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# 65. Seiji Miyano and Nobuhiro Abe: C-Alkylation of Active Methylene Compounds by Means of Alcohols. III.*1,2 A New Synthesis of 1,2-Dipyridylethylene and Related Compounds.

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A new method for the syntheses of 1,2-dipyridylethylene and its derivatives is described. The method involves condensation between N-oxides of picoline, lutidine, and quinaldine and pyridinemethanol in the presence of potassium hydroxide. Some stilbazole syntheses were also described.

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Carbon-benzylation of "active side-chain" attached to pyridine and quinoline ring by means of benzyl-alcoholic potassium hydroxide has previously been reported by Avramoff and Sprinzak[1] and the reaction was explained by the process involving 1) condensation of pyridine base with benzaldehyde*4 and 2) subsequent reduction of the resulting styryl derivative by benzyl alcohol (Chart 1).

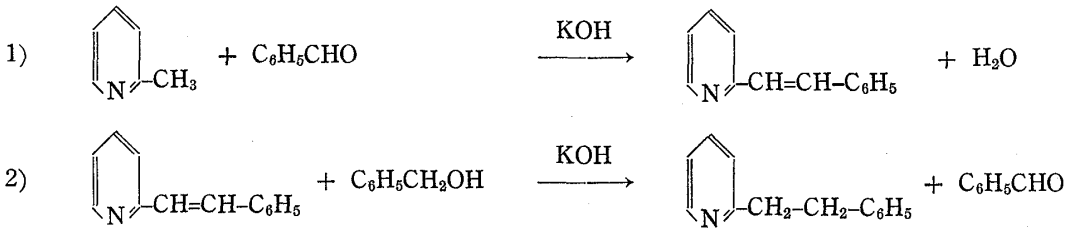


Chart 1.

In the course of an unrelated investigation one of the present authors recently reported[2] that the deoxygenation of pyridine and quinoline 1-oxides was readily effected by benzyl alcoholic or 2-pyridinemethanolic potassium hydroxide (Chart 2).

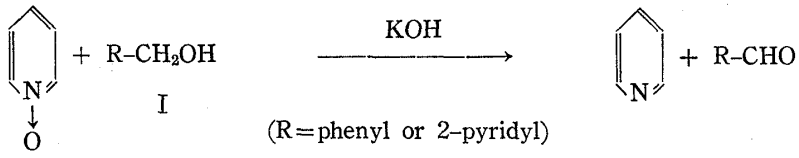


Chart 2.

This observation coupled with the Avramoff's has led us to attempt a synthesis of 2-stilbazole (II, R=phenyl) and related compounds starting with 2-picoline 1-oxide and benzyl alcohol since it seemed probable that 2-picoline 1-oxide, when treated with the above reagent, might be deoxygenated to 2-picoline which in turn react with benzaldehyde to give 2-stilbazole as final product (Chart 3).

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*1 Part I. S. Miyano, Y. Sako: This Bulletin, **13**, 1372 (1965).
*2 Part II. S. Miyano, N. Abe: Tetrahedron Letters, **14**, 1509 (1966).
*3 Nanakuma, Fukuoka (宮野成二, 安倍宣博).
*4 A small amount of benzaldehyde contained in benzyl alcohol induced the reaction, benzaldehyde reformed in equation 2 being reused to the equation 1. See ref. 1).

1) M. Avramoff, Y. Sprinzak: J. Am. Chem. Soc., **78**, 4090 (1956).
2) S. Miyano: This Bulletin, **14**, 663 (1966).

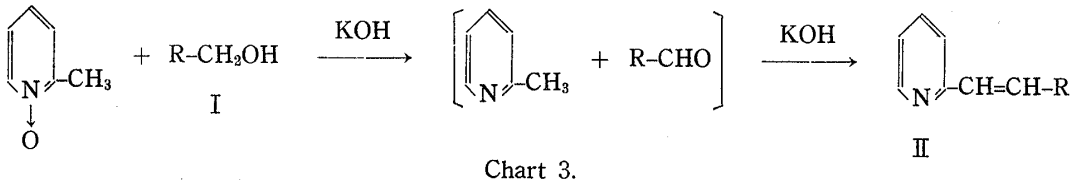

Chart 3.

