

718. *Attempts to prepare New Aromatic Systems. Part VII.\**  
15 : 16-Dihydro-15 : 16-diazapyrene. *The Synthesis of Di(pyridine-2 : 6-dimethylene).*

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The objective of the present work has been the preparation of a stable derivative (III) of *cyclotetradecaheptaene*, as a contribution to our knowledge of the higher, even-membered *cyclopolyolefins*. Di(pyridine-2 : 6-dimethylene) (I), a tetrahydro-derivative of (III), has now been made, starting from 2-methylpyridine-6-aldehyde and 2 : 6-dimethylpyridine which condense to give 1 : 2-di-(6-methyl-2-pyridyl)ethylene (IV). The related di-*N*-oxide (V) rearranges in acetic anhydride to (VI), which by successive hydrolysis, reduction, and treatment with hydrogen bromide yields 1 : 2-di-(6-bromo-methyl-2-pyridyl)ethane (VIII). Cyclisation to the new, ten-membered heterocyclic ring system (I) is best achieved by means of *n*-butyl-lithium.

CONSIDERABLE interest attaches to the preparation of higher vinylogues of benzene other than *cyclooctatetraene*. The *cyclopolyolefins*,  $C_nH_n$  (where  $n$  is an even number), which may formally be represented by Kekulé structures having closed systems of alternate double and single bonds, may either be fully conjugated and contain  $n$  identical, hybrid, carbon-carbon bonds as in benzene, or the olefinic bonds may fail to conjugate and the substance be accurately represented (except in conformation) by a Kekulé type formula as in *cyclooctatetraene*.<sup>1,2</sup> The Hückel rule<sup>3</sup> predicts that in this series of compounds only

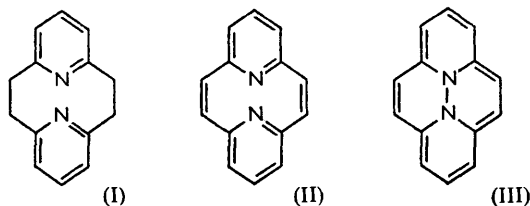
\* Part VI, *J.*, 1957, 4026.

<sup>1</sup> Baker, "The Development of the Concept of Aromaticity" in "Perspectives in Organic Chemistry," Ed. Sir A. Todd, Interscience Publishers, 1956, p. 44.

<sup>2</sup> Baker and McOmie, "Non-benzenoid Aromatic Compounds" in "Progress in Organic Chemistry," ed. J. W. Cook, Vol. III, pp. 48-49, Butterworths, 1955; "Cyclopolyolefines," in "Non-benzenoid Aromatic Compounds," ed. D. Ginsburg, Interscience Publ., 1958.

<sup>3</sup> Hückel, *Z. Physik*, 1931, 70, 204.

those having  $(4n + 2)$   $\pi$ -electrons will be of general benzenoid character. Two reasons, however, make it unlikely that this prediction can be directly tested. First, *cyclo*-polyolefins,  $C_{10}H_{10}$ ,  $C_{12}H_{12}$ ,  $C_{14}H_{14}$ , etc., if conjugated must have carbon-carbon bond angles close to  $120^\circ$  and be essentially planar, and the molecules therefore would have re-entrant angles with resultant severe steric clash between the interior hydrogen atoms.<sup>2,4</sup> There would be two such interior hydrogen atoms in *cyclodecapentaene*, and three in *cyclododecahexaene*; *cyclotetradecaheptaene* would have four interior hydrogen atoms irrespective of whether the molecule was shaped as the periphery of anthracene, phenanthrene, or pyrene. Secondly, such *cyclo*polyolefins would probably undergo very ready transannular bridging with formation of polycyclic structures, and these might further pass by movement of hydrogen atoms or by dehydrogenation into the related benzenoid compounds.<sup>5</sup>



The present paper describes an approach to the slightly indirect solution to this problem by a device which could be applied to a number of *cyclo*polyolefins. The steric clash of interior hydrogen atoms, and the possibility of transannular bridging are both avoided by replacing, *e.g.*, in *cyclotetradecaheptaene*, the four interior hydrogen atoms by two trivalent nitrogen atoms, as in 15 : 16-dihydro-15 : 16-diazapyrene (III), so that the molecule would possess a peripheral  $C_{14}$  conjugated system, which should be almost strainless, although it is possible that the two nitrogen atoms might be slightly displaced, one above and one below the plane of the fourteen carbon atoms.

A practicable synthesis of the tetrahydro-derivative of (III), namely, di(pyridine-2 : 6-dimethylene) (I), has now been achieved. Preliminary *X*-ray studies show that it may have a "stepped" molecule with slightly distorted pyridine rings as in the structurally very similar molecule of di-*m*-xylylene (I; having each N replaced by CH).<sup>6,7</sup> The properties of this compound (I) will be described in a later communication, but it may be observed now that loss of four hydrogen atoms should give di(pyridine-2 : 6-dimethylene) (II), and that this might undergo movement of electrons so as to avoid the repulsion of the two lone electron pairs of the nitrogen atoms by allowing a direct linking of these atoms and formation of the essentially planar, peripheral, conjugated system in (III). Formulæ (II) and (III) must be regarded as two of the extreme canonical forms of this molecule, but it appears that (III) and the other identical Kekulé-like structure would be the most important contributors to the hybrid molecule.

Synthesis of di(pyridine-2 : 6-dimethylene) (I) was achieved in the following way. 2-Methylpyridine-6-aldehyde, now technically available, was condensed with 2 : 6-dimethylpyridine (2 : 6-lutidine) in presence of acetic anhydride, giving 1 : 2-di-(6-methyl-2-pyridyl)ethylene (IV), and reaction with hydrogen peroxide in acetic acid then gave 1 : 2-di-(6-methyl-2-pyridyl)ethylene *N*-oxide (V). When the di-*N*-oxide was heated in acetic anhydride it underwent molecular rearrangement and diacetylation with formation of 1 : 2-di-(6-acetoxymethyl-2-pyridyl)ethylene (VI). In this reaction both oxygen atoms migrate to the adjacent methyl rather than to the methine groups, a behaviour which is consistent with the generalisation put forward by Boekelheide and Linn<sup>8</sup> that in these

<sup>4</sup> Mislow, *J. Chem. Phys.*, 1952, **20**, 1489.

