## EXPERIMENTAL

*Partial conversion of o-benzoylbenzoic-carboxyl-C$^{14}$ acid to labeled anthraquinone.* In 25 ml. of C.P. sulfuric acid, 850 mg. of *o*-benzoylbenzoic-carboxyl-C$^{14}$ acid was dissolved at room temperature to form a clear, red solution. This was heated in an oil bath 20 min. at 80°. The solution was poured onto ice, warmed to room temperature, and digested for 15 min. on a steam bath. The mixture was cooled in ice and the precipitated solid was collected on a filter and washed with water. The solid was extracted with $4N$ sodium hydroxide. The alkali-insoluble residue was washed with water and dried to give 130 mg. (16.5%) of labeled anthraquinone which was identified by its melting point after a recrystallization from ethanol. The alkaline solution was acidified and the recovered *o*-benzoylbenzoic-carboxyl-C$^{14}$ acid was collected on a filter, washed with water, dried, and recrystallized from a hexane-benzene solution. Degradation of the purified, recovered acid was performed by the method of Dougherty.[6] Radioassays were performed by a modification of the method described by Neville.[7]

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[6] G. Dougherty, *J. Am. Chem. Soc.*, **50**, 571 (1928).

[7] O. K. Neville, *J. Am. Chem. Soc.*, **70**, 3501 (1948).

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# 2,4′-Biquinolyl

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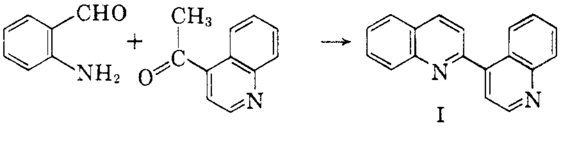
2,4′-Biquinolyl (I) is not among the series of known biquinolyls. The possibility that derivatives of this diquinolyl system might be formed in certain reductive coupling reactions that are currently under investigation prompted us to prepare the parent heteroaromatic compound for reference and for comparison with other known biquinolyls.

The intermediates for the synthesis of I were all known compounds. Starting from isatin, the sequence included 1-acetylisatin, 4-carboxycarbostyril, 2-chlorocinchoninic acid, cinchoninic acid, ethyl cinchoninate, and methyl 4-quinolyl ketone.[1] The last stage involved a Friedländer condensation of the ketone with *o*-aminobenzaldehyde to give 2,4′-biquinolyl.



I

The structure I for the final base is shown by the method of synthesis, its absorption spectra, and the preparation of salts. Spectroscopically, the base shows absorption in the ultraviolet like quinoline and other biquinolyls.[2] 2,4′-Biquinolyl forms a monopicrate salt in accord with the pattern observed by Abramovitch in the pyridylquinoline series.[3] Even with perchloric acid, the stable salt obtained was the monoprotonated derivative. Although a high-melting salt (m.p. 274°) was obtained from 2,4′-biquinolyl and concentrated perchloric acid, recrystallization from acidic methanol repeatedly afforded only a lower-melting monoperchlorate (m.p. 239–240°).[4]

Further evidence for the 2,4′-biquinolyl structure (I) is obtained from the infrared spectrum. There is no band in the region of 3.0 $\mu$(N–H) nor in the range 5.8–6.0 $\mu$ (ketone or aldehyde carbonyl). There is a series of bands (6.20, 6.28, 6.35, 6.40, and 6.43 $\mu$) of weak to medium intensity that show a general similarity to the spectra of other quinoline derivatives. However, the strongest bands appear in the region 11–14 $\mu$ where the C—H out-of-plane deformation vibrations arise. This portion of the spectrum has been widely used to study substitution in aromatic compounds, and it has been proposed that the correlations of the band positions with the number of adjacent hydrogens can be extended to pyridine and quinoline if the nitrogen is regarded as a substituted ring atom and, in the case of a bicyclic aromatic compound, if the two rings are considered separately.[5] For 2,4′-biquinolyl, however, there were only three strong bands observed within the usually accepted region. These were found at 11.96, 13.27, and 13.53 $\mu$. The first of these is like the band in *p*-disubstituted benzenes and may, as a single band, be ascribed to vibrations involving two adjacent hydrogens on both pyridine rings. The other two bands are like those found in the spectra of *o*-disubstituted benzenes and may arise from the C–H deformation frequencies associated with the two benzenoid rings. Moreover, the spectrum of 2,4′-biquinolyl is generally similar in the 11–14 $\mu$ region to a composite spectrum of quinaldine and lepidine.[6]

