

Synthesis of Some Binaphthoxazoles

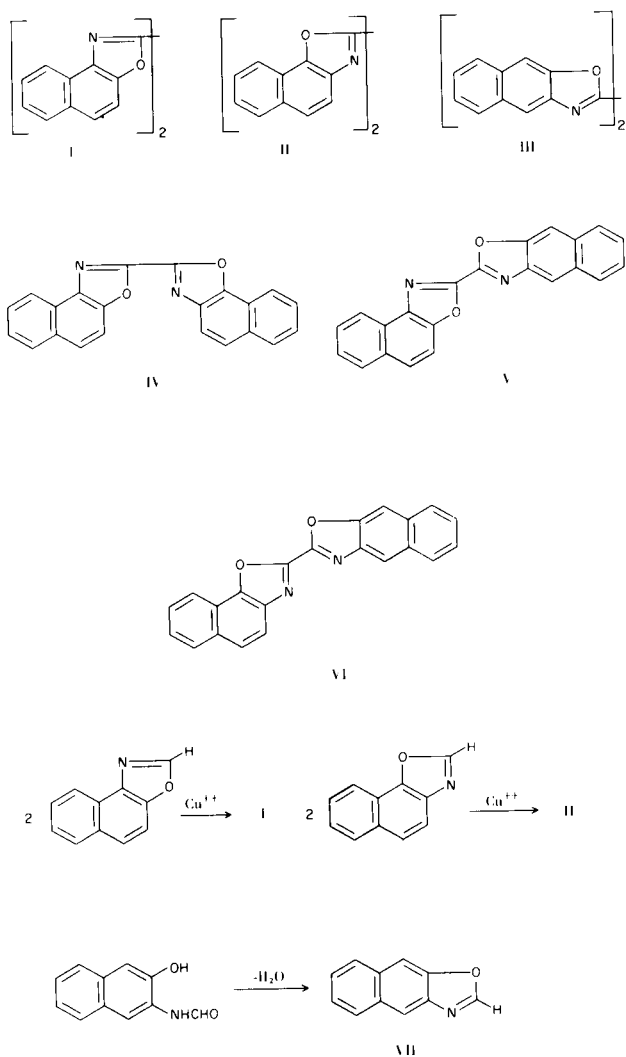
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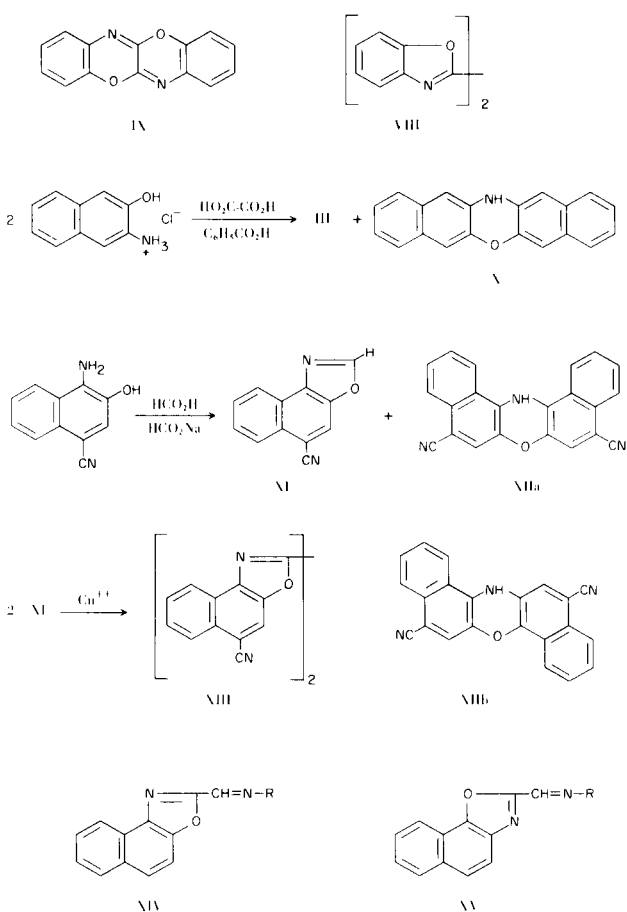
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Four of the six possible 2,2'-binaphthoxazoles, as well as several of their cyano derivatives, have been prepared. Naphth[2,3-*d*]oxazole was synthesized for the first time and 2,2'-binaphth[2,3-*d*]oxazole was made using a previously reported technique in which an incorrect assumption was made.

