Base-Catalyzed Reactions. XXXV.[1] The Alkali Metal Catalyzed Reactions of 2- and 4-Picoline with 2- and 4-Vinylpyridine. Disproportionation and Transaralkylation Reactions

NELSON E. SARTORIS[2] AND HERMAN PINES

The Ipatieff High Pressure and Catalytic Laboratory, Department of Chemistry, Northwestern University, Evanston, Illinois 60201

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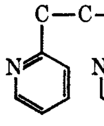
In the sodium- and potassium-catalyzed reactions of 2-picoline with 2-vinylpyridine and 4-picoline with 4-vinylpyridine, polymerization of the vinylpyridines is the initial reaction to occur. At temperatures near 100°, depolymerization occurs, followed by rapid addition reactions to yield **1** and **2**, respectively, as well as diaddition products. The reactions of 2-picoline with 4-vinylpyridine and 4-picoline with 2-vinylpyridine owing to disproportionation give a mixture of the three dipyridylpropanes. The disproportionation of **3** proceeds to yield 4-picoline and 2-picoline in a 2.6:1 ratio, indicating the greater acidity of 4-picoline *vs.* 2-picoline.

The preparation of 1,3-di(2-pyridyl)propane[3] (**1**) and of 1,3-di(4-pyridyl)propane[4,5] (**2**) from the corresponding picolines and vinylpyridines have been reported.

The preparation of the mixed dipyridylpropane, 1-(2-pyridyl)-3-(4-pyridyl)propane (**3**), by the sodium-catalyzed reaction of 2-picoline with 4-vinylpyridine and 4-picoline with 2-vinylpyridine, has also been reported.[5] In a more recent publication, however, Michalski and Zając[6] reported a 42% yield of **3** from 2-picoline and 4-vinylpyridine at reflux temperature. More surprising is their report that 4-picoline and 2-vinylpyridine with sodium did not give the expected mixed dipyridylpropane, but rather resulted in a 27% of **2**.



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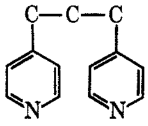

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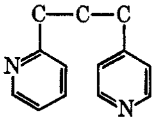

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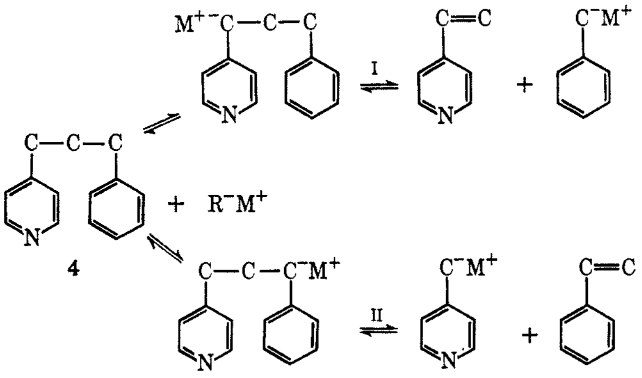
In view of these contradictory results, these reactions were reinvestigated. In the course of the aralkylation reactions studied in the preceding paper,[1] the question of the reversibility of the reaction has also emerged. If the disproportionation reaction can be forced to occur, the question of the path of disproportionation arises, for it is conceivable that the adduct, once formed, may disproportionate *via* two paths, I and II.



To elucidate the answer to these questions, the disproportionation reaction of 1-phenyl-3-(2-pyridyl)propane (**5**) and 1-phenyl-3-(4-pyridyl)propane (**4**) were undertaken. Depending on the relative ease of disproportionation of these two compounds an insight into the relative acidities and nucleophilicities of the compounds involved might be achieved. The disproportionation reaction of **3** was also performed. Depending on the relative amounts of 2- and 4-picoline produced, conclusions concerning their relative acidities may be made.

Discussion of Results

The alkali metal catalyzed reactions of 2- and 4-picoline were performed by first dispersing the alkali metal in the picoline and then adding the vinylpyridine slowly with a syringe. The progress of the reaction was followed by vapor phase chromatography, something which was not done in previous studies.