<sup>5</sup> Prelog, Boarland, and Polyak, *Helv. Chim. Acta*, 1955, **38**, 434.

<sup>6</sup> Baker, McOmie, and Norman, *J.*, 1951, 1114.

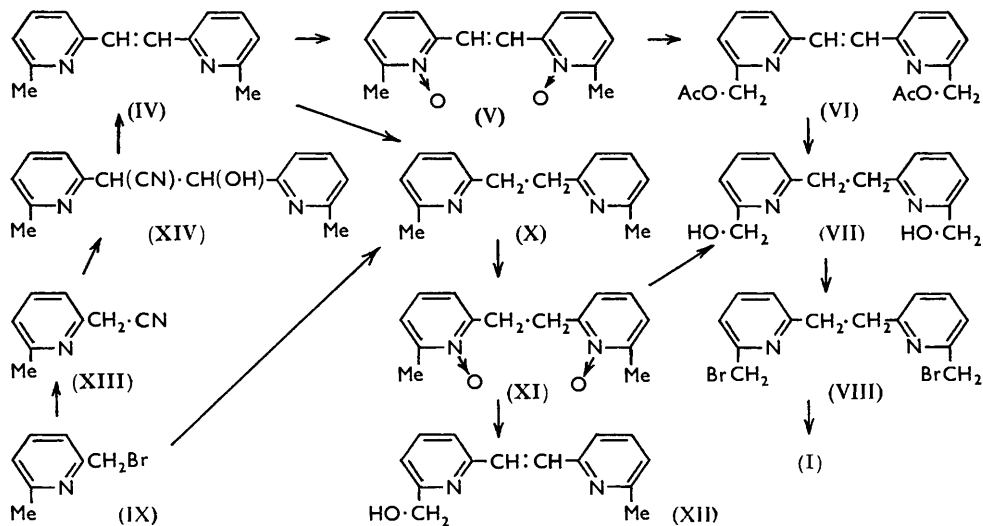
<sup>7</sup> Brown, *J.*, 1953, 3278.

<sup>8</sup> Boekelheide and Linn, *J. Amer. Chem. Soc.*, 1954, **76**, 1286.

rearrangements migration of the oxygen atom of the *N*-oxide to the  $\alpha$ -position of the side-chain in positions 2 or 6 occurs when at least two  $\alpha$ -hydrogen atoms are available for replacement. Acid hydrolysis of the diacetoxy-compound (VI) yielded 1 : 2-di-(6-hydroxymethyl-2-pyridyl)ethylene which was reduced catalytically in presence of Adams catalyst to 1 : 2-di-(6-hydroxymethyl-2-pyridyl)ethane (VII). Reaction of (VII) with hydrogen bromide in acetic acid then gave 1 : 2-di-(6-bromomethyl-2-pyridyl)ethane (VIII).

Many experiments were carried out in order to remove the two atoms of bromine intramolecularly and thus effect cyclisation to di(pyridine-2 : 6-dimethylene) (I). These included a Wurtz-Fittig reaction with sodium in boiling xylene (which gave material of high molecular weight) and simultaneous slow addition to ether of the dibromide in ether-benzene and of phenyl-lithium in ether, under moderately high-dilution conditions. The second reaction gave an approximately 3% yield of di(pyridine-2 : 6-dimethylene) (I). By far the most satisfactory method which has been found is the slow addition of *n*-butyllithium to 1 : 2-di-(6-bromomethyl-2-pyridyl)ethane (VIII) in ether, which gives di-(pyridine-2 : 6-dimethylene) in 28% yield.

The structure assigned to this key substance (I) is confirmed by (a) elementary analysis, (b) accurate determination of the molecular weight in the mass spectrometer which gave for the most prominent peak a value of  $210.184 \pm 0.01$  ( $C_{14}H_{14}N_2$  requires  $M$ , 210.183, after allowance for the usual isotopic ratios), (c) the ultraviolet absorption spectrum which shows that the compound contains no double bonds conjugated with a pyridine ring, (d) the infrared spectrum which shows the absence of olefinic bonds apart from those which may be regarded as associated with the aromatic nuclei of the pyridine rings, and (e) *X*-ray crystallographical analysis. The *X*-ray analysis shows that the orthorhombic crystals, specific gravity 1.242, have  $a$  13.48,  $b$  11.26,  $c$  7.41 Å, the mass in the unit cell being 842 equivalent to eight units of mass 105.25, or to four centrosymmetrical molecules of mass 210.5; the space group is *Pcab*.



A second approach to the preparation of the intermediate (IV) in the synthesis of the tricyclic compound (I) started from 2-hydroxymethyl-6-methylpyridine, which was either obtained technically or prepared by reducing methyl 6-methylpyridine-2-carboxylate with lithium aluminium hydride. The hydroxymethyl compound yielded 2-bromomethyl-6-methylpyridine (IX) when treated with hydrobromic acid, and with thionyl chloride it gave 2-chloromethyl-6-methylpyridine, converted by potassium cyanide into 2-cyanomethyl-6-methylpyridine (XIII). The methylene group of this 2-cyanomethyl compound is very reactive; in presence of piperidine it yields a benzylidene derivative,

1-cyano-1-(6-methyl-2-pyridyl)-2-phenylethylene, and condenses with 2-methylpyridine-6-aldehyde to give 1-cyano-1 : 2-di-(6-methyl-2-pyridyl)ethylene. When, however, the cyanomethyl compound is condensed with 2-methylpyridine-6-aldehyde, either in presence of *N*-ethylpiperidine, or by warming in its absence (these pyridine derivatives act as their own basic catalysts), the product is 2-cyano-1 : 2-di-(6-methyl-2-pyridyl)ethanol (XIV), which is dehydrated by acetic anhydride to the related olefin, 1-cyano-1 : 2-di-(6-methyl-2-pyridyl)ethylene (above), and undergoes dehydration, hydrolysis, and decarboxylation to give 1 : 2-di-(6-methyl-2-pyridyl)ethylene (IV) when boiled with hydrochloric acid. This preparation of (IV) is not as convenient as that previously described.

