atom. We have determined the heat of fusion calorimetrically and find it to be 0.69 ± 0.07 kcal./gram atom. The value agrees, within the rather large uncertainty of our measurements, with that of Bichowsky and Rossini,[3] which was calculated from the (calorimetric) entropies of fusion of the other alkali metals. Kelley's value[4] of 1.1 kcal./gram atom was calculated from freezing point–composition data for several binary alloys; his calculations for sodium gave values in agreement with those obtained calorimetrically, whereas for potassium the calorimetric value was less than the alloy value by approximately the same factor that we find for lithium. The melting point, which has been reported as 179 and 186°,[3] was found to be 179 ± 1°.

The heat of fusion was calculated from the heat content *vs.* temperature curve of an ampoule of $^3/_4$-in. o.d. stainless steel tubing containing slightly more than 13 g. of lithium. The lithium (99.5%) was handled in an atmosphere of argon, and the ampoule closed by heliarc welding. The heat content of the ampoule was measured by an adaptation of the method of mixtures for temperatures between 164 and 191°. The calorimeter was calibrated with pure copper for the same range of temperatures. Values for the heat capacity of copper were taken from the National Bureau of Standards compilation.[5]

(5) F. D. Rossini, D. D. Wagman, W. H. Evans, E. J. Blau and S. Levine, "Selected Values of Chemical Thermodynamic Properties," U. S. National Bureau of Standards, Washington, D. C., 1947.

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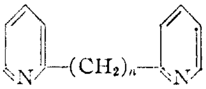
The Synthesis of 2,2'- and 4,4'-Polymethylenebipyridines

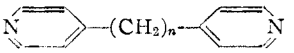
BY L. M. JAMPOLSKY, M. BAUM, S. KAISER, L. H. STERNBACH AND M. W. GOLDBERG

RECEIVED MAY 16, 1952

The present paper describes the preparation of several new 2,2'- and 4,4'-polymethylenebipyridines of the general structures I and II. They were required as intermediates for the synthesis of the corresponding polymethylene-bipyridinium compounds,[1] some of which were found to have interesting curare-like properties.[2]



I



II

Of the compounds of formula I, only the 2,2'-trimethylenebipyridine (I, n = 3) was known. It was obtained by Michael addition of 2-picoline to 2-vinylpyridine.[3] We have now prepared the corresponding pentamethylene (I, n = 5), hexamethylene (I, n = 6), heptamethylene (I, n = 7) and octamethylene (I, n = 8) homologs by treating 2-picolyllithium with the appropriate polymethylene dibromide. All four compounds were high boiling oils and gave crystalline dimethobromides.

The only known member of the 4,4'-polymethylenebipyridine series (II) was the dimethylene compound (II, n = 2). It was obtained by heating 4-picoline with sulfur.[4] We used the same method for its preparation, and synthesized the missing members of this series from the monomethylene to the octamethylene compound by a variety of other reactions. The monomethylene compound (II, n = 1) was made by treating 4-chloropyridine with 4-picolylpotassium in liquid ammonia. The trimethylene compound (II, n = 3) was prepared by condensing 4-picoline with 4-vinylpyridine in the presence of potassium (sodium was unsuitable for this purpose), and the tetramethylene compound (II, n = 4) was obtained by condensing 3-(4-pyridyl)-1-bromopropane with 4-picolylpotassium in liquid ammonia. We also attempted to prepare the tetramethylene compound by reacting ethylene dibromide with 4-picolylpotassium in liquid ammonia. However, the only product obtained in this case was the known 4,4'-dimethylenebipyridine (25% yield). The unexpected course of this reaction can best be explained by assuming a simultaneous formation of ethylene from the ethylene dibromide. Similar, but not completely analogous reactions are known, for example, the formation of bromobenzene, ethylene and lithium bromide from phenyllithium and ethylene dibromide.[5]

The 4,4'-pentamethylenebipyridine (II, n = 5) and the corresponding hexamethylene (II, n = 6), heptamethylene (II, n = 7) and octamethylene (II, n = 8) compounds were all prepared by reacting 4-picolylpotassium in liquid ammonia with the appropriate polymethylene dibromide. The lower members of the 4,4'-polymethylenebipyridine series crystallize readily. The hexamethylene compound was isolated in form of its crystalline dimethobromide and the hepta- and octamethylene homologs in form of their crystalline dihydrobromides.