The reaction of 2-picoline and freshly distilled 2-vinylpyridine was attempted at 0–120° with a 5:1 to 10:1 molar excess of 2-picoline. In each case, polymerization of the 2-vinylpyridine occurred immediately. The reaction was also attempted using undistilled 2-vinylpyridine, which contained *t*-butylcatechol as stabilizer, and by adding significant amounts of hydroquinone to the catalyst, as previous authors[3,6] had done, before the addition of 2-vinylpyridine.

Although polymerization is the primary reaction to take place at all temperatures, in the reactions at 100 and 120° secondary reactions occur with time, leading to the expected 1,3-di(2-pyridyl)propane (**1**). A catalytic depolymerization takes place. The polymers unzips to produce 2-vinylpyridine and immediately undergoes an addition reaction with 2-picoline to yield **1**. Also formed is a significant amount of diaddition product, presumably 1,3,5-tri(2-pyridyl)pentane (**6**). It is reasonable to conclude, therefore, that in work done by previous workers,[3,5] polymerization and depolymerization, although unnoticed, also occurred.

Also given in Table I are the results of a sodium-catalyzed reaction of 4-picoline with 4-vinylpyridine at 90°. In this reaction and in others attempted at various temperatures from 0 to 120°, polymerization of 4-vinylpyridine occurs initially.

Depolymerization occurs more readily with 4-vinylpyridine, since at temperatures near 70° the polymer starts to unzip leading to rapid addition reactions pro-

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[1] (a) Paper XXXIV: H. Pines and N. E. Sartoris, *J. Org. Chem.*, **34**, 2113 (1969). (b) Paper VI of the series Alkylation of Heteroaromatics. For other papers see 1a.

[2] Predoctoral Fellow, National Institutes of Health, 1965–1968.

[3] N. J. Leonard and J. H. Boyer, *J. Amer. Chem. Soc.*, **72**, 4818 (1950).

[4] L. M. Jampolsky, M. Baum, S. Kaiser, L. N. Sternbach, and M. W. Goldberg, *J. Amer. Chem. Soc.*, **74**, 5222 (1952).

[5] G. Magnus and R. Levine, *J. Org. Chem.*, **22**, 270 (1957).

[6] J. Michalski and H. Zając, *J. Chem. Soc.*, 593 (1963).

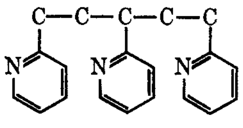
TABLE I

SODIUM-CATALYZED REACTIONS OF 2- AND 4-PICOLINE WITH 2- and 4-VINYLPYRIDINE

Expt	Picoline	Mole	Vinyl-pyridine	Mole	Sodium, g	Temp, °C	Time, hr	Conversion,[b,c] %	Product distribution,[a] % 1	3	2	Diadduct
1	2-	0.20	2-	0.04	0.1	110	4	71	70			21[d]
2	4-	0.20	4-	0.04	0.1	90	2.5	69			93	7[e]
3	2-	0.20	4-	0.03	0.15	105	0.5	16	15.5	84.5		*f*
							1.0	37	44.4	55.6		
							1.5	49	68.3	31.2	0.5	
							2.0	60	78.2	20.8	1.0	
4	4-	0.20	2-	0.03	0.15	105	1.0	9.3	1.0	81.0	18.0	
							2.0	18.4	4.0	65.0	31.0	
							3.0	25.5	7.5	56.9	35.6	
							5.0	38.1	9.0	48.4	42.6	

[a] *sec*-Butylcyclohexane (0.005 mole) was used as internal standard. [b] Percentages are corrected by thermal conductivity factors. [c] Based on vinylpyridine reacted. [d] The product is presumed to be 1,3,5-tri(2-pyridyl)pentane. [e] The product is presumed to be 1,3,5-tri(4-pyridyl)pentane. [f] Also formed small amounts of diaddition products.