A third approach to the synthesis of compound (I) was by an alternative route to the intermediate 1 : 2-di-(6-hydroxymethyl-2-pyridyl)ethane (VII). 2-Bromomethyl-6-methylpyridine undergoes a Wurtz-Fittig reaction when treated with sodium, giving 1 : 2-di-(6-methyl-2-pyridyl)ethane (X) and this compound is also produced by the catalytic reduction of 1 : 2-di-(6-methyl-2-pyridyl)ethylene (IV). Treatment of (X) with hydrogen peroxide gave the di-*N*-oxide (XI) and when this was heated with acetic anhydride it gave two products. One of these was the *O*-acetyl derivative of 1-(6-hydroxymethyl-2-pyridyl)-2-(6-methyl-2-pyridyl)ethylene (XII), which had been formed as the result of the migration of one of the oxygen atoms to a methyl group, and of the other to a methylene group with subsequent loss of water to give the olefin. The other product obtained after hydrolysis was 1 : 2-di-(6-hydroxymethyl-2-pyridyl)ethane (VII), arising from migration of both oxygen atoms to the adjacent methyl groups, but the yield was not more than 5% and the method is therefore much inferior to that already described involving the rearrangement of the di-*N*-oxide of the olefin (V) in which migration of the oxygen atoms occurs solely to the adjacent methyl groups and not at all to the methine groups.

A number of other experiments in this same group of 2 : 6-disubstituted pyridines has been carried out during the course of this work, and these will be described briefly.

2 : 6-Bischloromethylpyridine, formed in good yield from 2 : 6-bishydroxymethylpyridine by treatment with thionyl chloride, yields 2 : 6-biscyanomethylpyridine with potassium cyanide in aqueous methanol. 2 : 6-Bisbromomethylpyridine is readily prepared from 2 : 6-bishydroxymethylpyridine by treatment with aqueous hydrobromic acid. Attempts to convert this 2 : 6-bisbromomethylpyridine into di(pyridine-2 : 6-dimethylene) (I) by treatment with sodium were unsuccessful; this contrasts with the behaviour of *m*-xylylene dibromide which is converted into di-*m*-xylylene in 12% yield by this method.<sup>6</sup> 2 : 6-Bisbromomethylpyridine is strongly dermatitic and lachrymatory; the related chloromethyl compound is lachrymatory.

An interesting result was obtained when the *N*-oxide of 2 : 6-bisacetoxymethylpyridine was heated with acetic anhydride: rearrangement occurred to give 2-acetoxymethyl-6-diacetoxymethylpyridine, hydrolysed by hydrochloric acid to 2-hydroxymethylpyridine-6-aldehyde.

2-Carboxy-6-methylpyridine gave an *N*-oxide with hydrogen peroxide, but rearrangement of this in presence of acetic anhydride was accompanied by the liberation of carbon dioxide, and the product was 2-acetoxymethylpyridine which is also formed by treating 2-methylpyridine *N*-oxide with acetic anhydride.<sup>8</sup>

Condensation of pyridine-2 : 6-dialdehyde with 2 : 6-dimethylpyridine in presence of acetic anhydride did not give the conjugated tri- or tetra-cyclic aromatic system (II) or (III) by a double condensation between one molecule of each reactant, but the dialdehyde reacted with two molecules of 2 : 6-dimethylpyridine, giving 2 : 6-di-[2-(6-methyl-2-pyridyl)vinyl]pyridine, probably as a mixture of geometrical isomers; it could be reduced to 2 : 6-di-[2-(6-methyl-2-pyridyl)ethyl]pyridine. Theazine of 2-methylpyridine-6-aldehyde did not give 1 : 2-di-(6-methyl-2-pyridyl)ethylene (IV) when heated, but profound decomposition occurred.

The ultraviolet spectra of many of the derivatives of 2 : 6-dimethylpyridine are recorded in the Table. The derivatives of 1 : 2-di-(6-methyl-2-pyridyl)ethane (X), including

di(pyridine-2:6-dimethylene) (I), in which the two pyridine nuclei are united *via* saturated carbon atoms, possess a single, strong, absorption band at *ca.* 266 m $\mu$ ; in the corresponding conjugated olefins, *e.g.*, 1:2-di-(6-methyl-2-pyridyl)ethylene (IV), this band is slightly more intense, and a second stronger band appears at *ca.* 318 m $\mu$ . This suggests that all these olefins have the same geometrical configuration, and, in view of the shape of the curves, the methods of preparation, and the failure to undergo isomerisation in the presence of hydrobromic acid, they are assumed to be the *trans*-isomers. The

*Ultraviolet absorption spectra characteristics in ethanol.*

Compound	$\lambda_{\max.}$ (m $\mu$ )	$\log_{10} \epsilon$	$\lambda_{\max.}$ (m $\mu$ )	$\log_{10} \epsilon$
Di(pyridine-2:6-dimethylene) (I) .....	274	3.68	—	—
2:6-Lutidine .....	264	3.50	—	—
1:2-Di-(6-methyl-2-pyridyl)ethane (X) .....	267.5	3.95	—	—
2:6-Di-[2-(6-methyl-2-pyridyl)ethyl]pyridine .....	<i>ca.</i> 210	4.30	268	4.28
			274	4.22
1:2-Di-(6-acetoxymethyl-2-pyridyl)ethane .....	266	3.52	—	—
1:2-Di-(6-hydroxymethyl-2-pyridyl)ethane (VII) .....	266.5	3.85	—	—
1:2-Di-(6-methyl-2-pyridyl)ethane-1:2-diol (techn.) .....	266.5	3.91	—	—
2-Cyano-1:2-di-(6-methyl-2-pyridyl)ethanol (XIV) .....	255.5	3.53	—	—
1:2-Di-(6-methyl-2-pyridyl)ethane di- <i>N</i> -oxide (XI) .....	221	4.54	261	4.20
1:2-Di-(6-methyl-2-pyridyl)ethylene (IV) .....	265	4.16	318	4.58
1:2-Di-(6-acetoxymethyl-2-pyridyl)ethylene (VI) .....	266	4.15	317	4.49
1:2-Di-(6-hydroxymethyl-2-pyridyl)ethylene .....	265	4.12	318	4.48
1-(6-Hydroxymethyl-2-pyridyl)-2-(6-methyl-2-pyridyl)- ethylene (XII) .....	265	4.08	318	4.43
1-Cyano-1:2-di-(6-methyl-2-pyridyl)ethylene .....	222	3.38	266	3.17
			328	3.65
1:2-Di-(6-methyl-2-pyridyl)ethylene di- <i>N</i> -oxide (V) .....	220	4.50	—	—
	250	4.27	301	4.17
2:6-Di-[2-(6-methyl-2-pyridyl)vinyl]pyridine .....	266	4.35	303	4.48
			337	4.42
6-Methylpyridine-2-aldehyde .....	241	3.55	265	3.63
			271	3.61
Pyridine-2:6-dialdehyde .....	237	3.78	262	3.66
			267	3.67