The initial part of this investigation was directed at stilbazole synthesis. Having found that 2-stilbazole (II, R=phenyl) was obtained only in poor yield, the later work has been directed toward the synthesis of 1,2-di-(2-pyridyl)-ethylene (II, R=2-pyridyl) and derivatives employing 2-picoline 1-oxide and 2-pyridinemethanel (I, R=2-pyridyl) and this paper deals, for the most part, with the synthesis of 1,2-dipyridylethylene and derivatives.

When 2-picoline 1-oxide was condensed with benzyl alcohol in the presence of potassium hydroxide 2-stilbazole was formed in 19.3% yield. Similar type of condensations employing other three oxides of 4-picoline, quinaldine and lepidine with benzyl alcohol proceeded only in unsatisfactory yields, *i.e.*, 35.4%, 27.6%, and 11%, respectively. No advantage seems to be gained from this method for the synthesis of 2-stilbazole and derivatives since they can usually be prepared in better yields by direct condensation between picolines and benzaldehyde in a well-documented method.[3~5]

1,2-Di-(2-pyridyl)-ethylene (II, R=2-pyridyl) and related compounds are rarely encountered in literature in spite of the relatively simple structures, and this might be due to the less accessibility of 2-pyridinealdehyde as a starting material. The search for the literature revealed that only 1,2-di-(2-pyridyl)-[6] and 1,2-di-(4-pyridyl)-ethylene[7] had been synthesized by the condensation between 2- and 4-picoline and 2- and 4-pyridinealdehyde only in poor yields.

A method just outlined in stilbazole synthesis has now proved to be an effective means of synthesizing a series of 1,2-dipyridylethylenes in a convenient way. The procedure consists of dropwise addition*5 of picoline 1-oxides into the preheated mixture of pyridine alcohol and potassium hydroxide followed by reflux of the resulting mixture at 150~160° for the periods between two to five hours.

The yields of the condensations employing 2-pyridinemethanol are moderate (40~48%), whereas those with 4-pyridinemethanol (I, R=4-pyridyl) and 2-hydroxymethyl-6-methylpyridine (I, R=2-(6-methylpyridyl)-) are somewhat lower (15~35%). However, the present method is evidently simpler than the previous method[6~7] employing picoline and less accessible pyridine aldehydes[8] since readily available pyridine alcohols are used instead of pyridine aldehydes. 2-Pyridinemethanol is obtained[9~11] by rearrangement of 2-picoline 1-oxide in the presense of acetic anhydride followed by hydrolysis of the resulting 2-pyridinemethanol acetate, and 4-pyridinemethanol[10] and 2-hydroxymethyl-6-methylpyridine[12] can also be prepared in a similar fashon.

*5 Dropwise addition prevents frothing of the reaction mixtures.

3) P. Schwarz: Ber., **24**, 1676 (1891).
4) B. D. Shaw, E. A. Wagstaff: J. Chem. Soc., **1933**, 77.
5) C. E. Kaslow, R. D. Stayner: J. Am. Chem. Soc., **67**, 1716 (1945).
6) C. Harries, G. H. Lenart: Ann., **410**, 110 (1915).
7) H. J. Thayer, B. B. Corson: J. Am. Chem. Soc., **70**, 2330 (1948).
8) E. H. Rodd: "Chemistry of Carbon Compounds," Vol. IX, 552, Elsevier Publishing Company, London (1956).
9) G. Kobayashi, S. Furukawa: This Bulletin, **1**, 347 (1953).
10) V. Boekelheide, W. J. Linn: J. Am. Chem. Soc., **76**, 1286 (1954).
11) O. H. Bullitt, J. T. Maynard: *Ibid.*, **76**, 1370 (1954).
12) G. Kobayashi, S. Furukaka, Y. Kawata: Yakugaku Zasshi, **74**, 790 (1954).