ducing 2, and, presumably, 1,3,5-tri(4-pyridyl)pentane (7).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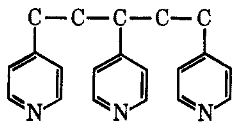
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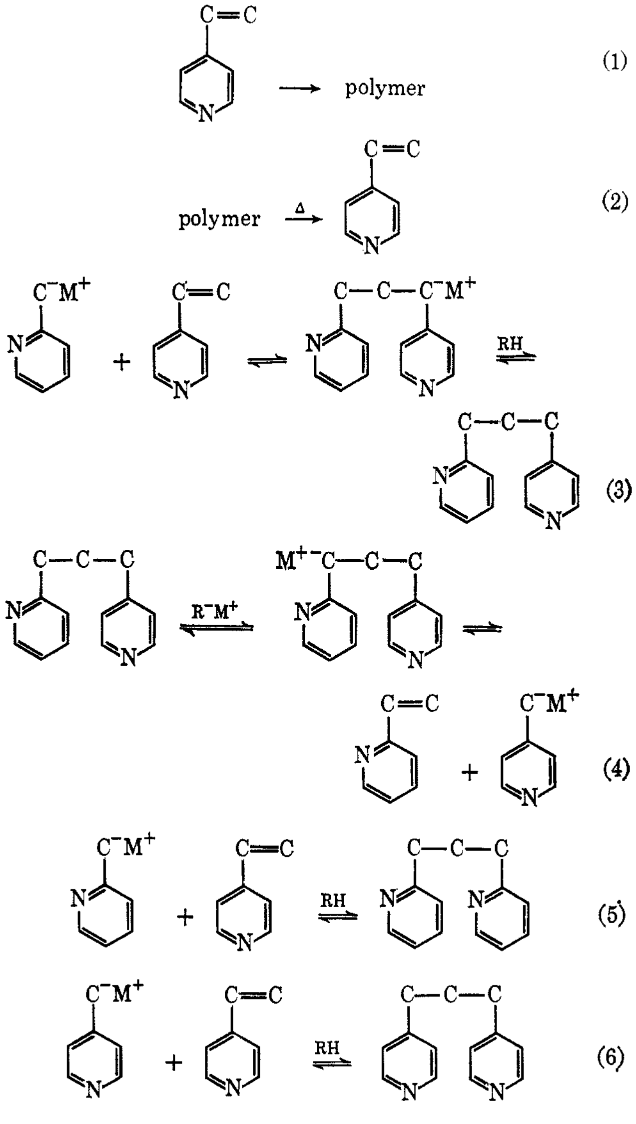
SCHEME I



In an attempt to prepare the mixed dipyridylpropane 3, the alkali metal catalyzed reaction of 2-picoline with 4-vinylpyridine was studied. At temperatures necessary to affect the depolymerization, however, the reaction is complicated by disproportionation of the mixed dipyridylpropane into 4-picoline and 2-vinylpyridine. The 2-vinylpyridine then undergoes an addition reaction with the excess 2-picoline to yield 1, while the 4-picoline reacts with depolymerizing 4-vinylpyridine to give 2 (Scheme I). Also produced are small amounts of diaddition products, presumably 1,3,5-tripyridylpentanes. The distribution of the 1,3-dipyridylpropanes changes substantially with contact time (expt 3 and 4, Table I). This type of reversal and resynthesis in the 1,3-dipyridylpropane system has recently been reported.[6,7]

It should be noted that Michalski and Zając[6] reported the formation of 3 upon refluxing 2-picoline and 4-vinylpyridines. Since vpc was not used in their study, it is conceivable that the product isolated in 42% yield is actually a mixture of 1,3-dipyridylpropanes.

The preparation of pure 3 was also attempted using 4-picoline and 2-vinylpyridine (Expt 4, Table I). Again, the course of the reaction was similar to that reported above.

Disproportionation and Transaralkylation Reactions.—The sodium-catalyzed disproportionation reactions of 4 and 1-phenyl-3-(2-pyridyl)propane (5), respectively, were studied by adding them to a dispersion of catalyst in a "scavenger" alkylpyridine. The olefin product of disproportionation, either styrene or a vinylpyridine, should then be picked up by the "scavenger" alkylpyridine or by another molecule of 4 or 5 in an addition reaction. In effect, a transaralkylation would take place.