There are six possible 2,2'-binaphthoxazoles (I-VI), none of which has yet been reported. However, four members of this series, I-IV, have now been prepared.



Compounds I and II were easily made by the oxidative coupling (1) of the corresponding naphthoxazole. To utilize this procedure for the synthesis of 2,2'-binaphth[2,3-*d*]oxazole (III), it was first necessary to prepare naphth[2,3-*d*]oxazole (VII) itself which was accomplished by the dehydrative ring-closure of 3-formamido-2-naphthol. However, the yield of VII was so poor that this route was considered impractical and two possible alternative routes were, therefore, investigated. Ried and Patschorke reported (2) that 2,2'-bibenzoxazole, VIII, can be formed by fusion of *o*-aminophenol and diethyl oxalate but this method was found to fail when attempted with 3-amino-2-naphthol. Kehrmann and Bener (3) reported the reaction of *o*-aminophenol hydrochloride and oxalic acid in molten benzoic acid to yield a colorless product, m.p. 259-260° which they formulated as [1,4]-benzoxazino[3,2-*b*][1,4]benzoxazine (IX). However, when this work was repeated, the product (m.p. 254-255°) was found to have infrared absorption identical with authentic 2,2'-bibenzoxazole (m.p. 253-254°) prepared by the method of Zerweck and Schwamberger (1). As a result of this observation 3-amino-2-naphthol hydrochloride was treated with oxalic acid in benzoic acid at 250°. Two products were isolated. One was the desired 2,2'-binaphth[2,3-*d*]oxazole (III), and the other, a jade green solid which becomes yellow-brown on heating, is believed to possess structure X. In addition to the parent systems described, the copper-catalyzed coupling reaction was used to prepare [2,2'-binaphth[1,2-*d*]oxazole]-5,5'-dicarbonitrile (XIII). The starting material for this coupling, naphth[1,2-*d*]oxazole-5-carbonitrile (XI) was made in the same manner used in the preparation of VII except that, in this instance, there was also isolated, along with low-melting XI, a red-brown, very high melting substance. From microanalytical and spectral data, as well as by analogy with structure X, the structure assigned to the red-brown product is XIIIa. (The alternative structure for