presence of the two oxygen atoms in the di-*N*-oxides of these compounds makes no very marked alteration to the ultraviolet spectra.

#### EXPERIMENTAL

1:2-Di-(6-methyl-2-pyridyl)ethylene (IV).—(a) A mixture of 2-methylpyridine-6-aldehyde (5.5 g.), 2:6-dimethylpyridine (20 g.; redistilled, b. p. 142—143°), and acetic anhydride (5.5 ml.) was heated at 175—180° for 3 hr. The very dark product was distilled under reduced pressure and yielded a fraction, b. p. *ca.* 136—137°/0.4 mm., as a yellow oil which solidified (yield variable, 5—7 g.). Recrystallisation from ethanol gave pale yellow crystals, m. p. 109—111°, and further crystallisation from benzene gave 1:2-di-(6-methyl-2-pyridyl)ethylene as almost colourless needles or prisms, m. p. 111—113° (Found: C, 80.1; H, 6.6; N, 13.5. C<sub>14</sub>H<sub>14</sub>N<sub>2</sub> requires C, 80.1; H, 6.7; N, 13.3%). The substance shows a brilliant yellow fluorescence in ultraviolet light. The *dipicrate* prepared in ethanol and recrystallised from nitromethane gave yellow crystals, decomp. 235—266° (Found: C, 46.8; H, 3.0. C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>.2C<sub>6</sub>H<sub>5</sub>O<sub>7</sub>.N<sub>2</sub> requires C, 46.7; H, 3.0%).

(b) 2-Cyano-1:2-di-(6-methyl-2-pyridyl)ethanol (XIV) (see below) (1.0 g.) was boiled for 5 hr. with acetic acid (5 ml.) and concentrated hydrochloric acid (5 ml.), poured into excess of aqueous sodium hydroxide, and extracted with ether. The extracts yielded a product which separated from light petroleum (b. p. 40—60°) in needles (0.4 g.), m. p. and mixed m. p. 110—113°.

1:2-Dibromo-1:2-di-(6-methyl-2-pyridyl)ethane.—1:2-Di-(6-methyl-2-pyridyl)ethylene (IV) (2.5 g.) in chloroform (8 ml.) was treated with bromine (1.9 g.) in chloroform (5 ml.) at 0°, then kept at room temperature for 1 hr. The solvent was removed under reduced pressure, and the solid crystallised from dioxan and then from benzene, giving 1:2-dibromo-1:2-di-(6-methyl-2-pyridyl)ethane as colourless needles (3.8 g.), m. p. 194—196° (decomp.) (Found: C, 45.1; H, 3.8. C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>Br<sub>2</sub> requires C, 45.4; H, 3.8%).

1 : 2-Di-(6-methyl-2-pyridyl)ethylene Di-N-oxide (V).—1 : 2-Di-(6-methyl-2-pyridyl)ethylene (2 g.) in acetic acid (120 ml.) was heated at 70–80° with 30% aqueous hydrogen peroxide (2 ml.) for 3 hr., and heating then continued for a further 9 hr. after addition of more hydrogen peroxide (1.4 ml.). The mixture was then evaporated to *ca.* 40 ml. under diminished pressure and again after the addition of water (40 ml.) and extracted with chloroform. After treatment with potassium carbonate and drying ( $\text{MgSO}_4$ ), distillation of the chloroform left a solid which was crystallised from ethanol-benzene, then benzene, and finally from ethanol, giving 1 : 2-di-(6-methyl-2-pyridyl)ethylene di-N-oxide (1.7 g.), m. p. 247.5–249° (decomp.) (Found: C, 69.0; H, 5.8.  $\text{C}_{14}\text{H}_{14}\text{O}_2\text{N}_2$  requires C, 69.4; H, 5.8%).

1 : 2-Di-(6-acetoxymethyl-2-pyridyl)ethylene (VI).—A mixture of the preceding di-N-oxide (4.2 g.) and acetic anhydride (30 ml.) was heated on the steam-bath for 6 hr., then distilled to dryness under reduced pressure. The residue was crystallised several times from a small volume of ethanol (charcoal), yielding 1 : 2-di-(6-acetoxymethyl-2-pyridyl)ethylene as needles (2.8 g., 50%), m. p. 133–134° (Found: C, 66.2; H, 5.6; N, 8.9.  $\text{C}_{18}\text{H}_{18}\text{O}_4\text{N}_2$  requires C, 66.3; H, 5.5; N, 8.6%). The overall yield from 1 : 2-di-(6-methyl-2-pyridyl)ethylene (*ca.* 35%) was not altered when the crude di-N-oxide, obtained directly from the oxidising mixture by evaporation to complete dryness, was used in this experiment.

1 : 2-Di-(6-hydroxymethyl-2-pyridyl)ethylene.—The preceding diacetoxy-compound (20 g.) was boiled for 10 hr. with concentrated hydrochloric acid (400 ml.), then cooled and neutralised by the addition of 30% aqueous sodium hydroxide (ice-cooling). The precipitate was collected, washed, and crystallised from ethanol, giving 1 : 2-di-(6-hydroxymethyl-2-pyridyl)ethylene as needles (12.0 g.), m. p. 142–144° (Found: C, 69.5; H, 5.7.  $\text{C}_{14}\text{H}_{14}\text{O}_2\text{N}_2$  requires C, 69.4; H, 5.8%).

