation on the yield of α-picoline when a homogeneous solution containing 2.0 g of pyridine, 4.0 g of methanol, and 0.5 g of $Ni(NO_3)_2 \cdot 6H_2O$ was irradiated with γ-rays at room temperature either in air or *in vacuo*. Inspection of Fig. 1 shows that the yield of α-picoline increases with increase in the duration of γ-ray irradiation at the initial stage of the reaction, reaches a maximum (27.8%) at an irradiation time between 8 and 10 h, and then decreases with further increase in the irradiation duration. The γ-ray irradiation of this homogeneous solution at room temperature in air for less than 8 h resulted in the formation of α-picoline only. At irradiation durations greater than 8 h, however, the formation of β-picoline was observed and its yield increased with increase of the irradiation time. However, the yield of β-picoline was found to be very low: *e.g.* 0.4 and 1.1% at irradiation durations of 12 and 24 h, respectively. On the other hand, when the solution was irradiated with γ-rays *in vacuo*, the yield of α-picoline was somewhat lower than that obtained in air. However, the accompanying formation of β-picoline was negligibly small even at an irradiation time of 24 h. In contrast to the thermal methylation of pyridine over Ni^{2+}-exchanged zeolites in the vapor phase,[1] 2,6-lutidine was not produced concomitantly

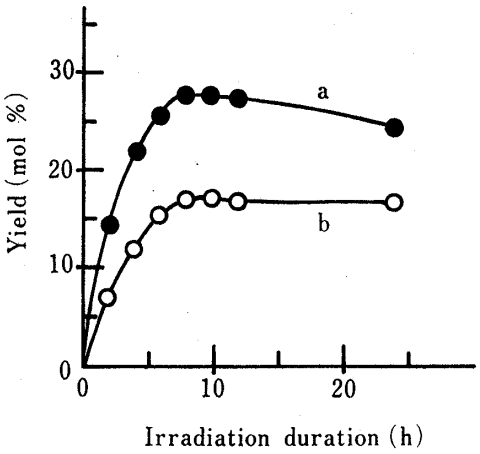


Fig. 1. The Effect of the Duration of γ-Ray Irradiation on the Yield of α-Picoline in the Methylation of Pyridine with Methanol Catalyzed by Nickel Nitrate

Atmosphere: a, in air; b, *in vacuo*.

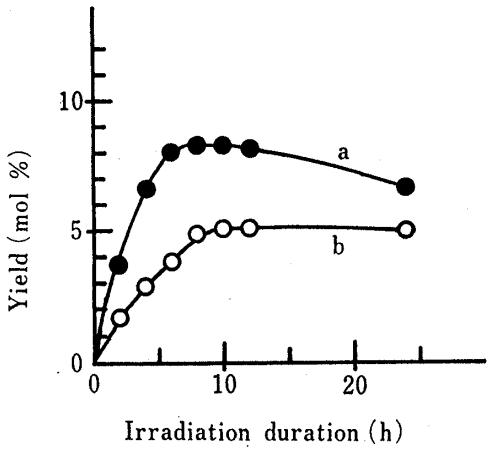


Fig. 2. The Effect of the Duration of γ-Ray Irradiation on the Yield of 2, 4-Lutidine in the Methylation of γ-Picoline with Methanol Catalyzed by Nickel Nitrate

Atmosphere: a, in air; b, *in vacuo*.

upon γ-ray irradiation in air or *in vacuo*. The mode of dependence of the yield of α-picoline on the γ-ray irradiation time in an atmosphere of nitrogen or of hydrogen was almost the same as that *in vacuo*, and the catalytic behavior of $Ni(NO_3)_2 \cdot 6H_2O$ in an atmosphere of oxygen was almost the same as that in air. The yield of α-picoline also varied with the amount of nickel nitrate catalyst used and with the composition of the homogeneous binary solution. For example, when a homogeneous solution consisting of 2.0 g of pyridine and 4.0 g of methanol was admixed with 0.1, 0.2, 0.3, or 0.5 g of $Ni(NO_3)_2 \cdot 6H_2O$, and the mixture was irradiated with γ-rays for 8 h at room temperature in air, the yield of α-picoline was 14.8, 21.6, 25.2, or 27.8%, respectively. Further, when a solution containing 1.0 g of pyridine and 0.25 g of $Ni(NO_3)_2 \cdot 6H_2O$ was admixed with 0.5, 1.0, 2.0, 5.0, or 10.0 g of methanol, and the mixture was irradiated with γ-rays for 8 h at room temperature in air, the yield of α-picoline was found to be 12.4, 19.0, 27.8, 34.8, or 37.1%, respectively.