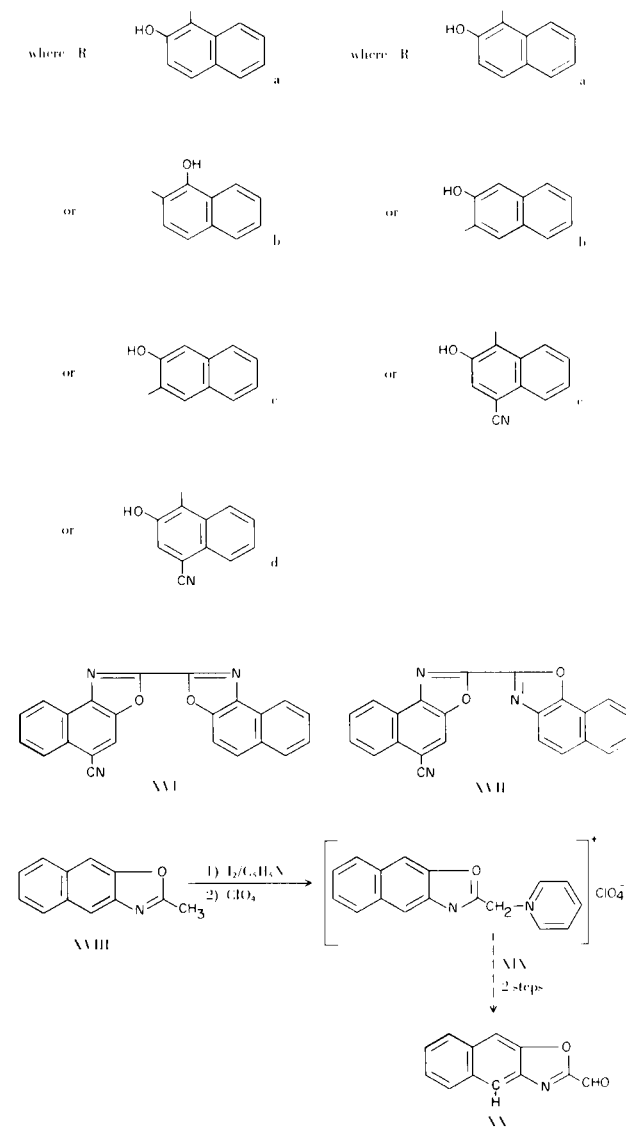


this product, XIIb, cannot be excluded).

In the case of the three unsymmetrical 2,2'-binaphthoxazoles (IV, V, and VI), the methods outlined above were obviously not suitable. Hence, the method for the already described (4) compounds, naphth[1,2-*d*]- and [2,1-*d*]oxazole-2-carboxaldehyde was utilized. When condensed with the appropriate aminonaphthol, the corresponding azomethines (structures XIVa-d and XVa-c) formed without great difficulty. Each of these were then treated with potassium permanganate in acetone according to the procedure of Postovskii, Pushkina, and Mazalov (5) but the results were not uniformly successful. 2-(Naph[2,1-*d*]oxazol-2-yl)naphth[1,2-*d*]oxazole (IV) was obtained readily from both XIVb and XVa. Oxidation of azomethine XIVa yield a product with properties identical to those recorded earlier for compound I. In addition, the azomethines XIVd and XVc were converted cleanly to the binaphthoxazole carbonitriles (XVI and XVII), respectively. However, both the azomethines derived from 3-amino-2-naphthol (XIVc and XVb), when oxidized, yielded only very insoluble and intractable brown powders.

As an alternative, the initial steps in the synthesis of V

and VI via the azomethines derivable from naphth[2,3-*d*]oxazole-2-carboxaldehyde (XX) were taken but, again, work was suspended when it was found that the yield in the first step (giving the salt XIX) of the three-step aldehyde synthesis was only 4%.



EXPERIMENTAL

2,2'-Binaphth[1,2-*d*]oxazole (I). Oxidative Coupling Method.

A mixture of 6.0 g. (0.0355 mole) of naphth[1,2-*d*]oxazole (6) and 3.0 g. of cupric butyrate was heated in a metal-bath (bath temperature 200°) for 1 hour. To the cooled reaction mixture was added 40 ml. of cyclohexane with swirling, and the solid was collected and washed with cyclohexane. The crude product was crystallized from chlorobenzene to give the yellow-green crystals, 1.8 g. (30%), m.p. 313-315°. Further crystallization from dimethylformamide and then from chlorobenzene provided

TABLE I

Compound	Melting Point	Solvent	Yield %	C	Analysis H	N
XIVa	ca. 220° resolidifies, re-m. ca. 275°	C ₆ H ₆	25	78.07 (a)	4.17	8.73
XIVb	237.5-239°	C ₆ H ₅ CH ₃	55	78.06 (a)	3.99	7.86
XIVc	ca. 220° (inst.)	C ₆ H ₆	25	77.84 (a)	4.28	8.02
XIVd	245-246°	1,2-C ₆ H ₄ Cl ₂	20	75.80 (b)	3.32	11.26
XVa	204-205°	<i>n</i> -C ₄ H ₉ OH	30	78.24 (a)	4.04	8.45
XVb	ca. 180° (inst.)	methyl- cyclohexane	20	77.75 (a)	4.10	8.02
XVc	273-278°	C ₆ H ₅ Cl	25	76.15 (b)	3.25	12.00

(a) Calcd. values for C₂₂H₁₄N₂O₂ are: C, 78.09; H, 4.17; N, 8.28. (b) Calcd. values for C₂₃H₁₃N₃O₂ are: C, 76.02; H, 3.61; N, 11.56.