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[1] (a) T. L. Jacobs, *et al.*, *Org. Syntheses*, **Coll. Vol. III**, 456 (1955); (b) K. N. Campbell and J. F. Kerwin, *J. Am. Chem. Soc.*, **68**, 1837 (1946); (c) C. F. Koelsch, *J. Am. Chem. Soc.*, **65**, 2460 (1943).

[2] M. Crawford and I. F. B. Smyth, *J. Chem. Soc.*, 1433 (1952).

[3] R. A. Abramovitch, *J. Chem. Soc.*, 3839 (1954).

[4] P. Krumholz, *J. Am. Chem. Soc.*, **73**, 3487 (1951) observed that the second dissociation constant for those dipyridyls in which one ring was linked at the 2-position was high compared to other isomers and that no biacid salt was formed for 2,2′-bipyridyl.

[5] L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, New York, 1958, p. 281. The principal limitation of this technique is that frequently the number of bands present exceeds that expected on the basis of the formulated rules, even in the carbocyclic series; *cf.* L. Cencelj and D. Hudzi, *Spectrochim. Acta*, **7**, 274 (1955); R. F. Curtis and G. Viswanath, *J. Chem. Soc.*, 1670 (1959); C. G. Cannon and G. B. B. M. Sutherland, *Spectrochim. Acta*, **4**, 373 (1951).

[6] Although the biquinolyl spectrum was recorded from a mulled sample and the two methylquinoline spectra were taken with liquid films, our examination of other closely related compounds does not indicate that there are appreciable variations from the two sampling techniques.

TABLE I

INFRARED ABSORPTION BANDS IN 11–14 $\mu$ REGION

| 2,4′-Biquinolyl (nujol mull) | 2,2′-Biquinolyl (nujol mull) | Quinaldine (liquid) | Lepidine (liquid) |
|---|---|---|---|
| 11.35 m[a] | — | 11.35 w | — |
| 11.50 w | 11.50 m | 11.52 vw | — |
| 11.59 w | — | — | 11.67 s |
| 11.96 s | 11.93 s | — | 11.93 vs |
| 11.28 w | 12.05 s | 12.22 vs | 12.32 m |
| 12.51 w | — | — | — |
| 12.71 m | 12.71 m | 12.80 s | 12.78 w |
| 13.05 w | 13.08 w | 13.05 vw | — |
| 13.13 w | — | — | — |
| 13.27 s | 13.45 i | 13.38 s | 13.25 vs |
| 13.53 vs | 13.52 s | — | — |

[a] Vs = very strong; s = strong; m = medium; w = weak; vw = very weak.

## EXPERIMENTAL[6]

*Methyl 4-quinolyl ketone.* Ethyl cinchoninate was prepared from 14 g. of cinchoninic acid in 75 ml. of absolute ethanol and 5 ml. of concd. sulfuric acid. The ester (12 g.) was distilled at 106–107° (0.2 mm.) [lit.,[1b] b.p. 120–123 (1 mm.)], with the following infrared bands (liquid film) ($\mu$): 5.72, (C═O), 12.50, 13.10. The picrate from the ester melted at 187–188° (lit.,[1c] m.p. 183–188°). The ester was condensed with ethyl acetate in toluene solution with sodium ethoxide and the condensation product was isolated as the sodium salt. To 6 g. of the sodio-derivative of ethyl 3-keto-3-(4-quinolyl)propanoate was added 75 ml. of water and 12 ml. of concd. sulfuric acid, and the solution was heated on the steam bath for 3 hr. The cooled solution was made weakly alkaline with sodium carbonate solution and extracted five times with ether. Evaporation of the dried ether extracts left only a small amount of a dark viscous oil that was distilled to give 0.9 g. of methyl 4-quinolyl ketone, b.p. 108–110° (0.2 mm.) (lit.,[7] b.p. 138°/2 mm.). Significant infrared bands follow (liquid film) ($\mu$): 5.86 (ketone C═O), 6.31, 11.75, 13.05. The ketone formed a picrate, m.p. 165–167° (lit.,[7] m.p. 165–167°).

