hydroxyadipaldehyde. The adipaldehyde derivative was also characterized as the tetraethyl mercaptal.

These results show that streptobiosamine is linked glycosidically at position 4 of streptidine.

RAHWAY, N. J. RECEIVED FEBRUARY 14, 1948

[CONTRIBUTION FROM KOPPERS CO., INC., MULTIPLE FELLOWSHIP ON TAR SYNTHETICS, MELLON INSTITUTE]

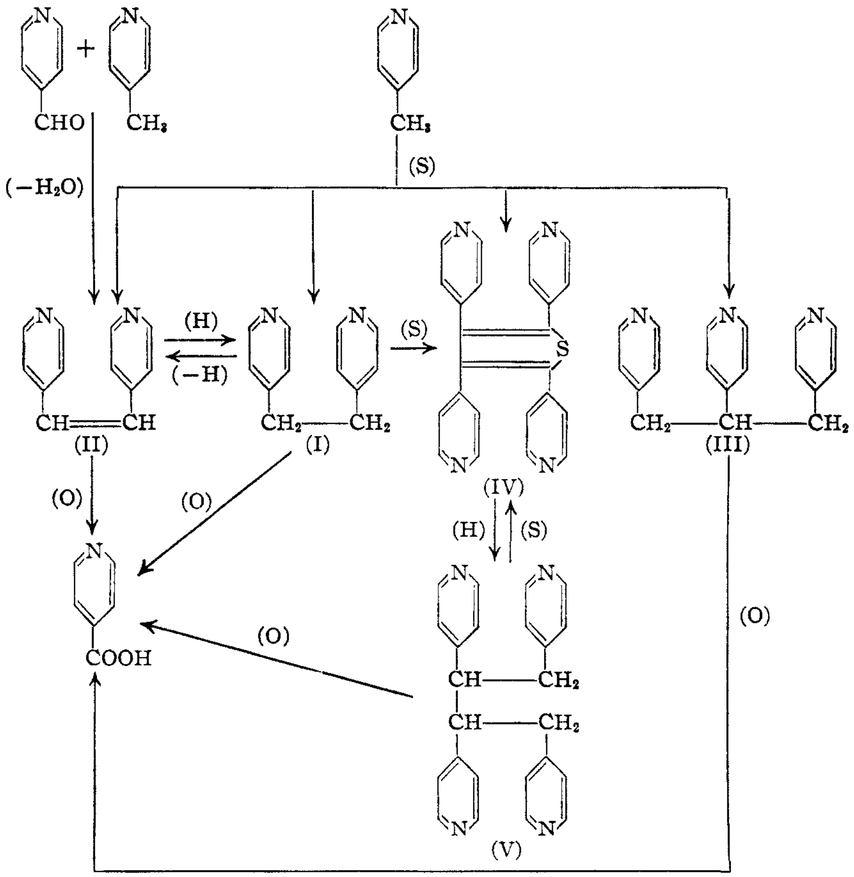
Action of Sulfur on Certain Pyridine and Quinoline Derivatives. I. Action of Sulfur on 4-Picoline

BY HELEN I. THAYER AND B. B. CORSON

The dehydropolymerizing action of sulfur on the picolines has not been previously noted, but certain examples of this action have been recorded in the methylbenzene series. For example, it is known that sulfur converts toluene to stilbene and tetraphenylthiophene, and xylenes to dimethylstilbenes and dimethylbenzyls.[1]

This paper describes the synthesis of several higher molecular weight bases from 4-picoline by the action of sulfur. Five products were obtained: hydrogen sulfide, 1,2-di-(4-pyridyl)-ethane (I), 1,2-di-(4-pyridyl)-ethylene (II), 1,2,3-tri-(4-pyridyl)-propane (III) and 2,3,4,5-tetra-(4-pyridyl)-thiophene (IV). In the absence of sodium hydroxide the yield of tetrapyridylthiophene (IV) was negligible, but it was the main product (85–90% yield) when the reaction mixture contained a catalytic amount of sodium hydroxide and the final reaction temperature was in the vicinity of 300°. In general, the presence of sodium hydroxide favored the production of the unsaturated compounds of dipyridylethylene (II) and tetrapyridylthiophene (IV) at the expense of the saturated compounds of dipyridylethane (I) and tripyridylpropane (III). The product-distribution was also affected by temperature, length of reaction time, and sulfur-picoline ratio.

