leaving a faint reddish yellow liquid of a characteristic odor, which reduced Fehling Solution when warmed. Yield, 0.6 g. Characterized as the hydrochloride, which forms colorless needles of m.p. 253° from MeOH-acetone. Yield of the pure hydrochloride was 20% based on (VII). *Anal.* Calcd. for $C_{13}H_{16}O_2N_2 \cdot HCl$: C, 58.1; H, 6.4; N, 10.4. Found: C, 57.9; H, 6.7; N, 10.0.

Summary

1, 2, 3, 6, 7, 12b-Hexahydro-4*H*-1, 3-dioxolo[*j*]pyridazo[3, 2-*a*]isoquinoline (II) was synthesized by cyclizing 2-(3, 4-methylenedioxyphenethyl)hexahydro-3-pyridazinone followed by reduction with sodium borohyride. This is the first exmple of azabenzoquinoline type of compound recorded in literature. Phrmacological property of the compound (II) is now being examined.

(Received July 31, 1956)

U. D. C. 547.821.411'361

90. Ikuo Suzuki: Rearrangement Reaction of Picolyl Ethers with Sodium Amide. II.

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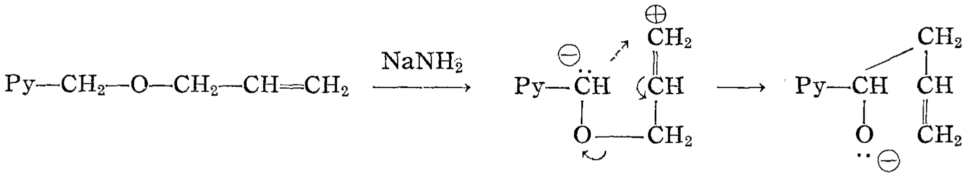
In the preceding paper,[1] it was shown that alkyl- or benzylpyridylcarbinols (α or γ) were obtained from alkyl or benzyl (α or γ)picolyl ethers by the application of sodium amide in decalin, xylene, or benzene.

In the present investigation, it has been found that allyl α-picolyl and γ-picolyl ethers underwent rearrangment to pyridylcarbinols with sodium amide in benzene or xylene, as in the foregoing cases, and further interesting reactions were observed, details of which are set in the present paper.

Reaction of allyl α-picolyl ether (I) or allyl γ-picolyl ether (I′) with equivalent amount of sodium amide in benzene, by boiling for 2～3 hours, respectively yields a viscous oil of b.p$_2$ 83～90° (picrate, m.p. 98～100°) and of b.p$_3$ 122～123° (picrate, m.p. 114～116°). These oily compounds were found to be respectively identical with allyl-α-pyridylcarbinol (II) and ally-γ-pyridylcarbinol (II′), obtained from α- and γ-pyridyl aldehydes by the application of allylmagnesium bromide in ether.



(Py = α or γ-substituted pyridine)

In the case of α-position the rearrangement occurs with good yield (84%) and the starting material is not recovered, but in the case of γ-substituent the rearrangement occurs with a poor yield (15%) and the starting material is recovered in a yield of 65%.

When the same reaction is carried out in xylene at an oil-bath temperature of 130～140°, the yield of rearrangement of the γ-compound increases to 60%, and that of the recovered starting material decreases (30%), while in the case of α-compound, a non-viscous oil of b.p$_5$ 75～81° (picrate, m.p. 91～92°) is obtained in a yield of 57.5%. The