When a homogeneous solution composed of 2.0 g of pyridine, 4.0 g of methanol, and 0.5 g of $Ni(NO_3)_2 \cdot 6H_2O$ was mixed with 0.1, 0.5, or 1.0 ml of concentrated hydrochloric acid, and the mixture was irradiated with γ-rays for 24 h at room temperature in air, the yield of α-picoline was 24.5, 24.6, or 24.6%, respectively. Therefore, the yield was not affected by the acidity of the solution. However, the yield of simultaneously produced β-picoline increased with increase in the acidity of the solution and was found to be 1.8, 2.8, or 4.2%, respectively. The γ-ray irradiation of α-picoline in the presence of a catalytic amount of $Ni(NO_3)_2 \cdot 6H_2O$ resulted in the formation of a small amount of β-picoline, and the yield of β-picoline was found to increase when hydrochloric acid was added before γ-ray irradiation. Therefore, the isomerization of α-picoline appears to occur readily at high acidity, whereas the α-methylation is not greatly affected by the acidity of the solution.

α-Methylation of γ-Picoline with Methanol

Fig. 2 illustrates the influence of the duration of γ-ray irradiation on the yield of 2,4-lutidine when a homogeneous solution composed of 2.0 g of γ-picoline, 4.0 g of methanol, and 0.5 g of $Ni(NO_3)_2 \cdot 6H_2O$ was irradiated with ^{60}Co γ-rays at room temperature either in air or *in vacuo*. A major product was found to be 2,4-lutidine. It can be seen from Fig. 2 that the yield of 2,4-lutidine upon irradiation in air is somewhat greater than that obtained *in vacuo*. When the solution was irradiated in air, the yield of 2,4-lutidine increased with increasing γ-ray irradiation duration, reached a maximum (8.3%) at an irradiation duration of

8—10 h, and then decreased with further increase of irradiation duration. When the above solution was irradiated with γ-rays at room temperature in air, the yields of pyridine and β-picoline were very low up to an irradiation time of 8 h, then increased with irradiation time, and reached 1.2 and 0.9%, respectively, at the irradiation time of 24 h. However, the formation of pyridine and β-picoline was found to be extremely small even at the irradiation time of 24 h upon irradiation *in vacuo*. Furthermore, the mode of dependence of the yield of 2,4-lutidine on the γ-ray irradiation time in an atmosphere of nitrogen or of hydrogen was found to be almost the same as that *in vacuo*, and the catalytic behavior of $Ni(NO_3)_2 \cdot 6H_2O$ in an atmosphere of oxygen was almost the same as that in air. Moreover, the yield of 2,4-lutidine varied with the amount of the nickel nitrate catalyst used and the composition of the starting solution. For instance, when 0.1, 0.2, 0.3, or 0.5 g of $Ni(NO_3)_2 \cdot 6H_2O$ was admixed with a solution containing 2.0 g of γ-picoline and 4.0 g of methanol, and the mixture was irradiated with γ-rays for 8 h at room temperature in air, the yield of 2,4-lutidine was 4.1, 6.1, 7.5, or 8.3%, respectively. In addition, when 0.5, 1.0, 2.0, 5.0, or 10.0 g of methanol was added to a mixture of 1.0 g of γ-picoline and 0.25 g of $Ni(NO_3)_2 \cdot 6H_2O$, and the whole was irradiated with γ-rays for 8 h at room temperature in air, the yield of 2,4-lutidine was found to be 3.7, 5.8, 8.3, 10.8, or 11.5%, respectively.

Other Reactions

α-Picoline, β-picoline, lutidines, and ethylpyridines were not methylated with methanol upon γ-ray irradiation even in the presence of the nickel nitrate catalyst. For most pyridines, more than 98% of the pyridine ring was recovered intact even at a γ-ray irradiation time of 24 h, and the yields of pyridine and other picolines formed were usually very low. However, the yield of pyridine from α-picoline and that of γ-picoline from 2,4-lutidine were found to be particularly high upon γ-ray irradiation in the presence of both methanol and nickel nitrate. For example, when a solution containing 2.0 g of α-picoline, 4.0 g of methanol, and 0.5 g of $Ni(NO_3)_2 \cdot 6H_2O$ was irradiated with γ-rays for 8, 12, or 24 h, the yield of pyridine was 28, 35, or 44%, respectively. In addition, when a solution containing 2.0 g of 2,4-lutidine, 4.0 g of methanol, and 0.5 g of $Ni(NO_3)_2 \cdot 6H_2O$ was irradiated with γ-rays for 8, 12, or 24 h, a 21, 28, or 37% yield of γ-picoline was obtained. Of course, the demethylation of either α-picoline or 2,4-lutidine no longer occurred in the absence of nickel nitrate. The α-methylation of pyridine seems to be reversible and may be expressed as Eq. (2).

