than the methyl ester. The apparent complete absence of chlorine derivatives in the decomposition products of α-amino-*iso*butyric esters is also significant.

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DIPYRIDYLS FROM PYRIDINE

BY C. R. SMITH

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Six isomeric dipyridyls are theoretically possible. At present five of these, α,α, β,β, γ,γ, α,β, and α,γ[1] have been identified. In this paper the preparation and properties of a sixth, β,γ, are described.

This investigation was begun primarily for the purpose of preparing chemical compounds toxic to insects, when used as ingredients of sprays and dusts. It happened that one sample of crude and one of pure γ,γ-dipyridyl, prepared by the usual method of treating pyridine with sodium and then with moistened or laboratory air, similar to the procedures of Anderson,[2] Weidel and Russo[3] and others, were tested for toxicity to certain plant lice. The purified γ,γ-dipyridyl had a negligible toxicity, while the impure sample showed appreciable toxicity. It was surmised that this impure sample contained one or more compounds of high toxicity.

The yield of toxic material in this reaction was very small and it was necessary to make an extended study to find the conditions under which the yield was increased. A method using sodium, pyridine, and air (or oxygen) has been evolved. A high proportion of isomeric dipyridyls other than γ,γ which, up to this time, has been the sole dipyridyl produced directly in this interaction, was obtained. These isomers have been separated and identified as α,α, β,β and a new dipyridyl, β,γ, which is the dipyridyl not previously reported. Anderson[2] prepared the first dipyridyl in 1870 but erroneously considered it to be dipyridine. Weidel and Russo[3] later showed that the substance was γ,γ-dipyridyl. Furthermore, these chemists did not obtain oily bases boiling between 120° and 180°, reported by Anderson in the action of sodium on pyridine, but claimed to have obtained an oil with the composition of dipyridine. Weidel and Russo's "dipyridine" is described as an oil boiling between 286° and 290° (uncorr.), with partial decomposition, easily soluble in water and alcohol. No crystalline salts were prepared. On oxidation with permanganate a small quantity of isonicotinic acid was obtained. "Dipyridine" was unaltered

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[1] Meyer and Meyer, [(a) *J. prakt. Chem.*, **102**, 280 (1921)], prepared the fifth isomer while this study was in progress.

[2] Anderson, *Ann.*, **154**, 270 (1870).

[3] Weidel and Russo, *Monatsh.*, **3**, 851 (1882).

by tin and hydrochloric acid. Weidel and Russo admittedly did not prepare a pure product, nor has any one since confirmed or extended this part of their work.

The writer has not been able to isolate a dipyridine by the method to be given but has obtained only a mixture of dipyridyls. As this method differs from the procedure of Weidel and Russo, it cannot be stated with certainty that these workers did not obtain dipyridine. It appears improbable, however, that they did.

Bruno Emmert[4] showed that sodium and other alkali metals form two series of compounds with pyridine, namely, $(C_5H_5N)_2.M$ and $C_5H_5N.M$, where M may be lithium, sodium or potassium. Sodium dipyridine is produced when the metal is placed in contact with the pyridine a sufficient length of time and the excess of pyridine is removed by vacuum below 40°. Sodium monopyridine is formed when the dipyridine is heated to 130° in a vacuum.

It appears probable that when sodium reacts with pyridine it is attached to the nitrogen and the bond in the *para* position is weakened, resulting in the production of sodium dipyridine, *p*-$NaNC_5H_5$-C_5H_5N(I).

The work of Emmert,[5] Dimroth and Heene[6] and Dimroth and Frister[7] proves that when an element or radical is attached to the nitrogen the *para* valence is set free, with the production of γ,γ-dipyridyl derivatives by the addition of a second pyridine ring. Acetic anhydride and zinc dust on pyridine, for example, results in the production of N—N′ diacetyl-tetrahydro-γ,γ'-dipyridyl.

When sodium dipyridine in excess of pyridine is oxidized by laboratory air or moistened air, the final product is γ,γ-dipyridyl. This reaction is probably effected through the intermediate production of γ,γ-tetrahydro-dipyridyl. The writer has found that when sodium dipyridine (I), dispersed in a large excess of pyridine, is maintained at 90° or below and oxidized by dry air or oxygen, the principal product is also γ,γ-dipyridyl. When, however, the mixture is given a preliminary digestion of several hours at temperatures between 90° and 115°, or higher under pressure, and is then oxidized at about 90°, increasing quantities of the isomeric dipyridyls are formed. The determining factors are the time and temperature of digestion, not the temperature of oxidation.