At the lower temperatures, sulfur-free compounds (I, II, and III) resulted, whereas at the higher temperatures the main product was the sulfur-containing tetrapyridylthiophene (IV). These results are similar to those of Aronstein and von Nierop,[1] who treated toluene with sulfur at 200° and 250–300° to obtain stilbene and tetraphenylthiophene, respectively. Likewise, Oddo and Raffa[2] obtained the sulfur-free compound 3,3′-biindole by treating indole with sulfur at 115–125° and sulfur-containing products at higher reaction temperatures.



The structures of I and II were established as follows: (1) oxidation of these compounds to isonicotinic acid; (2) hydrogenation of II to I; (3) dehydrogenation of I to II; and (4) the synthesis of 1,2-di-(4-pyridyl)-ethylene (II) by the condensation of 4-pyridylaldehyde with 4-pico-

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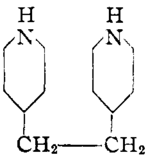
[1] Aronstein and von Nierop, *Rec. trav. chim.*, **21**, 448 (1902).

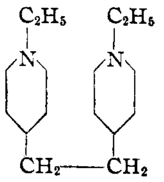
[2] Oddo and Raffa, *Gazz. chim. ital.*, **69**, 562 (1939).

line. The structure of 1,2,3-tri-(4-pyridyl)-propane (III) was based on its oxidation to isonicotinic acid. Evidence for the structure of 2,3,4,5-tetra-(4-pyridyl)-thiophene (IV) was threefold: (1) its synthesis from 1,2-di-(4-pyridyl)-ethane (I); (2) its conversion to the sulfur-free compound (V); (3) the similarity of its spectrum in the region 280–370 mμ (Fig. 1) to that of 2,3,4,5-tetraphenylthiophene. The synthesis of IV from 1,2-di-(4-pyridyl)-ethane (I) was accomplished by heating the latter with sulfur as in the synthesis of tetraphenylthiophene from dibenzyl and sulfur,[3] and tetrapyridylthiophene (IV) was degraded to tetrapyridylbutane (V) with zinc and hydrochloric acid as in the reductive fission of tetraphenylthiophene to tetraphenylbutane.[4] The structure of 1,2,3,4-tetra-(4-pyridyl)-butane (V) was based on its oxidation to isonicotinic acid, and the conversion of V to IV by reaction with sulfur.

Catalytic hydrogenation of 1,2-di-(4-pyridyl)-ethane (I) in cyclohexane solution gave 1,2-di-(4-piperidyl)-ethane (VI), whereas hydrogenation in ethanol gave the di-N-ethyl derivative (VII).[5]



(VI)



(VII)

The various reaction mixtures were scrutinized for intermediate products to serve as clues to the reaction mechanism. In the benzene series, polymeric thiobenzaldehyde, benzyl mercaptan and dibenzyl sulfide have been hypothesized as intermediates in the reaction of toluene with sulfur because they pyrolyze to certain of the end-products of this reaction, *viz.*, stilbene and tetraphenylthiophene.[1] However, in the present case, no analogous intermediates were isolated to justify the postulation of a reaction mechanism.

Experimental

4-Picoline.—The 4-picoline (95+% pure, b. p. 144.2–144.4° (743 mm.), n^{20}_D 1.5050, d^{20}_4 0.953) was a product of the Koppers Company, Inc.