Infrared spectra of all 1,2-dipyridylethylenes obtained by this procedure show strong absorption band at 975~991 $cm^{-1}$ which is characteristic to *trans* ethylenic double bonds.

## Experimental

**2-Stilbazole**——2-Picoline 1-oxide (10.9 g., 0.1 mole) was added dropwise onto preheated benzyl alcoholic KOH made from 1.5 g. (0.027 mole) of KOH and 10.8 g. (0.1 mole) of benzyl alcohol. The resulting mixture was stirred and refluxed at 160~165° for 4.5 hr. $H_2O$ was distilled as it formed. The cooled mixture was extracted with $CHCl_3$, the $CHCl_3$ layer was washed with $H_2O$, and extracted with 10% HCl. The aqueous layer was then neutralized with $K_2CO_3$, extracted with $CHCl_3$, and the solvent removed. The residual oil solidified on standing to a pale yellow prisms, m.p. 90.5~91°(from EtOH), reported[5] 90°. Yield 3.5 g. (19.3%).

**4-Stilbazole**——This was prepared from 10.9 g. (0.1 mole) of 4-picoline 1-oxide, 10.8 g. (0.1 mole) of benzyl alcohol in the presence of 1.5 g. (0.027 mole) of KOH according to the method described for the preparation of 2-stilbazole. The reaction mixture was refluxed at 160° until the evolution of $H_2O$ ceased. This required 3.5 hr. The cooled mixture was taken up in benzene, the benzene solution washed with $H_2O$ and extracted with 10% HCl. The extract was neutralized with $K_2CO_3$ to deposit crude crystals which was washed with $H_2O$, and extracted with ether. The ether layer was dried over anhydrous $K_2CO_3$ and the removal of ether gave 6.4 g. (35.4%) of pale yellow prisms, m.p. 118~124°. A sample recrystallized from EtOH has m.p. of 126~127°, reported[5] 127~128°.

**2-Styrylquinoline**——A mixture of 16 g. (0.1 mole) of quinaldine 1-oxide, 10.8 g. (0.1 mole) of benzyl alcohol and 1.5 g. (0.027 mole) of KOH was heated at 170° for 40 min. during which evolution of $H_2O$ was carried to completion. The reaction mixture was cooled and extracted with benzene. The organic layer was washed with $H_2O$ and the solvent removed *in vacuo*. The residue was triturated with conc. HCl thoroughly to separate HCl salt of 2-styrylquinoline as pale yellow needles which was neutralized with 10% NaOH to give 6.4 g. (27.6%) of the product. Two recrystallizations from ether gave colorless prisms, m.p. 99~100°, reported[5] 98~98.5°.

**4-Styrylquinoline**——A mixture of 8 g. (0.05 mole) of lepidine 1-oxide, 5.4 g. (0.05 mole) of benzyl alcohol was heated in the presence of 0.78 g. (0.014 mole) of KOH at 170~180°. The reaction proceeded vigorously and the whole mixture solidified to pale brownish cake after 30 min. The cooled mixture was taken up in $CHCl_3$, the $CHCl_3$ solution washed with $H_2O$ and the solvent removed. Conc. HCl was added to the residue and the precipitated HCl-salt was collected by filtration and washed with $CHCl_3$. 10% NaOH was added to the HCl-salt to liberate free base which was extracted with $CHCl_3$, the $CHCl_3$ extract dried over anhydrous $K_2CO_3$ and the solvent removed *in vacuo*. The product, m.p. 88~90°, was obtained in 11% yield. After recrystallization from EtOH, it melted at 92°, reported[5] 91.5~92°.