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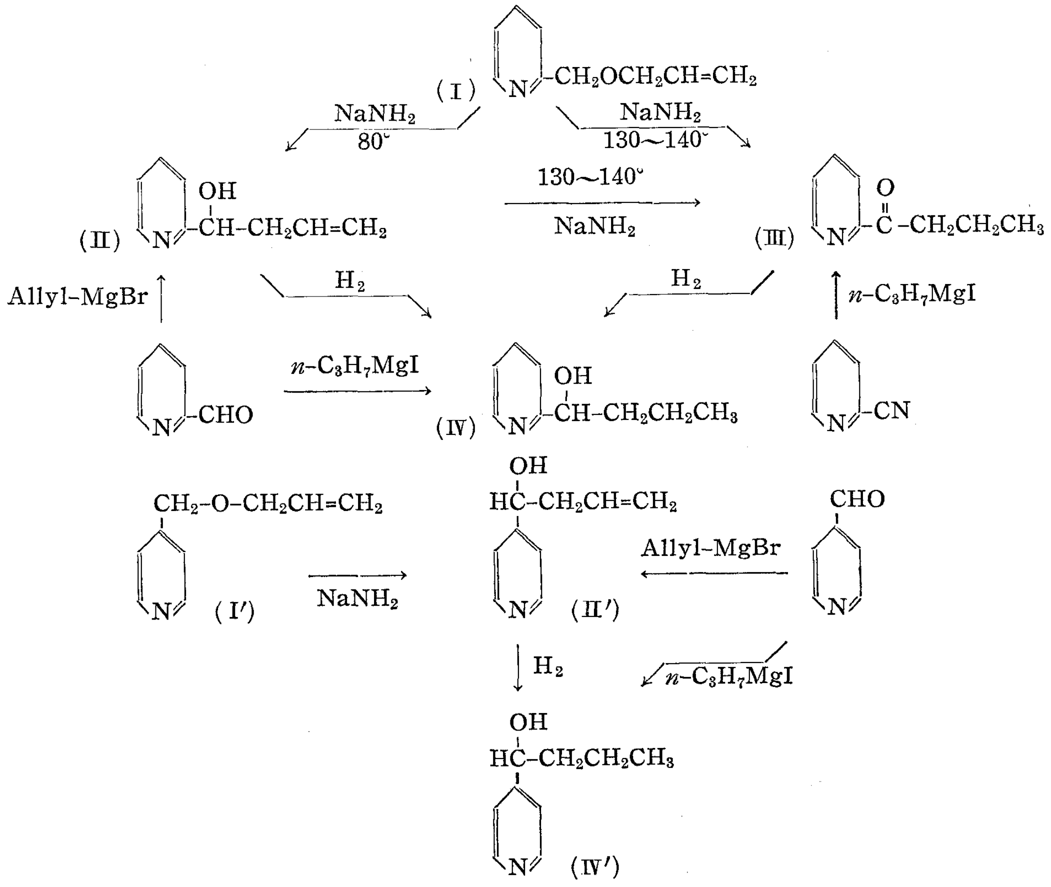
[1] Part I: This Bulletin, **4**, 211(1956).

infrared absorption spectrum of this compound exhibits a strong absorption at ca. 5.9 μ which corresponds to the absorption of a carbonyl (>C=O). At the same time, the absorptions at 10~11 μ and at 3 μ, respectively those of vinyl and hydroxyl groups have disappeared. Further, this compound forms a *p*-nitrophenylhydrazone, m.p. 151~153°. This non-viscous oil was found to be identical with propyl α-pyridyl ketone, obtained from α-cyanopyridine by the application of propylmagnesium iodide in ether.

To a solution of allyl-α-pyridylcarbinol dissolved in xylene, equivalent amount of finely pulverized sodium amide was added, the mixture turned to dark yellow at once, and evolution of ammonia was noticed. This mixture was heated for 2 hours in an oil bath of 130~140°. The reaction product was identical with allyl α-pyridyl ketone described above. On the other hand, in the case of γ-compound, evolution of ammonia was not noticed on addition of sodium amide at the room temperature and the reaction product, obtained on refluxing for 4 hours, was the starting material (20%) and a large amount of resinous substance.

It follows, therefore, that allyl α-picolyl ether underwent rearrangement to carbinol at a relatively low temperature and further formed propyl α-pyridyl ketone when heated to a higher temperature, while a ketone was not obtained from the γ-compound. It seems likely that a certain factor necessary for forming a conjugated system is larger in α-position than that in γ-position.