Experimental[6]

2,2'-Polymethylenebipyridines.—The compounds of this series were prepared by treating 2-picolyllithium in ether with the appropriate polymethylene dibromide. The 2,2'-pentamethylenebipyridine was obtained in 40% yield using trimethylene dibromide, the 2,2'-hexamethylenebipyridine in 62% yield using tetramethylene dibromide, the 2,2'-heptamethylenebipyridine in 46% yield using pentamethylene dibromide, and the 2,2'-octamethylenebipyridine in 41% yield using hexamethylene dibromide. All data on these new compounds and their derivatives are summarized in Table I. The reaction conditions were identical in all cases, and we describe, therefore, in detail only the preparation of the **2,2'-hexamethylenebipyridine**: To a stirred solution of phenyllithium, prepared from 31 g. (4.4 g. atoms) of lithium and 345 g. (2.2 moles) of bromobenzene in 1 liter of absolute ether, was added 186 g. (2 moles) of dry 2-picoline. This was followed by the dropwise addition of 152 g. (0.7 mole) of tetramethylene dibromide. The reaction mixture was refluxed for 2 hours. Ice and about 275 ml. of concentrated hydrochloric acid were then added and the aqueous phase separated. It was made strongly alkaline by the addition of 50% potassium hydroxide solution and extracted with ether. The ether extract was concentrated and the residue fractionated in high vacuum. The main fraction, b.p. 160–165° (0.5 mm.), gave a crystalline dimethobromide

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[1] To be reported in subsequent papers.

(2) See L. O. Randall, *Ann. N. Y. Acad. Sci.*, **54**, 460 (1951), and *J. Pharmacol. Exptl. Therap.*, **105**, 7 (1952).

(3) N. J. Leonard and J. H. Boyer, THIS JOURNAL, **72**, 4818 (1950).

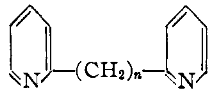
(4) H. I. Thayer and B. B. Corson, *ibid.*, **70**, 2330 (1948).

(5) G. Wittig and G. Harborth, *Ber.*, **77**, 306 (1944).

(6) All melting points are corrected.

TABLE I

2,2'-POLYMETHYLENEBIPYRIDINES AND DERIVATIVES

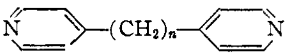


n	Type[a]	M.p., °C.	B.p. °C.	B.p. Mm.	n^t_D	t, °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
5	B		153–154	1	1.5478	25	$C_{15}H_{18}N_2$	79.60	79.49	8.02	7.85
5	MB	199–203					$C_{17}H_{24}N_2Br_2$	49.05	49.34	5.81	5.37
6	B		160–165	0.5	1.5408	25	$C_{16}H_{20}N_2$	79.95	80.12	8.39	8.24
6	MB	225–228					$C_{18}H_{26}N_2Br_2$	50.25	49.62	6.09	5.68
7	B		166–168	.8	1.5379	24	$C_{17}H_{22}N_2$	80.27	80.41	8.72	8.51
7	MB[b]	202–204					$C_{19}H_{28}N_2Br_2\cdot{}^1/_2H_2O$	50.34	50.16	6.45	6.30
8	B		177	.6	1.5339	26	$C_{18}H_{24}N_2$	80.55	79.99	9.01	9.10
8	MB[c]	200–201					$C_{20}H_{30}N_2Br_2.H_2O$	50.43	50.65	6.77	6.37

[a] B, base; MB, di-(methyl bromide). [b] Hemihydrate. [c] Monohydrate.