**1,2-Di-(2-pyridyl)ethylene**——A mixture of 1.5 g. (0.027 mole) of KOH and 10.9 g. (0.1 mole) of 2-pyridinemethanol was placed in a flask fitted with a mechanical stirrer, a dropping funnel and a distillation apparatus, and the temperature was raised to 150°. Then 10.9 g. (0.1 mole) of 2-picoline 1-oxide was added with stirring. Soon after the first addition was made $H_2O$ started to distil briskly. After completion of $H_2O$ distillation, the mixture was heated at 160° for 3.5 hr. The whole mixture solidified on cooling. $H_2O$ was added and insoluble crystals were filtered, washed with $H_2O$, and recrystallized from ether to give 8 g. (44%) of the product as colorless needles, m.p. 118~119°, reported[6] 118~119°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 991 (*trans* -CH=CH-)

**1-(2-Pyridyl)-2-(2-quinolyl)ethylene**——Quinaldine 1-oxide (6.3 g., 0.04 mole) was added portionwise to a mixture of 0.5 g. (0.009 mole) of KOH and and 4.3 g. (0.04 mole) of 2-pyridinemethanol and the mixture was stirred and refluxed for 3.5 hr. at 150~160°. Unreacted quinaldine was removed by steam distillation, the residue extracted with benzene, and the benzene extract chromatographed. 4.6 g. (46.5%) of light yellow needles were obtained and recrystallized from petroleum ether, m.p. 95~96°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 977 (*trans* -CH=CH-). *Anal.* Calcd. for $C_{16}H_{12}N_2$: C, 82.73; H, 5.21; N, 12.06. Found: C, 82.75; H, 5.31; N, 12.14.

**1-(2-Pyridyl)-2-(4-pyridyl)ethylene**——This compound was prepared by the two different procedures:

From 4-picoline 1-oxide and 2-pyridinemethanol: To a preheated mixture (bath temperature; 150°) of 10.9 g. (0.1 mole) of 2-pyridinemethanol and 1.5 g. (0.027 mole) of KOH, 10.9 g. (0.1 mole) of 4-picoline 1-oxide was added portionwise with stirring and the resulting mixture was stirred and refluxed for 3.5 hr. at 155~160°. The reaction mixture was extracted with $CHCl_3$, the $CHCl_3$ layer dried over anhydrous $K_2CO_3$ and the solvent removed. Vacuum distillation of the residue gave 8.75 g. (48%) of the product, boiling at 155~165°/5 mm. It solidified on standing to colorless platelets. A sample recrystallized from petroleum ether has m.p. 75~76°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 982 (*trans* -CH=CH-). *Anal.* Calcd. for $C_{12}H_{10}N_2$: C, 79.09; H, 5.53; N, 15.38. Found: C, 79.31; H, 5.77; N, 15.36.

From 2-picoline 1-oxide and 4-pyridinemethanol: 2-picoline 1-oxide (10.9 g., 0.1 mole) was dropped to 4-pyridinemethanolic KOH (made from 10.9 g. (0.1 mole) of 4-pyridinemethanol and 1.5 g. (0.027 mole) of

KOH) at 160° in 30 min. The reactants were stirred and refluxed for 3 hr. at 160° and worked up as before. A fraction boiling at 170~175°/7 mm. was collected. Yield 4 g. (22%). It solidified to colorless plates, m.p. 75~76° (from isopropyl ether or petroleum ether), undepressed upon admixture with the sample obtained by the procedure above and having an identical infrared spectrum.

**1-(2-Pyridyl)-2-[2-(6-methylpyridyl)]ethylene**——This was prepared by the following two procedures:

From 2,6-lutidine 1-oxide and 2-pyridinemethanol: 2,6-Lutidine 1-oxide (12.3 g., 0.1 mole) was added to a mixture of 1.5 g. (0.027 mole) of KOH and 10.9 g. (0.1 mole) of 2-pyridinemethanol at 170° in 30 min. The mixture was stirred and refluxed for 4 hr. at 170° and worked up in usual way. The product distilled at 157~162°/6 mm. and weighed 8 g. (40.4%). It solidified to colorless scales, m.p. 56.5~57.5° (from petroleum benzin). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 983 (*trans* -CH=CH-). *Anal.* Calcd. for $C_{13}H_{12}N_2$: C, 79.56; H, 6.16: N, 14.28. Found: C, 79.97; H, 6.33; N, 13.82.