The total yield of bases corresponds nearly to the ratio of one of sodium to six of pyridine. The theoretical ratio of sodium to dipyridyl, assuming the oxidation of compounds isomeric with (I), is nearly 1:6.8. No hydrogen is evolved during the preliminary digestion nor have piperidine or reduced dipyridyls yet been detected.

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[4] Emmert, *Ber.*, **49**, 1060 (1916).

[5] Emmert, *Ber.*, **50**, 31 (1917).

[6] Dimroth and Heene, *Ber.*, **54**, 2934 (1921).

[7] Dimroth and Frister, *Ber.*, **55**, 1223 (1922).

It appears probable that the preliminary digestion serves to produce isomeric sodium dipyridines with the rings united in the α,α, β,β, γ,γ and β,γ positions, which are then oxidized to the corresponding dipyridyls. When sulfur instead of oxygen is used to remove sodium, only pyridine, with some tarry matter, is produced. Similarly, iodine produces little dipyridyl. Evidently the simultaneous oxidation of the sodium and connecting hydrogen is produced by oxygen, but not by sulfur or iodine.

The assumption of the intermediate formation of isomeric sodium dipyridines explains the ratio of sodium to bases produced and the determining character of the preliminary digestion in affecting the proportion of the various dipyridyls formed. No attempt has been made to indicate the valence relations of the isomeric sodium dipyridines, particularly those of the terminal nitrogen atoms uncombined with sodium. In spite of this difficulty, the explanation tentatively offered agrees with all the known facts.

Since this paper was practically completed, α,γ-dipyridyl, previously referred to, was shown by Meyer and Meyer[1] to be formed when pyridine is passed through hot tubes. Their work confirms and extends the results obtained by Roth.[8] It can now be said that all possible dipyridyls are known.

Table I gives some of the important constants of the known dipyridyls.

TABLE I

CONSTANTS AND PROPERTIES OF THE ISOMERIC DIPYRIDYLS

Dipyridyl	M. p. °C.	B. p. °C.	M. p. picrate °C.	Sol. in water
$\alpha\alpha$[9]	69.5	272.5	155	Only slightly soluble
$\alpha\beta$[10a]	Liquid	287–289	149.5	Insoluble
$\beta\beta$[10b]	68	291–292	232	All proportions
$\gamma\gamma$[11]	114	305	213	Soluble in hot
$\beta\gamma$[12]	61	297	215	V. sol. in cold, sl. sol. in hot
$\alpha\gamma$[9,1a]	Liquid	280–282	208	Insoluble

Experimental Part

Sodium and Pyridine.—Sodium in excess of pyridine at from —10° to +10° slowly reacts, the mixture swelling to many times its original volume to form a mass of brownish product. When this mixture is heated to 50° or 60° it changes to a viscous blue liquid. When sodium reacts on pyridine at room temperature, a greenish-black product is formed. When heated, this also changes to a blue liquid, apparently the same as resulted before.

When sodium is used in the proportion of 1 part to 5 parts of pyridine,

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[8] Roth, *Ber.*, **19**, 360 (1886).

[9] Blau, *Monatsh.*, **10**, 378 (1889).

[10] Skraup and Vortmann, *ibid.*, (a) **3**, 599 (1882); (b) **4**, 591 (1883).

[11] Ref. 3, p. 855.

[12] This paper.

allowed to react for several days at room temperature, and then oxidized slowly by air dried over sulfuric acid, the principal product formed is γ,γ-dipyridyl. As a rule, violent explosions result, for the sodium appears to be oxidized to sodium peroxide, as observed by Emmert, and a little unaltered sodium readily fires the mass. When moist air is substituted for the dry air, explosions are averted and the principal product is γ,γ-dipyridyl, which probably results through the intermediate formation of tetrahydro-γ,γ'-dipyridyl. When instead of being treated with moist air the sodium pyridine compound is dropped into water a considerable quantity of yellow resin is produced, together with a pungent oil, probably γ,γ-tetrahydro-dipyridyl, which subsequently oxidizes to γ,γ-dipyridyl.