In preliminary reactions of 4 using 2-picoline as the "scavenger," the temperature was raised slowly as the progress of the reaction was followed by vpc. At 100°, the disproportionation is slow and proceeds exclusively in one direction to give 4-picoline and styrene. The styrene reacts immediately with the "scavenger" 2-picoline to yield 5, or more favorably (by 20:1) with another molecule of 4 to give 1,5-diphenyl-3-(4-pyridyl)-pentane (8) (Table II). At 120°, the disproportionation is considerably faster. The styrene is picked up again more readily by 4 (by 3:1) than by 2-picoline, although the selectivity is reduced in this case due to the higher temperature and by the fact that at these

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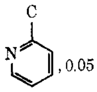
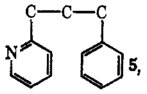
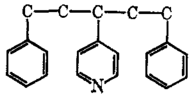
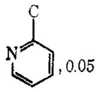
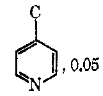
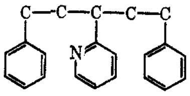
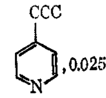
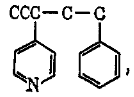
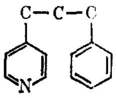
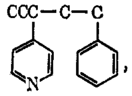
(7) J. Michalski and R. Bodalski, *Roczniki Chem.*, **41**, 549 (1967).

TABLE II

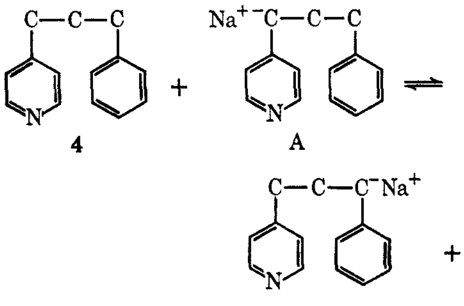
SODIUM-CATALYZED DISPROPORTIONATION AND TRANSARALKYLATION REACTIONS

Expt	Reactants,[a] moles		Temp, °C	Time, hr	Conversion,[b] %	Products,[b,c] %	
5	, 0.05	**4**, 0.05	100	48	9.0[d]	 **5**, 4.8	 **8**, 95.2
6	, 0.05	**4**, 0.05	120	24	21.3[d]	**5**, 27.0	**8**, 73.0
7	, 0.05	**5**, 0.05	120	21	7.1[e]	**4**, 75.8	 **9**, 24.2
8	, 0.025	**4**, 0.025	118	7	5.8[d]	, 47	**8**, 53
9	, 0.025	**5**, 0.025	118	7	2.9[e]	, 78	**9**, 22

[a] Isopropylcyclohexane (0.025 mol) was used as internal standard and 0.05 g of sodium as catalyst in expt 8 and 9 and *sec*-butylcyclohexane (0.005 mol) and 0.1 g of sodium in expt 5–7. [b] Percentages corrected by thermal conductivity factors. [c] A trace of toluene was detected in reactions made at 118 and 120°. [d] Based on 4-picoline produced. [e] Based on 2-picoline produced.

higher conversions of **4**, the greater relative concentration of 2-picoline becomes more important.

If the stability of the initial carbanion was the important factor in determining the path of disproportionation, *i.e.*, if the transition state more closely resembles the reactants, then the expected path of disproportionation would be of carbanion A to give toluene and 4-vinylpyridine. This is not the predominant path of disproportionation, however. Apparently, it is the stability of the resultant carbanion, and not that of the initial carbanion, that governs the path of disproportionation, *i.e.*, the transition states more closely resemble the products. The reaction proceeds to give the more stable carbanion of 4-picoline than of toluene, which is in agreement with their relative acidities.



Therefore, carbanion A, even though present in large concentration, does not tend to disproportionate. Instead, higher temperatures are necessary to shift the equilibrium toward greater amounts of the less stable carbanion B, which then reacts.