1 : 2-Di-(6-hydroxymethyl-2-pyridyl)ethane (VII).—1 : 2-Di-(6-hydroxymethyl-2-pyridyl)ethylene (3.5 g.) in methanol (175 ml.) was shaken vigorously with hydrogen at 4 atm. for 10 hr. in presence of Adams platinum oxide (0.2 g.). The filtered mixture was concentrated (to *ca.* 40 ml.) and cooled, and the solid collected and crystallised from ethanol-ethyl acetate and then from ethanol, giving 1 : 2-di-(6-hydroxymethyl-2-pyridyl)ethane (*ca.* 2.3 g.) as prisms, m. p. 157–159° (Found: C, 68.9; H, 6.3; N, 11.5.  $\text{C}_{14}\text{H}_{16}\text{O}_2\text{N}_2$  requires C, 68.9; H, 6.6; N, 11.5%). The *dipicrate* formed yellow plates (from acetone), m. p. 220–228° (decomp.) (Found: C, 44.9; H, 3.2.  $\text{C}_{14}\text{H}_{16}\text{O}_2\text{N}_2 \cdot 2\text{C}_6\text{H}_3\text{O}_7\text{N}_3$  requires C, 44.4; H, 3.1%).

1 : 2-Di-(6-bromomethyl-2-pyridyl)ethane (VIII).—1 : 2-Di-(6-hydroxymethyl-2-pyridyl)ethane (5.0 g.) was added to a solution (35 ml.; 50% w/w) of hydrogen bromide in acetic acid, and the mixture was gently warmed to initiate an exothermic reaction, after which it was heated on the water-bath for 24 hr. The cooled solution was added to water and neutralised at 0° by aqueous sodium hydroxide, and the solid 1 : 2-di-(6-bromomethyl-2-pyridyl)ethane collected and crystallised from benzene-light petroleum (b. p. 60–80°), giving needles (6.6 g.), m. p. 118–120° (decomp.). The substance is not very stable owing to self-quaternisation.

*Di(pyridine-2 : 6-dimethylene)* (I).—The strength of a solution of *n*-butyl-lithium, prepared by Gilman's method,<sup>9</sup> was found by titration. This solution of *n*-butyl-lithium (1.1 mols.) was then added during 1 hr., with vigorous stirring in an atmosphere of nitrogen, to 1 : 2-di-(6-bromomethyl-2-pyridyl)ethane (VIII) (3.7 g.) suspended in ether (250 ml.), after which the mixture was boiled for  $\frac{1}{2}$  hr. A further quantity (*ca.* 0.5 mol.) of the ethereal *n*-butyl-lithium was then added during 2 hr. and boiling was continued for 1 hr. more. Addition of water and extraction with benzene yielded a solid (2.5 g.) which was sublimed at 140–150°/12 mm. (1.0 g.; m. p. 240–250°), and then crystallised from benzene giving *di(pyridine-2 : 6-dimethylene)* as colourless plates, m. p. 256–258° (0.75 g., 28%) (Found: C, 79.8; H, 7.0; N, 13.2.  $\text{C}_{14}\text{H}_{14}\text{N}_2$  requires C, 80.0; H, 6.7; N, 13.3%).

2-Hydroxymethyl-6-methylpyridine.—Methyl 6-methylpyridine-2-carboxylate<sup>10, 11</sup> (7.5 g.) in ether (50 ml.) was added during  $\frac{1}{2}$  hr. to a stirred solution of lithium aluminium hydride (3.8 g.) in ether (80 ml.); water (50 ml.) was then added dropwise and the mixture was filtered. The solid was suspended in hot methanol, saturated with carbon dioxide, boiled, and filtered. The combined ether and methanol filtrates were evaporated to dryness under diminished pressure, and the product taken up in ether, dried ( $\text{K}_2\text{CO}_3$ ), and distilled at 105–110°/14 mm., giving a colourless oil (2.8 g.) which solidified as needles. The *picrate* separated from ethanol as yellow

<sup>9</sup> Gilman *et al.*, *J. Amer. Chem. Soc.*, 1949, **71**, 1499.

<sup>10</sup> Black, Depp, and Corson, *J. Org. Chem.*, 1949, **14**, 17.

<sup>11</sup> Mathes, Sauermilch, and Klein, *Chem. Ber.*, 1953, **86**, 584.

needles, m. p. 130—131° (Found: C, 44.1; H, 3.4.  $C_{13}H_{12}O_8N_4$  requires C, 44.3; H, 3.4%). The *O*-acetyl derivative, prepared by boiling with acetic anhydride and sodium acetate for 2 hr., was characterised as the picrate, yellow needles (from ethanol), m. p. 114—115° (this acetyl derivative was prepared by Boekelheide and Linn,<sup>8</sup> by heating 2 : 6-dimethylpyridine *N*-oxide with acetic anhydride; picrate, m. p. 114—115°); hydrolysis of the *O*-acetyl derivative with boiling hydrochloric acid and basification regenerated 2-hydroxymethyl-6-methylpyridine.

**2-Bromomethyl-6-methylpyridine (IX).**—2-Hydroxymethyl-6-methylpyridine (9.0 g.) was boiled for  $\frac{1}{2}$  hr. with 48% aqueous hydrobromic acid (100 ml.), then cooled in ice, neutralised with concentrated aqueous sodium hydroxide, and extracted with ether. The dried ( $MgSO_4$ ) extracts were evaporated at room temperature under diminished pressure leaving a strongly lachrymatory and dermatitic, partly crystalline mass (6.3 g., 60%) which was unstable even at room temperature, giving a red solid, but which could be kept in dry ethereal solution. The picrate formed yellow needles (from ethanol), m. p. 142—143°. Barnes and Fales<sup>12</sup> isolated 2-bromomethyl-6-methylpyridine as the picrate, m. p. 143°, in unstated but extremely low yield, from the product obtained by brominating 2 : 6-dimethylpyridine with *N*-bromosuccinimide.