TABLE II

4,4'-POLYMETHYLENEBIPYRIDINES AND DERIVATIVES



n	Type[a]	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
1	B	138–140	$C_{11}H_{10}N_2$	77.62	77.74	5.91	5.86
2	MB	285–292[b]	$C_{14}H_{18}N_2Br_2$	44.94	45.24	4.85	4.95
2	PB	251–253[b]	$C_{18}H_{26}N_2Br_2$	50.25	50.18	6.09	5.78
2	BB[c]	198–200[b]	$C_{20}H_{30}N_2Br_2\cdot{}^1/_2H_2O$	51.41	51.32	6.67	6.65
2	NB	271–280[b]	$C_{26}H_{24}O_4N_4Br_2$	50.66	50.45	3.92	4.02
3	B	57–60	$C_{13}H_{14}N_2$	78.75	78.95	7.12	7.01
3	MB	212–221[b]	$C_{15}H_{20}N_2Br_2$	46.41	46.33	5.19	5.11
4	B	111–115	$C_{14}H_{16}N_2$	79.21	79.37	7.60	7.76
4	NB	218–227[b]	$C_{28}H_{28}O_4N_4Br_2$	52.19	52.07	4.38	4.54
5	B	56–58	$C_{15}H_{18}N_2$	79.60	79.52	8.02	8.20
6	MB[d]	206–209[b]	$C_{18}H_{26}N_2Br_2\cdot H_2O$	48.23	48.62	6.29	6.13
7	HB	209–211[b]	$C_{17}H_{22}N_2\cdot 2HBr$	49.05	48.87	5.81	5.83
8	HB	284–290[b]	$C_{18}H_{24}N_2\cdot 2HBr$	50.26	50.60	6.09	6.30

[a] B, base; HB, dihydrobromide; MB, di-(methyl bromide); PB, di-(propyl bromide); BB, di-(butyl bromide); NB, bis-(p-nitrobenzyl bromide). [b] With decomposition. [c] Hemihydrate. [d] Monohydrate.

when treated with an excess of methyl bromide in acetone. It was recrystallized from methanol–acetone; m.p. 225–228°.

4,4'-Polymethylenebipyridines.—All data on the new compounds of this series are summarized in Table II. The preparation was carried out as follows:

4,4'-Methylenebipyridine.—To one liter of liquid ammonia containing 8.5 g. of potassium amide was added, with stirring at −80°, 14 g. of 4-picoline. After the mixture had stirred for 15 minutes at −80°, an ether solution containing 12.3 g. of 4-chloropyridine was added and the stirring continued at the same temperature for three additional hours. A small amount of ammonium chloride was then added and the ammonia allowed to evaporate. The residue so obtained was dissolved in water and extracted with benzene. The benzene was evaporated *in vacuo* at 100° and the residue crystallized from acetone–ether. The recrystallized material melted at 138–140°. The yield was 35%.

4,4'-Trimethylenebipyridine.—Eighty-four grams of 4-vinylpyridine and 372 g. of dry 4-picoline were added to 80 ml. of benzene containing 20 mg. of hydroquinone. While stirring, 1 g. of potassium was added and the temperature raised to 105°. After 45 minutes, the reaction mixture was cooled, the potassium destroyed with ethanol and the benzene solution extracted with water and with a saturated aqueous sodium bisulfite solution. The benzene solution was then dried and evaporated *in vacuo*. The oily residue was crystallized from acetone. The recrystallized material melted at 57–60°. The yield was 44%.

4,4'-Tetramethylenebipyridine.—Seventy-two grams of 3-(4-pyridyl)-1-methoxypropane[7] was refluxed with 700 ml. of 48% hydrobromic acid for four hours and the reaction mixture evaporated to dryness *in vacuo*. The residue, consisting of a mass of hygroscopic needles of 3-(4-pyridyl)-1-bromopropane hydrobromide, was directly converted into the unstable free base by dissolving it in ice-water, adding solid potassium carbonate and extracting with ether. The ether solution was dried, and an aliquot equivalent to 40 g. of 3-(4-pyridyl)-1-bromopropane hydrobromide was cooled to about −80°. This was slowly added to a stirred liquid ammonia suspension of 4-picolylpotassium, prepared by the addition of 20 g. of 4-picoline to 2 liters of liquid ammonia containing 12 g. of potassium amide. The reaction mixture was stirred for about three hours at about −30° and then the ammonia was allowed to evaporate. The residue so obtained was dissolved in water and extracted with ether. The crystalline residue obtained by evaporation of the dried ether extract was recrystallized from methanol and from acetone. The pure product melted at 111–115°. The yield was 20%.