*2,4′-Biquinolyl.* A solution of 0.72 g. of methyl 4-quinolyl ketone in 50 ml. of ethanol was treated with 0.70 g. of freshly prepared 2-aminobenzaldehyde[8] and 0.20 g. of potassium hydroxide. On warming a solid began to form, but this redissolved in hot ethanol. The solution, which turned red, was heated on a steam bath for 1 hr., filtered from a small amount of insoluble residue, and allowed to cool. From the solution 0.8 g. of a pink voluminous solid separated. Passage of the ethanolic solution of the biquinoline through a short column of alumina gave a colorless product, m.p. 153–154°; $\lambda_{max}^{C_2H_5OH}$ ($\log \epsilon$) 3.17 (4.04), 230 m$\mu$(4.56).

*Anal.* Calcd. for $C_{18}H_{12}N_2$: C, 84.35; H, 4.72; N, 10.93. Found: C, 84.40; H, 4.93; N, 10.69.

*2,4′-Biquinolyl monopicrate* was prepared in ethanol solution and recrystallized from acetonitrile as yellow plates, m.p. 261–262°.

*Anal.* Calcd. for $C_{24}H_{15}N_5O_7$: C, 59.35; H, 3.12. Found: C, 60.10; H, 3.35.

*2,4′-Biquinolyl perchlorate* was prepared in methanol solution and recrystallized from a mixture of methanol and water as pale yellow needles, m.p. 239–240°.

*Anal.* Calcd. for $C_{18}H_{13}N_2O_4Cl$: C, 60.60; H, 3.67; N, 7.85. Found: C, 60.77; H, 3.08; N, 7.99.

When 2,4′-biquinolyl or the monoperchlorate was treated with concd. perchloric acid, a salt melting at 274–276° was obtained, but recrystallization of this salt from acidic methanol gave only the salt melting at 239–240°.

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[6] Melting points were taken in a Drechsel melting point apparatus and are otherwise uncorrected. Analyses are by Schwarzkopf Microanalytical Laboratory. The infrared spectra were recorded on a Beckman IR-4 spectrophotometer with sodium chloride optics, and the ultraviolet spectrum was taken on a Beckman DK-1 instrument.

[7] A. Kaufmann, H. Peyer, and M. Kunkler, *Ber.*, **45**, 3090 (1912).

[8] F. G. Mann and A. J. Wilkinson, *J. Chem. Soc.*, 3346 (1957).

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## 2,4-Diamino-5-formylpyrimidine and 2,4-Diamino-5-hydroxymethylpyrimidine[1]

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In a study of the catalytic hydrogenation of heterocyclic nitriles,[3a,b] Huber has prepared a compound described as 2,4-diamino-5-hydroxymethylpyrimidine (I), which was formed from the hydrochloride of an amine characterized as di-(2,4 - diamino - 5 - pyrimidylmethyl)amine (II) on treatment with aqueous sodium hydroxide. This latter amine was formed along with 2,4-diamino-5-aminomethylpyrimidine (III) on hydrogenation of 2,4-diamino-5-cyanopyrimidine.[3a]

We have hydrogenated 2,4-diamino-5-cyanopyrimidine using a W-4[4] Raney nickel catalyst. Substances were formed which gave the approximate properties of the compounds previously described as the hydrochlorides of II and III. Treatment of the compound, presumed to be II, with aqueous sodium hydroxide gave a compound with properties different from those shown by a sample of I which had been prepared by Nairn and Tieckel-

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[3] (a) W. Huber, *J. Am. Chem. Soc.*, **65**, 2222 (1943). (b) W. Huber, *J. Am. Chem. Soc.*, **66**, 876 (1944).

[4] H. Adkins and A. A. Pavlic, *J. Am. Chem. Soc.*, **69**, 3039 (1947).