**2-Chloromethyl-6-methylpyridine.**—To 2-hydroxymethyl-6-methylpyridine (1.6 g.) was slowly added thionyl chloride (30 ml.) at 0°, and the mixture was then warmed on the water-bath for 4 hr. Evaporation to dryness under reduced pressure gave a solid hydrochloride (m. p. 152—154°) which yielded a rather unstable, ether-soluble free base (1.5 g.), b. p. 45—50°/0.4 mm., which darkened when kept. The picrate of 2-chloromethyl-6-methylpyridine formed yellow plates (from ethanol), m. p. 161—162° (Found: C, 42.4; H, 3.0; N, 14.9.  $C_{13}H_{11}O_7N_4Cl$  requires C, 42.1; H, 3.0; N, 15.1%).

**2-Cyanomethyl-6-methylpyridine (XIII).**—2-Chloromethyl-6-methylpyridine hydrochloride (5 g.) in methanol (50 ml.) was heated on the steam-bath for 2 hr. with potassium cyanide (5.0 g.) in water (20 ml.), basified with saturated aqueous sodium carbonate and extracted with ether. The extracts yielded a product which was distilled *in vacuo*, giving an oil (2.5 g.) which, after crystallisation from light petroleum (b. p. 40—60°) followed by sublimation at 70—80°/20 mm., formed needles, m. p. 40—41°. This 2-cyanomethyl-6-methylpyridine undergoes change when kept, and was characterised as the picrate, yellow needles (from alcohol), m. p. 179—180° (decomp.) (Found: C, 46.8; H, 3.0; N, 19.1.  $C_{14}H_{11}O_7N_5$  requires C, 46.5; H, 3.0; N, 19.1%).

**1-Cyano-1-(6-methyl-2-pyridyl)-2-phenylethylene.**—2-Cyanomethyl-6-methylpyridine (1.0 g.) and benzaldehyde (0.9 g.) were boiled for 2 hr. in ethanol (12 ml.) containing piperidine (0.5 ml.). Distillation then yielded an oil (1.1 g.), b. p. 135°/0.3 mm., which solidified, and after recrystallisation from light petroleum (b. p. 60—80°) the 1-cyano-1-(6-methyl-2-pyridyl)-2-phenylethylene was obtained as colourless crystals, m. p. 51—52°. The picrate formed yellow needles (from ethanol), m. p. 148—149° (Found: C, 56.2; H, 3.6.  $C_{15}H_{12}N_2C_6H_5O_7N_3$  requires C, 56.1; H, 3.3%).

**Condensation of 2-Cyanomethyl-6-methylpyridine with 2-Methylpyridine-6-aldehyde.**—(a) *In presence of piperidine.* A mixture of the cyanomethyl compound (2.0 g.) and the aldehyde (1.5 g.) in ethanol (30 ml.) containing piperidine (0.5 ml.) was boiled for 2 hr. Distillation then gave an oil, b. p. 155—160°/0.3 mm., which solidified and was crystallised from light petroleum (b. p. 60—80°), giving 1-cyano-1 : 2-di-(6-methyl-2-pyridyl)ethylene as needles (2.1 g.), m. p. 82—84° (Found: C, 76.3; H, 5.4; N, 18.4.  $C_{15}H_{13}N_3$  requires C, 76.6; H, 5.5; N, 17.8%). The substance is unstable in acid solution.

(b) *In presence of *N*-ethylpiperidine.* A similar experiment to the above was carried out but with *N*-ethylpiperidine in place of piperidine. Removal of the alcohol left a solid which was crystallised from benzene and then from light petroleum (b. p. 100—120°), giving 2-cyano-1 : 2-di-(6-methyl-2-pyridyl)ethan-1-ol (XIV) as needles (2.2 g.), m. p. 118—120° (Found: C, 71.3; H, 6.0; N, 16.2.  $C_{15}H_{15}ON_3$  requires C, 71.1; H, 5.9; N, 16.6%).

(c) *By heat.* The cyanomethyl compound (1.1 g.) and the aldehyde (1.0 g.) were mixed with gentle warming. After 10 min. at room temperature the mass solidified; crystallisation from benzene gave 2-cyano-1 : 2-di-(6-methyl-2-pyridyl)ethanol (XIV) (1.53 g.), m. p. and mixed m. p. 118—120°.

**Dehydration of 2-Cyano-1 : 2-di-(6-methyl-2-pyridyl)ethanol.**—The hydroxy-compound (0.5 g.) was boiled for  $\frac{1}{2}$  hr. with acetic anhydride (4 ml.) and acetic acid (2 ml.), and the mixture

<sup>12</sup> Barnes and Fales, *J. Amer. Chem. Soc.*, 1953, **75**, 3830.

poured into aqueous sodium hydroxide and extracted with ether. The ethereal solution yielded 1-cyano-1 : 2-di-(6-methyl-2-pyridyl)ethylene (0.2 g.), m. p. and mixed m. p. 82—84°.

1 : 2-Di-(6-methyl-2-pyridyl)ethane (X).—(a) 2-Bromomethyl-6-methylpyridine (10 g.) was boiled vigorously for 5 hr. in anhydrous xylene (350 ml.) with powdered sodium (7 g.). The cooled mixture was filtered, the black solid was washed with fresh xylene, and the combined filtrates were distilled, leaving an oil which solidified. This was sublimed twice at 120°/14 mm. giving 1 : 2-di-(6-methyl-2-pyridyl)ethane (X) as needles (1.8 g., 40%), m. p. 48—49°, b. p. 100—102°/0.25 mm. (Found: C, 79.5; H, 7.3; N, 12.9.  $C_{14}H_{16}N_2$  requires C, 79.5; H, 7.5; N, 13.2%). The *dipicrate* was prepared from alcoholic solution and recrystallised from nitromethane in yellow plates, m. p. 268° (decomp. from 254°) (Found: C, 46.5; H, 3.3; N, 16.3.  $C_{14}H_{16}N_2 \cdot 2C_6H_5O_7N_3$  requires C, 46.6; H, 3.3; N, 16.7%).

(b) 1 : 2-Di-(6-methyl-2-pyridyl)ethylene (IV) (6.0 g.) was hydrogenated in methanol for 3 hr. at 1 atm. in presence of Adams platinum oxide (0.1 g.). Filtration and isolation as described in paragraph (a) gave 1 : 2-di-(6-methyl-2-pyridyl)ethane (5.5 g.), m. p. and mixed m. p. 48—49°.