TABLE II

Binaphthoxazoles *via* Azomethines

Number	M.p., °C	Solvent	Yield %	UV Data	Em. Max		C	Analyses H	N
IV	226-227	<i>n</i> -C ₇ H ₁₆	9	274 (4.25), 295 (4.14) 365 (4.52); infl. 310 & 380 nm (EtOH)	427 nm (EtOH)	C. (a)	78.56	3.60	8.33
						F.	78.77	3.70	8.36
XVI	333-334	C ₆ H ₅ CH ₃	50	305 (4.10), 378 (4.61) 400 (4.51), infl. 317, 360 nm (DMF)	448 nm (DMF)	C. (b)	76.49	3.04	11.63
						F.	76.61	2.81	11.60
XVII	305.5-307	C ₆ H ₅ CH ₃	67	275 (4.18), 297 (4.15) 323 (4.16), 375 (4.55) 395 (4.45) (DMF)	449 nm (DMF)	C. (b)	76.49	3.04	11.63
						F.	76.40	2.89	11.91

(a) Empirical formula is C₂₂H₁₂N₂O₂. (b) Empirical formula is C₂₃H₁₁N₃O₂.

analytically pure material, m.p. 318-319.5°; uv maxima (nm) and absorptivities (log ϵ): in ethanol, 258 (3.94), 300 (3.98), 365 (4.48), 387 (4.36), infl. 310; fluorescence emission max. 428 nm.

Anal. Calcd. for C₂₂H₁₂N₂O₂: C, 78.56; H, 3.60; N, 8.33; O, 9.51. Found: C, 78.52; H, 3.41; N, 8.21.

2,2'-Binaphth[2,1-*d*]oxazole (II).

The procedure used was similar to that used in the preparation of I except that naphth[2,1-*d*]oxazole (6) was the starting material and, because the product was appreciably soluble in cyclohexane, it was necessary to concentrate the washings. The combined crops were washed with dilute ammonium hydroxide, dried and then crystallized twice from benzene, with decolorizing charcoal. The yield of sand-brown needles was 22%, m.p. 283.5-285°. A further crystallization from benzene provided material for analysis, m.p. 284.5-285.5°; uv data: in ethanol, 273 (4.51), 315 (4.28), 365 (4.48), infl. 380; fluor. em. max 426 nm.

Anal. Calcd. for C₂₂H₁₂N₂O₂: C, 78.56; H, 3.60; N, 8.33; O, 9.51. Found: C, 78.53; H, 3.30; N, 8.21.

Naphth[2,3-*d*]oxazole (VII).

A mixture of 1 g. 3-formamido-2-naphthol (7) and 0.5 g. of phosphorus pentoxide was heated at about 200° and 0.05 mm Hg

for 30 minutes. The white sublimate (ca. 0.1 g.) was crystallized from *n*-hexane, m.p. 125-125.5°; uv absorption: in ethanol, 288 (3.79), 302 (3.83), 330 (3.23); infl. at 280 and 315 nm.

Anal. Calcd. for C₁₁H₇NO: C, 78.09; H, 4.17; N, 8.28; O, 9.46. Found: C, 78.16; H, 4.18; N, 8.12.

2,2'-Binaphth[2,3-*d*]oxazole (III).

A mixture of 3.9 g. (0.02 mole) of 3-amino-2-naphthol hydrochloride, 0.9 g. (0.01 mole) of anhydrous oxalic acid and 30 g. of benzoic acid was heated carefully with a Bunsen flame. The internal temperature rose to 250° and was held there for 15 minutes. After allowing the dark reaction mixture to cool, ethanol (60 ml.) was added with swirling. The solid was collected, washed well with hot ethanol and then with water. The dry crude product was extracted with 200 ml. of boiling DMF. (A very small amount of light green solid remained on the filter-funnel). Upon cooling, the filtrate deposited 0.5 g. (15%) of yellow-brown needles, m.p. > 400°. A sample for analysis was prepared by recrystallization from DMF; uv data (qualitative only, due to trace solubility); in DMF, 267, 277, 300, and 354 nm. Fluor. em. max. 488 nm.

Anal. Calcd. for C₂₂H₁₂N₂O₂: C, 78.56; H, 3.60; N, 8.33; O, 9.51. Found: C, 78.82; H, 3.64; N, 8.21.

Isolation of Dibenzo[*b,i*]phenoxazine (X).