As previously stated, impure γ,γ-dipyridyl prepared in these reactions was toxic but when purified it was non-toxic. An extensive series of experiments was made in which conditions were altered in many ways until a procedure was evolved which increased enormously the yield of toxic oils which proved to be principally, if not wholly, the isomeric dipyridyls.

The following method is convenient for the laboratory, although an increased yield of oils has been obtained by digestion at higher temperatures under low pressures and at much shorter intervals of time. The variation in yields of the different isomers with temperature and pressure is being further studied.

Preparation of Isomeric Dipyridyls.—Ten g. of sodium is allowed to react with about 850 cc. of completely dried and purified pyridine (b. p., 115.3°) in a one-liter flask for 24 to 48 hours. The mixture is then slowly heated to, and maintained at 114° to 115° under a reflux condenser, but not allowed to boil, in a constant-temperature oven for 10 to 16 hours. The flask is then removed and the condenser is replaced quickly by a dry cork stopper carrying an inlet tube for the introduction of *dry air or oxygen* and an outlet tube for release of pressure and the subsequent distillation of the excess of pyridine.

During oxidation the flask is kept at 90–100° in an oil bath. The end of the oxidation is clearly indicated by the disappearance of the blue or green color (from a mixture of blue and brown) which changes to reddish-brown. The temperature is now increased and the excess of pyridine is distilled and recovered in a condition ready for a new treatment with sodium.

In order to separate the dipyridyls, ether is added to the residue, lumps are broken up with a flattened rod, and finally 10 to 15 cc. of water is added in small portions. This causes the separation of resins on the bottom of the flask and leaves the ether clear to be poured off. Fresh ether is added to extract more material. The combined ether solutions are dried with potassium hydroxide, the ether is evaporated and the residue of mixed dipyridyls distilled; the fraction distilling from 270° to 310° is collected.

Separation of γ,γ-dipyridyl is effected by evaporating the oil with an excess of concd. hydrochloric acid and then adding an equal volume of alcohol. After several hours in the cold the dipyridyl dihydrochloride is filtered off and washed with 95% alcohol. The combined filtrate and washings are evaporated to small volume, more alcohol is added and a second crop of the dihydrochloride is obtained. The filtrate is now freed from alcohol and the bases are liberated and dried by potassium hydroxide. The bases are redistilled, and the oil distilling above 300° to 305° is rejected. The distilled oil is cooled and seeded with α,α-dipyridyl. The α,α-dipyridyl thus precipitated is filtered off and crystallized from dil. alcohol. The melting point is 69.5°, and the boiling point is 272.5°. The picrate melts at 158° (corr.). The pure product gives an intense red color with ferrous salts and is undoubtedly the α,α isomer. According to a better method for separating the α,α isomer the distilled oil is dissolved in ether, an equal volume of gasoline added, and the β,γ and β,β dipyridyls washed out with several portions of water. The gasoline-ether mixture is evaporated to remove the solvents and the oily residue is crystallized from dil. alcohol. The oil filtered from the α,α isomer, or the oil obtained from the washings of the ether-gasoline solution by the addition of an excess of potassium hydroxide, is dissolved in benzene and the β,β isomer is washed out with small proportions of water. The β,γ isomer is largely left in the benzene. After removal of the benzene. the β,γ isomer is crystallized from gasoline (b. p., 35–75°), and washed with petroleum ether. If the β,γ isomer is not pure it may be converted into the picrate which is recrystallized and finally decomposed with alkali, and the base is extracted with ether. After removal of the ether, the residue is recrystallized from petroleum ether from which it separates in plates. Evaporation of water solutions yields radiating feathery needles. The melting point is 61°, and the boiling point is 297°.

Analyses. Calc.: C, 76.90; H, 5.17. Found: C, 77.01; H, 5.45.