1 : 2-Di-(6-methyl-2-pyridyl)ethane Di-N-oxide (XI).—A mixture of 1 : 2-di-(6-methyl-2-pyridyl)ethane (2.5 g.), acetic acid (14 ml.), and 30% aqueous hydrogen peroxide (2.3 ml.) was heated at 70—80° for 3 hr., more hydrogen peroxide (1.7 ml.) then added and heating continued for a further 9 hr. The mixture was evaporated to small bulk under reduced pressure, and again after the addition of water (20 ml.), and the solid product then collected and recrystallised first from ethanol-ethyl acetate and then from benzene, giving 1 : 2-di-(6-methyl-2-pyridyl)ethane di-N-oxide (1.4 g.), m. p. 183—185° (Found: C, 68.1; H, 6.8.  $C_{14}H_{16}O_2N_2$  requires C, 68.9; H, 6.6%).

Rearrangement of 1 : 2-Di-(6-methyl-2-pyridyl)ethane Di-N-oxide.—The di-N-oxide (XI) (4.5 g.) and acetic anhydride (15 ml.) were heated on the steam-bath for 9 hr., and the product distilled, giving a yellow oil (3.6 g.), b. p. 160—170°/0.2 mm. This oil had an ultraviolet absorption spectrum very similar to that of 1 : 2-di-(6-methyl-2-pyridyl)ethylene, and a derived *picrate*, yellow needles, m. p. 190—191°, from alcohol, is probably that of 1-(6-acetoxymethyl-2-pyridyl)-2-(6-methyl-2-pyridyl)ethylene (Found: C, 53.1; H, 4.1.  $C_{16}H_{16}O_2N_2 \cdot C_6H_5O_7N_3$  requires C, 53.1; H, 3.8%). A portion of the oil (2.7 g.) was hydrolysed with boiling hydrochloric acid (60 ml.) for 8 hr., the solution basified with strong aqueous potassium hydroxide and extracted with ether, and the product distilled at *ca.* 180°/0.3 mm., giving a viscous yellow oil (1.2 g.) which solidified. The solid was shaken several times with a little ether, and the insoluble material was crystallised twice from ethanol-ethyl acetate, giving 1 : 2-di-(6-hydroxymethyl-2-pyridyl)ethane (VII) (0.2 g.), m. p. and mixed m. p. 156—158° (ultraviolet absorption spectra were identical). The ether-soluble product was recovered and extracted with boiling light petroleum (b. p. 60—80°), evaporation of which left a solid which was crystallised from benzene, giving colourless crystals (0.78 g.), m. p. 89—91°, probably 1-(6-hydroxymethyl-2-pyridyl)-2-(6-methyl-2-pyridyl)ethylene (XII) (Found: C, 74.6; H, 6.0; N, 12.2.  $C_{14}H_{14}ON_2$  requires C, 74.3; H, 6.2; N, 12.4%).

2 : 6-Bischloromethylpyridine.—Thionyl chloride (150 ml.) was slowly added to 2 : 6-bis-hydroxymethylpyridine (10 g.) at 0°, and the mixture was warmed on the water-bath for 4 hr., then cooled, and treated with benzene. The precipitated hydrochloride (10.5 g.) was collected, washed with benzene, dried, dissolved in water, and neutralised with sodium hydrogen carbonate. The 2 : 6-bischloromethylpyridine was collected and crystallised from light petroleum (b. p. 40—60°) as needles (8.0 g.), m. p. 74—75° (Found: C, 47.9; H, 4.0; N, 8.3.  $C_7H_7NCl_2$  requires C, 47.7; H, 4.0; N, 7.9%).

2 : 6-Biscyanomethylpyridine.—A mixture of 2 : 6-bischloromethylpyridine hydrochloride (6.5 g.), potassium cyanide (6.5 g.), water (20 ml.), and methanol (70 ml.) was heated on the water-bath for 5 hr. After addition of water (100 ml.) and saturation with sodium carbonate, ether-extraction yielded a solid which was crystallised from ethanol (charcoal), giving 2 : 6-biscyanomethylpyridine as needles (0.7 g., 28%), m. p. 97—98° (Found: C, 68.6; H, 4.6; N, 27.0.  $C_8H_7N_3$  requires C, 68.8; H, 4.5; N, 26.8%). This biscyano-compound was similarly obtained in 40% yield from 2 : 6-bisbromomethylpyridine hydrobromide.

2 : 6-Bisbromomethylpyridine.—2 : 6-Bishydroxymethylpyridine (20 g.) and 48% aqueous hydrobromic acid (200 ml.) were boiled for 2 hr., and the mixture was then neutralised at 0° by the addition of a concentrated aqueous solution of sodium hydroxide. The solid product was collected, washed, and recrystallised from light petroleum (b. p. 40—60°), giving 2 : 6-bisbromomethylpyridine as needles or prisms (24 g., 62%), m. p. 84—89° (Found: C, 31.8; H, 2.5; N,



5.6. Calc. for  $C_7H_7NBr_2$ : C, 31.7; H, 2.7; N, 5.3%). Barnes and Fales<sup>14</sup> prepared this compound from 2 : 6-dimethylpyridine (a) in 1% yield by treatment with phenyl-lithium and then bromine and (b) in 2% yield by reaction with *N*-bromosuccinimide; they record m. p. 66—76° or 66—99° according to the rate of heating; the indeterminate m. p. is due to intermolecular quaternisation.