The light green solid (weighing perhaps 0.1 g.) which remained on the filter-funnel (above) was crystallized from chlorobenzene and then from DMF. The resulting green needles melted about 395-397°, becoming distinctly yellow-brown before melting. The material was recrystallized again from DMF prior to analysis. Its infrared absorption curve (Nujol) was very different from that of III showing, for example, a sharp singlet at 2.95 μ ; uv data (qualitative): in DMF, 328 and 385 nm; infl. at 368 nm. Fluor. em. max. 406 nm. It had a mass spectrum parent peak at 283 amu.

Anal. Calcd. for $C_{20}H_{13}NO$ (283.31): C, 84.78; H, 4.63; N, 4.94; O, 5.65. Found: C, 84.25; H, 4.37; N, 5.01.

Naphth[1,2-*d*]oxazole-5-carbonitrile (XI).

A mixture of 14 g. (0.071 mole) of 1-amino-4-cyano-2-naphthol (8), 15 g. sodium formate and 50 ml. of 98% formic acid was stirred at reflux for 26 hours. The mixture was cooled and then poured with stirring into a large volume of cold water. Concentrated ammonium hydroxide was added slowly until the mixture was nearly neutral and the solid was collected, washed with water and air-dried. The crude material was extracted with boiling 1,2,4-trichlorobenzene. On cooling this extract deposited dark brown granules (5 g.) which melted about 215° dec., and may have been 4-cyano-1-formamido-2-naphthol (strong ir absorption at 6.05 μ). Half (2.5 g.) of the dark brown granular solid was placed in a vacuum oven at 140°. After several hours the material had become a black mass coated with white crystals. This mixture was extracted with warm cyclohexane and the extract treated with decolorizing charcoal, filtered and concentrated. Pale yellow crystals (0.8 g.) separated from the filtrate. This material showed no carbonyl absorption in the infrared (but did have a nitrile band) and melted, after further crystallization from *n*-heptane, at 179-180°; uv absorption: in ethanol, 258 (3.58), 289 (3.93), 302 (3.98), 319 (3.79), 333 (3.81).

Anal. Calcd. for $C_{12}H_6N_2O$: C, 74.22; H, 3.11; N, 14.43; O, 8.24. Found: C, 74.27; H, 2.81; N, 14.54.

Isolation of 14*H*-Dibenzo[*a,j*]phenoxazine-5,9-dicarbonitrile (XIIa).

A portion of the brown granular product obtained from the trichlorobenzene extract (above) was crystallized from DMF. From the cool DMF filtrate there separated garnet red crystals, m.p. ca. 390° dec. This product displayed absorption bands in the infrared ascribable to N-H (2.97 μ) and nitrile (4.52 μ), but nothing in the carbonyl region; uv data: qualitative, in DMF, 288 and 401 nm; infl. at 315 nm. Fluor. em. max. 539 nm. Its mass spectrum showed a parent peak at 333 amu.

Anal. Calcd. for $C_{22}H_{11}N_3O$ (333.33): C, 79.27; H, 3.32; N, 12.61; O, 4.80. Found: C, 79.75; H, 3.01; N, 13.02.

[2,2'-Binaphth[1,2-*d*]oxazole]-5,5'-dicarbonitrile (XIII).

A mixture of 0.7 g. (0.0036 mole) of XI and 3 g. cupric butyrate was heated under nitrogen in a metal bath (bath temperature 220°) for 30 minutes. The cooled reaction mixture was broken up and washed well with dilute ammonium hydroxide. The dry, crude product was extracted with boiling 1,2,4-trichlorobenzene (300 ml.), and the extract filtered and concentrated to 50 ml. The yellow, crystalline solid was collected, washed and dried, 0.4 g. (57%), m.p. > 420°. The analytical sample was obtained after three crystallizations from 1,2,4-trichlorobenzene; uv data: in DMF, 315 (4.12), 382 (4.63), 406 (4.52) with infl. at 320 and 365 nm. Fluor. em. max. 419 and 444 nm with infl. at 471 nm.

Anal. Calcd. for $C_{24}H_{10}N_4O_2$: C, 74.63; H, 2.59; N, 14.53; O, 8.25. Found: C, 74.29; H, 2.54; N, 14.19.