Allylpyridylcarbinols can be reduced by catalytic reduction with palladium-carbon to propylcarbinols (α and γ) and the products were identical with the products obtained by the application of propylmagnesium iodide to pyridyl aldehydes (α and γ) in ether, and also similarly propyl ketone can be reduced with the same catalyst in hydrogen to propyl-α-pyridylcarbinol.



The writer expresses his gratitude to Dr. T. Kariyone, Director of the Laboratry, for giving him facilities for the present study, to Prof. Eiji Ochiai of the University of Tokyo for his kind advices and encourgement throughout the course of this study, and to Dr. T. Itai for his kind encouragement. The writer is also indebted to Mr. S. Tanaka of the University of Tokyo and Mr. T. Oba for determination of infrared spectra and to Miss Y. Ishigaki for the microanalytical data reported herein.

Experimental

1) **Allyl α-Picolyl Ether** (I)—A mixture of 2.1 g. of α-chloromethylpyridine dissolved in 20 cc. of dehyd. allyl alcohol and 0.4 g. of Na dissolved in 50 cc. of dehyd. allyl alcohol was warmed on a water bath for 30 mins., cooled, and NaCl that formed was removed by filtration. The filtrate was evaporated under a reduced pressure and the residual oil was distilled *in vacuo*. Colorless liquid, b.p$_4$ 76∼77°. Yield, 2.0 g. (81.3%).

Picrate: Yellow needles (from AcOEt), m.p. 108∼109°. *Anal.* Calcd. for $C_9H_{11}ON \cdot C_6H_3O_7N_3$: C, 47.62; H, 3.70; N, 14.81. Found: C, 47.96; H, 3.80; N, 14.65.

2) **Allyl γ-Picoly Ether** (I′)—The same treatment as (I) of 7 g. of γ-cholromethylpyridine hydrochloride afforded 5.0 g. (84.2%) of an oil, b.p$_5$ 94∼96°. Picrate: Yellow prisms (from AcOEt), m.p. 94.5∼96.5°. *Anal.* Found: C, 47.90; H, 3.95; N, 14.24.

3) **Rearrangement Reaction in Benzene**—a) **Allyl-α-pyridylcarbinol** (II): To a solution of 5 g. of allyl α-picolyl ether (I) dissolved in 15 cc. of benzene, finely pulverized $NaNH_2$ was added and the mixture was refluxed for 3 hrs., during which evolution of NH_3 was noticed. After cool, the mixture was poured into ice water, extracted with $CHCl_3$, and $CHCl_3$ and benzene residue was distilled *in vacuo*. Viscous oil, b.p$_2$ 83∼90°. Yield, 4.2 g. (84%). Yield, 3.8 g. of b.p. 94∼100° after redistillation.

Picrate: Yellow plates (from EtOH and benzene), m.p. 98∼100°, undepressed on admixture with the picrate of allyl-α-pyridylcarbinol obtained by the Grignard reaction described under (7). *Anal.* Calcd. for $C_9H_{11}ON \cdot C_6H_3O_7N_3$: C, 47.62; H, 3.70; N, 14.81. Found: C, 47.49; H, 3.69; N, 15.98.

b) **Allyl-γ-pyridylcarbinol** (II′)—To a solution of 2.0 g. of allyl γ-picolyl ether (I′) dissolved in 10 cc. of benzene, 0.6 g. of finely pulverized $NaNH_2$ was added and the mixture was boiled on a water bath for 3 hrs. After cool, the reaction mixture was treated as in (3)(a) and 0.3 g. (15%) of viscous oil, b.p$_3$ 122∼123°, was obtained besides recovery of 1.3 g. (65%) of the starting material (b.p$_3$ 85°; picrate, m.p. 94∼96°).

Picrate: Yellow needles (from MeOH), m.p. 114∼116°. This picrate was identical with that of allyl γ-pyridyl carbinol prepared by the Grignard reaction described under (7). *Anal.* Calcd. for $C_9H_{11}ON \cdot C_6H_3O_7N_3$: C, 47.62; H, 3.70; N, 14.81. Found: C, 47.73; H, 3.93; N, 14.54.