2 : 6-Bisacetoxymethylpyridine *N*-Oxide.—2 : 6-Bishydroxymethylpyridine (5 g.; technical) was boiled for 3 hr. with acetic anhydride (20 ml.) and anhydrous sodium acetate (5 g.), then distilled to dryness under reduced pressure, and the residue extracted with hot chloroform, filtered, and distilled, giving 2 : 6-diacetoxymethylpyridine (6.0 g.), b. p. 110—113°/0.1 mm. This substance (22.0 g.) was oxidised with 30% aqueous hydrogen peroxide (20.0 ml.) in acetic acid (60 ml.) at 70—80° for 3 hr.; hydrogen peroxide solution (7 ml.) was then added, heating continued for 9 hr., and the mixture cooled. The 2 : 6-di(acetoxymethyl)pyridine *N*-oxide which separated (5.0 g.) was collected and recrystallised from ethanol as needles, m. p. 141—143° (Found: C, 55.0; H, 5.9.  $C_{11}H_{13}O_5N$  requires C, 55.2; H, 5.4%). The filtrate was concentrated twice to small bulk after addition of water (2 × 25 ml.) and extracted with chloroform, and the extracts were treated with saturated, aqueous potassium carbonate, dried ( $MgSO_4$ ), and distilled, giving a further amount (10 g.) of the crude *N*-oxide.

2-Hydroxymethylpyridine-6-aldehyde.—Unpurified 2 : 6-di(acetoxymethyl)pyridine *N*-oxide (15.6 g.) was warmed on the steam-bath for 14 hr. with acetic anhydride (36 ml.); the mixture was next distilled *in vacuo*, yielding 2-acetoxymethyl-6-diacetoxymethylpyridine (12.0 g.), b. p. 158—159°/0.5 mm. (Found: N, 5.0.  $C_{13}H_{15}O_6N$  requires N, 5.0%). This afforded the *oxime* of 2-acetoxymethylpyridine-6-aldehyde as needles (from ethanol), m. p. 179—180° (Found: C, 55.2; H, 5.0; N, 13.9.  $C_9H_{10}O_3N_2$  requires C, 55.7; H, 5.2; N, 14.4%). Hydrolysis of 2-acetoxymethyl-6-diacetoxymethylpyridine by boiling concentrated hydrochloric acid, evaporation to small bulk, addition of potassium carbonate, and extraction with chloroform, gave 2-hydroxymethylpyridine-6-aldehyde as a cloudy oil (3.8 g., 70%), b. p. 80—86°/0.1 mm. (Found: N, 10.4.  $C_7H_7O_2N$  requires N, 10.2%). The aldehyde is hygroscopic and when kept changes to a pale yellow solid which leaves a residue when distilled *in vacuo*; the 2 : 4-dinitrophenylhydrazone, crystallised from ethanol and then from ethyl acetate, forms deep yellow needles, m. p. 233° (Found: C, 49.3; H, 3.3.  $C_{13}H_{11}O_5N_5$  requires C, 49.2; H, 3.5%).

2-Carboxy-6-methylpyridine *N*-Oxide.—2-Carboxy-6-methylpyridine<sup>12</sup> (2.5 g.), acetic acid (11 ml.), and 30% aqueous hydrogen peroxide (2 ml.) was heated at 70—80° for 3 hr., more hydrogen peroxide (1.5 ml.) then added, and heating continued for 9 hr. The solid was collected from the cooled mixture and recrystallised from ethanol, giving 2-carboxy-6-methylpyridine *N*-oxide as needles (1.8 g., 64%), m. p. 176° (Found: C, 54.8; H, 4.8; N, 9.1.  $C_7H_7O_3N$  requires C, 54.9; H, 4.5; N, 9.2%). A further amount (0.3 g.) was obtained from the acetic acid filtrate. This *N*-oxide was also obtained in 85% yield when 2-methoxycarbonyl-6-methylpyridine was oxidised in the same manner.

2-Acetoxymethylpyridine.—2-Carboxy-6-methylpyridine *N*-oxide (3.2 g.) was heated on the steam-bath for 8 hr. with acetic anhydride (5 ml.). The solution was next distilled under reduced pressure, giving 2-acetoxymethylpyridine (2.6 g., 80%), b. p. 120—121°/23 mm.; the picrate formed yellow needles (from ethanol), m. p. 166—168° (Found: C, 44.2; H, 3.2; N, 15.1. Calc. for  $C_{14}H_{12}O_9N_4$ : C, 44.2; H, 3.2; N, 14.7%). Boekelheide and Linn<sup>8</sup> prepared the compound by treating 2-methylpyridine *N*-oxide with acetic anhydride, and record b. p. 115—118°/22 mm., and picrate, m. p. 168°.

2 : 6-Di-[2-(6-methyl-2-pyridyl)vinyl]pyridine.—Pyridine-2 : 6-dialdehyde (1.5 g.; tech.), 2 : 6-dimethylpyridine (7.5 g.), and acetic anhydride (1.5 g.) were kept at 175° for 3 hr., the acetic anhydride removed under reduced pressure, and the residue crystallised twice from the minimum volume of benzene (charcoal). 2 : 6-Di-[2-(6-methyl-2-pyridyl)vinyl]pyridine was obtained as needles (0.8 g.), m. p. 148—156°, falling to 129—133° on further crystallisation from benzene (Found: C, 80.7; H, 6.0; N, 13.0.  $C_{21}H_{19}N_3$  requires C, 80.5; H, 6.0; N, 13.4%). This compound is almost certainly a mixture of two geometrical isomerides and perhaps also of different conformational forms.

2 : 6-Di-[2-(6-methyl-2-pyridyl)ethyl]pyridine.—The preceding compound (0.2 g.) was hydrogenated in methanol for 6 hr. in presence of Adams platinum oxide catalyst. Filtration, evaporation, and crystallisation from light petroleum (b. p. 40—60°) gave 2 : 6-di-[2-(6-methyl-2-pyridyl)ethyl]pyridine as needles, m. p. 108—109° (Found: C, 79.5; H, 7.4; N, 13.5.  $C_{21}H_{23}N_3$  requires C, 79.5; H, 7.2; N, 13.2%).

*2-Methylpyridine-6-aldazine.*—2-Methylpyridine-6-aldehyde (2.4 g.; tech.) was warmed with hydrazine hydrate (0.5 g.) and the solid was collected and crystallised from ethanol, giving the *azine* as yellow needles (2.5 g.), m. p. 175—176° (Found: C, 70.3; H, 5.9; N, 23.7.  $C_{14}H_{14}N_4$  requires C, 70.6; H, 5.9; N, 23.5%). It decomposes and darkens above its m. p., but 1 : 2-di-(6-methyl-2-pyridyl)ethylene could not be isolated from the decomposition products.

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