Reaction of 4-Picoline with Sulfur (below 200°).—Yield data on several experiments are listed in Table I. The general procedure was to heat a mixture of 4-picoline with flowers of sulfur (with or without sodium hydroxide) in a 3-neck flask equipped with condenser, stirrer and thermometer. The mixture darkened and hydrogen sulfide was evolved. The final temperature of the reaction mixture depended upon the length of the heating period. After cooling, unreacted picoline was removed through a short column at about 45 mm. pressure, distillation being discontinued when the pot temperature reached 180°. Redistillation of the overhead showed it to be at least 90% 4-picoline; no higher boiling material was present. The reaction product residue was stirred into a mixture of ice and 50% sulfuric acid; unreacted sulfur was removed by filtration, and the filtrate was made alkaline with 30% sodium hydroxide solution. The oil layer was separated while warm. The water layer was extracted with benzene and the extract was added to the oil. The crude product, dark brown and semi-solid after removal of water and benzene, was distilled at about 3 mm. into several fractions. These distillates crystallized in the receiver and were purified by crystallization; the pot residue was a black, charred solid.

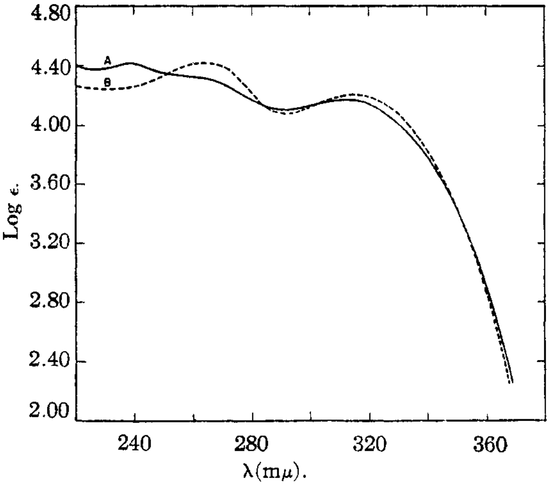


Fig. 1.—Absorption curves of tetraphenylthiophene (A) and tetra-(4-pyridyl)-thiophene (B) in 95% ethanol.

Effect of Reaction Variables (Table I).—In the absence of sodium hydroxide the main product was dipyridylethane; there was considerable tripyridylpropane, but little dipyridylethylene. Doubling the relative amount of sulfur (*e. g.*, increasing the sulfur–picoline ratio from 1:2 to 1:1) did not change the product-distribution, but it increased the picoline conversion somewhat. The effect of lengthening the reaction time was to increase the picoline conversion, partly due to the resulting higher final reaction temperature. As remarked above, the effect of sodium hydroxide was to favor the formation of dipyridylethylene and tetrapyridylthiophene at the expense of dipyridylethane and tripyridylpropane.

1,2-Di-(4-pyridyl)-ethane (I).—Repeated crystallization of the fraction melting at 107–110° (b. p. 167–174° at 3 mm.) from cyclohexane–benzene (3:1) gave compact, colorless crystals, m. p. (capillary) 110–111°, f. p. (cooling curve) 110.9–110.2°.[6]

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 78.2; H, 6.6; N, 15.2; mol. wt., 184. Found: C, 77.8; H, 6.9; N, 15.0; mol. wt., 189.[7]

The hydrochloride was precipitated from an alcohol solution of the base by hydrogen chloride; white crystalline powder, 95% yield, m. p. 329–330° (dec.).

Anal. Calcd. for $C_{12}H_{12}N_2 \cdot 2HCl$: Cl, 27.6. Found: Cl, 27.5.

1,2-Di-(4-pyridyl)-ethylene (II).—Three fractions boiling at 175–189° (2.5 mm.), 175–205° (2 mm.) and 193–220° (2 mm.), respectively, were combined and fractionally crystallized from benzene to yield impure I and II, the latter being long, white needles, m. p. 151–152°, f. p. 151.5–151.2°.

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(3) Szperl and Wierusz-Kowalski, *Chem. Polski*, **15**, 19 (1917); through *Chem. Zentr.*, **89**, I, 909 (1918).

(4) Fromm and Achert, *Ber.*, **36**, 534 (1903).

(5) This is another example of simultaneous N-alkylation-hydrogenation, see King, Baltrop and Walley, *J. Chem. Soc.*, 277 (1945); Adkins, Kuick, Farlow and Wojcik, THIS JOURNAL, **56**, 2425 (1934).

(6) All melting points were corrected. The cooling curve temperatures listed were the initial and the final temperatures (when about 50% of the sample was frozen).