4) **Rearrangement Reaction in Xylene**—a) **Propyl α-Pyridyl Ketone** (III): To a solution of 4 g. of allyl α-picolyl ether (I) dissolved in 10 cc. of xylene, 1.2 g. of finely pulverized $NaNH_2$ was added and the mixture was heated in an oil bath of 130∼140° for 3 hrs. After cool, the mixture was poured into ice water, extracted with $CHCl_3$, and the solvent was evaporated from the extract. After distilling off xylene under reduced pressure, the residue was distilled *in vacuo*. Colorless non-viscous oil, b.p$_5$ 75∼81°. Yield, 2.3 g. (57.5%). Resinous residue, 1.0 g.

Picrate: Yellow needles (from AcOEt), m.p. 91∼92°. This picrate was identical with the picrate of allyl α-pyridyl ketone obtained by the Grignard reaction described under (8). *Anal.* Calcd. for $C_9H_{11}ON \cdot C_6H_3O_7N_3$: C, 47.62; H, 3.70; N, 14.81. Found: C, 47.42; H, 3.52; N, 14.71.

p-Nitrophenylhydrazone: Orange needles (from EtOH), m.p. 151∼153°. *Anal.* Calcd. For $C_{15}H_{16}O_2N_4$: C, 63.38; H, 5.63; N, 19.72. Found: C, 63.29; H, 5.28; N, 19.90.

b) **Reaction of Allyl-α-pyridylcarbinol (II) and Sodium Amide**—To a solution of 1.5 g. of allyl-α-pyridylcarbinol (II) dissolved in 8 cc. of xylene, 0.45 g. of finely pulverized $NaNH_2$ was added and the mixture was heated in an oil bath of 130∼140° for 2 hrs. The treatment of this reaction mixture as in (4)(a) afforded 0.75 g. (50%) of colorless oil, b.p$_2$ 65∼66°. Resinous residue, 0.6 g.

Picrate: m.p. 90∼92°, undepressed with the picrate of propyl α-pyridyl ketone.

c) **Allyl-γ-pyridylcarbinol** (II′)—To a solution of 2.0 g. of allyl γ-picolyl ether (I′) dissolved in 10 cc. of xylene, 0.6 g. of $NaNH_2$ was added and the mixture was heated in an oil bath of 130∼140° for 3 hrs. The reaction mixture was treated as in (4)(a) and 1.2 g. (60%) of viscous oil, b.p$_3$ 122°, was obtained besides recovery of 0.6 g. (30%) of the starting material. The picrate, m.p. 114∼116°, was identical with the picrate of propyl-γ-pyridylcarbinol.

d) **Reaction of Allyl-γ-pyridylcarbinol (II′) and Sodium Amide**—To a solution of 2.0 g. of allyl-γ-pyridylcarbinol dissolved in 10 cc. of xylene, 0.45 g. of $NaNH_2$ was added and the mixture was refluxed for 4 hrs. The treatment of this reaction mixture as in (4)(a) afforded 0.3 g. of viscous oil, b.p$_3$ 115∼120°. The picrate, m.p. 114∼116°, was identical with the picrate of allyl-γ-pyridylcarbinol.

5) **Reduction of Allylpyridylcarbinols—a) Propyl-α-pyridylcarbinol (IV)** : A solution of 0.5 g. of allyl-α-pyridylcarbinol (II) dissolved in 10% HCl was catalytically reduced with Pd-C(30%), absorbing about 1 mole of H_2. After removal of the catalyst, HCl was distilled off, the residue was dissolved in a small amount of water, basified with K_2CO_3. and extracted with ether. The ether residue was distilled *in vacuo*. Colorless viscous oil, b.p$_2$ 80°. Yield, 0.4 g.