4,4'-Pentamethylenebipyridine.—To 2 liters of liquid ammonia containing about 28 g. of potassium amide (prepared in this and all other experiments by dissolving potassium metal in liquid ammonia in the presence of an iron catalyst) was added, with stirring at −80°, 47 g. of 4-picoline. After the mixture had stirred for 10 minutes at this temperature, a solution of 51 g. of trimethylene dibromide in 250 ml. of ether was slowly added.[8] The reaction mixture was stirred for 3 additional hours at −80°, and then 10 g. of ammonium chloride was added. The ammonia was allowed to evaporate, the residue was taken up in water and extracted with ether. The dried ether extract was evaporated to dryness, and the crystalline residue so obtained was recrystallized from benzene–petroleum ether; m.p. 56–58°. The yield was 64%.

4,4'-Hexa-, Hepta- and Octamethylenebipyridine.—These three compounds were made from 4-picolinepotassium and the appropriate polymethylene dibromide using the procedure for the pentamethylene homolog. Tetramethylene dibromide gave a 65% yield of 4,4'-hexamethylenebipyridine, pentamethylene dibromide a 36% yield of the heptamethylene homolog, and hexamethylene dibromide a 15%

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[7] T. R. Norton, R. A. Seibert, A. A. Benson and F. W. Bergstrom, THIS JOURNAL, **68**, 1572 (1946).

[8] The reaction can become violent if the trimethylene dibromide is added too quickly.

yield of the octamethylene compound. The hydrobromides of the two last mentioned compounds were prepared from the crude reaction products and recrystallized from aqueous acetone.

The bis-pyridinium compounds listed in Table II were prepared by heating a mixture of the polymethylenebipyridine with the appropriate alkyl or aralkyl bromide in acetone or benzene. They were recrystallized from methanol–acetone.

Acknowledgment.—We wish to express our thanks to Dr. Al Steyermark and his staff for the microanalyses.

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The Preparation of Nickel(II) Thiocyanate Complex Compounds with Picolines and the Determination of their Heats of Formation[1]

BY ALBERT V. LOGAN AND DON W. CARLE[2]

RECEIVED MAY 26, 1952

Work reported in an earlier paper[3] discussed the effect of negative groups upon the heat of formation of nickel(II) and cobalt(II) pyridinated compounds. We have now prepared a series of complexes in which the same metal salt has been combined with methyl substituted pyridines in an effort to determine the effect of the character of the base upon the heat of formation of the complexes. The heats of reaction of the simple salt, the amine and the complex with 2 N HCl were determined and the heat of formation of the complex calculated according to the equation

$$\Delta H_f = L_s + L_a - L_c$$

Preparation of Compounds

Nickel(II) Di-2-methylpyridine Thiocyanate.—17.48 g. (0.1 mole) of nickel thiocyanate was added to 300 ml. of α-picoline (b.p. 128.4–130°). The mixture was maintained at 125 to 130° for four hours under a reflux condenser. The salt changed to a red color immediately on contact with the hot α-picoline. The salt was completely dissolved after four hours heating producing a green solution. The solution was transferred to a large evaporating dish and low heating continued until a viscous mass was obtained. Rapid cooling produced a solid. The solid was pulverized and excess base removed in an air stream while the solid was continually stirred. The product, a brick red solid, was passed through a 60-mesh screen, air-dried for one-half hour. The compound may be kept indefinitely in a sealed container but will decompose almost quantitatively if left in the air overnight. The nickel content of this compound and others described later was determined by silver cyanide titration. *Anal.* Calcd. for $Ni(SCN)_2 \cdot 2C_6H_7N$: Ni, 16.25. Found: Ni, 16.07.

Nickel(II) Tetra-3-methylpyridine Thiocyanate.—The β-picoline available was the practical grade. Purification was effected by the method of Riethof.[4] The fraction distilling at 143–144° was collected for use in preparation of the complex compounds: 18.3 g. (0.077 mole) of $NiCl_2 \cdot 6H_2O$ was dissolved in 2 l. of H_2O, 33 ml. of β-picoline was added, a deep blue solution was formed. A solution of 15 g. (0.1544 mole) of KSCN in 200 ml. of H_2O was added slowly with constant stirring. A light blue microcrystalline precipitate formed immediately. The precipitate was obtained as a hard cake by use of a suction filter. The cake was pulverized and dried in air for four hours, then passed through a 60-mesh screen and placed in a desiccator over solid KOH for 2 days. The yield was nearly quantitative. The compound is stable in air for several days; at elevated temperatures it is readily converted to $Ni(SCN)_2$ and β-picoline. *Anal.* Calcd. for $Ni(SCN)_2 \cdot 4C_6H_7N$: Ni, 10.73. Found: Ni, 10.73.