(7) Molecular weights were determined by the method of Hanson and Bowman, *Ind. Eng. Chem., Anal. Ed.*, **11**, 440 (1939).

TABLE I

REACTION OF 4-PICOLINE WITH SULFUR (BELOW 200°)

Hr.	T, °C.	Reactants, moles: Pic[a]	S	NaOH	Pic reacted, %	Products, wt. %: $C_2H_4P_2$	$C_2H_2P_2$	$C_3H_5P_3$	TP_4	Pot residue	Unaccounted for
9	143–166	4	4	0	71	52	2	21	0	9	16
12	137–174	3	3	0	77	46	6	22	0	15	11
12	140–155	3	1.5	0	53	60	4	14	0	10	12
24	140–171	3	1.5	0	71	48	4	24	0	8	16
7	135–160	4	8	0.075	65	32	15	4	0	17	32
12	140–199	4	8	0.075	94	9	0	0	72	13	6
12	135–161	3	3	0.15	78	28	20	11	1	16	24
12	135–162	3	3	0.30	77	26	15	0	26	9	24

[a] Pic, $C_2H_4P_2$, $C_2H_2P_2$, $C_3H_5P_3$, TP_4 = 4-picoline, 1,2-di-(4-pyridyl)-ethane, 1,2-di-(4-pyridyl)-ethylene, 1,2,3-tri-(4-pyridyl)-propane, 2,3,4,5-tetra-(4-pyridyl)-thiophene, respectively.

TABLE II

REACTION OF 4-PICOLINE WITH SULFUR (ABOVE 200°)

Hr.	T, °C.	Reactants, moles: Pic	S	NaOH	Pic:S	Products: H_2S % Yield	S, g.	P_4T % Yield
2.5	150–300	0.05	0.075	0.00025	4:6	101	0	89[a]
2.8	175–330	.05	.0875	.00025	4:7	98	0.02	83[b]
2.5	160–290	.05	.100	.00025	4:8	97	0.5	90[b]
2.5	160–290	.05	.125	.00025	4:10	100	1.5	78[b]

[a] Based on sulfur. [b] Based on picoline.

Anal. Calcd. for $C_{12}H_{10}N_2$: C, 79.1; H, 5.5; N, 15.4; mol. wt., 182. Found: C, 78.8; H, 5.3; N, 15.6; mol. wt., 180.

Its hydrochloride, precipitated from alcohol in 99% yield, was a white crystalline solid, m. p. 347° (sealed tube, dec.).

Anal. Calcd. for $C_{12}H_{10}N_2{\cdot}2HCl$: Cl, 27.8. Found: Cl, 27.8.

1,2,3-Tri-(4-pyridyl)-propane (III).—The fraction boiling at 230–242° (2 mm.) was repeatedly crystallized from ethyl acetate to yield pale yellow crystals, m. p. 110–111°, f. p. 109.9–109.3°. Its melting point was depressed 10–12° by admixture with an equal amount of di-(4-pyridyl)-ethane (I) which also melted at 110–111°.

Anal. Calcd. for $C_{18}H_{17}N_3$: C, 78.5; H, 6.2; N, 15.3; mol. wt., 275. Found: C, 78.8; H, 6.3; N, 15.2; mol. wt., 282.

Its hydrochloride, precipitated from alcohol in 85% yield, was a white hygroscopic powder, m. p. 230–232° (dec.).

Anal. Calcd. $C_{18}H_{17}N_3{\cdot}3HCl$: Cl, 27.7. Found: Cl, 27.4.

Reaction of 4-Picoline with Sulfur (above 200°).—At temperatures above 200° in the presence of catalytic amounts of sodium hydroxide, the main products were 2,3,4,5-tetra-(4-pyridyl)-thiophene (IV) and hydrogen sulfide. The data listed in Table II were obtained from small experiments in which hydrogen sulfide was swept out of the reaction mixture by nitrogen and collected in Ascarite preceded by pumice–sulfuric acid. Approximately the theoretical amount of hydrogen sulfide was recovered; the maximum utilization of sulfur was at the picoline–sulfur ratios of 4:6 and 4:7. The decreased yield of tetrapyridylthiophene obtained at the smallest picoline:sulfur ratio of 4:10 (as compared with the theoretical ratio of 4:7) was probably due to inclusion of product in the recovered excess sulfur. In typical larger scale reactions, a mixture of 4 moles of picoline, 8 moles of sulfur, and 0.025 mole of sodium hydroxide was heated for fourteen hours (final temperature *ca.* 245°). The reaction mixture was poured into acid and unreacted sulfur was removed by filtration; the acid filtrate was made alkaline and the precipitated tetrapyridylthiophene isolated (85–90% yield).