$$C_6H_5N + CH_3OH \rightleftharpoons C_6H_4NCH_3 + H_2O \qquad (2)$$

However, the amount of water formed in the methylation of pyridine with methanol was very small. Further, when a solution containing 2.0 g of α-picoline, 4.0 g of water, and 0.5 g of $Ni(NO_3)_2 \cdot 6H_2O$ was irradiated with γ-rays at room temperature in air for 8 h, 29% pyridine and only 9% methanol were produced. Although methanol was probably produced from the methyl group of α-picoline and water, the yield of methanol was much lower than expected. Taking into account the yields of water and methanol, this α-methylation may not be reversible probably due to the decomposition of water or methanol by γ-ray irradiation.

None of the pyridines, including pyridine and γ-picoline, was alkylated upon γ-ray irradiation, even in the presence of nickel nitrate, when ethanol, propanol, or a higher alcohol was used in place of methanol. Consequently, this alkylation is applicable only to the α-methylation of pyridine and γ-picoline with methanol.

Reaction Mechanism

A possible reaction mechanism can be proposed on the basis of the results described above, using as an example the γ-ray-induced α-methylation of pyridine with methanol in the presence of nickel nitrate. In the first place, only two cations, Ni^{2+} and Co^{2+}, were able to promote the α-methylation of pyridine. Therefore, the α-methylation of pyridine is suggested to begin with the γ-ray-induced coordination of both pyridine and methanol to Ni^{2+}. Next, the presence

of oxygen was obviously advantageous for the formation of α-picoline because the yield of α-picoline in the presence of air was considerably higher than that *in vacuo*. This result suggests the formation of either a pyridine-methanol adduct as shown in Chart 2 or a complex of this adduct with Ni^{2+} as an intermediate of the reaction. The subsequent dehydration of this adduct by oxidizing agents gives rise to the formation of α-picoline. This dehydration take place even *in vacuo*, probably due to the formation of oxidizing agents by the decomposition of methanol. However, the presence of air was obviously advantageous for the formation of α-picoline. Further, the yield of α-picoline was found to increase with increase in the amount of the nickel nitrate catalyst. This result also supports the formation of the above adduct. That is to say, an increase in the concentration of nickel nitrate results in an increase in the yield of the pyridine-methanol adduct.

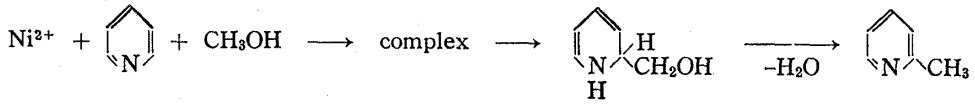


Chart 2

A possible reaction mechanism for the γ-ray-induced α-methylation of pyridine thus consists of three main steps, as shown in Chart 2. The first step is the complexing of both pyridine and methanol to Ni^{2+}, the second step is the formation of a pyridine-methanol adduct, and the third step is the oxidative dehydration of the adduct.

The demethylation of α-picoline to pyridine took place in the presence of the nickel nitrate catalyst both in an aqueous solution and in a methanolic solution of α-picoline. This suggests that the pyridine-methanol adduct can be produced in methanolic solution as well as in aqueous solution by γ-ray irradiation.

On the other hand, the simultaneous coordination either of methanol and a pyridine other than pyridine and γ-picoline, or of pyridine and an alcohol other than methanol to Ni^{2+} is inhibited stereochemically. Accordingly, Ni^{2+} cannot accelerate these reactions. Furthermore, addition of a small amount of ammonum chloride or aqueous ammoina to a solution containing pyridine, methanol, and nickel nitrate, and subsequent γ-ray irradiaton, resulted in a large decrease in the yield of α-picoline.

In any event, this is a unique γ-ray-induced replacement reaction of pyridines, in which γ-rays merely accelerate the catalytic reaction in the same way as heat in a usual thermal reaction, *i.e.*, no characteristic effect of γ-rays is involved in the reaction.

References and Notes

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