Picrate : Yellow prisms (from AcOEt), m.p. 133～135°, undepressed on admixture with the picrate of propyl-α-pyridylcarbinol, obtained by the Grignard reaction described under (7). *Anal.* Calcd. for $C_9H_{13}ON \cdot C_6H_3O_7N_3$: C, 47.37, H, 4.21; N, 14.74. Found : C, 47.05; H, 4.02; N, 14.92.

b) **Propyl-γ-pyridylcarbinol (IV′)**—A solution of 1.0 g. of allyl-γ-pyridylcarbinol (II′) dissolved in 10% HCl was catalytically reduced with Pd-C, absorbing about 150 cc. of H_2. After removal of the catalyst, HCl was distilled off and white crystalline residue of hydrochloride was obtained.

Hydrochloride : Colorless scales (repeated recrystallization from MeOH-AcOEt), m.p. 119～120°; yield, 1.0 g.

Picrate : Yellow needles (from AcOEt), m.p. 127～129°, was identical with the picrate obtained from the Grignard reaction described under (7). *Anal.* Calcd. for $C_9H_{13}ON \cdot C_6H_3O_7N_3$: C, 47.37; H, 4.21; N, 14.74. Found : C, 47.38; H, 3.85; N, 14.63.

6) **Reduction of Propyl α-Pyridyl Ketone**—A solution of 1.1 g. of propyl α-pyridyl ketone (III) dissolved in 10% HCl was catalytically reduced with Pd-C, absorbing about 180 cc. of H_2. The catalyst was filtered off, the filtrate was concentrated, basified with K_2CO_3, and extracted with ether. The ether residue was distilled *in vacuo*. Colorless viscous oil, b.p$_2$ 80～83°. Yield, 0.9 g. The picrate; m.p. 133～135°, was identical with the picrate obtained from (5) (a).

7) **Grignard Reaction of pyridyl Aldehydes**—To a solution of α- or γ-pyridyl aldehydes dissolved in dehyd. ether, dehyd. ether solution of alkylmagnesium bromide was added dropwise under stirring and the mixture was heated in a water bath for 30 mins. After all were added, the mixture was acidified with conc. HCl on cooling, basified with 10% NaOH, and extracted with ether. The ether residue was distilled *in vacuo*.

Pyridyl carbinols obtained	Yield	Grignard Reagt.	Picrate, m.p.(°C)
Allyl-α-	36%	Allyl•MgBr	98～99°
Allyl-γ-	36%	Allyl•MgBr	114～116°
Propyl-α-	64%	*n*-C_3H_7MgI	133.5～135°
Propyl-γ-	42%	*n*-C_3H_7MgI	127～129°

No depression of m.p. was observed on admixture with the alkylpyridylcarbinols obtained by the rearrangement reaction described above.

8) **Grignard Reaction of α-Cyanopyridine**—To a solution of 0.7 g. of α-cyanopyridine in dehyd. ether a dehyd. ether solution of propylmagnesium iodide was added dropwise under stirring and the mixture was heated in a water bath for 30 mins. The treatment of this reaction mixture as in (7) afforded 0.7 g. of colorless oil, b.p$_2$ 63～65°.

Picrate : m.p. 85～90°, repeatedly recrystallized from MeOH to m.p. 91°.

p-Nitrophenylhydrazone : m.p. 150～151°.

The picrate and *p*-nitrophenylhydrazone were identical with those of propyl α-pyridyl ketone, obtained by the rearrangement reaction. Infrared specturm of the oil of b.p$_2$ 63～65° was identical with that of propyl pyridyl ketone, obtained by rearrangement reaction.

Summary

Allylpyridylcarbinols (α or γ) were obtained from allyl picolyl ethers (α or γ) by the application of sodium amide in benzene. When the same reactions was carried out in xylene at 130～140°, the yield of rearrangement product increased in the γ-compound, while a non-viscous oil was obtained from the α-compound. This non-viscous oily product was found to be identical with propyl α-pyridyl ketone.

(Received August 27, 1956)