2,3,4,5-Tetra-(4-pyridyl)-thiophene (IV).—The crude product gave about 80% yield of compound IV, m. p. 251.8–252.6°, pale yellow crystals from methanol or pyridine.

Anal. Calcd. for $C_{24}H_{16}N_4S$: C, 73.4; H, 4.1; N, 14.3; S, 8.2; mol. wt., 393. Found: C, 73.6; H, 4.0; N, 14.2; S, 8.4; mol. wt., 401.

The hydrochloride, precipitated from ethanol in 95% yield, was a pale yellow hygroscopic solid, m. p. 283–285° (dec.).

Anal. Calcd. for $C_{24}H_{16}N_4S{\cdot}4HCl$: Cl, 26.3. Found: Cl, 26.0.

Proof of Structure

Oxidation of Compounds I, II, III and V.—1,2-Di-(4-pyridyl)-ethane (1.84 g.) in 100 cc. of water was oxidized at about 60° with 6 g. of potassium permanganate added in several portions during one and one-half hours. From the filtrate (at *p*H 3.6) two crops of isonicotinic acid were obtained, 1.81 g. (m. p. 317–319° (dec.)) and 0.36 g. (m. p. 314–316° (dec.)). The neutral equivalents were 124.3 and 125.6, respectively, compared with the theoretical of 123.1. The yield of isonicotinic acid was therefore 87%. In similar manner, 1,2-di-(4-pyridyl)-ethylene, 1,2,3-tri-(4-pyridyl)-propane, and 1,2,3,4-tetra-(4-pyridyl)-butane were oxidized to isonicotinic acid in 76, 84 and 74% yields, respectively.

Synthesis of 1,2-Di-(4-pyridyl)-ethylene (II) from 4-Pyridylaldehyde and 4-Picoline.—Selenium dioxide oxidation of 4-picoline in wet dioxane at 90° under nitrogen produced a small yield of 4-pyridylaldehyde, b. p. 68–74° (11 mm.), $n^{25}D$ 1.5382, m. p. of phenylhydrazone 177.5–178.5°.[8] 4-Pyridylaldehyde (1.79 g.) was heated with 1.56 g. of 4-picoline and 2.28 g. of zinc chloride for sixteen hours at 200–215°. The reaction mixture was cooled, dissolved in 20 cc. of 3 *N* sulfuric acid and two 5-g. portions of sodium hydroxide pellets were added. The cooled alkaline solution was repeatedly extracted with ether followed by chloroform. Removal of the solvent left a semi-solid product which was filtered; the filtrate was distilled (b. p. 182–189° (4 mm.)) to yield a distillate which partially solidified. The weight of the combined solids was 0.41 g. (13% yield). Three crystallizations from benzene with boneblacking gave colorless needles

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[8] Wibaut, Kooyman and Boer, *Rec. trav. chim.*, **64**, 30 (1945).

which melted at 151–152° and showed no depression in melting point when admixed with di-(4-pyridyl)-ethylene (II).

Anal. Calcd. for $C_{12}H_{10}N_2$: C, 79.1; H, 5.5; N, 15.4. Found: C, 78.9; H, 5.3; N, 15.7.

Hydrogenation of 1,2-Di-(4-pyridyl)-ethylene (II) to 1,2-Di-(4-pyridyl)-ethane (I).—Hydrogenation of dipyridylethylene in methanol with platinum gave a 76% yield of product which melted at 111–112° and did not depress the melting point of 1,2-di-(4-pyridyl)-ethane (I).