β,γ-Dipyridyl has a critical solubility point in water of about 12.8°. Below this temperature it is soluble in all proportions. Above 12.8° two layers are formed. The critical concentration is about 20%. These constants are greatly changed by the presence of impurities. It has not been determined whether or not the solubility curve closes at high temperatures under pressure.[13]

When pure, β,γ-dipyridyl does not produce a red color with ferrous salts. It is liquefied completely by small quantities of cold water. It reacts with zinc and acetic acid to give an intense blue color, similar to that produced with γ,γ-dipyridyl. This reaction is not given by α,α-dipyridyl or α,β-dipyridyl. β,γ-Dipyridyl is an extremely weak base without effect on red litmus. A crystalline dihydrochloride is obtained only under conditions in which hydrolysis is prevented. With mercuric chloride a double compound ($HgCl_2.C_{10}H_8N_2$) is produced. By analysis it contained 46.91% of mercury as compared with 47.10% calculated. Using concd. hydrochloric acid and platinic chloride, a crystalline double salt ($C_{10}H_8N_2.H_2PtCl_6$) is produced which contained 34.20% of platinum as compared with 33.9% calculated. To prove the constitution of β,γ-dipyridyl, the substance was digested overnight with neutral permanganate solution on the steam-bath, the mixture filtered from the manganese dioxide formed, and the filtrate neutralized with sulfuric acid, evaporated to low volume, and extracted with boiling alcohol. After the removal of the alcohol, copper acetate and acetic acid were added to precipitate the organic acids. The precipitate was filtered off and decomposed with hydrogen sulfide, and the acids were evaporated to small volume. Nicotinic acid was separated from the isonicotinic acid present by successive extractions and evaporations with alcohol. Nicotinic acid was finally crystallized from hot water in characteristic globular masses of needles; m. p., 229°. The alcohol-insoluble acid, crystallized from boiling water, was identified microscopically as isonicotinic acid. No picolinic acid was found. We were therefore dealing with β,γ-dipyridyl.

The washings from the benzene layer were treated with alkali, and the oil, recovered and crystallized from gasoline, was dried completely with potassium hydroxide. Crystallization is not always successful, but the picrate, which melts at 230–232° and consists of microscopic prismatic needles, proves the presence of β,β-dipyridyl.

Further study is being made of methods of separation, so that a plentiful supply of pure dipyridyls will be available. While the writer has not found

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[13] See Flaschner, *J. Chem. Soc.*, **95**, 668 (1909).

the α,β or α,γ derivatives in his mixtures, it is possible that refined methods may show that they also are produced, although probably in small quantities. The toxicity of these compounds is being investigated by Dr. Charles H. Richardson of the Bureau of Entomology, who will later report on his findings.

Summary

1. The preparation and separation of α,α, β,β, β,γ, and γ,γ dipyridyls produced by a new method involving the interaction of sodium, pyridine and dry oxygen or air is described.

2. β,γ-Dipyridyl has been isolated and some of its properties are given. This represents the only dipyridyl of the six possible isomers previously not reported.

3. The proportions of the various dipyridyls produced depend principally on the time, temperature and pressure of the preliminary digestion of the sodium dipyridine in an excess of pyridine before the oxidation is begun. These variations are being further studied.

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[CONTRIBUTION FROM THE CHEMICAL RESEARCH DEPARTMENT OF PARKE, DAVIS AND COMPANY]

AUTO-OXIDATION OF ETHERS

BY A. M. CLOVER

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In a previous article[1] on the auto-oxidation of ethyl ether, the writer has called attention to the fact that other ethers, when exposed to the action of the air, take on oxidizing properties, which may be shown by shaking them with an acidified solution of potassium iodide. As most ethers are insoluble it is necessary in order to obtain a complete reaction to add an equal volume of acetic acid to the solution of potassium iodide which contains an equivalent amount of hydrochloric acid. About 15 cc. of this solution is freshly prepared and half of this used as a control. One-half to 1 cc. of the ether to be tested is shaken with the solution for about a minute, then diluted with 20 volumes of water and the iodine determined by titration with thiosulfate solution. The results obtained in this way have been concordant.

As the peroxide is the primary product of oxidation, its determination from time to time is helpful in a study of this nature. However, the amount of peroxide found at any given time does not correspond to an equivalent amount of the ether because more or less of the total peroxide will have spontaneously decomposed. The peroxide usually accumulates until it reaches a definite maximum value. Further examination of such

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[1] Clover, THIS JOURNAL, **44**, 1107 (1922).