Nickel(II) Tetra-4-methylpyridine Thiocyanate.—This compound was prepared in a manner identical to that described for the β-picoline complex. The color and characteristics of the compound are the same. *Anal.* Calcd. for $Ni(SCN)_2 \cdot 4C_6H_7N$: Ni, 10.73. Found: Ni, 10.77.

Attempts were made to prepare the above compounds by chloroform extraction as had been previously employed in the preparation of a number of pyridinated compounds. The compounds obtained by this method indicated some entrapment of chloroform in the crystals of the complex. The slow evaporation of a chloroform solution, obtained by the extraction of an aqueous suspension of the β-picoline compound, produced large blue transparent crystals. These crystals contained 8.7% nickel. Each preparation by this method produced the same product. Test for water in the crystals was negative. To check for the presence of chloroform, a pure sample of $Ni(SCN)_2 \cdot 4BC_6H_7N$ prepared by precipitation from water, was dissolved in chloroform and the solution was evaporated. The large blue crystals obtained were crushed, then dried in air for an hour. Analysis showed 7.60% nickel. No attempt was made at the time to investigate the subject further since we were interested in the compound containing 4 molecules of the amine.

Determination of Heats of Reaction.—The method and the calorimeter employed in determining the heats of reaction of the $Ni(SCN)_2$, the bases and the complexes with 2 N HCl were similar to those employed by Logan, Bush and Rogers in this Laboratory.[3] The values obtained and the heats of formation calculated from them are recorded in Table I.

Results and Discussion

TABLE I

Substance	Heat of solution cal./mole at 25°[a]	Heat of formation cal./mole at 25°
β-Picoline	−9200 (±50)	
γ-Picoline	−9450 (±90)	
Pyridine[b]	−7860 (±25)	
$Ni(CNS)_2$	1140 (±10)	
$Ni(CNS)_2 \cdot 4\beta$-Pic	2340 (±60)	−36,000
$Ni(CNS)_2 \cdot 4\gamma$-Pic	1450 (±40)	−38,110
$Ni(CNS)_2 \cdot 4Py$[b]	7860 (±100)	−38,300

[a] Averages obtained from 3 to 5 determinations on each compound. [b] Reported in an earlier article (ref. 3).

The heats of formation of cobalt(II) (37,700 cal./mole) and nickel(II) (38,300 cal./mole) tetrapyridine thiocyanates and the cobalt(II) (22,300 cal./mole) and nickel(II) (18,500 cal./mole) hexapiperidine cyanates reported earlier, indicate that the negative groups play a more important role in the heat of formation of the complex compounds than do the metals. The fact that a stable tetra-α-picoline could not be obtained limited this study of the effect of bases on the heat of formation to the β- and γ-picolines. It is assumed that the proximity of the methyl group to the nitrogen atom in the amine prevented the formation of the tetra-α-picoline compound.

The relative basic strengths of pyridine, β-picoline and γ-picoline are evidenced by their heats of reaction with 2 N HCl recorded in Table I. By comparing the values calculated for the heats of formation of the complexes produced by the reaction of nickel thiocyanate with the three bases, Table I, it may be concluded that the heat of form-

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[1] Published with the approval of the Monograph Publishing Committee, Oregon State College, as Research Paper No. 206, School of Science, Department of Chemistry.

[2] This article is based on a thesis submitted by Don W. Carle in partial fulfillment of the requirements for the degree of Master of Science at Oregon State College, June, 1952.

[3] A. V. Logan, O. C. Bush and C. S. Rogers, THIS JOURNAL, **74**, 4194 (1952).

[4] G. Riethof, S. G. Richards, S. A. Savitt and D. F. Othmer, *Ind. Eng. Chem., Anal. Ed.*, **18**, 458 (1946).