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 78.2; H, 6.6; N, 15.2. Found: C, 78.2; H, 6.7; N, 15.3.

Dehydrogenation of 1,2-Di-(4-pyridyl)-ethane (I) to 1,2-Di-(4-pyridyl)-ethylene (II).—Dipyridylethane (117 g.) was passed over 60 g. of a ferruginous dehydrogenation catalyst[9] at 600°, atmospheric pressure, and one second contact time, with 15 volumes of diluent steam. The catalyst carbonized to the extent of 10.9 weight per cent. The catalyzate was a mixture of solid, oil and water (ammoniacal odor), from which were separated 30 g. of unchanged dipyridylethane, 20 g. of dipyridylethylene, and 14 g. of 4-picoline (identified as methiodide, m. p. and mixed m. p. 152–153.5°).

Sulfuration of 1,2-Di-(4-pyridyl)-ethane to 2,3,4,5-Tetra-(4-pyridyl)-thiophene.—A mixture of 3.68 g. of 1,2-di-(4-pyridyl)-ethane (I) and 1.60 g. of sulfur was heated for eight and one-half hours at 170–240°; 0.85 g. of hydrogen sulfide was evolved, 0.75 g. of sulfur was recovered, and 2.5 g. of a reddish-brown solid was obtained. Crystallization from methanol gave 1.69 g. of solid melting at 246–250°, and recrystallization gave yellow crystals melting at 251.5–252.5° whose melting point was not depressed by admixture with 2,3,4,5-tetra-(4-pyridyl)-thiophene (IV).

Anal. Calcd. for $C_{24}H_{16}N_4S$: C, 73.4; H, 4.1; N, 14.3. Found: C, 73.6; H, 4.2; N, 14.2.

Reductive Desulfurization of 2,3,4,5-Tetra-(4-pyridyl)-thiophene (IV) to 1,2,3,4-Tetra-(4-pyridyl)-butane (V).—A mixture of 7.84 g. of tetrapyridylthiophene, 20 g. of zinc dust, and 100 cc. of 25% hydrochloric acid was refluxed for two hours; 25 cc. of 25% hydrochloric acid was added and the refluxing was continued for another hour. The grayish solid was filtered, boiled for a short time with 25% caustic to decompose the zinc chloride complex, and the mixture was filtered. The solid was extracted with dilute hydrochloric acid, and the nitrogen base (4.21 g., 57% yield) was precipitated from the extract by caustic (m. p. 262–265° after recrystallization from 96% ethanol).

Anal. Calcd. for $C_{24}H_{22}N_4$: C, 78.6; H, 6.1; N, 15.3; mol. wt., 366. Found: C, 78.5; H, 6.1; N, 15.4; mol. wt. (Rast), 347.

Sulfuration of 1,2,3,4-Tetra-(4-pyridyl)-butane (V) to 2,3,4,5-Tetra-(4-pyridyl)-thiophene (IV).—A mixture of 1.44 g. of tetrapyridylbutane and 0.75 g. of sulfur was heated for two and one-half hours at 140–245° in a slow stream of nitrogen; 0.38 g. of hydrogen sulfide was collected in Ascarite and 0.31 g. of sulfur was recovered. The filtrate was made alkaline and 1.36 g. (89% yield) of tan-colored precipitate was filtered. Recrystallization from methanol gave pale-yellow crystals (m. p. 251.5–252.5°) whose melting point was not depressed by admixture with 2,3,4,5-tetra-(4-pyridyl)-thiophene (IV).

Anal. Calcd. for $C_{24}H_{16}N_4S$: C, 73.4; H, 4.1; N, 14.3; S, 8.2. Found: C, 73.7; H, 4.3; N, 14.6; S, 7.8.

Hydrogenation of 1,2-Di-(4-pyridyl)-ethane (I) to 1,2-Di-(4-piperidyl)-ethane (VI).—Dipyridylethane (114 g.) was hydrogenated in 300 cc. of cyclohexane at 135 atm. and 175–190° with nickel.[10] Distillation yielded 86 g. of material boiling at 125–130° (2 mm.) which solidified in the receiver. Crystallization from Skellysolve B-benzene (6:1) gave 68 g. of colorless crystals (m. p. 110–113.5°) which rapidly formed a carbonate on exposure to air. A recrystallized sample of carbonate-free material melted at 113–114°.