From 2-picoline 1-oxide and 2-hydroxymethyl-6-methylpyridine: A mixture of 10.9 g. (0.1 mole) of 2-picoline 1-oxide, 12.3 g. (0.1 mole) of 2-hydroxymethyl-6-methylpyridine and 1.5 g. (0.027 mole) of KOH was stirred and refluxed for 2 hr. at 160~165° and worked up as before. Vacuum distillation gave 7 g. (35.7%) of the product, b.p. 163~168°/8 mm. It solidified to colorless needles, m.p. 56~57°(from petroleum benzin), which was identical with the authentic sample prepared above in respect to mixed melting point determination and infrared spectrum.

**1,2-Di-[2-(6-methylpyridyl)]ethylene**——A mixture of 12.3 g. (0.1 mole) of 2,6-lutidine 1-oxide, 12.3 g. (0.1 mole) of 2-hydroxymethyl-6-methylpyridine and 1.5 g. (0.027 mole) of KOH was stirred and refluxed for 5 hr. at 165°. Working up the resulting mixture in usual way gave 5.5 g. (27.3%) of the product, b.p. 156~159°/6 mm. which quickly solidified as colorless needles, m.p. 112~113°(from isopropyl ether). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 975 (*trans* -CH=CH-). *Anal.* Calcd. for $C_{14}H_{14}N_2$: C, 79.96; H, 6.71; N, 13.32. Found: C, 80.02; H, 6.67; N, 13.15.

**1-[2-(6-Methylpyridyl)]-2-(4-pyridyl)ethylene**——This compounds was prepared by the following two procedures:

From 4-picoline 1-oxide and 2-hydroxymethyl-6-methylpyridine: A mixture of 10.9 g. (0.1 mole) of 4-picoline 1-oxide, 12.3 g. (0.1 mole) of 2-hydroxymethyl-6-methylpyridine and 1.5 g. (0.027 mole) of KOH was stirred and refluxed for 3 hr. at 165°. The reaction mixture was worked up to give 5.1 g. (26%) of the product. b.p. 170~173°/7 mm. which solidified on standing. One recrystallization from isopropyl ether gave colorless needles, m.p. 71°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 983 (*trans* -CH=CH-). *Anal.* Calcd. for $C_{13}H_{12}N_2$: C, 79.56; H, 6.16; N, 14.28. Found: C, 79.76; H, 6.07; N, 13.91.

From 2,6-lutidine 1-oxide and 4-pyridinemethanol: Equimolar amounts (0.1 mole) of the reactants were stirred and refluxed in the presence of 0.027 mole of KOH and the mixture was solidified after 3 hr. Working up as before gave 3 g. (15.3%) of the product, b.p. 170~175°/7 mm., which solidified to colorless needles, m.p. 71°(from isopropyl ether). This was identified by mixed melting point determination and infrared spectrum.

**1,2-Di-(4-pyridyl)ethylene**——The procedure described for the preparation of 1,2-di-(2-pyridyl)ethylene was used. A mixture of 10.9 g. (0.1 mole) of 4-picoline 1-oxide, 10.9 g. (0.1 mole) of 4-pyridinemethanol and 1.5 g. (0.027 mole) of KOH was stirred and refluxed at 160° for 3 hr. The resulting slurry was triturated with aliquot amount of $H_2O$ and filtered. The collected solid was washed with $H_2O$ and recrystallized from benzene to give 2.1 g. of colorless needles, m.p. 149~150°, reported[7] 151~152°. The filtrate was extracted with $CHCl_3$, washed and dried over anhydrous $K_2CO_3$. After removal of $CHCl_3$ the residual crystals were recrystallized from benzene, m.p. 149~150°. The yield combined with the first crop was 3.3 g. (18.1%). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 983 (*trans* -CH=CH-). *Anal.* Calcd. for $C_{12}H_{10}O_2$: C, 79.69; H, 5.53; N, 15.38. Found: C, 79.52; H, 5.66; N, 15.10.