These results are not without precedent, since Pines and Eschinazi[8] found that the stability of the resultant carbanion governs the reaction path in the sodium-catalyzed dealkylation of geminal alkylcyclohexadienes.

The disproportionation of 1-phenyl-3-(2-pyridyl)propane (**5**), using 4-picoline as the "scavenger" alkylpyridine, was studied. In contrast to **4**, the disproportionation of **5** does not proceed at an appreciable rate until the temperature nears 115–120°. Again, the predominant path of disproportionation is in the direction that yields the more stable carbanion, *i.e.*, the carbanion of 2-picoline rather than of toluene. Only a trace of toluene is detected.

The styrene produced is immediately captured by "scavenger" 4-picoline to yield **4**, or by another molecule of **5** to yield 1,5-diphenyl-3-(2-pyridyl)pentane (**9**) (Table II). At this temperature and conversion, the former route of capture is favored by 3:1. If the stability of the resultant carbanion is the important factor in determining the ease of disproportionation, then this would suggest that the carbanion of 4-picoline is more stable than that of 2-picoline, *i.e.*, 4-picoline is more acidic than 2-picoline.

To determine for certain the relative ease of disproportionation of **4** *vs.* **5**, these reactions were performed under identical catalytic conditions. This was accomplished by dispersing sodium in "scavenger" 4-*n*-propylpyridine, dividing the dispersion in two, and then adding **4** and **5**, respectively, to each half of the dispersion. Results of the reactions are given in expt 8 and 9, Table II. The disproportionation of **4** is twice as rapid as that of **5**.

To further examine the relative stabilities of the carbanions of 2- and 4-picoline, the disproportionation of **3** was also performed in the presence of 4-*n*-propylpyridine as scavenger of the vinylpyridines produced (Table III). The formation of 4-picoline was favored by about 2.6:1 over 2-picoline, and thus it can be concluded that 4-picoline is more acidic than 2-picoline. Also produced are adducts of 4-*n*-propylpyridine and 2- and 4-vinylpyridine, presumably, 1,3-di(4-pyridyl)pentane and 1-(2-pyridyl)-3-(4-pyridyl)pentane.

In contrast to these results is the work of Michalski and Zając,[6] who reported the preferred formation of

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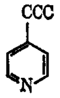
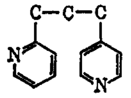
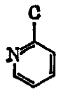
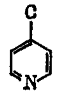
(8) H. Pines and H. E. Eschinazi, *J. Amer. Chem. Soc.*, **78**, 5950 (1956).

TABLE III

SODIUM-CATALYZED DISPROPORTIONATION REACTION OF 1-(2-PYRIDYL)-3-(4-PYRIDYL)PROPANE

		Reactants,[a] mole				Products,[b,d] %	
Expt	Time, hr			Temp, °C	Conversion,[b,c] %		
10	0.5	0.05	0.01	100	18.5	27.5	72.5
	1.0				27.5	28.5	71.5
	1.5				36.0	27.0	73.0

[a] Isopropylcyclohexane (0.005 mole) was used as internal standard and 0.05 g of sodium as catalyst. [b] Percentages corrected by thermal conductivity factors. [c] Based on 2- and 4-picoline produced. [d] Also produced were adducts of 2- and 4-vinylpyridine with n-propylpyridine.

TABLE IV

PHYSICAL CONSTANTS AND ELEMENTAL ANALYSES OF REACTION PRODUCTS

		Calcd, %			Found, %			
Compound	Formula	C	H	N	C	H	N	$n^{22}D$ or mp, °C
1,3-Di(2-pyridyl)propane (**1**)	$C_{13}H_{14}N_2$	78.75	7.22	14.13	78.94	7.22	13.94	1.5600 (lit.[3] 1.5607)
1,3-Di(4-pyridyl)propane (**2**)	$C_{13}H_{14}N_2$	78.75	7.12	14.13	78.75	7.11	14.09	61–63[a] (lit. 57–60,[4] 62–65[5])
1-(2-pyridyl)-3-(4-pyridyl)propane (**3**)	$C_{13}H_{14}N_2$	78.75	7.12	14.13	78.98	7.20	14.21	1.5585

[a] Product was recrystallized from hexane after separation by preparative gas chromatography.