Anal. Calcd. for $C_{12}H_{24}N_2$: C, 73.4; H, 12.3; N, 14.3. Found: C, 73.4; H, 12.1; N, 14.3.

The hydrochloride (colorless powder, 96% yield) melted at 366–368° (dec.).

Anal. Calcd. for $C_{12}H_{24}N_2 \cdot 2HCl$: Cl, 26.3. Found: Cl, 26.0.

Hydrogenation of 1,2-Di-(4-pyridyl)-ethane (I) to Di-(N-ethyl-4-piperidyl)-ethane (VII).—Dipyridylethane (18 g.) was hydrogenated in ethanol at 90 atm. and 200–220° with nickel. The crude product (21 g.) boiled at 139–143° (1.5 mm.); redistilled product (n^{20}_{D} 1.4836, d^{20}_{4} 0.9005) boiled at 153–156° (3.5 mm.). The colorless liquid base formed a solid hydrate which dehydrated over phosphorus pentoxide. The hydrochloride was obtained in 91% yield, a white, hygroscopic powder.

Anal. Calcd. for $C_{16}H_{32}N_2 \cdot 2HCl$: Cl, 21.8. Found: Cl, 21.8.

The picrate, yellow needles from benzene, melted at 178.5–180°.

Anal. Calcd. for $C_{16}H_{32}N_2 \cdot 2C_6H_3N_3O_7$: C, 47.3; H, 5.4. Found: C, 47.7; H, 5.4.

Ethylation of 1,2-Di-(4-piperidyl)-ethane (VI).—An ethanol solution (25 cc.) of 5.9 g. of dipiperidylethane and 9.8 g. of ethyl iodide was refluxed for two and one-half hours. The solid (9.8 g.), which separated on standing overnight, was filtered and treated with 65 cc. of 4% potassium hydroxide. The mixture was ether extracted, and the solid recovered from the ether was shaken with benzenesulfonyl chloride in 10% caustic. The solid sulfonamide of the non-ethylated dipiperidylethane was filtered and the filtrate was ether extracted. Double distillation of the ether-soluble oil gave a heart-cut (b. p. 149–150° (2.5 mm.) n^{20}_{D} 1.4839) which formed a picrate (m. p. 178.5–180°) which showed no depression with the picrate of compound VII.

Anal. Calcd. for $C_{16}H_{32}N_2 \cdot 2C_6H_3N_3O_7$: C, 47.3; H, 5.4. Found: C, 47.0; H, 5.3.

Acknowledgment.—Thanks are expressed to J. E. Nickels, B. F. Tatterson, and J. J. McGovern for assistance in dehydrogenation, hydrogenation and spectroscopy, respectively, and to J. L. Keller for initiation of the early phases of the work.

Summary

1,2-Di-(4-pyridyl)-ethane, 1,2-di-(4-pyridyl)-ethylene, 1,2,3-tri-(4-pyridyl)-propane and 2,3,4,-5-tetra-(4-pyridyl)-thiophene were obtained from the reaction of 4-picoline with sulfur, the product-distribution depending upon the conditions.

2,3,4,5-Tetra-(4-pyridyl)-thiophene was converted to 1,2,3,4-tetra-(4-pyridyl)-butane by reductive desulfurization.

1,2-Di-(4-pyridyl)-ethane and 1,2,3,4-tetra-(4-pyridyl)-butane reacted with sulfur to form 2,3,-4,5-tetra-(4-pyridyl)-thiophene.

1,2-Di-(4-pyridyl)-ethane was hydrogenated in cyclohexane solution to 1,2-di-(4-piperidyl)-ethane, and in ethanol solution to 1,2-di-(N-ethyl-4-piperidyl)-ethane.

PITTSBURGH, PA. RECEIVED FEBRUARY 13, 1948

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[9] Kearby, U. S. Patent 2,395,875 (1946).

[10] Ipatieff and Corson, *Ind. Eng. Chem.*, **30**, 1039 (1938).