General Conditions for Preparing Azomethines (XIVa-d and XVa-c).

To the appropriate aminonaphthol stirred at room temperature in glacial acetic acid (or aminonaphthol hydrochloride in acetic acid containing a slight molar excess of pyridine) was added rapidly an equimolar quantity of the naphthoxazole-2-carboxaldehyde (4) in acetic acid solution. The volume of acetic acid varied considerably depending on the solubility of the azomethine-product. Solid usually began to separate shortly after mixing although in some cases it was advantageous to allow the reaction mixture to stir for at least 30 minutes. Product was isolated by filtration; any additional product which could be obtained by diluting the acetic acid mother liquors was generally of much poorer quality. Melting points, solvents of crystallization and analyses are listed in Table I.

Oxidation of Azomethine Intermediates.

This procedure can be illustrated by a description of the preparation of 2-[naphth[2,1-*d*]oxazol-2-yl]naphth[1,2-*d*]oxazole (IV). It was adapted from the work of Postovskii, Pushkina, and Mazalov (5). The azomethine (XIVb) (3.4 g., 0.01 mole) in 250 ml. of C. P. acetone was stirred well at room temperature and treated with 1.1 g. (0.007 mole) of potassium permanganate solid, added gradually over 5 minutes. After 20 minutes, the dark mixture was poured into 1 liter of water containing several grams of sodium bisulfite. The precipitate was collected, washed with water and dried. The crude product was extracted with several hundred milliliters of methylocyclohexane, and the extract treated with decolorizing charcoal, filtered and then concentrated to about 50 ml. by evaporation. The dull yellow powder which separated weighed 0.3 g. (9%). Recrystallization from *n*-heptane afforded the pure compound, m.p. 226-227°. Absorptivity, microanalytical and other data are given in Table II. Oxidation of azomethine XVa gave a product in 40% yield whose melting point and infrared spectrum was the same as that obtained from azomethine XIVb. Oxidation of azomethine XIVa gave a product in 58% yield identical to that obtained by copper-catalyzed oxidative coupling of naphth[1,2-*d*]oxazole (*cf.* Preparation of I). When azomethines XIVc and XVb were treated with permanganate as described above, the brown powders obtained could not be crystallized. Extracts made with various hot solvents, although strongly fluorescent, yielded only very small amounts of yellow-brown solids which could not be further purified.

Preparation of 1-[(Naphth[2,3-*d*]oxazol-2-yl)methyl]pyridinium Perchlorate (XIX).

A solution of 3.7 g. (0.02 mole) of 2-methylnaphth[2,3-*d*]oxazole (XVIII) (9) and 5.1 g. (0.02 mole) iodine in 35 ml. of anhydrous pyridine was heated on a steam-bath for 20 hours. To the dark, cooled reaction mixture was added 35 ml. of benzene and the mixture shaken. The crystalline solid was collected, washed further with benzene and then air-dried. The crude product (iodide) was extracted well with 400 ml. of hot water and the aqueous extract treated with a solution of sodium perchlorate (15 g.) in water (50 ml.). The resulting mixture was chilled and the yellow crystals which deposited were collected. The crude perchlorate salt was crystallized from water containing a little sodium perchlorate. The weight of yellow crystals was 0.3 g. (4%). A further crystallization from water afforded the analytical sample, m.p. 213.5-215°.

Anal. Calcd. for $C_{17}H_{13}ClN_2O_5 \cdot H_2O$: C, 53.90; H, 3.99;

Cl, 9.36; N, 7.41; O, 25.34. Found: C, 54.05; H, 3.92; Cl, 9.15; N, 7.36.

Acknowledgments.

The microanalyses were made by Mr. J. Kobliska and his associates. The ultraviolet absorption spectra were determined on Beckman DU and DBG Spectrophotometers. The fluorescence emission maxima were determined on a Hitachi/Perkin-Elmer MP-2A Spectrophotofluorimeter. Ir curves were obtained on a Perkin-Elmer, Model 137, Spectrophotometer. Mass spectra determinations were performed on a Hitachi/Perkin-Elmer, RMU-6 Mass Spectrometer.

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