2-picoline over 4-picoline by a 4:1 ratio in the potassium-catalyzed reaction of **3** at reflux temperature for 5 hr. It is believed that the starting material **3** used by these authors might have been impure and contaminated with 1,3-di(2-pyridyl)propane, which upon disproportionation would give only 2-picoline.

Experimental Section[9]

Reagents.—2- and 4-picoline, 2- and 4-vinylpyridine, 1-phenyl-3-(4-pyridyl)propane, and 4-n-propylpyridine were obtained from Reilly Tar and Chemical Co. 1-Phenyl-3-(2-pyridyl)-propane was prepared from 2-picoline and styrene in the reactions described in the preceding paper.[1] All reagents were at least 99.5% pure.

General Reaction Procedure.—The catalyst was prepared and the reactions performed in an apparatus similar to that used in the preceding paper.[1]

Vapor Phase Chromatography.—The progress of all reactions was followed by vpc on an 8 ft × 0.25 in., 10% silicone gum rubber, SE-30, on Gas Pack WAB (60–80) column, programming at 9°/min from 80 to 275°, helium flow rate 85 ml/min. 1,3-Di-(2-pyridyl)propane (**1**) and 1,3-di(4-pyridyl)propane (**2**) were separated by preparative gas chromatography on a 1.5 ft × $^3/_8$ in., 15% silicone gum rubber, SE-30, on Gas Pack WAB (60–80) column, at 200°. 1-(2-Pyridyl)-3-(4-pyridyl)propane (**3**) was separated on a 3 ft × $^3/_8$ in., 15% Carbowax 20M and 5% KOH on Gas Pack W (60–80) column, at 210°.

Product Identification.—Compounds **1**–**3** were identified by ir and nmr spectroscopy, elemental analyses, and by comparison of physical constants. Elemental analyses and physical constants are given in Table IV.

1,3-Di(2-pyridyl)propane (**1**).—The nmr spectrum shows two α-, two γ-, four β-hydrogens of two α-substituted pyridine rings centered at 8.33, 7.36, and 6.88 ppm, respectively. Centered at 2.70 ppm are the four equivalent methylene hydrogens adjacent to the pyridine rings, while the other two methylene hydrogens are centered further upfield at 2.20 ppm.

1,3-Di(4-pyridyl)propane (**2**).—The nmr spectrum indicates four α- and four β-hydrogens of two γ-substituted pyridine rings centered at 8.28 and 6.88 ppm, respectively. The four equivalent methylene hydrogens adjacent to the pyridine rings are centered at 2.50 ppm, while centered further upfield at 1.93 ppm are the other two methylene hydrogens.

1-(2-Pyridyl)-3-(4-pyridyl)propane (**3**).—The nmr spectra show three α-, one γ-, and four β-hydrogens of one α- and one γ-substituted pyridine ring centered at 8.32, 7.38, and 6.90 ppm, respectively. Centered at 2.64 ppm are the four overlapping methylene hydrogens adjacent to the pyridine rings, while the other two methylene hydrogens are centered further upfield at 2.06 ppm.

Spectroscopic Analyses.—The infrared spectra of liquid products were taken as films between sodium chloride disks, while that of the only solid, **2**, was taken in a KBr pellet on a Baird Model 4-55 spectrophotometer. A Varian A-60 nmr spectrophotometer was used. All nmr spectra were taken in CCl_4 solvent using TMS as an internal standard.

Registry No.—**1**, 15937-81-2; **2**, 17252-51-6; **3**, 19978-13-3; 2-picoline, 109-06-8; 4-picoline, 108-89-4; 2-vinylpyridine, 100-69-6; 4-vinylpyridine, 100-43-6.

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[9] Experimental analyses were performed by M-H-W Laboratories, Garden City, Mich., and Micro-Tech Laboratories, Inc., Skokie, Ill.